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Guest Editors’ Message: American College of Physicians, Hawai‘i Chapter, Annual Meeting 2014

Gurdev Singh MD, FRCS, FACP; Donald Helman MD, FACP; and S. Kalani Brady MD, MACP; Co-Guest Editors

In this, our second year of publication of the proceedings of the Annual Scientific Meeting of The American College of Physicians Hawai‘i Chapter as a Supplement to the Hawai‘i Journal of Medicine and Public Health, we welcome Dr. S. Kalani Brady as a co-editor. Dr. Brady, as the immediate past governor of the ACP Hawai‘i Chapter, was instrumental in launching the Supplement to “the Journal” last year. It is with great pleasure that we announce to the readership that at this year’s National Annual Meeting of the ACP in Orlando, Florida, Dr. Brady was awarded the Mastership, only the 4th ever in the history of Hawai‘i and the first to a Native Hawaiian physician.

The high caliber of the 50 submissions to the scientific meeting this year made the work of the peer reviewers extremely difficult. However, after review, 29 abstracts were selected for poster presentation and 10 for delivery at the podium. The authors of seven of the highest scoring abstracts were invited to submit full-length manuscripts for publication.

Author affiliations ranged from as far North as Rochester, Minnesota, as far South as Houston, as far East as Boston, and as far West as San Diego and Los Angeles on the mainland United States. Institutional affiliations included the Keck School of Medicine, Massachusetts General Hospital, Mayo Clinic, and UCLA amongst others. Department affiliations outside of Medicine included Neurosurgery, Obstetric and Gynecology, Pathology, Anatomy, Biochemistry, and Physiology.

Topics covered were in the realms of critical care, dermatology, hematology/oncology, infectious diseases, internal medicine, nephrology, neurology, palliative care, psychology, pulmonology, rehabilitation, and rheumatology. No matter what area of interest and specialization, stage of training or practice, we think you will find something to stimulate your intellectual curiosity in this supplement.

We would like to thank Jenny Helman, Executive Director, ACP Hawai‘i Chapter, and Drake Chinen, Layout Editor, Production Manager, and Peer Review Coordinator with the “Journal” without whom the work of the co-editors would have been impossible.

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Dr. S. Kalani Brady receives the Mastership of American College of Physicians Award at the American College of Physicians Annual National Meeting, Orlando, FL, April 2014.

(Photo Credit: Emma Walsh)
Bodily Fluid Analysis of Non-Serum Samples using Point-of-Care Testing with iSTAT and Piccolo Analyzers Versus a Fixed Hospital Chemistry Analytical Platform

William Londeree MD; Konrad Davis MD; Donald Helman MD; and Jude Abadie PhD

Abstract

Introduction: Forward deployed military medical units can provide sophisticated medical care with limited resources. Point-of-Care Testing (POCT) may facilitate care and expedite diagnosis. This study assessed the accuracy of results for POCT for non-serum samples (pleural, peritoneal, and cerebrospinal fluid) using iSTAT and Piccolo hand-held devices compared with results obtained using a hospital chemistry analyzer.

Methods: Pleural, peritoneal, and cerebrospinal fluids obtained during routine care were simultaneously analyzed on a Vitros 5600 automated clinical chemistry hospital analyzer, iSTAT, and Piccolo POCT devices.

Results: POCT results were highly correlated with the Vitros 5600 for pleural fluid LDH, glucose, and triglycerides (TG); for peritoneal fluid bilirubin, TG, glucose, albumin, and protein; and glucose for cerebrospinal fluid.

Conclusion: POCT results for non-serum samples from pleural, peritoneal, and cerebrospinal fluid correlate with standard hospital chemistry analysis. The results of this study demonstrate potential for possible new diagnostic roles for POCT in resource-limited environments.

Introduction

The delivery of quality healthcare in developing countries has dramatically increased during the last 10-15 years. This growth is related to global health initiatives and advances in medical technology. The advent and expansion of point-of-care technology illustrates how diagnostic acumen in austere or low-income environments has changed. Point-of-care testing (POCT) offers rapid and accurate biochemical testing on serum samples. POCT has well established clinical utility for serum chemistry and blood gas analysis, as well as for the assessment of diabetes, pregnancy, HIV, and malaria.

Most point-of-care technologies have targeted blood tests, yet comprehensive laboratory testing (to include the evaluation of non-serum samples) continues to require conventional bench top analytic platforms, whose cost and size limit their practicality in resource constrained environments. Only two studies have compared POCT to traditional biochemical analysis of non-serum samples in humans. Kohn, et al, demonstrated that pleural fluid pH can be accurately performed on an iSTAT POCT device. Wockenfus, et al, demonstrated that the iSTAT is comparable to a validated blood gas analyzer for pleural fluid pH analysis.

An animal study on equine synovial fluid accurately measured lactate and glucose but was limited in the number of samples (N = 8). Overall, there is scant evidence-based literature regarding the use of POCT on non-serum samples, and those uses are not approved by the Food and Drug Administration (FDA).

The purpose of this study was to compare the accuracy of iSTAT and Piccolo devices to a standard hospital bench top analyzer using analyte measurement, in order to determine if the POCT devices have a potential role in the analysis of non-serum samples such as pleural, peritoneal, and cerebrospinal fluid.

Methods and Materials

Existing pleural, peritoneal, and cerebrospinal fluids collected for standard of care analysis were stored at -20°C for further POCT analysis. The samples were thawed and analyzed on an Ortho Clinical Diagnostics Vitros 5600 automated clinical chemistry analytical platform, considered the analytical reference standard in this study. All samples were simultaneously analyzed using an iSTAT and/or Piccolo POCT hand-held device, employing test-specific cartridges for individual analytes. The iSTAT used EC8+ cartridge, and the Piccolo used Lipid Panel, Basic Metabolic Plus, and General Chemistry 13 cartridges.

Pleural fluid analysis measured glucose and pH on the iSTAT using an EC8+ cartridge. The Piccolo POCT device measured LDH on the Basic Metabolic Panel Plus cartridge. Amylase, protein, and albumin were measured using the General Chemistry13 cartridge, and the Lipid Panel cartridge was used to quantify triglycerides (TG) and cholesterol levels in pleural fluid.

Peritoneal fluid analytes were only measured with the Piccolo POCT device. The Piccolo measured LDH with the Basic Metabolic Panel Plus cartridge and amylase, protein, albumin, bilirubin; however, the glucose was measured with the General Chemistry 13 cartridge while the Lipid Panel cartridge was used to measure triglycerides (TG).

The EC8+ cartridge was used to measure cerebrospinal fluid glucose using the iSTAT’s platform.

The null hypothesis was, “The differences of the means between POCT and bench top analysis is 0.” Bland-Altman charts were constructed to assess accuracy and precision of the POCT analyzer compared to the Vitros 5600. The Bland-Altman charts plot the difference of the paired measurements for each sample against the average, and also display 95% confidence intervals. A two-sided paired t-test assessed differences between the two measurements. A mean difference significantly different from zero indicated the average bias for the POCT analyzer. For analytes with a large number of measurements below the limit of detection, results were dichotomized as detected or non-detected, and a kappa statistic assessed concordance. A significance of $P \leq 0.05$ was used for all statistical tests. All analyses were performed using Statistical Analysis Software (SAS) v 9.2 software, SAS Institute, Cary, NC.
Correlation was determined using a correlation coefficient \( (r) \), reflecting a linear relationship of POCT (y-axis) versus control (x-axis) values with increasing correlation as 1.00 is approached. Because the sensitivity of the control and POCT analyzers varied, a concordance \( (k) \) value was calculated that represented the reliability of POCT to categorize samples as detectable or non-detectable when compared to the control, with increasing \( k \) as 1.00 is approached.

**Results**

**Pleural Fluid**

Table 1 summarizes the statistical results for pleural fluid. The number of samples for the analytes was 6-23 \( (n) \) with range of data values referenced in table 1. Statistical difference \( (P \leq .05) \) between testing modalities was demonstrated for LDH, albumin, glucose, and cholesterol based on the null hypothesis; however, protein, TG, and pH did not demonstrate a statistical difference, with \( P \) values of .96, .08, and .11, respectively. The mean values represented positive biases for protein, albumin, glucose, and pH at 0.01, 0.27, 11, and 0.01. A negative bias was calculated for LDH (-343), cholesterol (-16), and TG (-2.7). Correlation \( (r) \) values were determined for glucose (0.99), pH (0.98), LDH (0.97), protein (0.90), albumin (0.81), TG (0.91), and cholesterol (0.91).

The Bland Altman chart for pH is an example of how each analyte was plotted to demonstrate the difference of the paired measurements for each sample versus the average. Figure 1 is a representation of pH. Correlation is reflected in Figure 2 for pH as linear relationship of POCT versus Vitros 5600 values, with increasing correlation as 1.00 is approached.

<table>
<thead>
<tr>
<th>Table 1. Pleural Fluid Results</th>
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<tbody>
<tr>
<td>n</td>
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<tr>
<td>--------------------------------</td>
</tr>
<tr>
<td>LDH (U/L)</td>
</tr>
<tr>
<td>Protein (g/dL)</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
</tr>
<tr>
<td>Cholesterol (mg/dL)</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
</tr>
<tr>
<td>pH</td>
</tr>
</tbody>
</table>

![Bland Altman chart for pH (Pleural fluid)](image)
**Peritoneal Fluid**

Table 2 summarizes the statistical data for peritoneal fluid. Protein and TG were the only two analytes where statistical difference ($P \leq .05$) between the POCT and the control was not significant with $P$ values of .23 and .17. Glucose, bilirubin, and TG had correlation values of 1.00, 1.00, and 0.98. Albumin did not demonstrate a statistical difference, and only 3 of 16 samples were detectable on the testing modalities.

**Cerebrospinal Fluid**

Table 3 summarizes the data for cerebrospinal fluid. Fifty-five samples were obtained in total and glucose was the single analyte measured for cerebrospinal fluid. It did demonstrate statistical difference with a $P < .01$ but notably had a positive bias with a mean of 6 mg/dL and a strong correlation ($r = 0.97$).

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**Table 2. Peritoneal Fluid Results**

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Mean</th>
<th>Std</th>
<th>Mean 95% CI</th>
<th>$P$-value</th>
<th>Precision 95% CI</th>
<th>Correlation (r)</th>
<th>Concordance (k)</th>
<th>Data Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDH (U/L)</td>
<td>11</td>
<td>-301</td>
<td>398</td>
<td>-598/- 33.5</td>
<td>.03</td>
<td>-1114/466</td>
<td>0.88</td>
<td>0.11</td>
<td>1829</td>
</tr>
<tr>
<td>Protein (g/dL)</td>
<td>16</td>
<td>0.09</td>
<td>0.30</td>
<td>-0.07/0.25</td>
<td>.23</td>
<td>-0.50/0.69</td>
<td>0.92</td>
<td>1.00</td>
<td>2.6</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>16</td>
<td>0.20</td>
<td>0.30</td>
<td>0.04/0.36</td>
<td>.02</td>
<td>-0.40/0.80</td>
<td>0.90</td>
<td>0.46</td>
<td>1.4</td>
</tr>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>16</td>
<td>0.23</td>
<td>0.25</td>
<td>0.09/0.36</td>
<td>&lt;.01</td>
<td>-0.27/0.72</td>
<td>1.00</td>
<td>-0.12</td>
<td>9.0</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
<td>20</td>
<td>19</td>
<td>24</td>
<td>8/30</td>
<td>&lt;.01</td>
<td>-28/65</td>
<td>1.00</td>
<td>0.64</td>
<td>598</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>12</td>
<td>18.5</td>
<td>43</td>
<td>-9/46</td>
<td>.17</td>
<td>-66/103</td>
<td>0.98</td>
<td>1.00</td>
<td>190</td>
</tr>
</tbody>
</table>

**Table 3. Cerebrospinal Fluid Results**

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>Mean</th>
<th>Std</th>
<th>Mean 95% CI</th>
<th>$P$-value</th>
<th>Precision 95% CI</th>
<th>Correlation (r)</th>
<th>Concordance (k)</th>
<th>Data Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mg/dL)</td>
<td>55</td>
<td>6</td>
<td>4</td>
<td>5/7</td>
<td>&lt;.01</td>
<td>-1/14</td>
<td>0.97</td>
<td>1.00</td>
<td>53</td>
</tr>
</tbody>
</table>

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Figure 2. Correlation for pH. X axis is control measurement of pH. Y axis is POCT measurement of pH.
Discussion

Plural Fluid

Prior studies have demonstrated utility for pH measurement in plural fluid with POCT.\textsuperscript{4,5} In this study, no significant statistical difference was observed (\(P = .11\)) with slightly positive mean bias. POCT testing could be used at bedside for diagnostic purposes of diagnosing a parapneumonic effusion which can have a \(\text{pH} < 7.2\).\textsuperscript{7} All of the other samples had a \(\text{pH} > 7.4\) with 10 yielding a \(\text{pH} > 8.2\) on both devices. Alkaloid sampling might be from the delay in measuring pH since some of the samples were in the core laboratory freezer for a week. pH can become more alkaloid if there is a delay >4hrs between obtaining the plural fluid and analysis.\textsuperscript{8,10} A future improvement on this study would be to obtain a timely bedside measurement of pH versus a bench top control and assess the accuracy and the ability of the POCT device to correctly classify the effusion as a possible complicated parapneumonic effusion based on a \(\text{pH} < 7.2\) given the correct clinical scenario. A timely specimen collection and analysis would be classified as <2hrs since this should not affect the plural fluid pH.\textsuperscript{11}

Glucose demonstrated a statistical difference (\(P < .01\)) and a bias of 11mg/dL on the POCT when compared bench top analysis. The clinical utility of glucose is when it is \(\leq 60\text{mg/dL}\), usually in the setting of a parapneumonic effusion or malignant effusion.\textsuperscript{12} Glucose measurements on POCT correctly identified 6 of 7 effusions with glucose \(\leq 60\text{mg/dL}\). It would be 7 of 7 but one sample on POCT would be calculated at 62mg/dL while on the control analysis it would be 60mg/dL. Glucose has demonstrated the potential to be used for clinical assessment at the bedside in a future study.

LDH had statistically different values (\(P\)-value < .01) when comparing testing modalities with large negative mean bias (-343U/L); however, it had a strong \(r\) at 0.97. LDH had statistical differences in measurements on the POCT compared to the control due to measurement of different reaction products on each separate device. LDH is reported in international units on both devices but has different references ranges with a 99-192 U/L on the POCT and 313-618 U/L on the control. The control uses LDH as a catalyst for the oxidation of NADH to NAD\(^+\) monitored by reflectance spectrophotometry, and the activity of LDH corresponds to the LDH concentration.\textsuperscript{13} The POCT test for LDH was the Piccolo Basic Cartridge which uses the same reaction as above but carries out a second reaction measuring the formation of formazan by spectrophotometry.\textsuperscript{14} LDH is utilized diagnostically to characterize pleural fluid into exudative or transudative classes based on Light’s criteria.\textsuperscript{15} If using Light’s Criteria with LDH being 2/3 the upper limit of normal an exudate on the POCT device will be a value \(\geq 161\text{U/L}\) while on the control the value will be \(\geq 516\text{U/L}\). The POCT identifies 7 exudates and the control identifies 6. It would have identified the same seven but one of the value was only 503 U/L while 165 U/L on the POCT which is borderline exudative/transudative on both devices. LDH demonstrated potential for clinical use on POCT testing but further testing should be conducted to broaden the range of values and increase the sample size.

Protein had a positive bias at 0.01g/dL with no significant statistical difference (\(P = .96\)). Five of the 17 samples were <2.0g/dL on the POCT and control. The other 12 were detectable on both devices. Protein is another clinically important analyte in distinguishing exudate from a transudate with Light’s criteria, but a serum sample is needed to calculate a ratio.\textsuperscript{12,16} Future studies should investigate if the POCT device can categorize the pleural fluid as transudative or exudative.

TG had no significant statistical difference (\(P = .08\)) with a slightly negative bias (2.7mg/dL). The highest value measured was 60 mg/dL on the control. TG are routinely measured in pleural fluid if a chylothorax is suspected and confirmed with TG level > 110 mg/dL.\textsuperscript{17} The value range needs to be expanded to assess whether the POCT is clinically useful for diagnosing a chylothorax. The low concordance was due to the control detecting TG levels below 20, while POCT could not.

Albumin levels were analyzed because they have been used in studies to categorize transudative versus exudative effusions.\textsuperscript{16} Albumin demonstrated a statistical difference observed with a (\(P\)-value < .01) with a positive mean value at 0.27mg/dL with a low concordance value leading to the conclusion that albumin has limited if no potential future use on POCT.

Cholesterol had a negative bias at 16 mg/dL with statistically significant difference (\(P = .02\)) however, only 6 samples were measurable on the control. Cholesterol can categorize transudative and exudative pleural effusions. An exudative effusion has cholesterol level > 60 mg/dL for higher specificity or > 43mg/dL for higher sensitivity but neither is more sensitive nor more specific than Light’s criteria.\textsuperscript{16} POCT correctly identified 2 of 4 exudates with a cholesterol cutoff > 60mg/dL. If the cutoff is dropped to a cholesterol level > 43mg/dL then 6 of 6 exudates are identified. Future testing should be conducted to assess the accuracy of cholesterol measurement on POCT due to the low number of measurable samples.

