Urine Blastomyces Antigen Testing in an Integrated Medical System

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PROBLEM
- Blastomycosis is a potentially serious systemic and cutaneous fungal infection which mimics a variety of other diseases. Proper diagnosis is important to avoid increased morbidity and mortality.1,2
- Fungal culture is the gold standard for diagnosis of blastomycosis, however it is reportedly 86% sensitive and may take up to 5 weeks for the organism to grow. Fungal smears for rapid diagnosis vary from 24-55% sensitivity depending on the one sample, and serologic tests often have low sensitivity.3,4

OBJECTIVE
- Explore the geodemographic and clinical features of patients on whom BuAg is performed and compare its test performance to other non-invasive tests for Blastomycosis.

METHODS
- Design: Retrospective chart review of 834 BuAg performed on unique patients, June 2013 through May 2015, for test characteristics and geodemographic features. Of these, 100 cases from 2015 (year containing an outbreak) were randomly selected for detailed analysis of index illness features, testing and ultimate diagnosis. Descriptive statistics compared with chi-square/Fisher exact test or t-tests.
- Patients: Every patient having BuAg performed; first test within time period was studied.
- Setting: Large, integrated Eastern Wisconsin medical system.

RESULTS
- BuAg was performed on a population with mean age 55, 55% male, 79% White, representing 213 Zip codes.
- Tests were positive in 50/834 (6%), across 42 Zip codes
- 16/50 (32%) were part of a large 2015 outbreak [16/49 were positive among those tested with recorded exposure].
- BuAg positive patients were younger than those test negative, even when outbreak subjects were removed [48.6 v. 56.7 years, p = 0.014]; Asians and males were over-represented.

Table 1: Demographic features of subjects BuAg Positive vs. Negative

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Positive BuAg (N=50)</th>
<th>Negative BuAg (N=784)</th>
<th>Total (N=834)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>35 (7.6%)</td>
<td>425 (92.4%)</td>
<td>460 (55.2%)</td>
<td>0.042</td>
</tr>
<tr>
<td>Female</td>
<td>15 (4.0%)</td>
<td>359 (96.0%)</td>
<td>374 (44.8%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>27 (4.1%)</td>
<td>678 (95.9%)</td>
<td>655 (79.0%)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>6 (8.5%)</td>
<td>55 (91.5%)</td>
<td>71 (8.6%)</td>
<td>0.124</td>
</tr>
<tr>
<td>Hispanic</td>
<td>2 (2.8%)</td>
<td>51 (97.2%)</td>
<td>53 (6.4%)</td>
<td>1.000</td>
</tr>
<tr>
<td>Asian</td>
<td>12 (37.9%)</td>
<td>20 (62.1%)</td>
<td>32 (3.9%)</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Native American</td>
<td>11 (12.5%)</td>
<td>7 (87.5%)</td>
<td>8 (1.0%)</td>
<td>0.293</td>
</tr>
<tr>
<td>Unknown</td>
<td>2 (20.0%)</td>
<td>8 (80.0%)</td>
<td>10 (1.2%)</td>
<td>0.067</td>
</tr>
<tr>
<td>All Non-White</td>
<td>23 (18.0%)</td>
<td>51 (82.0%)</td>
<td>74 (21.0%)</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Mean Age</td>
<td>40.9</td>
<td>55.8</td>
<td>54.9</td>
<td>0.0001</td>
</tr>
<tr>
<td>Mean Age Adj</td>
<td>48.6</td>
<td>56.7</td>
<td>56.4</td>
<td>0.018</td>
</tr>
</tbody>
</table>

* Compared to White
*Includes 23 Southeast Asians, 9 were positive
*Outbreak related subjects removed

RESULTS, CONTINUED
- Sensitivity of BuAg was 91% (based on 32 culture-positive cases)
- Specificity 98%
- PPV=78%
- Only 2/19 (11%) culture positive cases were positive by Blasto Ab-ID, Q1/7 by CF.
- Of those with positive BuAg, 16% of co-tested were positive by Ab-ID, 4% by CF; all positive ID/CF were positive by BuAg.
- Histoplasma urine antigen was co-performed with BuAg in 69%, positive in 22/578; 16/25 were also BuAg positive (known cross-reactivity).
- 100 patient charts were examined for index illness details:
  - 7 were ultimately diagnosed with blastomycosis (6 had positive BuAg)
  - 7 with other fungal disease
  - 26 with non-fungal lung disease
  - 22 pneumonia
  - 5 skin lesions
  - 6 malignancies
  - 3 mycobacterial infections
  - 11 other diagnoses (plus 1 unknown entity)
  - 12 were tested based on symptoms.

Table 2: Time of onset to test, and test to diagnosis, by category

<table>
<thead>
<tr>
<th>Category</th>
<th>Time from onset to BuAg test (No. of Subjects)</th>
<th>Time from BuAg to diagnosis (No. of Subjects)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;7 days</td>
<td>24</td>
<td>78</td>
</tr>
<tr>
<td>7-30 days</td>
<td>33</td>
<td>13</td>
</tr>
<tr>
<td>1-3 months</td>
<td>19</td>
<td>6</td>
</tr>
<tr>
<td>3-6 months</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Total N</td>
<td>86</td>
<td>97</td>
</tr>
</tbody>
</table>

Among those 6/100 with positive BuAg:
- 1 patient was tested within 7 days of symptom onset
- 2 patients 7-30 days after onset
- 3 patients 1-3 months after onset

In the river associated Eastern Wisconsin outbreak, similar to non-outbreak cases, 88% of positive cases had at least one other test for Blastomycosis performed, yet BuAg was the only test positive in 9/16 (56%) in outbreak cases v. 6/54 (11%), p<0.009 other cases.

CONCLUSIONS
- BuAg is now commonly used in our region for work-up of broad differential diagnoses or known exposures.
- It may be particularly useful in outbreaks.
- Of those tested with BuAg, non-White patients (particularly Asians), and males were more likely to be positive.
- Not adding Blastomyces CF and ID tests ($40 each) to BuAg would save money without losing sensitivity.

REFERENCES

ACKNOWLEDGMENTS
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