Fusarium incarnatum/equiseti hemodialysis graft infection

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Abstract

Hemodialysis graft infections typically occur as a result of contamination by skin flora at the time of insertion or become secondarily infected after high-grade bacteremia. Infection of implanted vascular devices with filamentous fungi is rare. We report a case of infection of an implanted polytetrafluoroethylene dialysis graft with *Fusarium incarnatum/equiseti* that did not grow in cultures of tissue but was identified by molecular means.

Case Report

A 58-year-old woman with Crohn's disease, nephrolithiasis, and chronic renal insufficiency secondary to obstructive nephropathy required placement of a dialysis graft prior to the initiation of hemodialysis. The procedure was performed in a tertiary care hospital operating room. She was not receiving immunosuppressive agents for her Crohn's disease. Within 48 hours after placement of the graft she developed yellowish drainage, pain, erythema, and swelling at the distal incision just proximal to the antecubital fossa. She received multiple courses of treatment with oral cephalexin and IV vancomycin, without improvement in her symptoms. Over a period of a month she developed an enlarging, firm, nodular lesion at the site of her distal incision (Figure 1). She subsequently underwent surgical exploration and debridement. The graft was found to be poorly incorporated and was removed, as was the firm cyst-like lesion (Figure 2: histopathology). Fungal cultures of the tissue and graft were sterile. *Fusarium incarnatum/equiseti* species complex DNA was detected with a 28S primer set by the University of Washington Department of Laboratory Medicine from fresh tissue (not fixed in formalin).

Discussion

Fusarium is a ubiquitous mold found in soil and water and is a common pathogen of plants and stored grains. It is considered to be an agent of hyalohyphomycosis, which is defined as a human infection with a saprophytic mold with hyaline, branched or unbranched, hyphal elements without the presence of pigment in the cell wall.[1] Other common species in this group include *Aspergillus*, *Scopulariopsis*, *Pseudallescheria*, and *Scedosporium*. There are over 50 species contained within the *Fusarium* genus. The species most commonly associated with human disease are *Fusarium solani* (50%), *F. oxysporum* (20%), and *F. verticillioides* (10%).[2] Other less common species include *Fusarium chlamydosprum*, *F. dimerum*, as well as *F. incarnatum/equiseti*.

Fusarium species most often cause infection in immune compromised hosts such as stem cell transplant recipients or patients with prolonged neutropenia.[2,3] The usual portal of entry is the respiratory route versus direct inoculation of cutaneous structures or foreign bodies such as central venous catheters. Sinopulmonary disease and subsequent dissemination can occur in susceptible patients. In contrast to other filamentous fungi, *Fusarium* can be cultured from the blood in cases of disseminated disease. The dermatological manifestations of disseminated fusariosis consist of subcutaneous nodules or ecthyma-like skin lesions occasionally observed with a targetoid appearance with surrounding erythema. Other clinical syndromes include keratitis associated with contaminated contact lenses, endophthalmitis, onychomycosis, cutaneous infections from direct inoculation, and catheter/foreign body-associated infection. *Fusarium* infection of a dialysis access graft has not been reported previously. In our case, it is unknown how the implanted polytetrafluoroethylene dialysis graft became contaminated. The device had not yet been accessed for hemodialysis and no clinical evidence of disseminated disease was identified elsewhere. Thus, the device itself could have been contaminated prior to, or at the time of surgical implantation. No other cases of procedure-related invasive fungal infections were reported from the operating suite by the hospital's infection control surveillance team.

The cornerstone of treatment for patients with localized infection or infection of foreign bodies is surgical debridement, with removal of

all infected material, particularly any foreign bodies such as surgical implants. Antifungal therapy is also important in localized infection as well as disseminated disease. The best antifungal agent for the treatment of *Fusarium* infection has not been defined. For the most common *Fusarium* species: *F. solani* and *F. ver-*

Figure 1. Appearance of the right antecubital fossa prior to surgical resection.
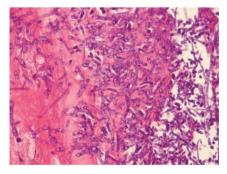

Figure 2. Hematoxylin and eosin stain of resected tissue (magnification 400X).

ticullioides, an amphotericin B preparation is considered to be the treatment of choice by some authors.[2] *In vitro* studies have shown that MICs to voriconazole and posaconazole are >8.0 μg/mL in these species while amphotericin B susceptibility is preserved in the 1.0 μg/mL range.[4,5] For the less common species such as *F. incarnatum/equisiti* there is less data. In a study that evaluated *in vitro* susceptibilities of this species from nine clinical isolates from India and Chile, the voriconazole MIC was 2-4 μg/mL with comparable posaconazole MICs.[6] Therefore, some experts have concluded that if *F. solani* or *F. verticillioides* is identified, high-dose amphotericin B should be used, and for other species amphotericin B and/or voriconazole can be administered.[2]

Currently, voriconazole is the only drug that is FDA approved for treatment of *Fusarium* sp. in the United States. In licensing trials for voriconazole, out of 21 patients with invasive *Fusarium* infection, 9 or 43% had a favorable response to voriconazole.[7] Three of the nine patients who had a successful outcome had an infection with *F. solani.* No other randomized trials or large case series are available. One group has reported a breakthrough infection with resistant *Fusarium* sp. while on treatment with voriconazole.[8] However, many other published case reports have described successful treatment with voriconazole in cases of soft tissue infection, disseminated infection, and endophthalmitis.[9-14] Successful outcomes utilizing combination therapy consisting of voriconazole with amphotericin B products have also been reported in similar cases.[15-19] Less experience is available regarding the use of posaconazole; however, this may also be an effective drug.[20-22] The echinocandins have been found to have high MICs to *Fusarium* (>16 μg/mL) and thus should not be used for primary treatment. However, synergy of echinocandins with amphotericin B has been demonstrated *in vitro*.[23]

In our case, voriconazole rather than an amphotericin B product was used, as the patient had stage IV-V chronic kidney disease and was at high risk for the need for hemodialysis. Initial treatment was complicated by transaminitis, with a measured plasma voriconazole level of 3.8 μg/mL. The dose was decreased to achieve levels of 1.4-1.9 μg/mL, with resolution of liver enzyme elevation. After six months of therapy, the surgical wound had completely healed and treatment with voriconazole was discontinued. This case illustrates the benefits of molecular testing to identify pathogens that are difficult to grow. Identifying clinical *Fusarium* isolates to the species level has important implications for the selection of an appropriate therapeutic regimen.

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