Peritoneal Fluid

LDH had 11 samples with a wide data range; however, it did not have a strong correlation. This test used the same cartridge as pleural fluid on the POCT device, and there was a large difference in values due to different analyte measurements on each device.\textsuperscript{13,14} This yielded a statistical difference between the values with a weaker correlation than pleural fluid. LDH measurement would not be particularly useful for peritoneal fluid in diagnosing spontaneous bacterial peritonitis or secondary bacterial peritonitis. A future study should be repeated with more samples.\textsuperscript{17}

Protein was measured on 16 samples but only detectable on 5 samples with a positive bias and no statistical significance. Since 11 of the samples read less than 2.0g/dL on both testing modalities and 5 detected samples >2.0 g/dL the concordance was 1.00. Only 5 samples had elevated protein levels so further testing should be conducted to assess potential use for protein measurement. If a sample is read as less than 2.0g/dL of protein on POCT testing it is most likely correct. It has demonstrated utility for use at bedside if it is negative or < 2.0g/dL but if the
level is positive there is not data to clinically utilize this testing modality.

Albumin demonstrated a statistically significant difference between the POCT device and the control with a mean bias of positive 0.2 mg/dl due to POCT reporting elevated albumin levels compared to the control. Of the 16 samples analyzed only 3 had a detectable albumin levels on the control and POCT device; however, the POCT device had 3 other samples with falsely high elevations when compared to the control. Albumin is diagnostically utilized to calculate a serum-ascites albumin gradient to aid in diagnosing portal hypertension.\textsuperscript{20, 21} A future study could assess a serum-ascites albumin gradient calculated from a control versus the POCT testing to account for the positive bias of the device but currently the POCT device should not be used to measure albumin in ascitic fluid.

Glucose demonstrated a large mean bias of 19 mg/dL with statistical significance (P < .01). However, there were 2 samples with larger values recorded on POCT at > 700 mg/dL and 699 mg/dL while control recorded values of 618 mg/dL and 611 mg/dL. These two results may have skewed the results and elevated the positive mean bias. The overall r was 1.00 demonstrating a relationship between testing modalities. Glucose is measured in ascites typically if there is a concern for secondary bacterial peritonitis with a level of < 50 mg/dL in this setting.\textsuperscript{22} Only 3 of the samples from the study had a reading on < 50 mg/dL and another 3 samples had a value of 50-70 mg/dL with the POCT and control agreeing for each set of 3 samples. Further testing should be conducted to assess the accuracy of glucose since it may be able to be utilized for aiding in the diagnosis of secondary bacterial peritonitis.

Bilirubin demonstrated a slightly positive mean on the 16 samples but only 3 of these samples had elevated bilirubin levels at > 1 mg/dL. The r was excellent at 1.00 but concordance was poor due to the slightly positive bias on the POCT testing which lead to detectable tests when the control read a negative result on 7 samples. Bilirubin is tested in ascitic fluid to investigate a possible choleperitonem from a gallbladder perforation which typically causes a bilirubin concentration greater than 6 mg/dL with an ascitic fluid-serum bilirubin ratio > 1.\textsuperscript{23} Only 1 sample in the study had a bilirubin > 6 mg/dL and at 8.7 mg/dL and 9.1 mg/dL on the POCT and control, respectively. POCT did demonstrate utility and even with a slightly positive mean bias it was able to detect elevated bilirubin levels. It should be assessed in further studies with a bedside assessment versus a control because it could impact patient care immediately.

TG testing demonstrated no statistical significance in the results between the two testing modalities but there was positive mean bias which is greatly affected by one sample where the POCT recorded 373 mg/dL and the control recorded 219 mg/dL. If this measurement is excluded since all the other measurements were less than a 109 mg/dL on both devices with 3 negative samples in agreement in both testing modalities, mean bias goes from 18.5 mg/dL to 6.2 mg/dl with an STD of 7.2 mg/dL (P = .017). It seems the testing could be used for lower TG levels but it remains uncertain of its clinical utility with levels > 109 mg/dL since there was only 1 sample which was elevated.

**Cerebrospinal Fluid**

55 samples demonstrated a mean positive bias of 6 mg/dL with statistical significance (P = < .01) but it may not be clinically relevant. The POCT device ranged higher on every sample except for one in which the POCT measured a low CSF glucose at 20 mg/dL with a control of 22 mg/dL. Both values still fall into the low range. Normal values of blood glucose typically range from 40-80 mg/dL or a CSF to serum glucose ratio of 0.6. Bacterial meningitis typically causes a ratio of CSF/serum glucose of < 0.4 .\textsuperscript{24–26} Forty-eight of the samples were within the range of 40-80 mg/dL and three samples were > 80 mg/dL. Four samples were less than 40 mg/dL. Future studies should sample glucose at bedside along with serum glucose on POCT and control devices. Further investigation needs to be conducted in values outside of 40-80 mg/dL.

**Conclusion**

Pleural fluid protein, pH, glucose, and TG, and peritoneal fluid protein, bilirubin, glucose, and TG correlated and had similar clinical results as the control, demonstrating potential for clinical use. Pleural fluid LDH had a strong correlation between the fixed platform and the POCT device; however, differences were noted between reference ranges and methodology. Further studies will need to be conducted to confirm the utility of LDH POCT. Cholesterol POCT requires further investigation, CSF glucose POCT results were promising, and future studies should study more samples with glucose < 40 mg/dL.

**Conflict of Interest**

None of the authors identify a conflict of interest.

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Aeroallergen Sensitivity in Hawai‘i: Association With Asthma and Increased Prevalence of Sensitivity to Indoor Allergens Since 1966

Kathleen Min BA; Marianne Yoshida RN; Rei Miike MPH; and Elizabeth Tam MD

Abstract

Asthma and allergic diseases have increased globally. Earlier studies suggest a history of excess asthma morbidity and mortality in Hawai‘i, with high prevalence of sensitization to outdoor aeroallergens among atopic children. This study was undertaken to test the hypotheses that specific allergens are more associated with asthma, and that sensitivity to common aeroallergens has increased in Hawai‘i since 1966. Adult participants were recruited between 2001-2013, according to approved protocols. Data from 211 adults who reported physician-diagnosed asthma and 404 non-asthmatic controls are included in this analysis. Skin test responses to 8 common aeroallergens were assessed, and association between specific aeroallergen response and asthma diagnosis evaluated, using Chi-squared analysis. P-values < .05 were considered statistically significant. Compared to non-asthmatic controls, asthmatic participants were older, more likely to be of Mixed and non-White race, and more likely to be obese. Allergen sensitivity (atopy) was found in 85% of asthmatic and 72% of the controls. Prevalence (%) of positive responses to specific aeroallergens in asthmatic, non-asthmatic, and all atopic subjects, were: D. farinae (74, 59, 83), D. pteronyssinus (68, 52, 75), roach (42, 31, 46), cat (45, 19, 37), dog (27, 15, 25), grasses (34, 26, 37), weeds (22, 18, 25), and molds (18, 11, 17). Adjusted for age, race, and BMI, highest prevalence ratios [PR (95% CI)] were: D. farinae [1.16 (1.1-1.2)], D. pteronyssinus [1.16 (1.1-1.3)], cat [1.34 (1.2-1.5)], and dog [1.19 (1.1-1.3)]. This data indicates a strong association with asthma, and an increased prevalence in sensitivity to indoor allergens.

Introduction

Atopic respiratory diseases, including asthma and allergic rhinitis, have increased in recent decades. Changes in environment, lifestyle, and migration, have been implicated in increased allergic sensitization. The epidemic may have plateaued in Western, more developed countries, but continues to increase in developing countries, including the Asia-Pacific region. Hawai‘i’s tropical climate and position in the crossroads of the Asia-Pacific region may particularly favor allergic sensitization and the development of asthma. One review suggests increased asthma morbidity and mortality in Hawai‘i.

This study was undertaken to test the hypotheses that physician-diagnosed asthma is associated with sensitization to specific aeroallergens, and that sensitization to indoor aeroallergens has increased in Hawai‘i since last described in 1966.

Methods

Adults with physician-diagnosed asthma (n=211), or no asthma diagnosis (n=404) were recruited at health fairs and on college campuses from 2001 to 2013, according to a protocol approved by the University of Hawai‘i Human Studies Program. The participants answered questionnaires indicating gender, age, race, smoking status, and whether or not they had previously been diagnosed with asthma. Height and weight were measured, and BMI determined. Participants were categorized into both standard BMI groups, and BMI groups according to WHO Asian population-specific criteria. Histamine and saline controls and 8 common aeroallergens, (Dermatophagoides farinae [Der f 1], Dermatophagoides pteronyssinus [Der p 1], roach [German and American cockroach], cat [Fel d 1], dog, grasses [Bermuda and Johnson grass], weeds [careless/pigweed, cocklebur, and lamb’s quarters], and mixed molds), were applied with a multiple testing system (allergens and Quintest testing system, Hollister-Stier, Spokane WA). Fifteen minutes later, wheals were outlined in ink, and the tracings transferred to paper with plastic tape for measurement. A wheal at least 2mm larger than the negative control was considered positive. Tests in which there was no histamine or allergen wheal at least 2mm greater than the negative control, were excluded from analysis.

Categorical values were compared using the Chi-squared analysis (SAS software, version 9.2, SAS Institute Inc., Cary, NC). P-values < .05 were considered statistically significant.

Results

Compared to controls, the asthmatic participants were significantly older, more likely to be of Mixed or non-White race, and more likely to be obese, especially after WHO BMI criteria for Asians was applied (Table 1). The two groups did not differ significantly in smoking status. The current smoking in both groups was less than the state-wide prevalence of 15-17%. The groups differed in prevalence of atopy, although prevalence exceeded 70% in both.

Overall the highest prevalence of sensitivity was to indoor allergens (Table 2). For all tested aeroallergens, the prevalence was higher in the asthmatic participants than in controls, with cat sensitivity having the highest prevalence ratio (PR) (adjusted for age, race, and BMI), (Table 2, Figure 1). Response to weeds was not associated with asthma.

Among all atopic participants, whether asthmatic or not asthmatic, response to Der f 1 or Der p 1 exceeded 75% (Table 3). The lowest prevalence of sensitization was to molds, at 17%.

Discussion

Association Between Asthma and Aeroallergen Sensitization

This is the first study since 1966 to document aeroallergen sensitization in Hawai‘i. Although this study is not population-based, it includes more than 200 asthmatic and more than 400
non-asthmatic adults, and reflects the racial diversity of Hawai‘i. The adults diagnosed with asthma were older, and more likely to be non-white and of mixed race. Given the high percentage of Asian participants, WHO Asian-specific criteria for overweight and obesity were applied. When this was done, more asthmatic participants were categorized as obese than were control participants. Asthma and control groups did not differ significantly in smoking status, although the percentage of former smokers was higher among the asthmatic participants. In both groups, the rate of current smoking was much lower than the statewide smoking rate of 15-17% during the study. Using aeroallergen skin test sensitivity as an indicator of atopy, the prevalence of atopy was significantly greater among asthmatic participants. Interestingly, 15% of the participants with asthma showed no response to common aeroallergens. Even among the non-asthmatic participants, atopy was documented in at least 75%.

After adjusting for differences in age, race, and corrected BMI, prevalence for all allergens except weeds were increased in the asthmatic vs non-asthmatic participants. Among the asthmatic participants, sensitivity to dust mites, cat, and roach, was detected in 74%, 45%, and 42% of the group. These rates of sensitivity exceed the rates described in inner-city children diagnosed with asthma in 1997 (35%, 24%, 36%, respectively). Sensitivity to the cat aeroallergen showed the greatest prevalence ratio (1.34 [95% CI 1.2-1.5]), standing out from the increased prevalence ratios also noted for dust mites, roach, dog, grasses, and molds. Nearly a half of the adult participants were sensitive to cat, perhaps reflecting changes in pets living indoors, wider use of carpeting and upholstery (serving as a reservoir of antigen), and decreased ventilation in modern homes in Hawai‘i. These factors, combined with the innate resilience, respirable size, and easily airborne nature of Fel d 1, increase exposure to threshold levels of cat allergen.

### Increased Prevalence of Aeroallergen Sensitivity in Hawai‘i Since 1966

To test the hypothesis that the prevalence of sensitization to indoor aeroallergens has increased over time, these findings were compared with an earlier Honolulu-based study of 500 children referred to two allergy clinics in Honolulu before 1966. The data from this earlier study allows estimation of prevalence of sensitivity among atopic individuals. Comparisons between the two studies are limited to atopic individuals and aeroallergens that were similar in both (Table 3). Those aeroallergens in the current vs earlier study include: dust mite proteins (Der f 1 and Der p 1) vs “House dust”; cat (Fel d 1) and dog vs “animal danders” (cat, cattle, dog, goat, and rabbit); Bermuda and Johnson grasses vs “grasses” (Bermuda, Johnson, Blue, Red Top, Timothy, and sugar cane grasses); careless/pigweed, cocklebur, and lamb’s quarters weeds vs “weeds” (careless/pigweed, cocklebur, lamb’s quarters, common ragweed, false ragweed, Russian thistle, and saltbush), and mixed molds vs “molds” (11 species).

The comparison indicates that prevalence of sensitivity to dust mites among atopic individuals has doubled, since 1996; whereas sensitivity to the outdoor allergens (grasses, weeds, and molds) decreased. There was no apparent change in sensitivity to cat and dog. Roach sensitivity could not be compared.

Limitations of the study include: differences in the populations and in the tested aeroallergen mixes. The current study consisted of adults (with age-related decline of allergic mediators and markers) of different racial distribution from the children of the earlier study (Asian 25%, Filipino 8%, none Mixed, Pacific Islander 4%, White 50%, and Other 15%). In addition, 38% of the atopic adults were asthmatic, compared to 79% of the children in the earlier study. Antigen mixes also differed in that the earlier study included more species in each of their animal, grass, weed, and mold mixes. This could have led to an apparent reduction in sensitivity to outdoor allergens over time, but does not detract from the clear increase in dust mite sensitivity.

### Table 1. Characteristics of participants

<table>
<thead>
<tr>
<th>Smoking Status</th>
<th>Asthma</th>
<th>No Asthma</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>60</td>
<td>66</td>
<td>.145</td>
</tr>
<tr>
<td>Past</td>
<td>33</td>
<td>26</td>
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</tr>
<tr>
<td>Current</td>
<td>7</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Atopic</td>
<td>85</td>
<td>72</td>
<td>&lt;.001</td>
</tr>
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</table>

<table>
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<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>Asian</td>
<td>39</td>
<td>39</td>
<td>.95</td>
</tr>
<tr>
<td>Filipino</td>
<td>5</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Mixed</td>
<td>34</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Pacific Islander</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>18</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>4</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>BMI*</th>
<th>Asthma</th>
<th>No Asthma</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>1</td>
<td>4</td>
<td>.003</td>
</tr>
<tr>
<td>Normal</td>
<td>46</td>
<td>49</td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>27</td>
<td>23</td>
<td>.015</td>
</tr>
<tr>
<td>Obese</td>
<td>26</td>
<td>25</td>
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</tr>
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</table>

<table>
<thead>
<tr>
<th>BMI**</th>
<th>Asthma</th>
<th>No Asthma</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight</td>
<td>1</td>
<td>4</td>
<td>.008</td>
</tr>
<tr>
<td>Normal</td>
<td>39</td>
<td>49</td>
<td></td>
</tr>
<tr>
<td>Overweight</td>
<td>24</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Obese</td>
<td>35</td>
<td>25</td>
<td></td>
</tr>
</tbody>
</table>

*Underweight (< 18.50), Normal (18.50-24.99), Overweight (25.00-29.99), Obese (≥ 30.00). **Corrected according to WHO Asian population-specific criteria.*
Table 2. Prevalence of positive skin tests among participants diagnosed with asthma and non-asthmatic controls, with unadjusted and adjusted prevalence ratios.

<table>
<thead>
<tr>
<th>Allergen</th>
<th>All N=615 (%)</th>
<th>Asthma n=211 (%)</th>
<th>No asthma n=404 (%)</th>
<th>P-value</th>
<th>PR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted</td>
<td>Adjusted*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dust mites (Der f 1)</td>
<td>64</td>
<td>74</td>
<td>59</td>
<td>&lt;.001</td>
<td>1.17 (1.1-1.3)</td>
</tr>
<tr>
<td>Dust mites (Der p 1)</td>
<td>58</td>
<td>68</td>
<td>52</td>
<td>&lt;.001</td>
<td>1.16 (1.1-1.3)</td>
</tr>
<tr>
<td>Roach</td>
<td>35</td>
<td>42</td>
<td>31</td>
<td>.008</td>
<td>1.11 (1.0-1.2)</td>
</tr>
<tr>
<td>Cat (Fel d 1)</td>
<td>28</td>
<td>45</td>
<td>19</td>
<td>&lt;.001</td>
<td>1.33 (1.2-1.4)</td>
</tr>
<tr>
<td>Dog</td>
<td>19</td>
<td>27</td>
<td>15</td>
<td>&lt;.001</td>
<td>1.20 (1.1-1.3)</td>
</tr>
<tr>
<td>Grasses</td>
<td>28</td>
<td>34</td>
<td>26</td>
<td>.009</td>
<td>1.10 (1.0-1.2)</td>
</tr>
<tr>
<td>Weeds</td>
<td>19</td>
<td>22</td>
<td>18</td>
<td>.205</td>
<td>1.06 (0.96-1.2)</td>
</tr>
<tr>
<td>Molds</td>
<td>13</td>
<td>18</td>
<td>11</td>
<td>.021</td>
<td>1.14 (1.0-1.3)</td>
</tr>
</tbody>
</table>

*Adjusted for age, race, and BMI.

