Open Forum Infectious Diseases

ID TEACHING CASES

Prosthetic Finger Joint Infection Due to *Aspergillus terreus*

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Fungal periprosthetic joint infections (PJIs) are rare but associated with significant mortality. We report a case of a finger PJI secondary to *Aspergillus terreus* in an immunocompetent patient with soil exposure, successfully treated with surgical debridement and voriconazole. Identification of *A terreus* is important because of intrinsic amphotericin B resistance.

Keywords. *Aspergillus terreus*; fungal prosthetic joint infection.

CASE

A 74-year-old female with a history of severe osteoarthritis of her bilateral hands underwent left ring finger proximal interphalangeal (PIP) joint arthroplasty with a silicone implant to improve functional use of the finger. At her 2-week postoperative follow up, her surgical wound was healing well. She presented 1 month after her initial surgery with complaints of acute redness, swelling, and pain at the surgical site. She also complained of a small blister at the surgical site that drained purulent fluid. She denied fever, chills, or weight loss. The patient did not have any other medical problems other than dry eyes for which she used artificial tears eye drops. She had not been on any antibiotics recently. She had no recent travel or any pets at home. She enjoyed gardening and liked creating miniature fairy gardens. She stated that she used soil and moss in her gardening. She also maintained several bird feeders at home that were noted to be moldy. Initial vitals were unremarkable, without fever. Physical examination revealed erythema and edema at the PIP joint of the left ring finger (Figure 1). A blister was noted that when unroofed, revealed a small sinus tract with purulent drainage. Laboratory work up revealed a normal white blood cell count, liver function, and kidney function tests. C-reactive protein was less than 0.5 mg/dL and erythrocyte sedimentation rate was 12 mm/hour. Human immunodeficiency virus testing was negative. X-ray of the left finger showed periprosthetic lucency and mild periosteal reaction at the middle phalanx suggesting osteolysis versus infection (Figure 2). Given concern for infection, the patient underwent irrigation and debridement of the left ring PIP joint. During the surgery, purulent material was seen, and the old implant was removed with placement of a new silicone implant. Joint fluid and tissue samples were sent for culture, which subsequently grew *Aspergillus terreus* in all 3 sets of cultures that were sent. Unfortunately, tissue was not sent for histopathology during the procedure. She was seen by an infectious diseases physician and was started on voriconazole. Given that she had a fungal PJI, the decision was made to remove the implant 2 months later to ensure eradication of infection. Tissue cultures sent during the explantation of the implant remained negative. She was continued on voriconazole for 3 additional months after the second surgery for a total of 5 months from initial surgery. At follow up, the patient had a well healed incision with no motion at the PIP joint but good range of motion at the distal interphalangeal joint and metacarpophalangeal joint at which time voriconazole was stopped. Plans were made to consider reimplantation arthroplasty or fusion of the joint at 3 to 6 months after stopping antifungal medications. At 1-year follow up, the incision was well healed (Figure 3) and the patient did not have any pain or swelling. She was able to do all her daily activities including lifting weights, knitting, and sewing. Therefore, the decision was made to not reimplant or fuse the joint. At 2-year telephone follow up, the patient continued to do well with no concerns for infection.

PATIENT CONSENT STATEMENT

The patient's written consent was obtained.

DISCUSSION

Aspergillus species are ubiquitous in nature, and infection may occur after inhalation of conidia or through direct inoculation. Infection is uncommon in immunocompetent patients

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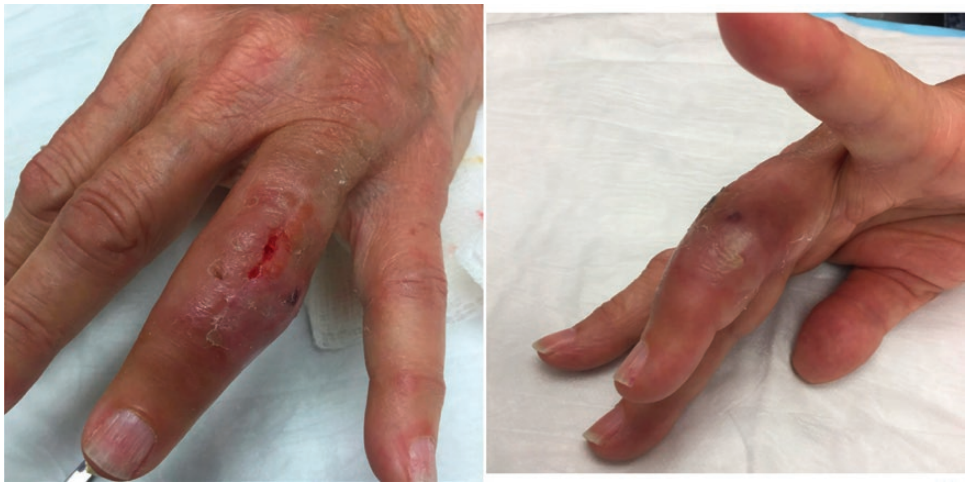

