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Case Report

Humeral Osteomyelitis with *Apophysomyces ossiformis* in an Immunocompetent Patient: A Case Report

Travis J. Miller MD^{1,2*}, Clifford C. Sheckter MD¹ and Andrew J. Watt MD²

¹Department of Surgery, Division of Plastic and Reconstructive Surgery, Stanford University School of Medicine, Stanford, CA 94304, USA

²The Buncke Clinic, San Francisco, CA 94114, USA

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ABSTRACT

Introduction: Osteomyelitis of a limb can lead to devastating functional consequences. Fungal osteomyelitis is rare in immunocompetent patients, and compared to bacterial osteomyelitis, fungal infections are more difficult to eradicate.

Case Report: We present a case of a 59-year-old male who suffered traumatic left open radius and ulna fractures at the elbow with significant soft tissue loss. He underwent spanning fixation across the elbow, and soft tissue coverage was provided with a free latissimus flap. At the time of flap coverage, the patient was found to have fungal osteomyelitis with the organism *Apophysomyces ossiformis*. The patient achieved wound closure and functional use of the left upper extremity.

Conclusion: The reported case demonstrates the pathogenicity of a microorganism not previously described in human disease. In this case, treatment was successful with local debridement, placement of antibiotic beads, and long-term antifungal therapy.

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Introduction

Osteomyelitis is a challenging problem for clinicians to face. Either through direct inoculation or hematogenous spread, pathogenic invasion of the bone leads to destruction of native architecture and biophysical signaling pathways, leading to impaired mechanical stability and fracture healing capacity [1]. In severe infections, patients may also have systemic, life-threatening symptoms. More commonly, osteomyelitis presents as a localized infection. In the limbs, this has profound implications on functional capacity. While antibiotic therapy alone may be effective in certain cases of acute infection, surgical intervention is commonly required concurrently to remove all sequestra and nonviable tissue, allowing healing of the bone and soft tissue envelope [2]. Implanted hardware most commonly needs to be removed. In more severe cases, reconstruction of the bony and soft tissue defect with or without bone lengthening and/or free tissue transfer may be needed [3]. If a limb is not salvageable or the disease cannot be cleared, amputation is required. Osteomyelitis caused by fungal pathogens is much less common than bacterial osteomyelitis, and cases are more typical in immunosuppressed and/or diabetic patients [4]. Given the typical

indolence of these pathogens, surgical intervention is often mandatory in combination with prolonged antifungal therapy [5]. Here we describe a case of fungal osteomyelitis of the humerus in an immunocompetent patient who was treated successfully and has regained use of the affected limb.

Case Report

A 58-year-old healthy male was involved in a motor vehicle accident, suffering thoracic spine fractures, rib fractures, a pneumothorax, and left open fractures of the radius and ulna including the olecranon. The patient was stabilized from a trauma perspective and underwent multiple debridements to the left elbow. Ultimately the ulna and radius underwent internal fixation and a spanning plate was placed across the humerus to the ulna (Figure 1). However, the patient had insufficient soft tissue envelope to cover the elbow wound and underlying bone and hardware. The patient underwent prolonged wound care using vacuum assisted suction devices for over a month.

*Correspondence to: Travis J. Miller MD, The Buncke Clinic, 45 Castro St #121, San Francisco, CA 94114, 415-565-6136; E-mail: travismi@stanford.edu

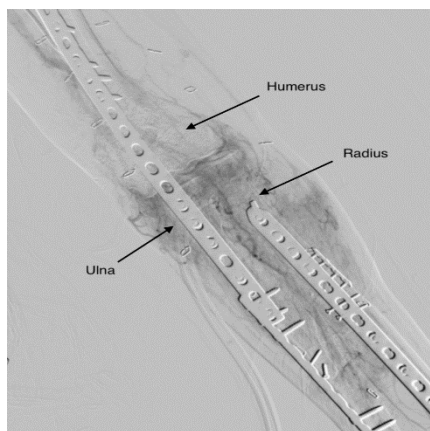


Figure 1: Pre-operative angiogram image of the left elbow demonstrating internal fixation. Note the fixation plates on the radius and ulna as well as the spanning plate across the humerus and ulna.

The wound failed to close over this period, and the patient was transferred to a specialized reconstructive microsurgery facility for soft tissue coverage. The patient's wound at this point was 400 cm² with exposure of the elbow hardware and bone. Free tissue transfer was planned for coverage. At the time of reconstruction, it was noted that gross fungal elements were growing on the distal humerus and lateral epicondyle (Figure 2).