Table 3. Comparison of prevalence of positive skin tests among atopic participants 2001-2013 and 1966

<table>
<thead>
<tr>
<th>Allergen</th>
<th>2001-2013 Prevalence (%)</th>
<th>1966 Prevalence (%)</th>
<th>Allergen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dust mites (Der f 1)</td>
<td>83</td>
<td>41</td>
<td>House dust</td>
</tr>
<tr>
<td>Dust mites (Der p 1)</td>
<td>46</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>Roach</td>
<td>37</td>
<td>30</td>
<td>Not tested</td>
</tr>
<tr>
<td>Cat (Fel d 1)</td>
<td>25</td>
<td>30</td>
<td>Cat, dog, cattle, goat, rabbit</td>
</tr>
<tr>
<td>Dog</td>
<td>37</td>
<td>75</td>
<td>Grasses</td>
</tr>
<tr>
<td>Grasses</td>
<td>25</td>
<td>51</td>
<td>Weeds</td>
</tr>
<tr>
<td>Weeds</td>
<td>17</td>
<td>68</td>
<td>Molds</td>
</tr>
</tbody>
</table>

Figure 1. Risk of physician-diagnosed asthma by various aeroallergens
Conclusion
This study confirms the hypothesis that physician-diagnosed asthma is associated with sensitization to specific aeroallergens. Although not population-based, the current study indicates that dust mite sensitivity has increased in Hawai‘i, insofar as rates of sensitivity in adults recruited from the community from 2001 to 2013 exceeded rates in children referred for “major allergic disease” to allergy specialists in 1966.6

Understanding this association between asthma and indoor allergens, and that the majority of Hawai‘i residents may be sensitized, can inform practical environmental controls and public policy.

Conflict of Interest
None of the authors identify a conflict of interest.

Acknowledgements
Supported by American Lung Association of Hawai‘i, Leahi Fund, Hawai‘i Community Foundation, NIH/NCRR Grants G12RR003061, P20RR11091.

References
Streptococcus suis Meningoencephalitis with Seizure from Raw Pork Ingestion: A Case Report

Suwarat Wongjittraporn MD; Ornusa Teerasukjinda MD; Melvin Yee MD; and Heath H. Chung MD

Abstract

Background: Streptococcus suis meningocerebralitis is a rare but increasingly important condition. Good history taking will give clues to the diagnosis. This is the fourth case report in the United States.

Case: A 52-year-old Filipino man who recently returned from a trip to the Philippines was admitted with classic symptoms of bacterial meningitis. His cerebrospinal fluid culture grew Streptococcus suis. His clinical course was complicated by seizures, hearing loss, and permanent tinnitus.

Conclusion: Clinicians should be aware of this emerging disease especially in patients with recent travel history to endemic areas. Early recognition and appropriate management could potentially prevent complications.

Keywords

Case Report, Streptococcus suis meningocerebralitis, seizure, hearing loss, tinnitus

Introduction

Streptococcus suis is an emerging zoonotic pathogen found in the upper airway, reproductive system, and digestive tracts of pigs. This organism can enter the human bloodstream via direct contact through open wounds, or through inhalation.

The first case report of human Streptococcus suis infection was in 1968 in Denmark. Since then, over 100 cases have been reported worldwide. The majority of the cases are in Asia (Vietnam, Thailand, and China). An outbreak in China involved 215 human cases and 39 deaths.2 There were 4 cases reported in the United States before February 2013. In 3 of these cases, infection was acquired domestically (New York, Hawaii, and Minnesota) and one (California) was probably acquired in the Philippines.3

Clinical Presentation

A 52-year-old Filipino man was admitted to a tertiary care hospital in Hawaii for a diagnosis of bacterial meningitis. The patient recently returned from a trip to the Philippines. He reportedly ingested raw pork in the Philippines. On the day of admission, the patient was febrile and confused. Examination was significant for meningeumus, however, there was no focal neurologic deficit. Computed Tomography (CT) of his brain showed multiple calcifications consistent with previous neurocysticercosis with no active lesions. Lumbar puncture revealed cloudy cerebrospinal fluid (CSF) with a white blood cell count (WBC) of 880 cells/mL with 63% of segmented neutrophils. The initial gram stain of CSF showed gram positive cocci. The sample of CSF and blood cultures showed bacterial growth. An echocardiogram was negative for bacterial endocarditis. The patient received initial treatment with vancomycin, ceftriaxone, and ampicillin that was subsequently transitioned to linezolid and ampicillin, and finally to ceftriaxone 2 gram intravenous injection every 12 hours when identification and sensitivities showed a sensitive streptococcus suis isolate. The repeat blood cultures on day 2 of hospitalization were negative and the repeat lumbar puncture on day 10 after admission showed resolving CSF with WBC of 57 cells/mL (5% segmented neutrophils) with negative gram stains and cultures.

Clinical Course

The patient developed bilateral deafness with high-pitched tinnitus and unbalanced gait within 24 hours of admission. He completed 4 weeks of antibiotics and a tapering course of steroid. The patient’s symptoms of deafness and ataxia persisted. He developed generalized tonic-clonic seizures 4 weeks after admission. He was started on levetiracetam for seizure control.

Discussion

Seizures occur in up to 12-30 percent of adults with meningitis and are also associated with higher neurologic deficit. The incidence of seizures is significantly increased in Streptococcal meningitis.

Streptococcus suis meningitis is also known to result in hearing loss (at a rate of 54%-68.8%).6 Hearing loss due to this infection can be irreversible7 and is more common than in other causes of bacterial meningitis.8 Magnetic Resonance Imaging (MRI) may show some involvement in the cochlea and the severity of this process is proportional to hearing loss.9 Mortality is between 4.8%-6.7%.6 Our patient developed seizures, which is not common for Streptococcus suis meningitis. There is an association with neurocysticercosis. However, our patient’s lesions appeared old with no active inflammation. There were only 2 other streptococcus suis cases reported that involved seizures and both of them in alcoholics.6 It was still unclear whether or not the seizures were related to streptococcus suis meningitis or not. Our patient is at risk of developing unprovoked seizures from meningitis due to high indices of CSF inflammation (CSF WBC less than 1,000 cell/mL and high CSF protein level) and abnormal cranial CT lesions from prior neurocysticercosis. Focal abnormalities on cranial CT are related to seizures > 48 hours after admission.

There is no standard treatment duration. One case series reported that there were 2 relapses reported after treatment with vs 4 weeks,10 so prolonged therapy should be considered for infections caused by this pathogen. Dexamethasone sodium
phosphate administration can reduce the risk of severe hearing loss and neurologic sequelae; however, there is no specific treatment duration recommendation for *Streptococcus suis* meningitis.

This case is reported to increase awareness of this particular disease and its common association with hearing loss. Further clinical investigation is warranted to characterize the epidemiology, long-term complications, and optimal treatment of this pathogen.

**Conflict of Interest**

None of the authors identify a conflict of interest.

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**Correspondence to:**
Suwarat Wongjittraporn MD; Email: suwarat.w@gmail.com

**References**

**Mycobacterium avium Complex Empyema in a Patient with Interferon Gamma Autoantibodies**

Thomas T. DeLeón MD; Heath H. Chung MD; Steven M. Opal MD; and Jonathan D. Dworkin MD

**Abstract**
Interferon gamma (IFN-γ) autoantibodies are a relatively recently discovered clinical entity, which have been shown to be associated with disseminated non-tuberculous mycobacterial (NTM) infections and other opportunistic infections. Interestingly, isolated NTM infections (without disseminated NTM infection) have not been shown to be a good predictor of the presence of IFN-γ autoantibodies. This case describes an isolated NTM empyema in a patient with IFN-γ autoantibodies and makes the argument that the development of an NTM empyema in a patient with no known immunodeficiency should prompt consideration for IFN-γ testing. Additionally, this case underscores the importance for clinicians to recognize that an unusual infection without the typical cause of impairment in immunity should prompt a more thorough investigation of the patient’s immune system.

**Background**
Interferon gamma (IFN-γ) autoantibodies have been described since 2004. From its initial description IFN-γ autoantibodies were found to have a relationship with nontuberculous mycobacterial (NTM) infections in HIV negative patients. The relationship was found to be particularly strong in patients with disseminated NTM infections (infections in two non-contiguous organ systems). The presence of IFN-γ autoantibodies leads to deficits in cellular immunity and infection with opportunistic pathogens, such as NTM, which are normally eradicated by the IFN-γ, IL-12, TNF-a pathway. NTM empyemas have been described in the literature in patients with impairment of cellular immunity (transplant patients, AIDS patients, and patients on chronic immunosuppressive therapy). The presence of IFN-γ autoantibodies has been strongly linked to IFN-γ autoantibodies and the patients history of these conditions provided a reason to test for the presence of IFN-γ autoantibodies.

**Case Presentation**
The patient is a 77-year old Filipino man born in the Philippines but lives in Hawai‘i, who presented with abdominal pain, dry cough, and nausea of 2 weeks duration. The patient’s previous history was significant for cutaneous Sweet’s syndrome (2005) and Salmonella Typhimurium bacteremia (2006). Disseminated nontuberculous mycobacterial infections or bacterial infections such as Streptococcus, Staphylococcus, Klebsiella, or anaerobic species. NTM empyemas are rare occurrences that have been described in cases of an immunocompromised host. In this case the patient presented with a MAC empyema without the typical causes for deficits in cellular immunity. Salmonellosis and Sweet’s syndrome have been strongly linked to IFN-γ autoantibodies and the patients history of these conditions provided a reason to test for the presence of IFN-γ autoantibodies.

Interestingly, isolated pulmonary NTM infections by themselves have not been found to be a useful predictor of the presence of IFN-γ autoantibodies. IFN-γ autoantibodies have been found to be strongly associated with HIV negative patients with a history of (1) disseminated nontuberculous mycobacterial infections (infection in two non-contiguous organs) and (2) opportunistic infections such as Cryptococcus neoformans, Histoplasma capsulatum, Penicillium marneffei, disseminated...
Figure 1. Chest X-ray and CT-Chest of Empyema

<table>
<thead>
<tr>
<th></th>
<th>Day 2</th>
<th>Day 5</th>
<th>Day 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram Stain</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Aerobic &amp; Anaerobic Culture</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
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<td>+</td>
<td>+</td>
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<td>+</td>
<td>+</td>
</tr>
<tr>
<td>M. Avium DNA Probe</td>
<td>+</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>M. Tuberculosis DNA Probe</td>
<td>-</td>
<td>-</td>
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</tr>
</tbody>
</table>
salmonellosis, and severe herpes zoster infections. Currently there are no clear guidelines for IFN-γ autoantibody testing. However, based on the current evidence, it seems reasonable to consider testing in patients for IFN-γ autoantibodies who are HIV negative and have a history of a characteristic opportunistic infection (as listed above) or disseminated NTM infection as depicted in Figure 2. This is particularly true in patients of East Asian descent. The relationship with IFN-γ autoantibodies and isolated NTM empyemas is not clear. However, acquired antibodies against the IFN-γ pathway are a consideration in these cases, as there have been a few reports of immunocompetent hosts developing NTM empyemas who may benefit from IFN-γ autoantibody testing.

Unfortunately for patients found to have IFN-γ autoantibodies there is no proven therapeutic treatment available for this condition. Many patients diagnosed with IFN-γ autoantibodies will respond to anti-microbial agents alone, but many patients will also develop an infection that is refractory to treatment or develop recurrent disease. Browne, et al, found that 4 of the 11 patients with IFN-γ autoantibodies were refractory to anti-microbial agents alone. In these patients they found Rituximab to be a promising treatment. Browne, et al, conducted a very small pilot study (4 patients), which found that using Rituximab in conjunction with anti-microbial agents led to resolution of refractory nontuberculous mycobacterial infections in all patients enrolled in the study.

In conclusion, this case report illustrates that the question of adult onset immune deficiency is more complex than consideration of HIV status, use of immunosuppressive agents, and other common risk factors. There are many pathways in the innate and cell-mediated immune systems that are crucial to a host’s defense against infection. These pathways are continuing to become better understood. It is particularly important for clinicians to recognize that an unusual infection without the typical cause of impairment in immunity should prompt a more thorough investigation of the patient’s immune system.
Lupus Erythematosus Tumidus: A Unique Disease Entity

Rodger Stitt MD; Colby Fernelius MD; Jefferson Roberts MD; Troy Denunzio DO; and Navin S. Arora DO

Abstract
Lupus erythematosus tumidus (LET) is a photosensitive skin disease characterized by succulent, edematous, and non-scarring plaques. Histologic features include perivascular and periadnexal lymphocytic infiltration and interstitial mucin deposition. Despite being first described in 1909, there are few case reports in the current literature describing this disease and even fewer that discuss treatment. We describe a case of a 22-year-old woman with systemic lupus erythematosus (SLE) and secondary class V lupus nephritis. She was referred to Dermatology for an intermittent pruritic facial eruption that was clinically and histologically consistent with LET.

There is much controversy in literature as to whether or not LET is a unique variant of cutaneous lupus erythematosus. Interestingly, the mainstay of treatment for LET, in the limited case reports and series that exist, is with antimalarial drugs, which our patient had already been taking for SLE. This case exemplifies the need for complete disease characterization, evidence-based treatment, and a multidisciplinary approach.

Keywords
Lupus erythematosus tumidus, systemic lupus erythematosus, lupus nephritis, cutaneous lupus erythematosus

Case Presentation
A 22-year-old caucasian woman with a one-year history of systemic lupus erythematosus (SLE) was referred to dermatology clinic for a persistent eruption of a rash on her face and arms. Significant past medical history included systemic lupus erythematosus (SLE) manifested by polyarticular arthritis, malar rash, photosensitivity, positive serology with anti-nuclear antibody titer of 1:2560, low C4, positive dsDNA antibody, anti-cardiolipin antibody, and beta2-glycoprotein. She was also being treated for biopsy proven class V lupus nephritis with mycophenolate mofetil 720mg twice a day, tacrolimus 2mg twice a day, and hydroxychloroquine sulfate 200 mg daily (4.5mg/kg/day). She was previously treated with oral prednisone while pregnant and then transitioned to the above immunosuppressants following delivery.

The eruption had been present for one week and had occurred several months ago for a similar duration and had resolved without treatment or scarring. She complained of mild pruritus and tenderness. Exam was remarkable for blanching, inflamed plaques with raised borders, proximally on both arms, cheeks, and temples with coalescing of lesions (Figure 1 and Figure 2). A punch biopsy of her right upper extremity revealed a superficial and deep periadnexal and interstitial infiltrate (Figure 3). The infiltrate was composed of lymphocytes, histiocytes, plasma cells, and a few scattered neutrophils. Increased dermal mucin was noted and confirmed by a colloidal iron stain (Figure 4). Notably, the epidermis was unremarkable with no significant vacuolar changes. Given her clinical presentation and histopathologic findings, a diagnosis of lupus erythematosus tumidus (LET) was made.

Fluocinonide 0.05% and hydrocortisone valerate 0.2% ointments were prescribed resulting in complete resolution within two weeks without scarring. One month later, she returned to clinic with a similar eruption, consistent with another episode of LET and was prescribed a low dose prednisione taper, 10mg for three weeks followed by 5mg for two weeks. Following the five week prednisone taper, she has been without any further eruptions to date.

Discussion
LET is a photosensitive skin disease that is characterized by succulent, edematous, non-scarring plaques.1 The disease was first described by the German dermatologist, E. Hoffman, in 1909.2 There are a limited number of case reports and case series with most of the literature originating in Europe. It remains controversial whether LET is a separate disease entity or rather an entity on the cutaneous lupus erythematosus (CLE) disease spectrum.3

Clinical Presentation
LET disease is more photosensitive than CLE and patients can have numerous flares with no scarring.2 Kuhn, et al, described 40 cases of LET and suggested that extreme photosensitivity, histological findings, and effective treatment with antimalarial therapy are so characteristic of this disease that it should be classified as a separate entity separate from any other variant of lupus erythematosus. Schmitt, et al, studied the characteristics of 44 patients with CLE, 24 of whom were diagnosed with LET, and found that LET had significantly decreased damage scores and increased mucin deposition, absent interface dermatitis, and alteration of hair follicles on histology when compared to other variants of CLE.3

Histology
Histological features include perivascular and periadnexal lymphocytic infiltration and interstitial mucin deposition.1 LET is unique in that epidermal changes and vacuolar degeneration of the dermoeipidermal junction or basement thickening are absent, while the typical lesions in CLE (discoid) and subacute cutaneous lupus erythematosus involving the skin are noted in Table 1.
Figure 1. Photograph of face showing blanching inflamed plaques with raised borders and coalescing of lesions.

