ABSTRACT

Background: Burkholderia pseudomallei is endemic in the tropics and associated with high mortality. We performed a retrospective study analyzing the clinical and microbiologic features of melioidosis, and predictors of mortality. Patients with culture-positive melioidosis from 2006-2016 were identified from microbiologic records.

Methods: Clinical data including demographics, treatment and outcomes were extracted from medical records. Categorical variables were compared using χ2 test or Fisher exact test while continuous variables were compared using Student’s t test or Mann-Whitney U test.

Results: Forty-three cases of melioidosis were identified. Presentations included fever (41.9%), respiratory symptoms (25.9%) and joint swelling (9.3%). 76.7% were bacteremic and 69.7% were culture-positive from a non-blood source. Mean time from presentation to positive microbiological data was 5.1 ± 6.4 days. Infection sites included pulmonary (62.8%), spleen (27.9%), skin/soft tissue (25.6%) and bone/joint (25.3%). Antibiotic susceptibility were as follows: ceftazidime (97.5%), imipenem (100.0%), trimethoprim-sulfamethoxazole (92.1%), amoxicillin-clavulanate (94.7%), doxycline (94.7%). Mean time from presentation to melioidosis-active coverage was 6.8 ± 9.1 days. Thirty-day all-cause mortality occurred in 9 patients (from first positive culture); 1 patient died within 5 months. Univariable analysis associations with 30-day all-cause mortality were: intensive care unit (ICU) admission (OR 26.3, 95% CI 4.0-173.1, P <0.01), mechanical ventilation (OR 15.0, 95% CI 2.6-85.0, P<0.01), higher median Pitt Bacteremia Score (PBS) (4.0 vs 2.0, P<0.01), receipt of ceftazidime (vs a carbapenem) as primary induction antibiotic therapy (OR 0.2, 95% CI 0.03-0.91, P=0.847) and not receiving melioidosis-active induction intravenous antibiotics (P=0.04). Multivariable analysis found ICU stay to be an independent predictor for 30-day mortality (P = 0.018, OR 12.1 95% CI 1.5-96.0).

Conclusions: ICU admission, a high PBS, and in particular, receipt of mechanical ventilation may help identify patients with high mortality risk. Delay in melioidosis-active therapy was not uncommon. Prompt recognition of melioidosis and early institution of active therapy, especially in the critically ill, may reduce mortality.

BACKGROUND

• Burkholderia pseudomallei is a gran-negative saprophytic soil endemic in Singapore and the tropics.

• Burkholderia pseudomallei infections are associated with high mortality.

• We performed a retrospective study analyzing clinical and microbiologic features of melioidosis, and Predictors of mortality.

METHODS

• Culture-positive melioidosis (from blood and non-blood sources) patients between 2006-2016 were identified from microbiologic records.

• Clinical data including demographics, treatment and outcomes were extracted from medical records.

• Categorical variables were compared using χ2 test or Fisher exact test.

• Continuous variables were compared using Student’s t test or Mann-Whitney U test.

• P values <0.05 were regarded as statistically significant.

• Multivariable backward logistic regression was performed for variables with P < 0.2.

• All data was analyzed using SPSS.

RESULTS

See Table 1 for summarised key points.

(A) Demographic Data

• Forty-three cases of melioidosis were identified.

• Median age of presentation was 60.0 years old (IQR 51.0 – 68.5).

• Patient ethnicity were as follows: Chinese (65.1%), Indians (20.9%), Malays (14.0%).

• Majority of patients were male (83.7%).

• Presentations included fever (41.9%), respiratory symptoms (20.9%) and joint swelling (9.3%).

• Thirty four patients (79.1%) were diabetic, with mean glycated haemoglobin (HbA1c) level at presentation of 10.1.

• Diabetes mellitus was not significantly associated with 30-day mortality (OR 0.4, 95% CI 0.3 – 2.2, P = 0.37).

(B) Microbiological data

• 76.7% were bacteremic.

• 69.7% were culture-positive from a non-blood source.

• Culture-positive infection sites included pulmonary (62.8%), spleen (27.9%), skin/soft tissue (25.6%) and bone/joint (25.3%).

• Mean time from presentation to positive microbiological data was 5.1 ± 6.4 days.

• Mean time from presentation to melioidosis-active coverage was 6.8 ± 9.1 days.

• Antibiotic susceptibility were as follows: ceftazidime (97.5%), imipenem (100.0%), trimethoprim-sulfamethoxazole (92.1%), amoxicillin-clavulanate (94.7%), doxycline (94.7%).