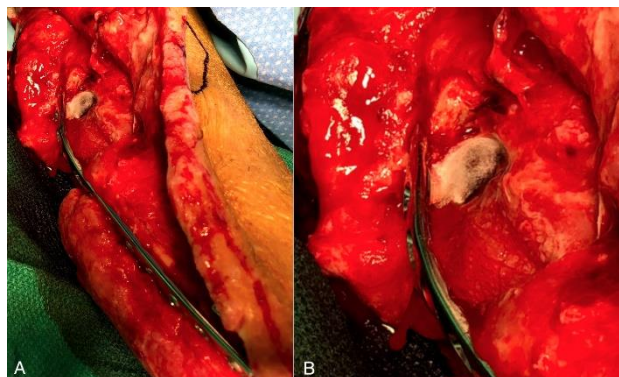


Figure 2: Intraoperative view of left elbow wound. Panel A: View demonstrating wound size and exposed structures. Note the exposed spanning plate from the humerus superiorly to the ulna inferiorly. Panel B: Zoomed view demonstrating gross hyphal elements growing on the humerus/lateral epicondyle.

The fungal elements and underlying necrotic bone were debrided back to healthy tissue, and specimens were sent for laboratory analysis. Prior consultation with the referring orthopedist noted that removal of the hardware would likely preclude limb salvage, and thus soft tissue reconstruction proceeded without removal of the in-situ plates. Given the fungal element findings, polymethylmethacrylate beads impregnated with amphotericin B were placed at the distal humerus site. A free latissimus flap was then placed over the wound, utilizing the thoracodorsal pedicle with end-to-side anastomosis to the brachial artery and end-to-end anastomosis to the basilic vein. A split thickness skin graft was placed over the latissimus muscle.

The patient was placed in a splint which was taken down post-operative day 5. Some skin graft loss was evident at the edges of the flap, but the bulk of the flap remained healthy (Figure 3). Ultimately the areas of skin graft loss healed with wound care. Pathology confirmed fungal osteomyelitis, and subsequent polymerase chain reaction (PCR) isolated *Apophysomyces ossiformis*. After consultation with infectious disease

specialists, the patient was placed on a 6-month regimen of oral voriconazole 200 mg twice per day. At 7 months post-operatively, the patient is off of antibiotics, and the wound is closed without apparent swelling, sinus tracts, or drainage. The patient remains fused at the elbow but is able to bring his left hand over his head and use the hand for daily activities. The patient currently declines further intervention to restore elbow motion.



Figure 3: View of free latissimus flap 5 days after surgery and takedown of splint. Note necrosis of the skin graft at the perimeter of the flap, while the center bulk of the flap is viable with skin graft take.

Discussion

Over 100,000 fungal species have been defined, and approximately 150 species are known to be pathogenic to mammals. Common species include *Candida*, *Aspergillus*, *Coccidioides*, *Histoplasma*, *Blastomyces*, and *Cryptococcus* [4]. *Apophysomyces* species (which are causative agents of zygomycosis) are opportunistic and typically affect immunocompromised patients [7]. *A. trapeziformis* has been found as a causative agent in septic arthritis, *A. elegans* has been seen as a causative agent of rhino-oculo-cerebral mucormycosis, and *A. variabilis* has been implicated in necrotizing fasciitis [8-10]. *A. ossiformis* was only described as a distinct species in 2010 and is characterized by its bone-shaped sporangiospores. Amphotericin B and posaconazole have been described as effective anti-fungal agents in vitro, but no clinical guidelines for treatment are available [11]. At the time of this case report, there have been no other documented human infections by this organism.

Based on this case, it appears that this organism can be controlled by following current standards of care for osteomyelitis. Indeed, in this case radical removal of all potentially infected tissue and hardware was not performed. This implies that while *A. ossiformis* is virulent enough to infect immunocompetent patients, it is not so aggressive to require radical debridement; this is in contrast to other *Apophysomyces* species [12]. While amphotericin B was utilized locally, systemic therapy with this agent was avoided, sparing the patient from potential morbidity from this macrolide [13]. However, it must be highlighted in this case that follow up was only 7 months, and the resurgence of underlying infection remains a possibility.

Conclusion

This case report demonstrates *A. ossiformis* as a human pathogen causing osteomyelitis. Traditional surgical technique and antibiotic therapy appear effective in treating an infection with this organism in an

immunocompetent patient; however, current evidence-based guidelines are needed.

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