Figure 2. Right upper arm with blanching inflamed plaques with raised borders.

Table 1. Histologic features of the major clinical variants of lupus erythematosus involving the skin.

<table>
<thead>
<tr>
<th>Histologic Changes</th>
<th>Discoid</th>
<th>Tumid</th>
<th>Subacute</th>
<th>Systemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidermal</td>
<td>+</td>
<td>-</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Vacuolar change</td>
<td>+</td>
<td>-</td>
<td>++</td>
<td>++</td>
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<tr>
<td>Civatte bodies</td>
<td>+</td>
<td>-</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>Follicular plugging</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Atrophy</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Basement Membrane thickening</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Dermal</td>
<td>+</td>
<td>+</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Dermal mucin</td>
<td>++</td>
<td>+ to ++</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Superficial and deep infiltrate</td>
<td>+++</td>
<td>+ to ++</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Treatment

There are few evidence-based pharmacologic treatments for LET beyond case reports and series. Kuhn, et al, reported complete resolution of skin lesions in 18 patients (45%) who were treated with topical corticosteroids or sunscreens of SPF 15 or greater. The remaining patients were treated with antimalarial therapy with 91% (20 of 22) having complete resolution over the course of 4-6 weeks at a daily dose of hydroxychloroquine sulfate 3.5 to 4 mg/kg/day. In 3 patients, the dose had to be increased to 6-6.5 mg/kg per day to achieve remission. Systemic corticosteroids or immunosuppressants were only temporarily necessary in 2 patients. Cozzani, et al, described a case series of 21 patients, of which 16 were treated with antimalarial therapy (hydroxychloroquine sulfate, chloroquine phosphate, and mepacrine hydrochloride) of unknown dose-weight ratio. All initially had complete resolution of skin lesions but there were varying rates of relapses, mostly occurring in spring and summer months approximately 3 weeks following sun exposure. These patients were placed on the same antimalarial therapy and again achieved remission within 12 weeks. Kreuter, et al, reported a retrospective study of 36 patients with LET treated with either hydroxychloroquine sulfate (n=10) or chloroquine phosphate (n=26). The median Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) score was 4 at baseline and decreased to 1 following 3 months of therapy. Twenty-two patients achieved complete or almost complete remission. There was no significant difference in outcome between the two different antimalarial treatments.
Figure 3. A punch biopsy of right upper extremity revealing a superficial and deep periadnexal and interstitial infiltrate composed of lymphocytes, histiocytes, plasma cells, and a few scattered neutrophils. (H&E staining 10x)

Figure 4. Punch biopsy of right upper extremity revealing dermal mucin. (Colloid iron stain)
In our patient, despite already being treated with hydroxychloroquine sulfate, mycophenolate mofetil, and tacrolimus for SLE and lupus nephritis, she developed lesions of LET. She had complete resolution with topical corticosteroids, however the lesions returned a month later and a low dose oral prednisone taper was required to achieve remission. A general stepwise approach to treatment can be partially extrapolated from Kuhn, et al’s, series of 40 patients from a progressively more systemic and toxic lineation; sunscreen (sun exposure avoidance), topical steroid treatment, antimalarial therapy, followed by systemic steroids, and other immunosuppressants. If lesions recur for a third time, it may be reasonable to increase our patient’s hydroxychloroquine sulfate therapy to 6-6.5mg/kg/day. This, however, places our patient at risk for adverse drug reactions such as retinopathy or agranulocytosis with hydroxychloroquine therapy. Multiple prednisone tapers may lead to adrenal insufficiency and other excess corticosteroid effects. What if there is a fourth recurrence? Our patient is young and would benefit from steroid sparing treatments. However, she is already taking mycophenolate and tacrolimus. Further immunosuppression will inevitably lead to a higher risk of infection and considering her age, there is a high probability of developing a serious infection in her lifetime. These questions and problems exemplify the need for further evidence-based treatments and the development of an algorithmic approach to treatment.

Summary
It is important to distinguish LET from other variants of CLE based on histology and clinical features since the course of disease and treatment response significantly differs. As this disease entity becomes more recognized, there will be an increase growth in incidence and thus a need for larger treatment studies to create an evidence-based algorithmic approach to this unique disease entity, especially in medically complicated cases, such as this young woman.

Conflict of Interest/ Disclosure
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References
Diagnosis of Atypical Hemolytic Uremic Syndrome and Response to Eculizumab Therapy

May H. Nguyen MD; Jacob J. Mathew DO; Troy M. Denunzio DO; and Mark G. Carmichael MD

Abstract

Atypical hemolytic uremic syndrome (aHUS) has a high mortality rate if not detected and treated early. While in the past, it was associated with renal failure in children, today, it has become increasingly identified among adults. Due to recent advances in the pathogenesis of aHUS and other major thrombotic microangiopathies (TMA), diagnosing it has become a lot easier. We present a case of a 62-year-old man who was initially thought to have thrombotic thrombocytopenic purpura (TTP), but after further evaluation was diagnosed with aHUS. We will discuss how to distinguish aHUS from other major TMA and the role of eculizumab in the management of aHUS.

Introduction

Atypical hemolytic uremic syndrome is the rarest form of thrombotic microangiopathy (TMA) and affects people of all ages. It is caused by mutations in the alternative complement pathway resulting in the failure of regulators to inactivate C3b.1-3 Then overactive complements will attack not only foreign antigens but also normal host cells leading to endothelial cell injury, platelet activation and aggregation, coagulation, and multi-system microthrombosis. Eculizumab is a monoclonal antibody that blocks the formation of C5a and membrane attack complex (MAC). It was first approved for paroxysmal nocturnal hemoglobinuria (PNH), a related complement mediated disease, and now it is also used for aHUS. Multiple case studies have proven the effectiveness of eculizumab in reversing multi-organ dysfunction caused by TMA.4 Before the discovery of eculizumab, plasma exchange (PEX) was considered to be the first line therapy for all three major TMA syndromes: TTP, Shiga toxin-producing Escherichia coli (STEC-HUS), and aHUS. Patients with aHUS sometimes transiently respond to PEX. However, approximately 65% would progress to end-stage renal disease (ESRD) or die within a year of diagnosis.5 Clinical trials have shown that treatment with eculizumab improves and reverses the effect of TMA in 80% of patients with aHUS.6 Thus, it is very important to distinguish aHUS as a separate entity early in its course in order to implement appropriate therapy. This report will explain the distinguishing factors among the three major TMA and highlight the treatment of aHUS with eculizumab.

Case Report

A 62-year-old Filipino man with a history of chronic kidney disease stage 3 and diabetes mellitus type 2 experienced a decline in renal function with abdominal pain, arthritis, and palpable purpura a year prior to diagnosis of aHUS. Renal biopsy at the time revealed, on immunofluorescence microscopy, mesangial IgA deposits consistent with IgA vasculitis. He was treated with six months of steroid therapy with improvement of his symptoms and renal function back to baseline. Six months later he again presented with a one month history of progressively worsening dyspnea on exertion with orthopnea, disorientation, confusion, fatigue, abdominal pain, and loose stools. Labs showed acute and chronic renal failure with creatinine 8.0 mg/dL, BUN 115.0 mg/dL, sodium 131.0 mmol/L, potassium 6.2 mmol/L, chloride 98.0 mmol/L, bicarbonate 19.0 mmol/L. Complete blood count was significant for hemoglobin of 8.9 g/dL, hematocrit 28.5%, mean corpuscular volume 88 fl., and platelets 140 x 10(9)/L.

The patient was admitted to the intensive care unit for initiation of continuous renal replacement therapy and, thereafter, dialysis for volume overload, uremia, and hyperkalemia. Within 48 hours, a rapid fall of his hemoglobin and platelets was noted. Hemoglobin and platelets dropped to 6.7 g/dL and 66 x 10(9)/L respectively. Lactate dehydrogenase rose to 1155 IU/L and haptoglobin decreased to <26 mg/dL. Review of his peripheral smear revealed extensive microangiopathic hemolytic anemia with thrombocytopenia (see Figure 1). PEX was initiated for possible TTP while further workup for TMA was performed. He was started on high dose steroid therapy. Further laboratory and imaging evaluations excluded antiphospholipid antibody syndrome, systemic lupus erythematosus, heparin-induced thrombocytopenia, malignant hypertension, autoimmune hemolytic anemia, infections, disseminated intravascular coagulation, toxin producing bacterial colitis, and malignancy. He transiently responded, minimally, to plasma exchange and high dose steroids. However, after PEX and steroids were stopped, his anemia and thrombocytopenia worsened. A therapeutic trial of rituximab was initiated and was unsuccessful. TTP was excluded and aHUS favored when the ADAMTS13 (a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13) level returned at 33% and TMA relapsed despite 14 days of PEX and steroids, and 1 month of rituximab. Since clinical evidence supported the diagnosis of aHUS, further investigation with complement genetic testing was not pursued. Eculizumab was started using published dosing guidelines for aHUS and we documented a rapid normalization of his hemoglobin, platelet, and lactate dehydrogenase levels within 2 weeks of therapy. While there was a rapid improvement in his hematologic parameters, his renal function did not recover and he remains on dialysis despite therapy.

Discussion

The similarities in clinical features among the major TMAs have made it challenging to distinguish them apart. All of them, more or less, have microangiopathic hemolytic anemia, thrombocytopenia, and multi-organ system involvement. However, in
Figure 1. Patient’s blood smear showing microangiopathic hemolytic anemia with red cell fragmentation and thrombocytopenia.

The last two decades, there have been many discoveries in the pathogenesis of aHUS and TTP. For instance, an autoantibody-mediated deficiency of the von Willebrand factor (vWF) cleaving protease ADAMTS13 has been shown to be the leading cause of platelet aggregation and microvascular thrombi formation in TTP.6-8 On the contrary, aHUS is mediated by genetic dysfunction in the complement alternative pathway. Normally, in the alternative complement pathway, C3b is inactivated by complement regulators, thus preventing the formation of SCa and MAC (C5a-9). However, due to gene mutations or autoantibodies to these regulators, C3b is always active and goes on to generate SCa and MAC. These overactive complements then cause endothelial cell damage, inflammation, activation of the coagulation cascade, and thrombotic microangiopathy.2-3

The first step in diagnosing aHUS is to recognize TMA: schistocytes, elevated lactate dehydrogenase (typically >600 IU/L), decreased haptoglobin, decreased hemoglobin, and thrombocytopenia (platelet count less than 150,000 or >25% decrease from baseline).9 These lab abnormalities should also coincide with one or more of the following: neurological symptoms, acute renal failure, or gastrointestinal symptoms. Early initiation of PEX for TTP is indicated as the definitive evaluation is started given the increased mortality of untreated TTP. Etiologies that mimic TMA should be excluded and they include systemic infections, medications, disseminated malignancy, scleroderma, antiphospholipid antibody syndrome, systemic lupus erythematosus, heparin-induced thrombocytopenia, malignant hypertension, autoimmune hemolytic anemia, disseminated intravascular coagulation, and pregnancy-related syndromes such as preeclampsia and HELLP syndrome.10 aHUS can be distinguished from STEC-HUS by PCR or culture-based assays for the Shiga-toxin producing E. coli. TTP can be distinguished from aHUS by measuring ADAMTS13 level. Clinicians should be aware that ADAMTS13 activity alone could not be used to definitively exclude TTP. It is only an adjunct in the evaluation and diagnosis of aHUS and TTP. If ADAMTS13 is >5% and the patient is resistant to plasma exchange, then the diagnosis is more likely to be aHUS than TTP.5,6,9,11 If the diagnosis is still elusive, then screening for complement mutations and antibodies should be performed. Unfortunately, laboratories that offer complement genetic testing are not widely available.6,11 Once aHUS is diagnosed, eculizumab may be used as first line therapy.

Eculizumab is a recombinant, fully humanized monoclonal antibody, which is effective in treating aHUS due to its high binding affinity for C5 thus preventing the formation of C5a and C5a-9. It was recently approved as first line therapy for aHUS in 2011.8 In 2013, Legendre, et al, studied the outcome of 37 patients after 26 weeks of eculizumab therapy in 2 clinical trials. Patients included in the trials were >12 years of age, had clinical evidence of hemolysis, had previous treatment with PEX, and had impaired renal function. They were excluded from the trials if they had documented STEC infection, ADAMTS 13 activity <5%, and previous treatment with eculizumab. Eighty percent of patients treated with eculizumab had improvement in thrombocytopenia, anemia, and renal function resulting in
eventual cessation of dialysis. The trials also showed that patients had a significantly greater improvement in their estimated glomerular filtration rates (GFR) if eculizumab was initiated earlier. Given that 90% of patients relapse during the first year after an aHUS episode, long term therapy with eculizumab is encouraged. The optimal duration of therapy thereafter is yet to be determined.

Our patient experienced complete hematologic response and tremendous improvement in fatigue, gastrointestinal symptoms, and neurological symptoms. Unfortunately, he remains dialysis dependent and this is likely due to previous damage to his kidneys from concomitant IgA vasculitis, hypertension, and diabetes. We also suspect that he may have had an unknown duration of undiagnosed aHUS prior his initial presentation to us which may have contributed to this irreversible renal function.

**Conclusion**

TMAs and TMA-mimicking diseases should be excluded before making a diagnosis of aHUS. Eculizumab is a complement inhibitor that has been shown to be effective in reversing the TMA effect in patients with aHUS, especially when it is used early on in the course of the disease. While early administration of eculizumab has been shown to be successful in treating aHUS, further studies are needed to determine the optimal duration of therapy.

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**Conflict of Interest**

None of the authors identify a conflict of interest.
Group B streptococcal (GBS) Bacteremia with Mycotic Thoracic Aortic Aneurysm and Suppurative Pericardial Effusion

Brent Matsuda MD; Aaron Hoo MD; Ornusa Teerasukjinda MD; Heath Chung MD; and Jinichi Tokeshi MD

Abstract
Mycotic aortic aneurysm associated with suppurative pericardial effusion is a rare and serious clinical phenomenon that is linked with significant morbidity and mortality. We report a case of a 78-year-old man who presented with purulent pericardial effusion with tamponade physiology in association with a progressively enlarging, transverse aortic arch, mycotic aneurysm due to group B streptococci. To our knowledge, this is only the second reported case of this nature. Despite advances in the current era of antibiotics and surgical techniques, early diagnosis and aggressive treatment remain sentinel to successful management of the cardiovascular complications of group B streptococcus bacteremia.

Introduction
Invasive Group B Streptococcus (GBS) disease has emerged as an important cause of morbidity and mortality in adults. Although traditionally considered predominantly a neonatal pathogen, recent data has shown increasing prevalence of GBS infection in elderly patients with chronic medical conditions. Preventable outcomes include sepsis and meningitis in neonates; however, of concern is the growing number of similar events.

Case Report
A 78-year-old Japanese man with a past medical history significant for diabetes mellitus type 2, hypertension, and squamous cell carcinoma of the penis status post penectomy in 1993, presented to Kuakini Medical Center in Honolulu with a non-productive cough and shortness of breath of 1-week duration. On physical examination, the patient was afebrile (Temp 34.5 degrees Celsius), tachycardic (heart rate 119 beats per minute), with coarse crackles bilaterally. Blood tests revealed an elevated white blood cell (WBC) count of 19.7 x 10^9/L with 10% bands, and elevated creatinine of 2.6 mg/dL consistent with acute kidney injury. Chest x-ray revealed central and bibasilar infiltrates. Following initial workup, he was admitted for presumed community-acquired pneumonia. Blood cultures were obtained and the patient was started on ceftriaxone and azithromycin.

The following day, blood cultures were positive for group B streptococcus in 4/4 bottles. Based on culture sensitivities and in light of renal impairment, ceftriaxone was continued. WBC count continued to rise, eventually peaking at 25.8 x 10^9/L. Repeat blood cultures were negative. Due to worsening leukocytosis and minimal improvement in symptoms on antibiotic treatment, a computed tomography (CT) scan of the chest without contrast was obtained which revealed an aortic aneurysm in the inferior aspect of the transverse aorta measuring approximately 4 x 2 cm and a moderate-sized pericardial effusion (Figure 1). Notably, there were no CT findings suggestive of pneumonia. Subsequent transthoracic echocardiogram showed a large circumferential purulent pericardial effusion with tamponade physiology.

The patient underwent elective pericardiocentesis and grossly purulent fluid was aspirated (Figure 2). Pericardial fluid studies revealed a WBC count 126,500 cell/mm3, with no growth on culture. His symptoms and leukocytosis significantly improved following the procedure. Since previous infectious workup including pan-culture failed to provide evidence for a potential source, a tagged white blood cell scan was ordered. This imaging modality demonstrated increased uptake surrounding the cardiac silhouette, proximal region of the aortic root, aortic arch, and left femoral artery (Figure 3).

Serial CT scans revealed a marked, progressive increase in the aortic arch aneurysm to approximately 10 x 8 cm (one week following initial study). Due to the location and characteristics of the aneurysm along with associated co-morbidities, the patient was deemed a poor candidate for surgical intervention. Thus management was limited to intravenous esmolol infusion and ultimately supportive care. The patient expired during this hospitalization from hemorrhagic shock due to left femoral artery aneurysmal rupture.

