Pythium insidiosum necrotizing fasciitis in an immunocompetent patient exposed to a New Mexico hot spring: a rare human case of "swamp cancer" in the southwest United States

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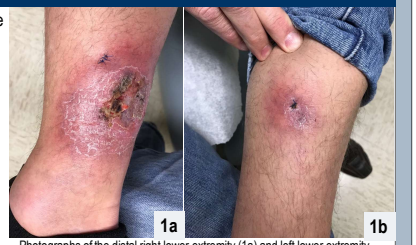
History and Examination

- A 58 year old man presented with three progressive necrotic ulcerative plaques in bilateral lower extremities present for 1 month
- Lesions began as four papules 5-6 days after a hot springs exposure and enlarged to become indurated, non-painful, erythematous plaques (Figures 1a-b) despite treatment with doxycycline and amoxicillin/clavulanate for presumed cellulitis
- He had no other associated systemic symptoms of fevers, chills, night sweats, weight loss and swollen lymph nodes.



Photographs of the distal right lower extremity (1a) and left lower extremity (1b) skin lesions

Epidemiologic History: He is an office-worker, an ex-smoker and occasionally drinks alcohol. He has multiple pets including a dog, an iguana, multiple snakes, birds and fish. He denies any unusual dietary habits such as raw meat or unpasteurized dairy.

Physical Examination: The patient was a well-appearing adult male in no acute distress. The blood pressure was 131/87mm Hg, pulse 77 beats per minute, temperature 97°F (36.1°C), and respirations 20 breaths per minute. On skin examination he had two well-circumscribed, indurated, erythematous plaques approximately 2x2 cm and 10x6 cm in diameter on the right lower extremity, the larger plaque was medial and proximal to the ankle and the smaller plaque anterior and distal to the knee. The inferior lesion had central ulceration and necrosis (Figure 1a). An approximately 3x3 cm indurated, erythematous, scaly plaque was present proximal to the left ankle (Figure 1b).

Diagnostic Studies

- MRI of the bilateral lower extremities: diffuse subcutaneous inflammatory changes in the right lower extremity and subcutaneous inflammatory changes in the medial left lower extremity
- Pertinent lab findings: Mild eosinophilia (White blood cells 10.8x10^3 cells/ µl, absolute eosinophil count 778 cells/ µl), platelets 463 x10^3 cells/ µl, HIV/Hg electrophoresis/immunoglobulins/lymphocyte subsets normal
- Skin punch biopsy specimens with fungal elements described as broad hyphae with ribbon-like architecture with rare septae concerning for cutaneous agent of mucormycosis on Grocott's methenamine silver (GMS) stain (Figure 2).
- Tissue samples were plated directly onto Sabouraud-dextrose agar and on day 3 of culture, fine white hyphae were noted to be growing on agar plates (Figure 3).
- Tissue sample and subculture of growth from Sabouraud-dextrose agar plate were sent to reference laboratories. Three weeks after admission the organism was identified as *Pythium insidiosum* via 18S ribosomal RNA gene sequencing.

References

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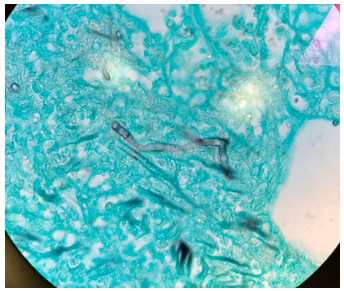

Figure 2: GMS stain of skin biopsy from affected areas showed hyphal elements. These hyphae were focally twisted and ribbon-like, with only rare septae formation (100x+ magnification)

Figure 3: Growth of fine, white hyphae seen on sabouraud-dextrose agar plate

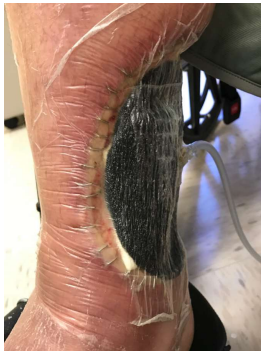

Figure 4: Photograph of right lower leg one week after discharge from hospital, with wound-vacuum system in place

