Fracture treatment in the setting of cutaneous aspergillosis: a case report
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Abstract
The authors present the case of a patient who developed an Aspergillosis flavus (A flavus) superficial cutaneous infection which was identified at the time of cast removal, 2 weeks after immobilization of a closed distal third humerus fracture. Clinical and microbiological findings, as well as the treatment of this patient, are reported. An otherwise healthy 27-year-old male presented to the orthopaedic surgery clinic 2 weeks after a closed distal humerus fracture, which was initially immobilized with a functional removable brace. Upon cast removal, the patient was noted to have significant brown hyperkeratotic patches and plaques, studded with pustules in an annular configuration on his left posterior and lateral arm. Fungal culture later grew A flavus. The patient was started on both oral and topical antifungals and operative management of the displaced fracture was delayed until skin lesions resolved. Once clinical examination and negative repeat bedside potassium hydroxide were confirmed, open reduction and internal fixation was performed. The fracture healed uneventfully, and the patient did not develop any signs or symptoms of postoperative infection.

Keywords: cutaneous aspergillosis, fracture, treatment

1. Introduction
Aspergillus spp. are ubiquitous filamentous fungi found in the environment but rarely cause infection in immunocompetent hosts. Aspergillus infections are predominately observed in immunocompromised individuals, such as individuals who are immunosuppressed, have a hematologic malignancy, HIV, transplant patients, burn victims, or have a granulomatous disease. Clinical presentation is variable, and ranges from life-threatening angioinvasive disease to cutaneous only involvement, such as in primary cutaneous aspergillus (PCA). PCA clinical presentation is variable, and can present as studded small pustules, violaceous papules and plaques, dermatophyte-like, or with deeper cutaneous involvement, such as subcutaneous nodules. Regardless, PCA infections are very rare in immunocompetent individuals and typically occur at sites of surgical wounds, exposure to large spore burden, or traumatic inoculation. In immunocompetent hosts, these infections are typically limited, but can progress to vesicular lesions that ulcerate.

Infections attributed to the genus aspergillus have been on the rise. Common species triggering infection include Aspergillus flavus (A flavus), which is the second leading cause of invasive aspergillosis and is the most common cause of superficial infection. A flavus grows better with water activity between 0.86 and 0.96 and is more active in humid, tropical environments as a result. The optimum temperature for A flavus growth is 37°C, but fungal growth can be observed at temperatures ranging from 12 to 48°C. These high optimum temperatures contribute to the A flavus pathogenicity in humans.

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Nonoperative treatment of distal humerus fractures with a functional brace is common and associated with satisfactory outcomes.\(^7\)–\(^9\) In the case of patients with insufficient immobilization or delayed healing, operative treatment may be a good option. We report the delayed surgical management of a patient who sustained a distal humerus fracture, for which surgical fixation to correct deformity was not immediately available given cutaneous infection with \(A\) \textit{flavus}.

2. Case report

The patient has provided written informed consent for publication of this material in a medical journal and understands that radiographs and clinical photographs obtained during the course of clinical care may be used for these purposes. A healthy, right-hand dominant 27-year-old male sustained a closed distal third humerus fracture to his left arm while wake boarding in Florida. Initial injury radiographs are shown in Figure 1. The patient was initially immobilized at a local urgent care in a removable functional brace with stockinette next to skin for compression prior to presentation at the Orthopedic Surgery clinic at our institution 2 weeks after his initial injury. As shown in Figure 2, X-rays demonstrated 37 degrees of varus malalignment, and surgical fixation was recommended.

Upon removal of the brace for the first time since its application in Florida, the authors observed significant brown hyperkeratotic patches and plaques, studded with pustules in an annular configuration on his left posterior and lateral arm (Fig. 3). Patient was unaware of the skin eruption, as it was asymptomatic. Patient denied any systemic symptoms or past history of herpes eruptions. Patient was immediately referred to Dermatology.

Upon dermatologic consultation, a potassium hydroxide (KOH) prep was performed of one of the pustules and a fungal infection was noted to affect the lateral (A) and posterior (B) aspects of the left upper arm, as well as the stockinette overlying the arm (C).
culture was obtained. Clinical findings were highly suggestive of a superficial cutaneous fungal infection; however, the KOH prep was nondiagnostic. The decision was made to start a systemic and topical antifungal regimen (oral terbinafine 250 mg daily for 14 days and 2% topical ketoconazole cream applied twice daily). Surgical treatment was postponed on account of the cutaneous fungal infection, which involved the region of the proposed surgical incision.

Results of the fungal culture identified *A. flavus* as the causative organism. Considering this culture result and the virulence of *A. flavus*, an Infectious Disease specialist at our institution was consulted and involved in the patient’s care. Weighing the associated risks and benefits of exposure to antifungal therapy vs the risks of deep infection in the setting of orthopaedic implants, a more cautious treatment regimen was recommended that provided the best chance to avoid deeper infection. At this time (2 weeks after antifungal treatment had been initiated), oral voriconazole was started at a loading dose of 400 mg twice daily for the first day, followed by 200 mg twice daily thereafter. Topical ketoconazole treatment was continued during this time, while oral terbinafine was discontinued. Baseline complete blood count with differential, kidney function tests, and liver function tests were obtained and within normal limits including a negative HIV antibody screening.