Figure 1. Swelling and erythema demonstrated at the left ring finger proximal interphalangeal (PIP) joint. Slight wound dehiscence with purulent drainage noted from this area. Exam noted minimal motion at the PIP joint.

and occurs most frequently in the setting of immunosuppression associated with therapy for hematologic malignancies, hematopoietic cell transplantation, and solid organ transplantation. Most invasive infections are caused by members of the *Aspergillus fumigatus* species complex, followed by *Aspergillus flavus*, *Aspergillus niger*, and *A terreus* [1, 2].

Aspergillus terreus is a thermotolerant fungus found worldwide in soil, compost, dust, and decaying plant matter [3]. It is an industrially relevant fungus because its metabolites lovastatin and itaconic acid have been used as a cholesterol-lowering drug and in the polymer industry, respectively [4]. *Aspergillus terreus* is cinnamon brown in color in slide culture, unique among common *Aspergillus* species, and gets darker as it ages while maintaining a nonpigmented reverse (Figure 4). *Aspergillus terreus* conidia are small (2.0 to 2.5 μm), smooth walled, and can be light yellow in color. Unique to this species is the production of aleurioconidia (Figure 5) [3]. *Aspergillus terreus* has been recognized as an emerging opportunistic fungus that constitutes 4% of all invasive aspergillus infections [5]. *Aspergillus terreus* can cause a spectrum of disease including invasive pulmonary infections, allergic bronchopulmonary aspergillosis, bronchitis and/or tracheobronchitis, and disseminated aspergillosis including at extrapulmonary sites such as the skin, brain, heart, etc [3, 6, 7]. Identification of this species has become increasingly important because of its intrinsic resistance to amphotericin B [8]. *Aspergillus terreus* infections are associated with higher mortality and treatment failure than infections due to other *Aspergillus* species. Although there are not antimicrobial susceptibility breakpoints, voriconazole is considered first-line treatment because of superior outcomes [9].

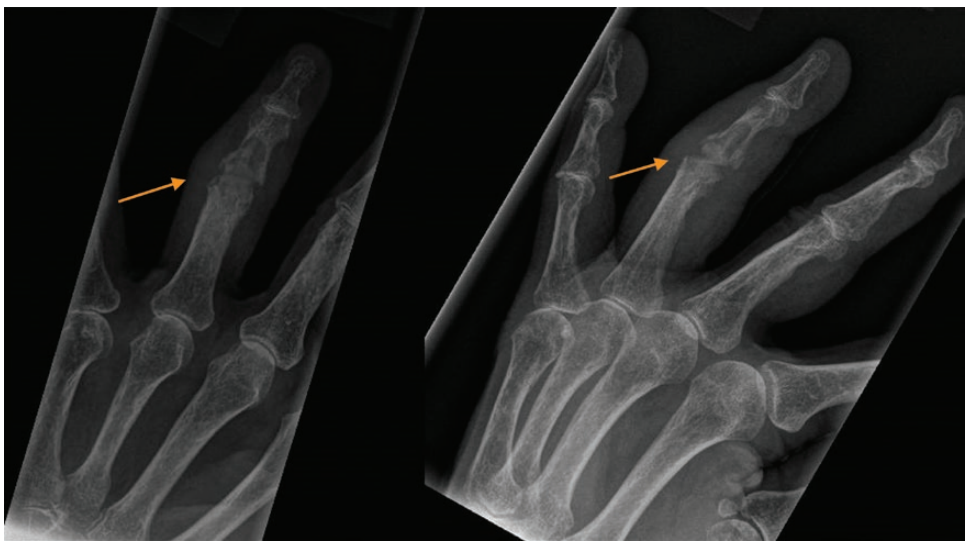

Figure 2. X-ray of left ring finger showed periprosthetic lucency and mild periosteal reaction at middle phalanx concerning for infection.