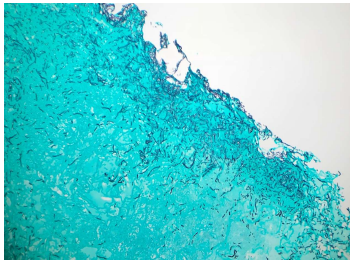

Figure 5: GMS stain of repeat skin debridement showed abundant ribbon-like hyphae with rare septae (40x magnification)

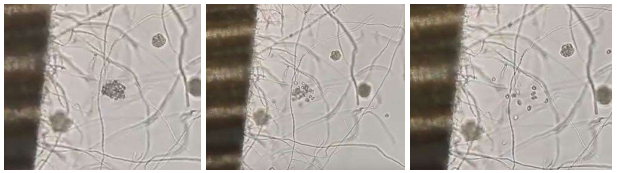

Figure 6: Light microscopy of *Pythium insidiosum* zoosporogenesis in aqueous culture achieved in William Beaumont Army Medical Center microbiology lab (40x magnification)

Treatment and Clinical Course

- Prior to identification of *P. insidiosum*, treatment with intravenous liposomal amphotericin B 5mg/kg daily and oral posaconazole 300mg daily was initiated for presumed mucormycosis. Serial surgical debridements were performed. Amphotericin B solution was also irrigated into the wounds. He was discharged on posaconazole.
- At outpatient follow-up, one week post-discharge, increased erythema and induration was present at previously debrided lesions (Figure 4). He was readmitted and underwent additional exploration of his wounds. Extensive tissue necrosis was noted surrounding the previously-debrided right lower extremity wound which necessitated a below-the-knee amputation.
- Tissue samples sent for histopathology showed persistent presence of the organism (Figure 5) from abnormal-appering areas, but all surgical margins at the site of amputation were clear. CT angiography showed no evidence of vascular involvement.
- An immunotherapeutic veterinary *Pythium insidiosum* antigen vaccine was administered (3 doses). He was transitioned to itraconazole, terbinafine, minocycline, and caspofungin. Caspofungin was discontinued after six weeks. Plan is for one year of therapy with no evidence of active infection after six months on the above regimen.

Discussion

- *Pythium insidiosum* is a fungus-like oomycete found in standing water which mainly infects non-human mammals[1]. Pythiosis can occur in the immunocompetent, but hemoglobinopathies and immunocompromise are risks for severe disease. Rare cases are reported in North America[2, 3] Human pythiosis is described predominantly in Thailand[2, 4].
- Four clinical syndromes have been described: cutaneous/ subcutaneous, vascular, ocular, and disseminated[2]. Mortality rates of cutaneous/subcutaneous and ocular pythiosis may be low, although treatment often involves aggressive surgical debridement and enucleation[2]. In one series, the vascular and disseminated forms carried a 40% and 100% mortality rate, respectively[2].
- Most cases have been linked to exposures to natural bodies of water. The New Mexico Department of Health was notified and investigated the hot spring where the exposure was thought to have occurred. No environmental samples were taken.
- Human pythiosis is frequently mistaken for an agent of mucormycosis due to similar histopathology[3]. Management is based on case reports given disease rarity in human hosts.
- *Pythium insidiosum* is resistant to traditional antifungals as it lacks ergosterol in its cytoplasmic membrane[1].
- An experimental immunotherapeutic *Pythium insidiosum* vaccine (Pan American Vet Lab) developed for equine and canine pythiosis has been utilized in human cases[2]. Human and animal data suggest an approximate 60% efficacy rate.[5]
- Due to lack of known effective medical therapy, early and radical surgical debridement with confirmed negative tissue margins is recommended and necessary for effective treatment[2].

Acknowledgements and Disclaimer

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- Disclaimer. The views expressed are those of the authors and do not necessarily reflect the official policy or position of William Beaumont Army Medical Center, Department of the Army, Department of Defense, or the US Government.