Pythiosis with renal involvement: Rare but Fatal Disease: A Systematic Review

Sirisak Chanprasert, Patompong Ungprasert, Charat Thongprayoon, Wisit Cheungpasitporn, Narat Srivali, and Jackrapong Bruminhent

Pythiosis is a form of infectious disease caused by Pythium insidiosum. Infected patients can present with 1) cutaneous/subcutaneous, 2) vascular, 3) ocular, and 4) disseminated diseases. Systemic disease occurs following vascular invasion and is considered fatal when large arteries are involved. Infection/sepsis, commonly from bacterial infection, is one of major causes of AKI in hospitalized patients. Invasive fungal infections can also cause septic shock and is associated with high mortality. However, the incidence of renal involvement in these patients with pythiosis and their outcomes are still unclear. Therefore, we performed a systematic literature search for reported cases of pythiosis with kidney involvement. We found two case reports of systemic pythiosis with renal involvement. The locations of acquired infection were reported in Mexico and Texas, United States. Although systemic pythiosis with renal failure is rarely reported, it is serious and fatal condition. Journal of Nature and Science, 1(5):e92, 2015

Introduction
Pythiosis is a form of infectious disease caused by Pythium insidiosum. Infected patients can present with 1) cutaneous/subcutaneous, 2) vascular, 3) ocular, and 4) disseminated diseases (1). Pythiosis is considered as one of the opportunistic fungal infections in the Asia-Pacific region (2, 3). Pythiosis is more common in animals than human (4), however, human pythiosis has high rates of morbidity and mortality (3). 75% reported an agricultural occupation. Systemic/disseminated disease occurs following vascular invasion and is considered fatal when large arteries are involved (5-7). Serious comorbidities include limb amputation in cases with vascular involvement and enucleation/evisceration in cases with severe ocular pythiosis (3, 8, 9). Indeed, in a large multi-institutional study from Thailand with a total of 102 cases of pythiosis, 60 patients received a diagnosis of vascular pythiosis, and only the patients who had undergone amputation survived (3).

Acute kidney injury (AKI) is a common clinical problem in hospitalized patients, independently associated with both short and long-term mortality (10-14). Infection/sepsis, commonly from bacterial infection, is one of major causes of AKI in hospitalized patients (15, 16). Invasive fungal infections can less commonly cause septic shock, but is also associated with high mortality (17). However, the incidence of renal involvement in these patients with relatively rare invasive fungal infection, pythiosis and their outcomes are still unclear. Therefore, we performed a systematic literature search for reported cases of pythiosis with kidney involvement.

Methods
Search strategy
Two investigators (C.T. and W.C.) independently searched published studies indexed in MEDLINE, EMBASE, and Cochrane Database of Systematic Reviews from inception through February 2015 using keywords described in Table 1. A manual search for additional relevant studies using references from retrieved articles was also performed.

Inclusion criteria
The inclusion criteria were as follows: (1) randomized controlled trials (RCTs), observational studies (case-control, cross-sectional or cohort studies), case series, case reports published as original studies or abstracts or letters to evaluate the risk of renal involvements including AKI, chronic kidney disease (CKD), glomerulonephritis (GN) and end stage renal disease (ESRD) in patients with pythiosis. Study eligibility was independently determined by the two investigators noted above.

Data extraction
A standardized data collection form was used to extract the following information: reported location(s) of acquired infection, patient age, coexist medical problem(s), organ Injury/failure(s), following information: reported location(s) of acquired infection, study population, and outcome of interest.

Results
Our search strategy yielded 4 potentially relevant articles. 2 articles were excluded based on title and abstract for clearly not fulfilling inclusion criteria on the basis of the type of article, study design, population, or outcome of interest. There have been only two case reports of systemic pythiosis with renal involvement (5, 18) as described in Table 2.

Discussion
Our systematic review found only two case reports of systemic pythiosis with renal involvement. Although most of the cases of human pythiosis have been reported in Thailand, and less commonly in Australia, and North, Central and South America, the locations of two cases of systemic pythiosis with renal involvement were reported in Mexico and Texas, United States. The first patient was transferred to Galveston, Texas from Mexico for intensive treatment. The first case developed systemic pythiosis with renal failure during her severe burn injury (5). The second patient was 14-year-old female who had Diamond-Blackfan anemia, requiring monthly blood transfusions since infancy (18).
A variety of therapeutic modalities have been used to treat this disease, including antibiotics, antifungals, and immunotherapy, but the ultimate management of vascular pythiosis is surgical source control (6). Despite aggressive treatment and multiple antifungal therapies, both patients died during hospitalization with multiple organ failures. The second patient was on continuous venovenous hemodialysis for renal replacement therapy during her septic shock. In summary, although systemic pythiosis with renal failure is rarely reported, it is serious and fatal condition. In addition, although pythiosis is more common in Asia, these 2 cases were reported in America. Thus, there is a possibility of underreport. Physicians should increase their awareness of this fatal form of Pythiosis.


<table>
<thead>
<tr>
<th>Case 1 (5)</th>
<th>Case 2 (18)</th>
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</thead>
<tbody>
<tr>
<td>Reported location(s) of acquired infection</td>
<td>Mexico</td>
</tr>
<tr>
<td>Age, year</td>
<td>10</td>
</tr>
<tr>
<td>Sex</td>
<td>female</td>
</tr>
<tr>
<td>Coexist medical problem(s)</td>
<td>65% total body surface area burns</td>
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<tr>
<td>Organ Injury/Failure(s)</td>
<td>Septic shock, acute kidney injury and developed disseminated intravascular coagulation.</td>
</tr>
<tr>
<td>Treatment</td>
<td>-Treated at different times with voriconazole, colistin, amphotericin B body washes, anidulofungin, and posaconazole as well as bacterial antibiotics with no success. - bilateral below knee amputations and multiple excision and debridement procedures.</td>
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<tr>
<td>Outcomes</td>
<td>Death with a total 18-day hospitalization</td>
</tr>
</tbody>
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