

Fusarium Osteomyelitis of the Lower Extremity: A Two–Case Series Highlighting Diagnostic and Therapeutic Challenges



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Case 1

CASE 1

Prior healthy patient status post open reduction internal fixation (ORIF) of the left great toe, followed by a prolonged, evolving bone and joint infection.

- **Index surgery:** ORIF of the left great toe proximal phalanx and medial sesamoid.
- **Month 1:** Postoperative wound infection → I&D; cultures grew *Klebsiella oxytoca* and *Enterococcus faecalis*; treated with oral antibiotics.
- **Month 4:** MRI negative for abscess/osteomyelitis. Hardware removed—cultures grew coagulase-negative staphylococci and *Corynebacterium* sp. No improvement despite antibiotics; persistent deep pain and drainage.
- **Month 5:** Repeat I&D of the left 1st MTP joint—cultures grew *Aspergillus terreus*. PICC placed; started IV vancomycin and oral voriconazole.
- **Month 6:** Subtherapeutic voriconazole level (dose increased). Wound dehiscence after suture removal → repeat I&D/washout and bone biopsy again grew *Aspergillus*; IV micafungin added.
- **Month 7:** Further I&D—bone/tissue culture grew *Fusarium* species, speciated at a reference laboratory as *F. brachygibbosum* (*Fusarium sambucinum* complex); isolate essentially pan-resistant in vitro (see Results).
- **Month 8:** Escalated to triple antifungal therapy (micafungin + voriconazole + amphotericin B); electrolyte wasting (K, Mg, Ca) managed with supplementation.
- **Month 9:** Immunology workup revealed an underlying **IgG subclass deficiency**; enrolled in an investigational protocol for **fosmanogepix** given the refractory course.
- **Months 9–10:** Transitioned IV → oral fosmanogepix 800 mg BID; amphotericin B discontinued for drug-associated AKI; wound steadily improved.
- **Months 11–12:** Wound healed; regained full, pain-free ambulation; completed a half marathon.
- **Ongoing:** Maintained on long-term oral fosmanogepix plus IVIG/SCIG replacement for IgG deficiency.
- **Most recent follow-up (~2 years):** Incision well-healed, only mild residual stiffness on passive ROM; completed a 25-mile race and training for a 126-mile ultramarathon—full functional recovery.