Discussion
Infection with GBS is widely recognized as the leading cause of sepsis and meningitis in neonates; however, of concern is the increasing incidence of GBS disease particularly in adults above age 65. Chronic medical conditions associated with higher rates of infection include diabetes mellitus, chronic liver or renal disease, malignancy, human immunodeficiency virus infection, or stroke. In our report, we describe a case of GBS bacteremia associated with severe cardiovascular manifestations, and upon further literature review, we express alarm regarding the growing number of similar events.

Mycotic aortic aneurysms comprise a minority of all aneurysms (0.7%) since the advent of antibiotic therapy. Hematogenous seeding of a damaged atherosclerotic wall is the most frequently described pathogenesis for infected aortic...
The thin, endothelial, intimal lining of the aorta is naturally impervious to infection. However, local disruption of this barrier by atherosclerosis reduces this resistance. The abdominal and thoracic aorta are frequent targets for mycotic aneurysm development, lending further support for this hypothesis. Additional proposed mechanisms include local extension of an infected focus and direct trauma with contamination. Several studies on the virulent nature of the *Staphylococcus aureus* and *Salmonella sp.* suggest these organisms carry the potential to invade normal intima and result in early aneurysm rupture. Whether or not GBS will be considered pathogenically analogous to these organisms has yet to be elucidated.

Mycotic aneurysm of the aorta and concomitant pericardial effusion due to GBS infection is rare, with only one previously described case by Akashi, et al. Risk factors for development of purulent pericarditis include a compromised immune system, infective endocarditis, or septicemia. Prompt diagnosis and early provision of antibiotic treatment is required to prevent subsequent complications including death, septic shock, cardiac tamponade, and development of constrictive pericarditis. In our patient, the effusion was incidentally found on CT scan, with tamponade physiology seen on follow-up echocardiogram. Although the pericardiocentesis revealed grossly purulent fluid, pericardial fluid culture results were negative, presumably due to early administration of antibiotic therapy. However, despite aggressive management in the current antibiotic era, mortality rates in treated patients are reported to be near 40%.
Both aforementioned cardiovascular complications pose significant diagnostic challenges, particularly due to the often non-specific clinical presentation of infected patients. One study found only 16% of patients with infective aortic aneurysms present with the classic triad of fever, back pain, and pulsatile mass. Subsequently diagnosis is often made in late stages of the disease process with fulminant sepsis and aneurysmal rupture. Similarly, the diagnosis of purulent pericarditis is often delayed due to the absence of typical pericarditis features including chest pain and pericardial friction rub. Thus early suspicion is crucial, and CT imaging plays a central role in mycotic aneurysm detection, and in our case, coexistent pericardial effusion. Patients with positive blood cultures and arterial aneurysms should be suspected to have a mycotic aneurysm until proven otherwise. Evaluation for infective endocarditis should also be explored, and transesophageal echocardiogram is the method of choice.

In our case, inability to identify the source of infection resulted in elective utilization of the tagged white blood cell (WBC) scan as an investigative tool. This scan may be useful early in the course of disease for localization of occult sites of infection, as well as other unsuspected sites of infection. Additionally, the WBC scan might provide a useful preoperative assessment of the severity of aortic wall inflammation of the aneurysm, and thus predict treatment outcome and potential complications. Unfortunately, the WBC scan did not detect a potential source of infection in the presented case, accentuating the point that a high degree of suspicion remains the most vital instrument for initiation of early successful treatment.

According to Oderich, et al, early mortality in patients with mycotic aneurysms and pericardial effusion likely reflects a combination of aggressive presentation with consequent high rupture rate, and treatment limitations due aneurysm location. Following identification of GBS on initial blood cultures, and in light of concurrent renal injury, we chose ceftriaxone for antimicrobial therapy based on culture sensitivities. Despite evidence of infection clearance on repeat cultures, the patient continued to deteriorate clinically with ongoing progression in aneurysmal size. Although antibiotic therapy theoretically limits progression, mycotic aneurysms tend to inflate due to a weakened arterial wall, which increases the risk of rupture. In fact, conservative treatment of infective aortic aneurysms without surgery is associated with a mortality rate of >90%. Surgical repair is the first-line treatment for a mycotic aneurysm by synthetic extra anatomic bypass or in situ reconstruction with graft. Previous case reports of GBS bacteremia associated mycotic aneurysm recognized that successful early and long-term treatment is conceivable with extensive emergent surgery. A life-long antibiotic course post-operatively remains controversial. In our case, we were unable to pursue operative intervention primarily due to the aneurysm location on the transverse aortic arch near the great vessels, which upon surgical consultation was deemed inoperable.
Conclusion

GBS bacteremia in adults is of growing concern in the healthcare community. In light of the invasive nature of this pathogen, we encourage high suspicion for potential cardiovascular manifestations, along with acquisition of early imaging and institution of antibiotic therapy.

Conflict of Interest

None of the authors identify a conflict of interest.

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References

Total and Differential White Blood Cell Counts Predict Eight-Year Incident Stoke in Elderly Japanese-American Men: The Honolulu Heart Program

Ji Young Huh MD; G. Webster Ross MD; Randi Chen MS; Christina Bell MD, PhD; Bradley Willcox MD; Robert Abbott PhD; Lenore Launer PhD; Brock Kaya MD; and Kamal Masaki MD

Abstract
Background: Previous studies have found that a higher white blood cell (WBC) count is associated with incident stroke. There have been few studies examining differential WBC counts in elderly or Asian populations. We studied the association between total and differential WBC counts and incident stroke in an older Asian population.

Methods: The Honolulu Heart Program is a prospective population-based study of cardiovascular diseases in Japanese-American men that started in 1965. At exam 4 (1991–93), 3,741 men ages 71-93 years participated, and total and differential WBC counts were measured in 3,569 men using a Coulter counter machine. Data on incident stroke (all strokes [ALL-CVA], thromboembolic [TE-CVA] and hemorrhagic [HEM-CVA]) were available through December 1999 (8 years follow-up) from a comprehensive hospital surveillance system. After excluding 227 subjects with prevalent stroke, 3,342 subjects were divided into quartiles of total WBC, neutrophil (segmented and band), granulocyte (neutrophil, eosinophil and basophil), lymphocyte, and monocyte counts for separate analyses.

Results: Age-adjusted incident ALL-CVA rates increased significantly with total WBC quartiles (7.68, 9.04, 9.26, 14.1, per 1,000 person years follow-up, respectively, P = .0014). Relative risks for ALL-CVA for each quartile of total and differential WBC counts were obtained using Cox proportional hazards, using the lowest quartile as the reference group. After full adjustment including age, cardiovascular risk factors, fibrinogen, prevalent CHD, cancer or COPD, and aspirin/NSAID use, the relative risks in the highest quartiles of total WBC, neutrophil, and granulocyte counts were 1.63 (95%CI = 1.05-2.54, P = .03), 2.19 (95%CI = 1.41-3.39, P < .001) and 1.91 (95%CI = 1.25-2.92, P = .003), respectively. These significant associations were also seen for TE-CVA, but not for HEM-CVA. No significant associations were found between lymphocyte or monocyte counts and incident stroke or subtypes.

Conclusions: In elderly Japanese-American men, higher total WBC, neutrophil, and granulocyte counts were independent predictors of overall stroke, as well as thromboembolic stroke. Further studies are needed to establish cut-points and treatment options.

Conflict of Interest
The authors report no conflict of interest.

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Abstract

Objective: Late-life hoarding is a serious psychiatric condition with significant implications in health and functioning. Geriatric hoarding patients show greater impairment in activities of daily living and have a greater number of medical conditions compared to same-aged non-hoarders. This study examined the relationship between geriatric hoarding severity and disability severity.

Methods: Sixty-five subjects age 60 or older with hoarding disorder (HD) participated in the current study. Participants were assessed with measures of hoarding severity, psychiatric symptoms, and general disability. Hierarchical regression was used to test the unique association of hoarding symptoms with disability beyond the effects of demographic factors, anxiety, and depression.

Results: When controlled for demographics (age and gender) and psychiatric symptoms (anxiety and depression), hoarding severity predicts disability severity. Analyses also show that clinician-administered measures of hoarding are stronger predictors of disability than patient self-report measures.

Conclusions: When treating older adults with HD, clinicians must consider symptom impact on daily life. A multidisciplinary team must be utilized to address the wide ranging consequences of hoarding symptoms. Future work should examine how psychiatric treatment of hoarding disorder affects disability.
Diffusion Tensor Imaging in PSEN1-Related Spastic Paraparesis Reveals Widespread White Matter Abnormalities

Steffan K. Soosman BS; Meredith N. Braskie PhD; Jeffry Alger PhD; Yvette M. Bordelon MD, PhD; David Wharton BS; and John M. Ringman MD, MS

Abstract

Objective: To investigate white matter changes in familial Alzheimer’s disease (FAD) patients with spastic paraparesis (SP) using diffusion tensor imaging (DTI).

Background: Though FAD due to PSEN1 mutations typically recapitulates late onset AD, it can have unusual clinical features including SP. SP is seen with specific PSEN1 mutations and is frequently associated with “cotton wool” amyloid plaques. The pathophysiology underlying SP in FAD is not well understood, though disproportionate degeneration of the corticospinal tracts has been implicated.

Design/Methods: We compared white matter integrity in two persons with the A431E PSEN1 mutation with early and severe SP to that of 8 symptomatic PSEN1 mutation carriers without SP from DTI images obtained on a 3T Siemens Trio scanner using 64 direction EPI sequence. Fractional Anisotropy (FA) images were generated using FSL Diffusion Toolbox. FA images were then processed using FSL Tract Based Spatial Statistics toolbox to obtain group level voxel-based statistical maps.

Results: The patients with SP were men, mean age of 48, duration of illness of 5.5 years, and CDR SOB scores of 8.5. The 8 subjects without SP (5 men) had various PSEN1 mutations, mean age of 54 years, illness duration of 4.6 years, and CDR SOB scores of 6.1 (all P-values > .05). Using the false discovery rate to correct for multiple comparisons, significantly lower FA were seen in subjects with SP in widespread areas including in the orbitofrontal region, corpus callosum, bilateral precentral gyri, and the anterior limb of the right internal capsule. The reverse contrast revealed no areas in which persons without SP had lower FA relative to those with SP.

Conclusions: SP is the most evident clinical manifestation of widespread FA decreases in persons with the A431E PSEN1 mutation, suggesting it may be mediated by a generalized effect of this mutation on white matter.
Age Disparity in Palliative Radiotherapy Among Elderly Patients with Advanced Cancer

Jonathan Wong BS and James D. Murphy MD, MS

Abstract

Objective: Radiotherapy (RT) is often utilized in cancer care with palliative intent. The purpose of this study was to verify that differences exist in rates of palliative radiotherapy relating to the age of the patient that go beyond the expected survival differences in older people.

Methods: Using the Surveillance, Epidemiology, and End Results (SEER) – Medicare Linked Database, 56,519 patients were identified with Stage IV breast, lung, prostate, or colorectal cancer diagnosed between 2000 and 2007. Multivariate logistic regression was performed with Statistical Analysis System (SAS, 1976) to determine rates of palliative radiotherapy accounting for known confounding factors.

Results: Thirty-four percent of the study population received palliative radiotherapy with a disease distribution of lung (65%), colorectal (20%), prostate (8%), and breast (6%) cancer. Upon multivariate analysis, it was revealed that older patients ($P < .001$) and patients with higher Charlson comorbidity scores ($P < .001$) were less likely to receive palliative RT. Black patients ($P < .001$) and married patients ($P < .001$) were also correlated with reduced likelihood of receiving palliative RT.

Conclusion: An age disparity exists among older patients, who are less likely to receive palliative radiotherapy, even when controlling for the length of survival. This suggests that a physician and/or patient bias exists against the elderly. Identifying the cause for these discrepancies in the receipt of palliative RT is important, so that we may improve access to quality palliative RT.

Conflict of Interest

The authors report no conflict of interest.

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Safety Net Patients with Diabetes Experience Less Rapport Building When Providers Demonstrate High Computer Use

Michael Wu BA; Jennifer Barton MD; Dean Schillinger MD; Ed Yelin PhD; and Neda Ratanawongsa MD, MPH

Abstract

Introduction: Limited research on how computer use influences physician-patient communication has yielded both positive and negative effects.

Methods: This study aims to determine the effects of computer use on rapport building in diverse safety-net settings. Utilizing video recordings of patient encounters in both primary and specialty settings, we conducted an observational study at a large US public hospital with a basic electronic health records (EHR) system. Eligible patients included English and/or Spanish-speaking adults (≥18 years old) with diabetes who receive primary and subspecialty care at five hospital clinics. We coded verbal communication behaviors using an adapted version of the Roter Interaction Analysis System (RIAS, 2002). The primary outcome was rapport-building statements (such as reassurance, concern, empathy, or partnership statements) by patients and providers. The primary predictor was high concurrent computer use, categorized as encounters in which >15% of total statements (provider and patient) had concurrent provider computer use. Analysts also rated overall computer use using a 3-item observation instrument (total possible score 0-9), categorizing high use as score ≥4. We performed regression analysis using generalized estimating equations to account for clustering by providers, controlling for patient age and gender.

Results: To date, we have coded 15 encounters among 15 English-speaking patients and 13 providers. Among patients, 53% were women. Although all encounters were in English, 29% preferred Spanish. Among providers, 62% were women; 62% PCPs. Patients were less likely to use any rapport building statements with providers who demonstrated high concurrent computer use (IRR=0.989; 95% CI=0.977-1.000). Specifically, both providers and patients were less likely to use emotional rapport building statements (IRR = 0.968, 95% CI = 0.941-0.996; IRR = 0.950, 95% CI = 0.907-0.996, respectively). In addition, high overall computer use was associated with less positive rapport-building by providers and patients (IRR=0.961, 95% CI=0.954-0.968; IRR = 0.993, 95% CI=0.987-0.999, respectively). However, both providers (IRR = 1.173, 95% CI = 1.084-1.268) and patients (IRR = 1.302, 95% CI = 1.100-1.542) were more likely to offer personal remarks and social conversations during encounters with high overall computer use.

Conclusions: Preliminary analyses suggest that high computer use may be associated with less overall rapport-building, but personal conversations or “chit-chat” occur more frequently. EHR use may influence patient-provider conversations towards more biomedically-oriented agendas. Future analyses will examine the relationship between computer use and other communication outcomes, such as biomedical and psychosocial statements. Although EHRs are promoted as tools to improve efficiency and safety, it is crucial to gain a better understanding of the how computer use alters patient-provider relationships and communication.

Conflict of Interest

The authors report no conflict of interest.

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Accumulation of Iron in a Model of Myocardial Infarction and Its Cell Toxicity in Cardiomyocytes

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Abstract
Introduction: Despite advancements in medicine leading to a marked decline in mortality due to acute myocardial infarction (MI), mortality due to post-MI heart failure (HF) remains high. Left ventricular (LV) remodeling is important in the pathogenesis of HF following MI. Previous reports investigating iron overload in anemia and chronic liver cirrhosis suggest that excess iron exhibits cell toxicity in multiple organ systems. During acute MI, ischemia/reperfusion (I/R) injury caused by temporary coronary ischemia results in massive necrosis followed by fibrosis. Previous reports studying tissue injury demonstrated that iron accumulation suppresses wound healing and exacerbates tissue injury in other organs. However, the role of iron in scar formation and LV remodeling is not well characterized.

Methods: To address this, we investigated iron, transferrin, and fibrosis in heart tissue sections after I/R injury, and potential cytotoxic effects of iron in the form of FeCl₃ on HL-1 and H9C2 cardiomyocytes. Mice underwent surgical I/R injury using left anterior descending coronary ligation to induce 30-minute transient ischemia. The hearts were harvested 1 week later and prepared for histological assays.

Results: Masson’s trichrome staining revealed fibrosis from the anterior to posterior wall in the mid-myocardium. Perl’s iron staining revealed non-transferrin bound iron localized in scar tissue at anterior and posterior aspects of the heart. Immunohistochemistry found ferritin localization to areas of fibrosis, specifically in the extracellular fluid of mid-myocardium and intracellular fluid of fibroblasts and surrounding cardiomyocytes. While iron was undetectable in iron stains of sham operated mice, more than 50 cells were positive with the iron stain in I/R group. Image J (NIH) showed increased anti-ferritin staining in the I/R group compared to sham controls (more than a four-fold increase). To further investigate this, HL-1 and H9C2 cardiomyocytes were cultured with doses of 1 µM to 1 mM FeCl₃ for 24 hours, and cell death was analyzed with Live/Dead Cell Viability Assay (Invitrogen). Treatment greater than 100 µM decreased cell viability, and significant cell death (n=6, *P*<.05) was observed in cardiomyocytes exposed to 50 µM FeCl₃ or more, and that excess iron leads to cell death.

Conclusions: These results suggest that iron accumulation may play a role in cardiac cell death and fibrosis in ventricular myofiber remodeling after I/R injury. Taken together, excess iron in MI may induce cell death, leading to LV remodeling following I/R injury. Understanding the role of iron accumulation in the heart could develop new therapeutic strategies for treating multiple heart diseases including HF.

Conflict of Interest
The authors report no conflict of interest.