The patient was seen in the Dermatology Clinic 5 days later. At this point, he had received nearly 3 weeks of topical and systemic antifungal therapy. The patient showed marked clinical improve-

Figure 4. Clinical photograph showing a lateral view of the left upper arm after 3 weeks of oral and topical antifungal therapy, prior to open reduction and internal fixation of the distal humerus fracture.

Figure 5. Immediate postoperative anteroposterior (A) and lateral (B) radiographs of the left humerus after open reduction and internal fixation (ORIF).
ment with the above treatment regimen, and the superficial cutaneous lesions were completely resolved at this point (Fig. 4). After communicating once more with the Infectious Disease consultant, the patient was scheduled for surgery the following day.

On postinjury day 33, he underwent open reduction, internal fixation of the left distal humerus fracture. A posterolateral surgical approach was utilized, and extensive mobilization of the fracture fragments was required due to the significant degree of callus formation. The fracture was secured with multiple lag screws and a precontoured locking plate using a combination of nonlocking and locking screws (Fig. 5). Postoperatively, oral voriconazole was continued at 200mg twice daily for 1 month. Repeat complete blood count with differential, kidney function tests, and liver function tests were obtained and remained normal. At the 6 week postoperative follow-up appointment, the patient was doing well with no sign of deep or recurrent superficial infection. Radiographs showed maintained fixation and signs of fracture healing at the 3-month follow-up visit (Fig. 6). The patient had regained full elbow range of motion and had a normal neurovascular examination. The wound healed uneventfully and there were no signs of recurrent cutaneous fungal infection. He was discharged from further care with no restrictions.

3. Discussion

A *flavus* is the second leading cause of invasive aspergillosis and it is the most common cause of outbreaks of superficial infection, including those affecting the skin and oral/nasal mucosa.[9] *A flavus* grows better with water activity between 0.86 and 0.96. The optimum temperature for *A flavus* to grow is 37°C, but fungal growth can be observed at temperatures ranging from 12 to 48°C. This broad range of optimum temperatures contributes to its pathogenicity in humans.[10] *A flavus* has also been shown to be more prevalent in tropical air.[10] Cutaneous infection caused by *A flavus* is commonly classified as either primary or secondary. Specifically, primary infection is caused by direct inoculation, including intravenous catheter sites, traumatic inoculation, occlusive dressings, burns or surgery; secondary skin infection is from hematogenous spread.[9]

Treatment for disseminated aspergillosis in immunocompromised individuals is better delineated in the literature. However, there is a paucity of literature regarding the treatment of primary cutaneous aspergillosis in immunocompetent persons. It is understandable how it could have occurred in this case, as *A flavus* can be water-associated, especially if moisture stagnated beneath the stockinette after its initial placement following injury. The risks and benefits of exposure to antifungal therapy vs those of infected hardware were weighed, and treating physicians opted for a more aggressive antifungal regimen along with open reduction internal fixation to address malalignment of the distal third humeral shaft fracture. In this case, the patient had an excellent response to initial combination therapy including systemic and local antifungal agents. He ultimately tolerated continued systemic therapy with no complication or side effects. In general, treatment of cutaneous aspergillosis infection does not pose a risk to health care workers as long as they are immunocompetent.

The authors present here a case of primary cutaneous aspergillosis infection caused by *A flavus* in an immunocompetent individual with a closed distal humeral shaft fracture initially...
treated in a functional removable brace. In this case, the antecedent of his primary cutaneous infection was direct inoculation of *A. flavus* on the cutaneous surface of his arm, which was entrapped under stockinette creating a genial environment for this fungal species to grow and propagate for a prolonged period of time. To diminish the risk of similar infections, we recommend removal of functional removable braces every 1 to 2 days for visual inspection as well as hygiene (showering or sponge-bathing). We also provide patients with 2 or more stockinette sleeves so that one can be laundered and a clean stockinette placed each time after hygiene is performed. For patients who sustain closed fractures in freshwater environments, if patient comfort allows, thorough cleansing of the skin with antimicrobial soap and water should be performed prior to application of external immobilization devices. A complete inspection of the overlying skin envelope should be performed at the first follow-up visit, which ideally should be scheduled within a week of injury. If primary cutaneous aspergillosis infection is identified in this setting, we recommend early involvement of a multidisciplinary care team (including Orthopaedics, Dermatology, and Infectious Disease specialists). Bedside KOH prep and fungal culture should be performed, and an antifungal regimen comprised of a systemic and topical antifungal agent should be initiated. Modifications to the antifungal regimen should be made according to the fungal culture results. Operative fixation should not be considered until complete resolution of the cutaneous lesions. Finally, systemic antifungal therapy should be continued for a period of time after operative treatment in order to prevent cutaneous recurrence or deep fungal infection.

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