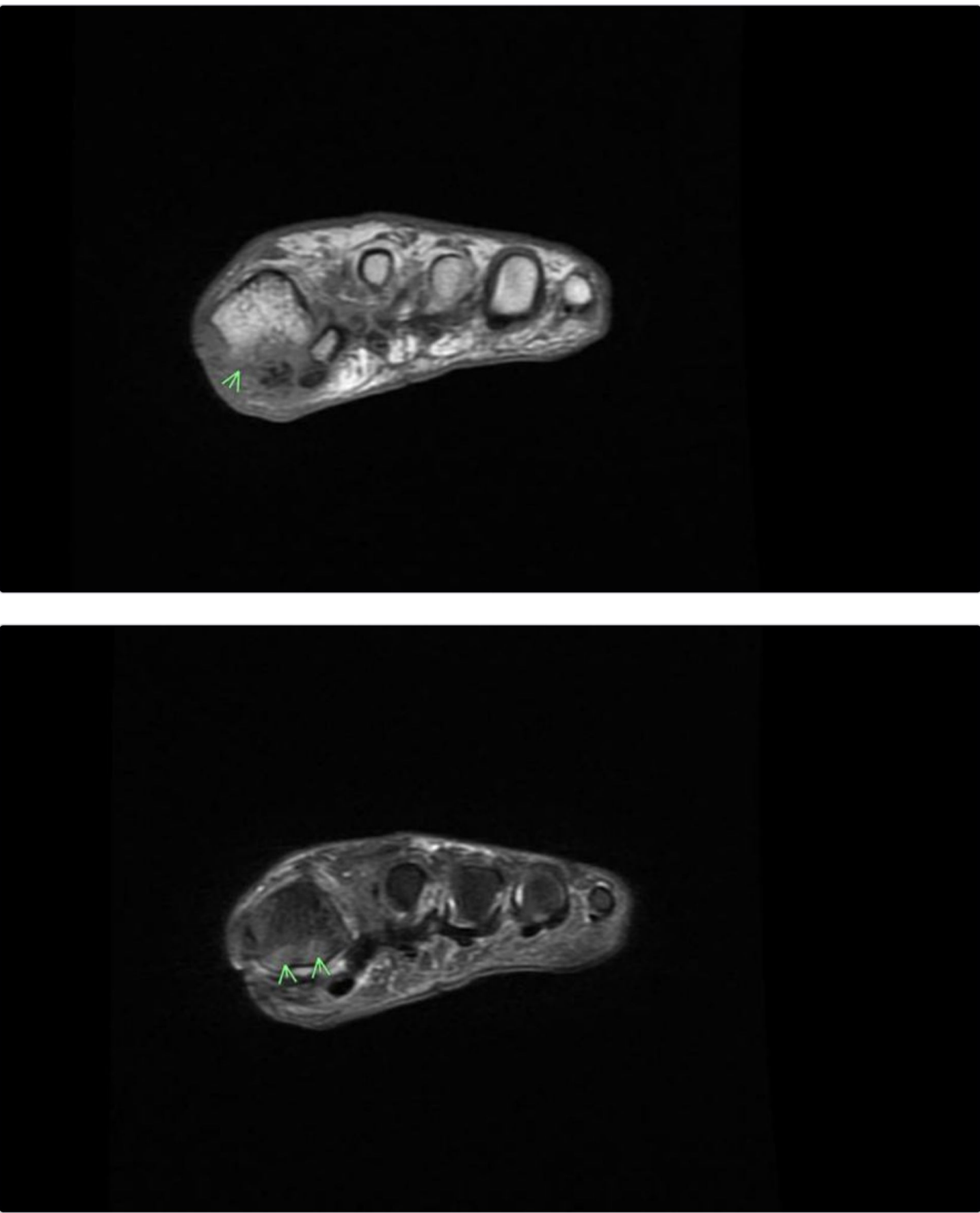


Figure 1. Coronal T1 (left) and fat-saturated PD (right) MRI of the left forefoot, same level. Signal abnormality centered at the first metatarsal head (arrows) prompted biopsy, ultimately yielding *Fusarium brachygibbosum*.

Case 2

CASE 2

65-year-old woman with congestive heart failure, atrial fibrillation on anticoagulation, and type 2 diabetes.

- **Presentation:** Sepsis with group B *Streptococcus* bacteremia complicated by cervical/lumbar epidural abscess-discitis (I&D ×2), an abdominal wall abscess (drained), and a right empyema (chest tube). Treated with 6 weeks IV penicillin.
- Lumbar wound failed to heal → operative re-exploration, duraplasty; cultures negative.
- Re-admitted for a full-thickness right knee wound with concern for gangrene.
- **Intra-operatively:** extensive, cadaveric-appearing necrosis of the proximal tibia—described by the operating surgeon as among the most severe bone necrosis/infection encountered in a combined ~20 years of practice.
- Tibial bone / pes tendon cultures: *Fusarium* sp. with scant *C. albicans* and *C. parapsilosis*; tibial bone fungal culture: yeast.
- → **Right above-knee amputation** for source control.
- +2 days: lumbar wound dehiscence—bone (spinous process): *C. auris*, *C. albicans*; soft tissue: *C. auris*, vancomycin-resistant *E. faecium*.
- +5 days: left leg wound debrided and closed—subcutaneous tissue: *Fusarium* sp. with scant yeast.
- *Fusarium* isolate pan-azole non-susceptible (see Results); amphotericin B MIC 1 µg/mL.
- Antifungal therapy: IV micafungin ×3 months → long-term oral isavuconazole (combined *Fusarium/Candida* coverage).
- ~4 months later: new sacral wound—plain films unremarkable, MRI showed sacral osteomyelitis/discitis; bedside bone biopsy grew MSSA, *Pseudomonas aeruginosa*, anaerobes; blood culture (1/2 bottles): *Streptococcus anginosus*.
- **Outcome:** transitioned to hospice; patient died.