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Symptoms of Autonomic Dysfunction in HIV-Infected Stable Patients on Combined Antiretroviral Therapy

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**Background:** Autonomic dysfunction was a common co-morbidity associated with HIV-infection particularly with acquired immunodeficiency syndrome (AIDS) prior to the advent of combination antiretroviral therapy (cART). The burden of autonomic symptoms in the era of cART is unknown. Our study aims to evaluate the prevalence of autonomic symptoms in HIV infected (HIV+) subjects on stable cART.

**Methods:** This retrospective study evaluated the prevalence of symptoms associated with autonomic dysfunction in HIV+ subjects on a stable cART compared to HIV- controls. Subjects completed an Autonomic Symptom Profile (ASP) questionnaire from which a clinically relevant Composite Autonomic Symptom Scale (COMPASS) score was calculated. A COMPASS score ≥30 was used as the cutoff for the presence of autonomic dysfunction.

**Results:** Seventy subjects, 48 HIV+ and 22 HIV- were analyzed. Forty percent of the HIV+ group had a total COMPASS score ≥30 compared to 9% of HIV- control (P<.01). HIV+ subjects reported a higher prevalence of symptoms in the autonomic domains related to secretomotor, pupillomotor, and male sexual dysfunction. Eighty percent of HIV+ subjects with a COMPASS score of ≥30 had abnormalities on formal autonomic function testing.

**Conclusions:** HIV+ subjects on cART have a higher prevalence of dysautonomia symptoms compared to HIV- controls.

**Conflict of Interest**
The authors report no conflict of interest.

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Body Mass Index and Non-Hodgkin’s Lymphoma Survival in an Ethnically Diverse Population: The Multiethnic Cohort Study

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Introduction: Obesity increases the risk of death from several malignancies including breast and colon cancer. However, for non-Hodgkin’s lymphoma (NHL), the association between pre-diagnostic body mass index (BMI) and survival is unclear. We examined the association between pre-diagnostic BMI overall and NHL-specific survival in the Multiethnic Cohort (MEC) study of African Americans, Native Hawaiians, Japanese Americans, Latinos, and Caucasians.

Methods: MEC participants free of NHL at cohort entry and diagnosed with NHL during follow-up were included in the analyses (N=1348). Body mass index (BMI) was based on self-reported weight and height at cohort entry. Cox proportional hazards regression was used to calculate hazard ratios (HR) and 95% confidence intervals (CI) for pre-diagnostic BMI categories in relation to all-cause and NHL-specific mortality while adjusting for known confounders.

Results: The mean time from cohort entry to NHL diagnosis was 7.2±3.9 years (range: 0.0-15.0 years). The mean age at NHL diagnosis was 70.6 (range 45-89) years and the mean BMI at cohort entry was 26.5±4.7 kg/m². After a mean follow-up of 4.3±3.5 years, 679 deaths including 457 NHL-specific deaths occurred. In multivariable models, obese patients (BMI ≥ 30.0) had higher all-cause (HR = 1.55, 95%CI = 1.21 - 2.00) and NHL-specific (HR = 1.84, 95%CI = 1.35 - 2.52) mortality compared to patients with high-normal BMI (22.5-24.9 kg/m²). For overweight patients (BMI 25.0 – 29.9), the respective HRs were 1.29 (95%CI = 1.05 - 1.58) and 1.47 (95%CI = 1.14 - 1.89). Stratification by NHL type suggested higher NHL-specific mortality risk for chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) than for diffuse large B-cell lymphoma (DLBCL).

Conclusions: Pre-diagnostic obesity may be related to poorer overall and NHL-specific survival in NHL patients. Therefore, pre-diagnostic BMI may be a suitable prognostic marker for NHL patients.

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The authors report no conflict of interest.

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Inflammation and Albuminuria in HIV-infected Patients Receiving Combination Antiretroviral Therapy

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Abstract

Background: The observed higher prevalence of albuminuria among HIV-infected patients has been strongly associated with cardiovascular disease and higher mortality. In HIV-seronegative patients with metabolic syndrome, malignancies and infections, pro-inflammatory cytokines, and acute phase reactants have been associated with albuminuria. However, the pathophysiology of albuminuria in HIV-seropositive individuals is poorly understood. We investigated the association of albuminuria with inflammatory biomarkers among HIV-infected patients on combination antiretroviral therapy.

Methods: This is a cross-sectional analysis of the entry data of the participants enrolled in the Hawai‘i Aging with HIV-Cardiovascular Cohort. Participants were ≥ 40 years old, lived in Hawai‘i, documented HIV-positive, and had been on antiretroviral therapy for at least 6 months prior to recruitment. Albuminuria was defined as urine albumin-to-creatinine ratio (ACR) of 30 mg/g or higher, as assessed from single random urine collection. Microalbuminuria was defined as urine ACR between 30 and 300 mg/g and macroalbuminuria as urine ACR more than 300 mg/g. Plasma inflammatory biomarkers were assessed by multiplexing using Milliplex Human Cardiovascular Disease panels. Differences in clinical and laboratory characteristics between subjects with and without albuminuria were compared using a non-parametric Wilcoxon rank test for continuous variables and a chi-squared test for categorical variables. Univariate and multivariate logistic regression analyses were utilized to assess the association between presence of albuminuria as the dependent variable and plasma biomarkers as independent variables. Univariate and multivariate logistic regression analyses were utilized to assess the association between presence of albuminuria as the dependent variable and plasma biomarkers as independent variables. Log-transformed plasma inflammatory biomarkers with P-value less than .1 in univariate logistic regression analysis were selected for examination in separate multivariate logistic regression models, adjusting for previously reported risk factors for albuminuria (age, gender, race, diabetes, hypertension, CD4 percent, current ritonavir, and tenofovir use).

Results: Among a cohort of 111 HIV-infected patients (median age of 52 (Q1:46, Q3:57); male 86%; diabetes 6%; hypertension 33%; median CD4 count of 489 cells/mm³ (Q1:341, Q3:638); HIV RNA PCR <48 copies/ml 85%), eighteen subjects (16.2%) had microalbuminuria, and two subjects (1.8%) had macroalbuminuria. There was no significant difference in CD4 count and HIV viral loads between patients with and without albuminuria. In univariate logistic regression analysis, higher levels of log-transformed soluble E-selectin (sE-selectin), tissue plasminogen activator inhibitor-1 (tPAI-1), C-reactive protein (CRP), serum amyloid A (SAA), serum amyloid P (SAP), interleukin-1β, interleukin-8, and tumor necrosis factor-α (TNF-α) were associated with albuminuria (P<.10). In multivariate logistic regression models, sE-selectin, sVCAM-1, tPAI-1, CRP, and SAP remained significant (P<.05) even after adjustment for previously reported risk factors for albuminuria.

Conclusions: This study has shown an association between inflammation and albuminuria independent of previously reported risk factors for albuminuria in HIV-infected subjects on stable combination antiretroviral therapy. Chronic low-grade inflammation despite potent antiretroviral treatment may be one of the factors causing higher rates of albuminuria among HIV-infected patients. Future studies are needed to further elucidate the pathophysiologic mechanisms of chronic inflammation in HIV and its impact on kidney disease.

Conflict of Interest

The authors report no conflict of interest.

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Bone Mineral Density and Frailty Among HIV-infected Patients on Stable Antiretroviral Therapy

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Abstract

Introduction: It is estimated that the rate of frailty in middle-aged adults is approximately 4%. Chronic inflammation in HIV is associated with accelerated aging and frailty. Frailty among HIV-infected persons is increasingly recognized but the correlation between frailty and osteoporosis in HIV-infected patients is not completely elucidated. We aimed to determine frailty prevalence and factors associated with frailty score in a cohort of HIV-infected patients on stable antiretroviral therapy.

Methods: Patients were enrolled into the Hawai’i Aging with HIV-Cardiovascular Cohort (HAHC-CVD) study. Entry into the cohort required patients to be ≥ 40 years old, documented to be HIV-infected, and to have been on antiretroviral therapy for at least 6 months prior to recruitment. Physical Frailty was measured approximately three years after recruitment, defined by presence of > 3 of 5 factors: unintentional weight loss, self-reported low physical activity, self-reported exhaustion, weak grip strength, and slow walking time. Bone mineral density (BMD) was measured by dual-energy X-ray absorptiometry (Lunar Prodigy scanner, GE Medical Systems, Inc, Milwaukee, WI).

Results: Analysis was conducted among 90 patients with frailty data in the HAHC-CVD cohort. Mean age at entry was 52.7 (SD 7.48) years, 90% males, 61.1% Caucasian, CD4 nadir of 173 (SD 158) cells/microliter, and 83.3% with undetectable HIV RNA (< 48 copies/ml). About half of the subjects (57.8%) had frailty score of 0, while 6 (6.6%) had a frailty score > 3 (patient is positive for frailty when score > 3). Mean hand grip was 36.8 (9.4) kg, walking speed of 3.6 (0.8) seconds, and BMD of the left femoral neck was 0.93 (SD 0.15) g/cm². Handgrip correlated with BMD of the right femoral neck (Pearson correlation [r] = 0.35, P = .001) and with BMD of the left femoral neck (r = 0.40, P < .001). BMD of the femoral neck did not correlate with total frailty score or average walking speed.

Conclusions: Higher rate of frailty was found in our cohort of HIV-infected patients compared to published studies in the general population of the same age group. A significant association between hand grip and BMD was seen. Earlier screening for frailty among HIV-infected adults should be considered. Furthermore, the utility of using hand grip to detect HIV-infected patients who may need osteoporosis screening should be investigated.

Conflict of Interest

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Hypercalcemia in Clear Cell Sarcoma

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Abstract
Hypercalcemia is a frequently encountered clinical problem in patients with cancer.\(^1\) It occurs in up to 30% of patients during their clinical course and is associated with a poor prognosis. While typically associated with certain primary tumors (breast & squamous cell cancers, multiple myeloma, lymphoma), it is less frequently seen in the adult sarcoma population.\(^2,3\) Hypercalcemia has not been previously reported in clear cell sarcoma (CCS), and consequently no underlying mechanism has been described. We present the case of a 35-year-old man with metastatic cutaneous clear cell sarcoma, who developed severe hypercalcemia, thought to be secondary to osteolytic metastasis. Though CSS is a rare neoplasm, physicians should be aware of this potential clinical development, particularly in the presence of metastatic bone disease. CCS should be included among the other tumor types known to be associated with hypercalcemia of malignancy. Early recognition can ensure optimal patient management and palliation, despite the poor prognosis associated with this disease.

Conflict of Interest
The authors report no conflict of interest.

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References
A Bimonthly Interdisciplinary State-wide Palliative Care Case Conference Promotes Education, Networking, and Emotional Support

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Abstract

Background: Meeting emotional, educational, and professional development needs for palliative care practitioners is a priority of clinical practice guidelines for quality palliative care. Here, we introduce and evaluate Palliative Pupus, a novel, state-wide, interdisciplinary, case conference designed to meet these needs.

Methods: Palliative Pupus is a free, interdisciplinary case conference open to all hospice and palliative care clinicians in Hawai‘i. The conference has convened every other month since 2010 and is jointly sponsored by Hawai‘i’s largest hospital-based palliative care program and Kokua Mau, Hawai‘i’s hospice and palliative care organization. Twenty to forty participants typically meet on the island of O‘ahu and are joined by participants from other islands who attend remotely via audio or video conferencing technology. Attendees at the Palliative Pupus on May 15th, 2013 were asked to complete an anonymous evaluation tool designed for this purpose. Demographic data were analyzed using SPSS software (IBM, 1911) and inductive content analysis was carried out on open-ended questions.

Results: Twenty-four attendees participated in the study. The majority of participants were women (75%). The leading disciplines of attendees were nursing (46%), medicine (25%), and chaplaincy (12.5%). The primary work settings were hospice (67%) and hospital (25%). Participants cited education (96%), networking (87%), and emotional support (37%) as reasons for attending. Inductive content analysis revealed the most valued benefits of attending were educational (71%), an enhanced sense of being part of a community of providers (24%), and emotional/psychological support (24%). Respondents agreed that the format of the conference would work in other communities (100%) and that they would recommend attending the conference to others (100%).

Conclusions: Palliative Pupus is an innovative and sustainable state-wide approach to meeting diverse educational, emotional, and networking needs for practitioners in palliative care. Participants expressed confidence that this approach could be successfully disseminated to other states.

Conflict of Interest

The authors report no conflict of interest.

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Does Gastric Bubble Location on Plain X-ray Predict the Presence of Splenomegaly?

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Abstract
Introduction: When there is medial displacement of the gastric bubble on chest X-ray, splenomegaly is frequently suggested as the etiology of this finding. Data to support this association are lacking. We sought to compare the gastric bubble location in patients with and without splenomegaly.

Methods: We identified individuals who had a chest X-ray done concurrently with a CT scan noting a measured splenic index. A concurrent X-ray was defined as having been within +/- 30 days of the CT scan. The data source was a convenience sample from a radiology query at our facility including scans between January 2003 and July 2012. Splenomegaly was defined as a splenic index of > 480 ml. We then reviewed chest X-rays and assessed for a visible gastric bubble. The gastric bubble location was noted as (1) the distance from the apex of the gastric bubble to the left lateral chest wall and (2) as a ratio of the distance of the apex to left lateral chest wall, to the total transverse distance across the chest at the level of the apex of the bubble. Statistical analysis to compare mean ratios between patients with and without splenomegaly, as well a correlation between splenic index and the displacement ratio was conducted.

Results: Preliminary results demonstrate, 223 cases were found to have a measured splenic index with a corresponding concurrent chest X-ray demonstrating presence of gastric bubble. Mean age was 39.5 years, with a gender distribution of 74.4% male and 25.6% female, which is reflective of the overall patient base at our institution. Of the 223 patients identified, only 12 had splenic indexes < 480 ml (additional data will be available for presentation). Mean splenic index was 1022.31 ml (range of 39-8588 ml, SD 825.68), with a mean gastric bubble ratio of 0.28 (range 0.08-0.47, SD 0.05). Differences in gastric bubble ratios in patients with and without splenomegaly, 0.2851 and 0.2853, respectively, were not statistically significant ($P = .99$, CI -0.03-0.03). When viewed as a continuous variable, there was only a weak association between splenic index and gastric bubble ratio using Pearsons $r$ ($r=0.167$, $P = .01$).

Conclusions: Our results refute the commonly held assertion that a medially displaced gastric bubble is suggestive of splenomegaly. There was no statistical significance between the mean ratios in patients with and without splenomegaly. However, there is a weak correlation between splenic size and position of the gastric bubble. Additional data analysis is ongoing in an effort to better test our hypothesis and to test whether an association between gastric bubble location and varying degrees of splenomegaly is present.

Conflict of Interest
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Blood Pressure and Physical Function

Melissa H. Corson; Nketi Forbang MD; Joachim Ix MD, MAS; Michael Criqui MD; and Dena Rifkin MD, MS

Abstract

Background: Hypertension in older adults is a dynamic process, with significant diurnal fluctuation. Little research has been done on the associations between increased short-term blood pressure variability and blunted night-time dipping in respect to decreased physical function in the elderly. Our aim is to use a cross-sectional analysis to illuminate any associations.

Methods: A cross-sectional sub-study (mean age: 72, 67.5% female) was performed on selected participants from the San Diego Population Study (Criqui, et al, 2003). Blood pressure was measured both in the office (3 independent blood pressure readings) and using a 24-hour ambulatory blood pressure monitoring cuff. Blood pressure variability was measured using average real variability (ARV). Physical function was measured using the Short Physical Performance Battery (SPPB) test. Statistical analysis was performed on IBM SPSS Statistics (1911) software.

Results: An unadjusted univariate analysis adjusted for age and gender showed associations between 24-hr ARV of SBP ($P=0.001$), 24-hr ARV pulse pressure ($P<0.001$), and percent systolic dipping ($P=0.011$) and SPPB score. After multivariate analysis adjusted for age and gender was performed, the results were substantially attenuated. However, the association of ARV of SBP was not significant with a $P$-value of 0.052 and the ARV of pulse pressure remained significant with a $P$-value of 0.022. Multivariate hierarchical linear regression models revealed insignificant trends.

Conclusions: Increased short-term variability and blunted night-time dipping were associated physical function but were not independent of age and body mass index (BMI). Further research can be done as to the biology of how both age and BMI influence blood pressure patterns. The trends observed in this study may warrant the investigation of abnormal blood pressure patterns in those who are either elderly or have increased BMI.

Conflict of Interest

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Asian and Pacific Islander Populations Have Higher Rates of Short Interpregnancy Intervals

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Abstract

Introduction: A short interpregnancy interval (IPI) is associated with poor maternal and neonatal outcomes. There is currently little known about rates of IPIs in Asian and Pacific Islander populations. We sought to determine rates of IPIs among Pacific Islanders and Asian subgroups in California.

Methods: Data from all birth records in California between 1999 and 2004 were linked with hospital discharge data. For women with a first birth in 1999-2000 and a second birth before the end of the study period, IPIs were calculated as the interval between the first birth and conception of the next pregnancy. We use bivariate and multivariable modeling to determine whether specific Asian ethnicities are associated with greater risk of short IPIs (<6 months, 6-18 months).