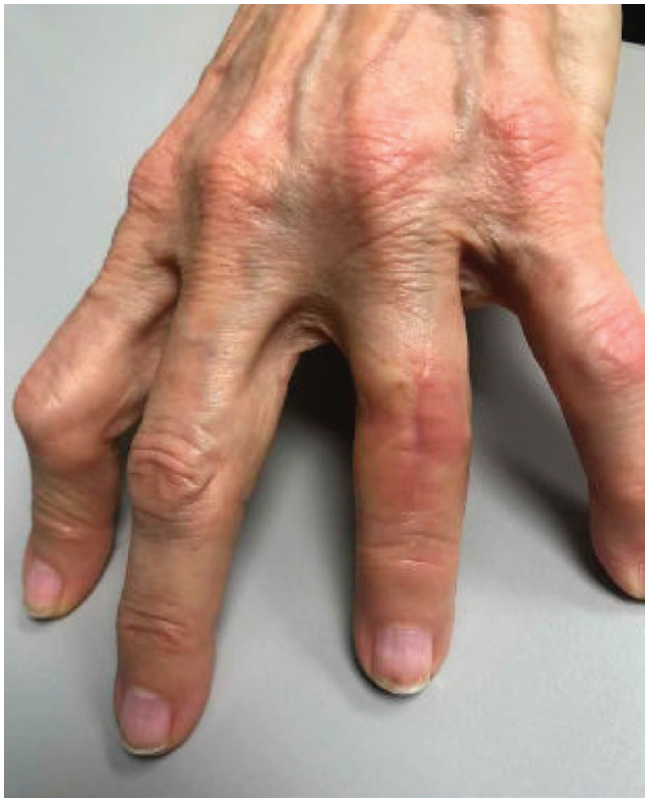

Figure 3. No swelling or erythema seen at 1-year follow up.

Fungal periprosthetic joint infections (PJIs) are rare and account for approximately 1% of all PJIs, with the majority of cases attributed to *Candida* species [10]. Prior bacterial PJI, preceding antimicrobial use, immunosuppressive therapy, and diabetes have been suggested as risk factors [11, 12]. Periprosthetic joint infections due to *Aspergillus* spp are extremely rare with several of the reported cases occurring in immunocompetent

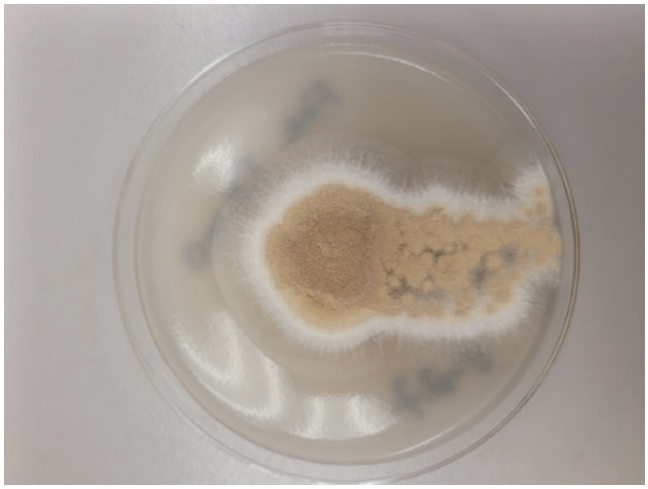

Figure 4. *Aspergillus terreus* complex grow moderately rapidly on potato flake media to form a cinnamon-brown velvety colony.

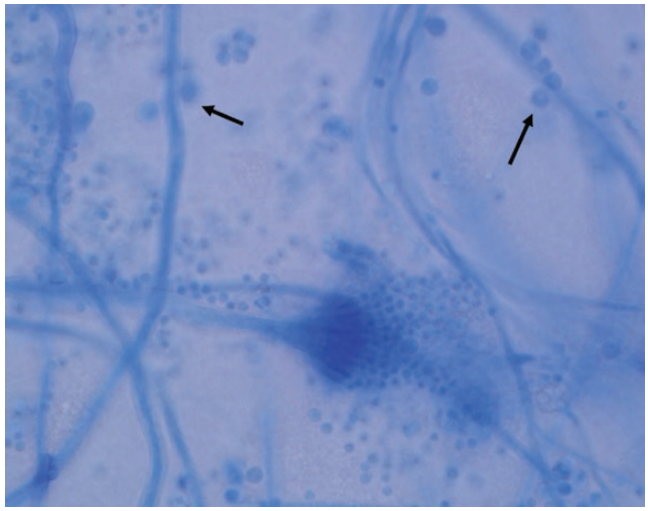

Figure 5. *Aspergillus terreus* complex produce vesicle with biseriate phialides over the top half. Aleurioconidia (asexually reproduced conidia) are indicated (lactophenol aniline blue, ×1000).