Figure 2. (Left) Left lower-extremity wound with exposed necrotic tissue at the time of debridement; subcutaneous tissue culture grew *Fusarium* species. (Right) Coronal MRI of the right tibia/fibula showing extensive marrow signal abnormality spanning the proximal tibia (8.81 cm)—the site of fungal osteomyelitis preceding above-knee amputation.

Introduction

- *Fusarium* species are ubiquitous environmental molds and increasingly recognized opportunistic pathogens.
- In immunocompromised or critically ill hosts, *Fusarium* can cause disseminated disease with cutaneous, soft-tissue, and—rarely—osteoarticular involvement.
- Intrinsic resistance to most azole antifungals is common, severely limiting standard treatment options.
- We report two culture-confirmed cases of *Fusarium* musculoskeletal infection managed in Southern Arizona, illustrating divergent diagnostic pathways and outcomes—one salvaged with source control, immunologic workup, and a novel antifungal; one fatal despite maximal therapy.

Materials & Methods

- Retrospective case series; chart review of patients with culture-confirmed *Fusarium* musculoskeletal infection at a Southern Arizona academic medical center.
- Clinical, microbiologic, and antifungal susceptibility data (CLSI M38 broth microdilution) abstracted from the medical record.
- Patient identifiers removed in accordance with institutional case-report policy.

Results

ANTIFUNGAL SUSCEPTIBILITY (MIC, MG/ML)

Case	Organism	AMB	MICA	ITRA	POS	VORI	ISAV	MGX
1	<i>Aspergillus terreus</i>	0.5	≤0.015	≤0.03	0.06	0.125	—	—
1	<i>Fusarium brachygibbosum</i>	4	>8	>16	>16	16	>16	≤0.008
2	<i>Fusarium</i> sp.	1	—	>16	>16	>16	>16	—

CLSI M38 broth microdilution. AMB amphotericin B; MICA micafungin; ITRA itraconazole; POS posaconazole; VORI voriconazole; ISAV isavuconazole; MGX manogepix (active moiety of investigational fosmanogepix). No CLSI interpretive breakpoints are established for *Aspergillus* or *Fusarium* spp. against most agents; MICs shown for reference only.

CASE 1 – CULTURE PROGRESSION

Timepoint	Source	Organism(s)
Month 1	Left foot wound	<i>K. oxytoca</i> , <i>E. faecalis</i>
Month 4	Hardware / wound	Coag-neg staph, <i>Corynebacterium</i> sp.
Month 5	Left 1st MTP (I&D)	<i>Aspergillus terreus</i>
Month 6	Left 1st MTP (bone biopsy)	<i>Aspergillus</i> sp.
Month 7	Left 1st MTP head (bone)	<i>Fusarium brachygibbosum</i>

CASE 2 – MULTI-SITE MICROBIOLOGY

Site	Organism(s)
Right tibia / pes tendon	<i>Fusarium</i> sp.; scant <i>C. albicans</i> , <i>C. parapsilosis</i>
Lumbar spinous process (bone)	<i>C. auris</i> ; <i>C. albicans</i>
Left LE subcutaneous tissue	<i>Fusarium</i> sp.; scant yeast
Sacral bone (biopsy)	MSSA, <i>P. aeruginosa</i> , anaerobes
Blood (1 of 2 bottles)	<i>Streptococcus anginosus</i>

Full site list in the clinical timeline (Case 2); femoral marrow at the amputation margin was culture-negative.

Discussion & Conclusion

- Musculoskeletal *Fusarium* infection should be considered in patients with atypical, indolent, or treatment-refractory wounds—particularly when initial bacterial or *Candida/Aspergillus* cultures fail to explain a worsening course.
- Intrinsic pan-azole resistance, seen in both isolates here, is common; amphotericin B retains variable in vitro activity, and clinical response remains unpredictable.
- Case 1 responded to aggressive source control, an underlying immunodeficiency work-up, and salvage therapy with investigational fosmanogepix—to which the isolate was highly susceptible in vitro—achieving full functional recovery.
- Case 2, with multifocal disease across bone, joint, and soft tissue in a critically ill host, progressed despite amputation and prolonged combination antifungal therapy and was ultimately fatal.
- Early recognition, source control, susceptibility-guided therapy, and evaluation for underlying immune dysfunction are central to improving outcomes in this rare but consequential infection.

References

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