Results: Our sample included 178,000 women. In multivariable analyses adjusted for maternal demographic, social, and clinical factors, Pacific Islanders and all other Asian subgroups were more likely to have an IPI <6 months than were white women (Pacific Islanders: OR 3.31 (95% CI [2.7, 4.1]); Filipinas: OR1.51 (95% CI [1.33, 1.71]); Southeast Asians: 1.93 (95% CI [1.73, 2.1]); East Asians: OR 1.65 (95% CI [1.48, 1.84]); Other Asians: OR 2.04 (95% CI [1.70, 2.4])). Other risk factors for shorter IPIs included young maternal age, lower educational attainment, public insurance, and prior preterm birth. Similar findings were noted for IPIs of 6-18 months.

Conclusions: There were significantly higher rates of IPI <6 months compared to >18 months in the Pacific Islander group and Asian sub groups. In addition, there were higher rates of IPI 6-18 months compared to >18 months in the Pacific Islander and Southeast Asian groups. More work should focus on rates of adverse maternal and neonatal outcomes associated with a short IPI in these populations. A better understanding of whether short intervals are the result of intended or unintended pregnancies will be critical in informing effective interventions.

Conflict of Interest

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An Unusually Extensive Extranodal Head and Neck Non-Hodgkin Lymphoma

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Abstract
The second most common site for extranodal lymphoma is the head and neck. Typically these extranodal head and neck lymphomas have subtle manifestations. This case, however, describes a rather large extranodal Diffuse Large B-Cell Lymphoma that distorted facial structures and protruded externally from the patient’s orbit. This unusually extensive lymphoma completely filled and destroyed the patient’s right orbit, right paranasal sinuses, and involved the cranium. It is rare to have involvement of all these structures. Because of the profound osseous destruction there was concern whether this patient would have the structural stability to tolerate chemotherapy and facial reconstruction. This case report chronicles the patient’s treatment course and discusses the therapeutic approach used for this patient’s lymphoma.

Conflict of Interest
The authors report no conflict of interest.

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A Rare Presentation of Community Acquired Methicillin Resistant
Staphylococcus Aureus

Jeremy Docekal MD and Tomas Ferguson MD

Abstract

Introduction: Prostatic abscess is a rarely described condition, and is typically caused by gram-negative organisms such as Enterobacteriaceae. However, as the prevalence of Methicillin resistant Staphylococcus aureus (MRSA) increases in the community, unusual infections due to this organism have recently been published. In this abstract, we describe a patient with diabetes mellitus type 2, who presents in diabetic ketoacidosis, later found to be due to a prostatic abscess from which MRSA was cultured.

Case Presentation: A 56 year-old male resident of a homeless shelter presented to the Emergency Department with complaints of dysuria, polyuria, polydypsia, and difficulty urinating. He was found to be hyperglycemic, and other laboratory findings were consistent with the diagnosis of diabetic keto-acidosis (DKA). On evaluation, the patient had rectal pain and urinary retention. The rectal exam revealed no fluctuance, mass, or fissures, but an enlarged and tender prostate was noted. A CT of the abdomen and pelvis was obtained, showing a 9 cm prostatic abscess, the presumptive etiology of his diabetic keto-acidosis. The patient underwent an IR-guided abscess drainage. Cultures from the abscess were positive for MRSA, and treatment with Vancomycin was initiated. Repeat imaging noted re-accumulation of fluid in the prostatic abscess, which necessitated a transurethral resection of the prostate (TURP), with unroofing of the abscess. Following this procedure, the patient’s inflammatory markers and serum prostate specific antigen trended downward. The patient continued to improve, and was discharged with a plan to complete 6 weeks of Vancomycin therapy.

Discussion: Prostatic abscess is an uncommon condition that has been associated with the presence of chronic indwelling catheters, genito-urinary instrumentation, diabetes mellitus, or other immune compromising conditions. Prior to the widespread use of broad spectrum antibiotics for patients with lower urinary tract infections, this condition was primarily caused by Neisseria gonorrhoeae. Currently, E. coli and other gram negative bacteria are the primary pathogens responsible for prostatic abscesses. However, prostatic abscess due to MRSA is exceedingly rare, and we feel that recently reported cases reflect the evolving prevalence and pathogenicity of MRSA in human disease.

Conclusion: This case highlights the need for increased vigilance among physicians for atypical presentations of invasive infection with MRSA.

Conflict of Interest

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Rare Presentation of Thiamine Deficiency as Gastrointestinal Syndrome

James Duca MSIII and Cory Lum DO

Abstract
Introduction: Thiamine deficiency is prevalent among nutritionally deficient persons and manifests as Wernicke encephalopathy or beriberi. Rare accounts of a primary syndrome consisting of GI symptoms are described in the literature.

Case Report: The following report illustrates the case of a 30-year-old man with intractable nausea and vomiting, leukocytosis, transaminitis, and lactic acidosis that resolved rapidly after thiamine infusion. The patient was admitted with severe epigastric pain, nausea, and vomiting over the previous week and abdominal pain for the previous 2 weeks. Past medical history was significant for a four-year history of intermittent abdominal pain, and no alcohol consumption. The patient was started on IV pantoprazole for peptic ulcer disease or other gastritis. He was given IV ciprofloxacin and metronidazole for possible infection given his leukocytosis. CT and ultrasound were unremarkable. His condition improved briefly on day 5, but he failed to tolerate a clear liquid diet. Lactic acidosis began to increase on day 7, with hydration failing to alleviate the acidosis. An upper endoscopy on day 9 showed a deep duodenal ulcer, and pantoprazole was restarted. AST and ALT rose from day 4, peaking at 98 and 154 on day 11. The patient was switched from pantoprazole to famotidine on day 11 with no improvement in his LFTs. On the 12th day the patient reported numbness and tingling on his chest. He was treated with thiamine. Lactate levels that had risen to 8.7mmol/L dropped to 2.3 within 24 hours, and the leukocytosis, nausea, and vomiting resolved. The patient stated he felt “the best he had felt in weeks” and was discharged on day 13. Abnormal signs, symptoms, and lab values resolved over the following weeks. Blood drawn on day 12 was positive for low thiamine.

Discussion: Thiamine deficiency is a rare cause of GI symptoms of nausea, vomiting, abdominal pain, and lactic acidosis. An under-diagnosed condition, failure to recognize and treat it may result in morbidity and death. Clinicians should have increased awareness of this problem, consider it in all patients with GI symptoms, and lactic acidosis, and have a low threshold to treat with thiamine.

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The authors report no conflict of interest.

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Sarcoidosis with Multi-organ Involvement Presenting as Ventricular Tachycardia

Sarah Gordon MD (ACP Associate); Jamalah Munir MD; Donald Helman MD (ACP Fellow)

Abstract
Introduction: Sarcoidosis is a granulomatous disease which can affect any organ, but most commonly presents with pulmonary manifestations. We present an unusual case of sarcoidosis with multiorgan involvement which initially manifested as ventricular tachycardia; the patient was subsequently found to have extensive cardiac, respiratory, skin, and hepatic involvement.

Case Report: An otherwise healthy 35-year-old African American soldier presented to emergency care with hypotension and tachycardia greater than 200 beats per minute. He was found to be in sustained ventricular tachycardia with a pulse. Defibrillation was performed, the patient was loaded with amiodarone, and hospitalized. Cardiac catheterization showed no evidence of atherosclerotic coronary artery disease. A cardiac MRI revealed high density lesions in the lateral wall and apex, and diffusely decreased left ventricular wall motion. An implantable cardiac defibrillator (ICD) was placed. Further questioning revealed a six month history of twenty pounds weight loss, persistent nasal congestion, and subcutaneous nodules. Biopsy of two subcutaneous nodules from the left upper extremity and nasal mucosa biopsy demonstrated noncaseating granulomas. His evaluation was notable for a mixed pattern hepatic injury, normocytic anemia, elevated lactate dehydrogenase, and a CT chest showing hilar and mediastinal adenopathy with multiple pulmonary nodules. Sarcoidosis was suspected and additional testing for HIV, EBV, vasculitis, lymphoma, fungal infection, and mycobacterial infection was negative. Pulmonary function tests showed normal basic spirometry and DLCO. Transthoracic echocardiogram demonstrated normal ejection fraction, and an 8mm cystic structure partially incorporated in the left ventricular wall. This was suspected to be a granulomatous accumulation. Sestamibi imaging showed a dense defect involving the apex and a medium sized, moderate severity, inferior wall defect consistent with an infiltrative process. Interrogation of his ICD six months after placement demonstrated no recurrence of arrhythmia. Initially, he was treated with 40mg prednisone daily. After a three-month course he had continued active disease and was treated with infliximab. His treatment is ongoing; lab parameters are improving.

Discussion: Cardiac sarcoidosis is rare. Conduction abnormalities are the most common finding, and arrhythmias are second. Heart failure, valvular dysfunction, and chronic effusion are also frequently observed, and one case report describes a large left atrial mass which behaved like a myxoma. This patient’s case is unusual because of his large degree of sinus and cardiac involvement, as well as his unusual left ventricular cystic structure. Sarcoidosis should be considered in all patients who have unexplained structural heart disease, particularly young individuals. Treatment of cardiac sarcoidosis is aimed at controlling inflammation and preventing compromise of cardiac structure or function. Sources agree that steroids are an effective initial treatment, but the initial dose and optimal duration are unclear. This patient’s course suggests that infliximab is an efficacious treatment option in severe cases.

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Central Diabetes Insipidus Masquerading as Benign Prostatic Hyperplasia in a Native Hawaiian

Robert F. Greenwood DO (ACP Associate); Rodger Stitt MD (ACP Associate); Arthur Guerrero MD (ACP Member); Warren Ishida MD

Abstract

Introduction: Central diabetes insipidus (DI) develops when production or release of antidiuretic hormone is disrupted. A large number of cases are idiopathic with the vast majority of all remaining adult cases a result of primary or secondary hypothalamic tumor, infiltrative disease, neurosurgery, or trauma. Pituitary adenoma is not typically a cause of central diabetes insipidus. We present a case of previously undiagnosed pituitary macroadenoma resulting in central diabetes insipidus that presented critically after months of polyuria and nocturia that had previously been attributed to benign prostatic hyperplasia.

Case Presentation: A 67-year-old man with a history of hypertension and taking no medications initially presented to the Hilo Medical Center with headache, nausea, nocturia, and polyuria. He had had symptoms for a year and presented to the ED after acute worsening. He was hypotensive and tachycardic with an initial sodium of 145. He quickly became hemodynamically unstable, unresponsive to fluid resuscitation, and was admitted to the ICU, briefly requiring vasoressors for blood pressure support. He was noted to have large volume output of dilute urine and elevated serum sodium. An MRI demonstrated a concentric sellar mass, with lymphocytic hypophysitis as a resultant working diagnosis. He was transferred to TAMC for Neurosurgical evaluation and further management. He was started on corticosteroids but after no improvement a follow up MRI showed a 2.0 x 1.3 x 2.5 cm lobulated, heterogeneously enhancing mass seen centered within the sella with T2 hyperintensity concerning for necrosis. After stabilization the patient underwent a transspenoidal excision of the mass. Pathology was consistent with nonsecreting pituitary adenoma. He responded appropriately to treatment with PO and nasal desmopressin.

Discussion: Central diabetes insipidus is frequently seen with tumors that involve the hypothalamus such as craniopharyngiomas. It is also frequently seen in metastatic spread of lung or breast cancer to the posterior pituitary or hypothalamus. However, tumors originating from the anterior pituitary very rarely cause DI. This led to a working diagnosis of lymphocytic hypophysitis in this patient but a lack of response to therapy with corticosteroids led to excision and final diagnosis of adenoma. There is also an interesting cultural twist to this case. The patient was working as a construction worker on the Big Island of Hawaiʻi and noted that there was significant social pressure to avoid drinking water while at work. Several coworkers were in this patient’s age range and had similar symptoms of frequent urination and nocturia and had been diagnosed with BPH. They managed their symptoms with decreased PO water intake at work and the patient felt pressure to do the same. As a result the patient had developed a significant ability to ignore his thirst response and this contributed to his not seeking medical care for his persistent symptoms before becoming very ill. The patient required coaching prior to discharge in order to adequately respond to his thirst response to achieve stable serum sodium levels with scheduled PO and intranasal desmopressin.

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Sarcoma: An Unusual Tumor in a Patient with Lynch Syndrome

Qi Jie Nicholas Leo MBBS (ACP Associate) and Dennis Bolger MD

Abstract
Introduction: Lynch syndrome is an autosomal dominant disorder caused by germ line mutations in DNA mismatch repair (MMR) genes. It is characterized by an increased risk of colon cancer, endometrial cancer, and ovarian cancer. Sarcoma is not a typical cancer associated with Lynch syndrome but has been reported. We report a case of sarcoma in a patient who was eventually diagnosed with Lynch Syndrome.

Case Report: A 71-year-old woman with personal history of endometrial cancer treated with total abdominal hysterectomy and radiation therapy 20 years ago, presented with a 2-month history of left leg pain and weakness. Family history was significant for both daughter and sister diagnosed with synchronous ovarian and uterine cancer at ages 42 and 48 respectively. Physical examination revealed weakness of the left quadriceps and decreased sensation to L4 dermatome. Magnetic resonance imaging of the lumbar spine showed an 8cm enhancing mass in the left psoas muscle, causing complete erosion and collapse of the L4 vertebral body, with moderate to severe spinal stenosis. Biopsy of the psoas mass showed high-grade sarcoma of unknown primary. As the patient’s family history was suspicious of Lynch syndrome, microsatellite instability testing of the sarcoma by immunohistochemical staining of MMR proteins was performed. Results of MMR testing showed loss of expression of MSH2 protein in malignant cell nuclei. MSH2 gene testing was positive for deleterious mutation R621X, confirming the diagnosis of Lynch syndrome. The patient underwent palliative radiation therapy with improved pain control. Her relatives at risk were informed of MSH2 gene mutation in the family and counseled about screening and medical management of healthy individuals who test positive for the mutation.

This case illustrates the importance of family history in identifying patients at risk for Lynch syndrome. Identification of specific mutations in an index case is very helpful in order to identify relatives at risk of inheriting the mutation. Appropriate screening can then be offered to affected relatives to reduce cancer risk. Although sarcoma is not a typical tumor of Lynch syndrome, the absence of MSH2 protein on immunohistochemistry suggests that a germ line mutation contributed to the development of sarcoma. Sarcoma may be part of the hereditary nonpolyposis colorectal cancer (HNPCC) tumor spectrum, and Lynch syndrome should be considered in patients with family history of sarcoma.

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Septic Cavernous Thrombosis Due to Campylobacter Rectus Infection

Qi Jie Nicholas Leo MBBS (ACP Associate) and Dennis Bolger MD

Abstract

Introduction: Cavernous sinus thrombosis is a rare but serious disease associated with significant morbidity and mortality. Early recognition and prompt treatment is necessary to improve patient outcomes in this potentially fatal disease.

Case Report: A 55-year-old man visiting from mainland China with no significant past medical history presented with eight days of headache. One day prior to admission, the patient developed diplopia and ptosis of his left eye. Physical examination revealed a fixed, dilated left pupil and left third, fourth, and sixth nerve palsies with loss of sensation in the left supraorbital region. Initial magnetic resonance imaging (MRI) of the brain showed fullness of the left cavernous sinus and dilated left superior ophthalmic vein consistent with cavernous sinus thrombosis. Treatment was initiated with broad spectrum antibiotics, high-dose corticosteroids, and anticoagulants.

Hours after admission, he developed new proptosis, ophthalmoplegia, and marked chemosis of his right eye. Bilateral carotid artery angiogram ruled out indirect or direct carotid cavernous fistula. Computed tomography (CT) angiogram of the neck showed right internal jugular vein thrombosis extending into the right sigmoid sinus, while CT of the chest revealed solid and cavitary pulmonary nodules consistent with septic pulmonary emboli. Repeat MRI two days later showed progression of thrombosis to the contralateral cavernous sinus and superior ophthalmic vein. MRI venogram showed decreased, and in some portions, lack of flow in the right transverse, sigmoid sinuses and visualized internal jugular vein.

Blood cultures eventually grew Campylobacter rectus identified by 16S rRNA sequencing. Additional history revealed that the patient had an uncomplicated tooth extraction of a decayed upper left molar 3 months ago. As Campylobacter rectus is a member of the human oral flora associated with human periodontal disease, we hypothesized that the patient’s infection likely started from left upper molar removal causing bacteremia and resulting in left cavernous sinus and right internal jugular vein thromboses with septic pulmonary emboli. The patient’s condition improved and he was discharged from hospital to continue medical care in China.

Discussion: Despite the very few cases of invasive Campylobacter rectus infections reported in literature, this case illustrates that Campylobacter rectus can be pathogenic. Dental infections may result in serious complications and an odontogenic source of infection should always be considered in patients with cavernous sinus thrombosis.

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A Case of Recurrent Cardiac Arrest and Light Chain Cardiac Amyloidosis

Brent Matsuda MD and Steven Azuma MD

Abstract
Introduction: Light chain amyloidosis is a clonal plasma cell disorder characterized by monoclonal light chain deposition in body organs. The diagnostic challenge belies the variable, often elusive nature of amyloid disease presentation. Cardiac involvement in particular may be seen in up to 50% of cases, and is associated with poor prognosis. We present a case of light chain cardiac amyloidosis, with multi-system derangements, leading to recurrent cardiac arrest despite resuscitative efforts.