individuals [10, 13]. A review of the literature from 1967 to 2015 identified only 31 reported cases of *Aspergillus* arthritis [14]. In the article, 55% of the patients were immunocompromised with conditions such as neutropenia, chronic steroid use, diabetes mellitus, etc and likely had hematogenous seeding of their joints. Our patient who was immunocompetent likely acquired the infection through direct inoculation as suggested in this article. We postulate that our patient acquired her infection through direct inoculation of her incision with the organism while gardening. Soil in potted plants has been postulated as a source of nosocomial *Aspergillus* infections [15]. Clinical manifestations include pain (87%), edema (26%), and limited function (23%), with knees (35%), intervertebral discs (26%), and hips (16%) being most commonly affected. *Aspergillus fumigatus* constituted 77% of cases followed by *A flavus* in 13%, *A niger* in 3%, and species not specified in 7% [14]. A review article on *Aspergillus* osteomyelitis (excluding septic arthritis and PJI) by Gamaletsou et al [16] demonstrated *A terreus* as the etiology of infection in only 3% (5 of 180) of the cases. There are only a handful of PJIs secondary to *A terreus* reported to date [14, 17, 18]. To the best of our knowledge, our case is the first case of a finger PJI secondary to *A terreus*.

Diagnosis of fungal PJI is made by histopathological examination and culture in concert with clinical and radiological findings. Although tissue was not sent for histopathology in our case, it is an important tool to define the diagnostic significance of positive culture results when contamination is suspected. *Aspergillus terreus* infections may produce high levels of serum galactomannan; however, serum galactomannan was negative in our case and the other PJI case reported in the literature due to *A terreus* [18]. This is likely because these infections are limited to the joint and are not disseminated. Therefore, PJI should

still be suspected in the presence of negative serum fungal markers. If *Aspergillus* species is isolated from a joint, it should be considered a true pathogen and treated appropriately [14].

Fungal PJIs are not only difficult to diagnose but are challenging to treat. Guidelines for the treatment of PJI published by the Infectious Diseases Society of America (IDSA) do not address the treatment of fungal PJIs [19]. However, IDSA guidelines on management of *Aspergillus* infections do recommend voriconazole as first-line treatment for all invasive aspergillus infections with liposomal amphotericin B and isavuconazole as alternative options [20]. Successful treatment of fungal PJIs including infections caused by *Aspergillus* spp require both a surgical and medical approach [17, 21]. According to a review of 31 reported *Aspergillus* cases, 19 patients (61%) were managed with combined medical and surgical therapy, 10 (32%) with medical therapy only, and 2 (6%) surgery only [14]. Amphotericin B and itraconazole were the most frequently used agents with median duration of therapy of 219 days (range, 30–545). Complete response of *Aspergillus* arthritis was achieved in 22 cases (71%), partial response in 5 (16%), relapse in 5 (16%), and death in 11 (35%). Voriconazole is the drug of choice for first-line treatment of infections due to *A terreus* because this organism is inherently resistant to amphotericin B [3, 22]. Limited data are available for itraconazole, posaconazole, isavuconazole, or caspofungin. There are reports of cases successfully treated with posaconazole, whereas the resistance rate of *A terreus* to posaconazole in European countries was reported to be approximately 5% [18, 23]. In our case, the patient was treated with voriconazole for 5 months with removal of the infected prosthesis and resolution of infection. A patient with *Aspergillus terreus* PJI in a total elbow arthroplasty was successfully treated with 2 debridements followed by definitive resection arthroplasty and 8 weeks of caspofungin, followed by a short course of voriconazole [12]. Another case of PJI due to *A terreus* in a total hip arthroplasty was treated with resection of hardware and posaconazole although the duration of treatment was not mentioned [18]. Given the association with higher mortality and treatment failure, prospective studies are needed to investigate the optimal agent and the treatment duration for PJI due to *A terreus*.

CONCLUSIONS

Fungal periprosthetic joint infection due to *Aspergillus* species is rare but is associated with significant cost and morbidity. *Aspergillus* spp need to be considered as an etiology of joint infection even in immunocompetent patients. Identification of *A terreus* has become increasingly important because of its intrinsic resistance to amphotericin B, and treatment with voriconazole is associated with better outcomes.

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