Table 1: Important clinical features of Melioidosis patients

<table>
<thead>
<tr>
<th>Category</th>
<th>All Patients (n=43)</th>
<th>Patients who lived (n=34)</th>
<th>Patients who died (n=9)</th>
<th>Alive vs Dead</th>
<th>P value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Past Medical Conditions</strong></td>
<td></td>
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<tr>
<td>Diabetes mellitus, no. (%)</td>
<td>34 (79.1)</td>
<td>28 (82.4)</td>
<td>6 (66.7)</td>
<td></td>
<td>0.37</td>
<td>0.4 (0.3 – 2.2)</td>
</tr>
<tr>
<td>Mean HBA1C at presentation, no. (SD)</td>
<td>10.1 (3.0)</td>
<td>10.0 (2.8)</td>
<td>10.4 (3.9)</td>
<td></td>
<td>0.77</td>
<td>-</td>
</tr>
<tr>
<td><strong>Disease Characteristics</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Any positive blood cultures, no. (%)</td>
<td>33 (77.3)</td>
<td>25 (73.5)</td>
<td>8 (88.9)</td>
<td></td>
<td>0.66</td>
<td>2.9 (0.3-26.4)</td>
</tr>
<tr>
<td>Mean time from presentation to any positive culture, days (IQR)</td>
<td>5.1 ± 6.2</td>
<td>5.2 ± 6.5</td>
<td>4.6 ± 6.4</td>
<td></td>
<td>0.81</td>
<td>-</td>
</tr>
<tr>
<td>Mean time from presentation to Melioid-active coverage, days, (SD)</td>
<td>6.8 ± 9.1</td>
<td>6.5 ± 6.7</td>
<td>9.7 ± 17.9</td>
<td></td>
<td>0.44</td>
<td>-</td>
</tr>
<tr>
<td>Median Pitt Bacteremia score (IQR)</td>
<td>2.0 (0.0-4.0)</td>
<td>2.0 (2.0-4.0)</td>
<td>4.0 (2.5-10.0)</td>
<td></td>
<td>0.002</td>
<td>-</td>
</tr>
<tr>
<td>Need for ICU stay, no. (%)</td>
<td>11 (25.6)</td>
<td>4 (11.8)</td>
<td>7 (77.8)</td>
<td></td>
<td>&lt;0.001</td>
<td>26.3 (4.0 – 173.1)</td>
</tr>
<tr>
<td>Requiring mechanical ventilation, no. (%)</td>
<td>10 (23.3)</td>
<td>4 (11.8)</td>
<td>6 (66.7)</td>
<td></td>
<td>0.002</td>
<td>15.0 (2.6 – 85.0)</td>
</tr>
<tr>
<td>Septic shock, no. (%)</td>
<td>20 (46.5)</td>
<td>13 (38.2)</td>
<td>7 (77.8)</td>
<td></td>
<td>0.06</td>
<td>5.7 (1.0 – 31.5)</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Use of Ceftazidime (referent group) vs Carbapenem as initial induction antibiotic therapy, no. (%)</td>
<td>31/41* (75.6)</td>
<td>28/34</td>
<td>3/7 (42.9)</td>
<td></td>
<td>0.047</td>
<td>0.2 (0.3 – 0.9)</td>
</tr>
<tr>
<td>Non-recipient of melioidosis-active therapy</td>
<td>2 (4.7)</td>
<td>0 (0.0)</td>
<td>2 (22.2)</td>
<td></td>
<td>0.04</td>
<td>-</td>
</tr>
</tbody>
</table>

1: P values by Fisher exact test except as indicated. Values given as no./no. indicate number of patients for whom results were available (if less than total no. patients in category). ICU, intensive care unit; OR, odds ratio; CI, confidence interval.

2: Student T test

3: Mann-Whitney U test

4: Excluded patients not on melioidosis-active therapy (n=2)

RESULTS

(C) Predictors of mortality

• Thirty-day all-cause mortality occurred in 9 patients (from first positive culture); 1 patient died within 5 months.

• Univariable analysis showed that the following features were associated with 30-day all-cause mortality:

  • Intensive care unit (ICU) admission (OR 26.3, 95% CI 4.0-173.1, P <0.01).
  • Mechanical ventilation (OR 15.0, 95% CI 2.6-85.0, P<0.01).
  • Higher median Pitt Bacteremia Score (PBS) (4.0 vs 2.0, P<0.01).
  • Receipt of ceftazidime (vs a carbapenem) as primary induction antibiotic therapy (OR 0.2, 95% CI 0.03-0.91, P=0.047).
  • Not receiving melioidosis-active induction intravenous antibiotics (P=0.04).

• Septic shock was present in 20 patients (46.5%), although it was not significantly associated with 30-day mortality (OR 5.7, 95% CI 1.0-31.5, P=0.06).

• Multivariable analysis was performed using two different models:

  • Model 1: Backwards (Wald) [for risk factors with P <0.2 on univariate analysis] found mechanical ventilation to be an independent predictor for 30-day mortality (P = 0.03, OR 18.8, 95% CI 2.7-131.0).
  • Model 2: Backwards (LR) [for the 3 most significant variables] found ICU stay to be an independent predictor for 30-day mortality (P = 0.18, OR 12.1, 95% CI 1.5-96.0).

CONCLUSIONS

ICU admission, a high PBS, and in particular, receipt of mechanical ventilation may help identify patients with high mortality risk.

• Delays in melioidosis-active therapy were not uncommon.

• Prompt recognition of melioidosis and early institution of active therapy, especially in the critically ill, may reduce mortality.