Case Report: A 59-year-old man with a history of end-stage renal disease presented with the complaint of sudden onset of shortness of breath. Atrial fibrillation with rapid ventricular response was noted. While undergoing treatment, complications arose on 3 separate occasions at which time the patient experienced a precipitous fall in heart rate, cardiac arrest, and successful resuscitation. An echocardiogram was performed which revealed a 25% reduction in ejection fraction and new left ventricular septal thickening in comparison to an evaluation 3 months prior. Cardiac catheterization was unremarkable for coronary artery disease. Over the course of hospitalization, there was progressive muscle weakness. Nerve conduction studies were performed, revealing diffuse axonal sensorimotor neuropathy. The link between diffuse polynuropathy, autonomic instability, persistent hypotension requiring intravenous vasoactive support, and recurrent asystole remained unclear. Amyloidosis workup with immunofixation electrophoresis revealed free kappa light chain excess. Before further workup, the patient went into asystole, unresponsive to resuscitative efforts. Post-mortem findings suggest cardiac arrest due to amyloidosis of the heart secondary to multiple myeloma. Of note, amyloid deposits were found focally in blood vessels of the kidney and peripheral nerves.

Discussion: Early detection of cardiac involvement is crucial as illustrated above. Advanced echocardiographic techniques including speckle tracking plus strain imaging, may lead to earlier, amyloid-specific identification. Gadolinium-enhanced cardiac MRI has also been employed, with futility reserved for infiltrative cardiac disease states without renal insufficiency. Potentially, utilizing the above imaging studies, in association with cardiac biomarkers such as NT-pro BNP, may lead to the development of prognostication tools to identify patient’s at high risk for death. Goal for early detection and institution of prognosis models are aimed at early implementation of treatment strategies including heart transplantation, high-dose chemotherapy, and autologous stem cell support. For patients with a myriad of symptoms and suspicion of amyloidosis, we encourage early lab and imaging studies, because any delay in diagnosis and initiation of treatment is inevitably too late.

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Tumor Necrosis Factor Receptor-associated Periodic Syndrome, 
A Rare Cause of Fever of Unknown Origin

Pichaya O-charoen MD; Erlaine F. Bello MD; and Ken C. Arakawa MD

Abstract
Introduction: Tumor necrosis factor receptor-associated periodic syndrome (TRAPS) is an autosomal dominant auto-inflammatory disease characterized by recurrent episodes of fever and localized sites of inflammation. We report a case of a young man who was diagnosed with fever of unknown origin (FUO) until he developed acceleration of fevers, myocarditis, pericarditis with tamponade, septic shock-like syndrome, and ischemic small bowel.

Case Report: A 19-year-old Japanese man presented with recurrent severe fevers for two years, associated with myalgias and sore throat. He was initially diagnosed with adult-onset Still’s disease (AOSD). The fevers, as high as 106 degrees Fahrenheit, varied from several times per day to several times per month and did not respond to naproxen or colchicine. He was completely asymptomatic between each episode. The severity and frequency of his symptoms were such that he dropped out of college and all athletic activities. Subsequently, he developed acute myocarditis with hypotension. Shortly afterwards he developed acute pericarditis with tamponade associated with bilateral pleural effusions, requiring pericardial window and thoracentesis. Both conditions rapidly resolved with high dose steroid therapy. Infectious disease workup and autoimmune serologies were all negative. Bone marrow aspiration and bone scan were negative for malignancy. Every episode was characterized by severe leukocytosis and elevated acute phase reactants including ferritin. We diagnosed him with TRAPS based on fever pattern and a lack of typical AOSD rash. He was started on etanercept in addition to high dose steroid. However, he still developed intermittent fevers associated with erythematous papules involving the extremities and trunk. Three weeks later, he developed epigastric pain, vomiting, and septic shock-like syndrome. Following these events, he developed severe bloody diarrhea secondary to ischemic jejunitis and ileitis. High dose steroid partially relieved his symptoms. After infectious causes were excluded, etanercept was changed to an interleukin-1 receptor antagonist. His symptoms have completely resolved and he has been tapered off steroids. He has been able to return to school and running. TNFRSF1A gene sequencing was negative for known mutations. However, the rate of detection of auto-inflammatory gene mutations is reported to be low. The negative genetic test does not necessarily exclude this condition. His case is likely sporadic with no family history.

Discussion: A high index of suspicion for TRAPS is needed to diagnose and promptly treat patients who present with severe recurrent fevers after exclusion of infectious diseases, autoimmune disorders, and malignancies. Delay in diagnosis can lead to serious, life-threatening complications. Treatment can be difficult and currently interleukin-1 receptor antagonist has the best efficacy. For this patient, recognition of the disease and appropriate treatments had great impact on preservation and quality of life.

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Cardiac MRI and Iron Overload Cardiomyopathy in Thalassemia Major: A Case Report

Jun Onitsuka MD and Steven Azuma MD

Abstract
Introduction: Heart failure is the leading cause of death in patients with Thalassemia major and primarily results from transfusional iron overload. It is essential to assess myocardial iron load. Previous studies have shown that neither serum ferritin nor liver iron concentration gives a reliable measure of cardiac iron accumulation. Cardiac T2* MRI technique offers noninvasive measurement of myocardial iron load.

Case Report: A 39-year-old man with a past medical history significant for beta thalassemia major requiring blood transfusions every three-weeks and on iron chelation, presented with a cough, high fevers, and chills. He was subsequently found to have community acquired pneumonia and was treated with ceftriaxone and doxycycline. His hospital course was significant for episodes of atrial fibrillation and non-sustained ventricular tachycardia. An echocardiogram showed normal left ventricular function with an ejection fraction of 70%, which hadn’t changed from 2011. Although, the patient didn’t have symptoms of heart failure, he likely had ventricular dysfunction that could be masked by the basal high cardiac output which can be seen in patients with chronic anemia and we decided to start the patient on sotalol 80 mg twice a day. The MRI software for multiecho T2* measurement was installed at Queens Medical Center in September 2011 and we were able to obtain images for our patient at that time. His myocardial T2* value was estimated to be 9 milliseconds which suggests an increased risk for the development of future cardiac arrhythmias and heart failure. The repeat cardiac MRI images after discharge showed 8 milliseconds which suggested an interval worsening of the iron deposition within the myocardium.

Discussion: We were able to keep track of the progression of his iron cardiomyopathy, and start additional treatment. The patient continues to be followed by a hematologist for management of his hemochromatosis and a cardiologist for his infiltrative heart disease both resulting from his need for chronic blood transfusions. In patients with iron overload cardiomyopathy, their systolic function is preserved until a very late stage as iron deposition begins within the epicardium and extends to the myocardium. This case illustrates the importance of assessing cardiac iron content utilizing cardiac MRI as it is less invasive than cardiac biopsy and may show earlier involvement than echocardiogram.

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Unexplained Hypercalcemia: Atypical Presentation of (Disseminated) Miliary Tuberculosis

Edison So MD and Dennis Bolger MD, MPH

Abstract

Introduction: Miliary tuberculosis may not present with typical chronic respiratory symptoms. Metabolic disturbances like hypercalcemia may be an important clue to its diagnosis.

Case Report: We report an unusual case of miliary tuberculosis in a 77-year-old Filipino man with hypertension, diabetes mellitus type 2, and nephrolithiasis (status-post left nephrectomy), presenting with a one-month history of fever, generalized weakness, and weight loss. Laboratory data was significant for anemia, hypercalcemia, and acute kidney injury. Chest radiograph showed ground glass opacities and interstitial infiltrates. Empiric antibiotics for community acquired pneumonia were initiated, however, fever persisted. Extensive workup was performed to evaluate fever and hypercalcemia. Malignancy, hormonal, and septic workup were all unremarkable. PPD skin test was negative. Sputum, pleural fluid, bronchoalveolar lavage, and cerebrospinal fluid were AFB smear negative. Remarkably, urine AFB smear was positive. Anti-tuberculosis therapy was initiated which lead to defervescence and clinical improvement. However, his hospital course was complicated by small bowel obstruction and respiratory failure. He subsequently developed loss of cardiac electrical activity and expired. Postmortem autopsy confirmed the presence of tuberculosis in multiple organs including his remaining kidney.

Discussion: Diagnosis of miliary tuberculosis can be very challenging especially in patients with an unusual presentation. A high index of suspicion is warranted, and as in our case, miliary tuberculosis should always be one of the differential diagnoses of fever of unknown origin with hypercalcemia. Moreover, workup for renal tuberculosis with urine AFB should be done in high-risk patients with a history of kidney stones.

Conflict of Interest

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Large Cerebral Intraventricular Neurocysticercosal Tumor in an Asymptomatic Patient: A Treatment Dilemma

Ornusa Teerasukjinda MD; Suwarat Wongjitraporn MD; Chawat Tongma MD; and Heath Chung MD

Abstract
Introduction: Neurocysticercosis (NCC) is a growing health problem in the United States and worldwide due to an increasing number of immigrants. Cysticercosis is caused by ingestion of the larval form of Taenia solium. The intraventricular form, NCC is seen in 7%-45% of the cases. We present a case of a young Chinese man who presented with headache and finding of an impressive intraventricular cyst related to NCC. Our case emphasizes the importance of recognition of NCC, especially in immigrant populations.

Case Report: A 37 year-old male Chinese immigrant with no significant past medical history presented to our facility after sustaining a head injury from a car accident. He lost consciousness briefly during the incident and had transient headache. He was admitted to the hospital for further evaluation. On physical exam, he had no neurological deficits. Non-contrast Head Computed tomography (CT) was obtained to rule out intracranial hemorrhage and found a large cystic lesion measuring 5x6x7cm in the right lateral ventricle, with partially calcification. Gadolinium-enhanced magnetic resonance imaging (MRI) of the brain was obtained and revealed a large solitary, right lateral ventricular cystic lesion containing a partially calcified mural nodule. No surrounding edema or inflammation was observed. The findings were highly suggestive of intraventricular NCC. He was born and raised in China, moved to Mexico and then to Hawai‘i three years ago. He denied previous history of headache, weakness, seizure, or visual impairment. The MRI result prompted neurosurgical evaluation. As the patient was asymptomatic and had no hydrocephalus, no surgical intervention was pursued and close outpatient follow-up was recommended. After 6 months of follow up, the patient has remained asymptomatic. Follow-up MRI after admission showed no changes in size of the cystic lesion or evidence of surrounding inflammation.

Discussion: Treatment for NCC should be tailored individually. In our patient who was asymptomatic, the large intraventricular cyst was an incidental finding on neuroimaging. The decision whether or not to perform endoscopic neurosurgery is very complicated; endoscopic surgery is an invasive procedure with multiple possible complications. Removal of the large cyst may decrease the risk of mechanical obstruction but may increase the risk of secondary hydrocephalus due to inflammatory damage. We present an atypically-large intraventricular NCC managed by close observation in an asymptomatic patient. The conservative approach in a seemingly complicated patient implies and emphasizes the importance of managing NCC on an individual basis.

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Native Valve Endocarditis Due to Citrobacter Chronic Prostatitis

Michael Tom MD; Corey Lum DO; Dennis Bolger MD; and Erlaine Bello MD

Abstract

Introduction: Citrobacter koseri is a gram-negative bacillus that rarely causes infection in immunocompetent hosts and typically is associated with urinary or respiratory tract infections. Rarely will Citrobacter be a cause of infective endocarditis.

Case Report: We present a case of a 77-year-old man with no known immunocompromising conditions who was hospitalized for infective aortic endocarditis due to Citrobacter koseri originating from a chronically infected prostate. Unusually, he also developed a C. koseri diskitis and phlegmon, which, along with the aortic vegetations, increased in size despite appropriate antibiotics. The patient thus met indications for aortic valve replacement and had improved appearance of lesions in follow-up imaging.

Conflict of Interest

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Multiple Intramuscular Gouty Tophi Mimicking Deep Tissue Abscesses: A Case Report

Chawat Tongma MD and Van T. Luu MD

Abstract

Introduction: Gout is a common metabolic disorder resulting from supersaturation of uric acid in extracellular fluid and deposition of monosodium urate monohydrate crystals in tissues triggering inflammatory response. Depositions of uric acid crystal outside articular structures cause tophi and are commonly found at peripheral areas of the body which have a lower temperature. Deposition of uric acid crystals in the central area of the body is not uncommon and may be overlooked.

Case presentation: A 55-year-old Pacific Islander man with a history of chronic tophaceous gout was admitted because of acute right knee pain. Physical examination revealed signs of inflammation over the right knee. Arthrocentesis was performed but no synovial fluid obtained. The patient was empirically treated with prednisone, colchicine, and febuxostat. On the next day, there was progression of inflammation up to the right mid-thigh. MRI of the right femur was obtained to exclude abscess and necrotizing faciitis. Multiple pockets of abscesses were identified within the vastus medialis and vastus intermedius adjacent to the femoral shaft. This prompted immediate surgical consultation and incision and drainage. Intraoperative findings revealed healthy muscles and deposition of soft-tan material in the vastus medialis and vastus intermedius along and above the shaft of the femur. Culture of the surgical aspirate was negative and pathology showed needle-shaped structures consistent with uric acid crystals. Empiric antibiotic was discontinued. The patient’s condition improved after treatment for acute gout. Pegloticase was also added to the treatment regimen during an outpatient follow up visit with his rheumatologist. At six month follow up, the patient reported excellent improvements in clinical symptoms.

Discussion: Atypical presentations of chronic tophaceous gout can be a great mimicker, causing diagnostic challenges for clinicians. Our patient who had multiple intramuscular tophi presented with abrupt signs and symptoms of inflammation of lower extremity resembling cellulitis, abscess, or necrotizing fasciitis. On MRI, tophi typically exhibit low signal on T1-weighted images and medium to high signal on T2-weighted images, indicating the presence of cellular tissues surrounding or infiltrating the crystalline mass. The vascularity of this tissue influences the degree of MRI post-contrast enhancement on T2-weighted images. With varying degrees of cellular response and vascularity, distinguishing tophi from abscesses by MRI is still difficult.

Conclusion: Our report focuses on the fact that tophi can also trigger acute inflammatory responses mimicking those of acute infection. At atypical locations, it can lead to misdiagnosis and inappropriate treatment. MRI is not a sensitive tool to differentiate abscess from tophaceous gout. Tissue diagnosis obtained from biopsy or aspiration is warranted to guide appropriate treatment and distinguish these different entities.

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Cardiac Rehabilitation Program at Rehabilitation Hospital of the Pacific

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Abstract

Introduction: For the past 20 years, multiple studies have demonstrated that cardiac rehabilitation and secondary prevention programs reduce cardiovascular risk and event rates significantly (up to 20%-25%) in patients with acute coronary syndrome (ACS), stable ischemic heart disease (IHD), and patients who have undergone percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG). Consequently, the American Heart Association (AHA) and American College of Cardiology (ACC) designated cardiac rehabilitation as a Class I indication for these patients.

Status: On the island of O‘ahu, comprehensive cardiac rehabilitation programs have not been available at any of the major hospitals for at least the past several years. Because of the desperate need for these services, Rehabilitation Hospital of the Pacific (REHAB) officially instituted a comprehensive cardiac rehabilitation program that is the only cardiac rehab program on the island of Oahu that contributes to the American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR) data registry and has been going through the process of national certification effective as of December 1, 2012.

It is well-known that the major problem of cardiac rehabilitation programs in this country is suboptimal participation, ie, only 25%-30% of eligible patients are actually referred to these programs. Our data suggests that underutilization of cardiac rehab programs is extremely severe here in Honolulu where probably less than 5% of eligible patients are actually referred to this program. We will discuss the importance of improving utilization at the patient level, physician level, third-party payer level, in the general medical community as well as in the general public to positively impact overall mortality and morbidity in the state of Hawai‘i.
Premature Ventricular Contraction (PVC)-induced Cardiomyopathy

Nath Zungsontiporn MD; Ittikorn Spanuchart MD; David Singh MD; and Osamu Fukuyama MD, FACP

Abstract

Introduction: Frequent cardiac tachyarrhythmias (incessant atrial fibrillation or flutter, supraventricular tachycardia, or ventricular tachycardia) can result in cardiomyopathy which is reversible once the underlying tachyarrhythmia is successfully treated. For the past several years, frequent monomorphic PVCs (without ventricular tachycardia) has been implicated in the development of a reversible form of dilated cardiomyopathy.

Case Report: We present a case of an elderly man who had moderate left ventricular systolic dysfunction secondary to hypertensive heart disease who was originally treated with a beta-blocker and an ACE-inhibitor with improvement of ejection fraction from 35% to 45%, where it leveled off. He was also noted to have over 50,000 PVCs on 24-hour Holter monitoring. Symptoms presented were only mild exertional dyspnea and fatigue without any other symptoms attributable to frequent PVCs. Therefore, initially, his PVCs were not treated. Once his ejection fraction leveled off at 45% with symptomatology only partially improved, it was elected to treat his frequent PVCs with amiodarone. With chronic amiodarone therapy, his exertional fatigue and dyspnea resolved while his ejection fraction further improved from 45% to 55%. Repeat Holter monitoring after three months of amiodarone therapy showed over 95% reduction in the number of PVCs in a 24-hour period.

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