CASE REPORT

The mysterious joint: Septic arthritis and acute osteomyelitis due to *Fusarium* species in a child with type II Chiari malformation

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Fungal bone infection due to *Fusarium* species is unusual. We report a case of a child who presented with septic arthritis and osteomyelitis due to *Fusarium* species. The lack of clinical trials and the organism's intrinsic resistance to most antifungal agents make antimicrobial management difficult. Our patient attained a favourable response to therapy with amphotericin B and voriconazole. This case report highlights a rare manifestation of joint- and bone-related *Fusarium* infection in a child.

Keywords: *Fusarium* infection, septic arthritis, osteomyelitis, spina bifida, fusariosis

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Fusarium is a large genus of filamentous fungi that is ubiquitous, typically known for its mycotoxin production and related plant and animal pathogenicity.[1,2] It belongs to the *Ascomycota* division and comprises >300 species, with ~10 complexes thought to be associated with human pathology.[3,4] Infections by this mould are highly dependent upon the portal of entry and host immune status; superficial clinical manifestations such as keratitis and onychomycosis predominate in healthy hosts, while more disseminated disease occurs in the immunocompromised.[5,6]

The most typical cause of acute septic arthritis in children of all ages is *Staphylococcus aureus*.[7] Data on fusariosis with bone or joint involvement are scarce, with limited case reports in immunocompromised children, where the condition usually arises in the setting of cutaneous damage.[8,9] Owing to the paucity of clinical trials and the critical role of immune reconstitution on clinical outcome, the optimal treatment strategy for patients with *Fusarium* infection remains unclear.[8,10]

We report a rare, and to our knowledge, the first case of septic arthritis and osteomyelitis due to *Fusarium* species in a paediatric patient in South Africa (SA).

Case presentation

A 7-year-old child with lower limb diplegia due to congenital Chiari II malformation presented to the paediatric emergency unit at a tertiary-level hospital following a local clinic referral for a left moderately swollen knee joint. Two weeks prior, she had experienced accidental bilateral lower limb superficial scald burns while exiting the bathtub, simultaneously sustaining a fall onto her left knee. The insidious unilateral swelling was first noticed by primary care nursing practitioners during routine burn wound inspection and dressing changes.

The patient had impaired lower limb sensorimotor function and no sphincter control, owing to the Chiari II malformation, for which a postnatal myelomeningocele repair had been done. Crawling had thereafter become her primary mode of mobility. Her caregiver claimed an up-to-date immunisation history (Road to Health card unavailable for confirmation) and an alleged left leg fracture at the age of 9 months, for which further information was unavailable.

Marked swelling, warmth, a ballotable patella and reduced joint range of motion were pertinent findings on a focused clinical examination of the left knee. She was wheelchair-bound, comfortable in room air and apyrexial, and had no palpable lymphadenopathy. Her vital signs were essentially normal, and the remainder of the systemic examination was unremarkable. Osteosarcoma, haematoma secondary to trauma and subacute osteomyelitis were the differential diagnoses entertained at this stage.

Plain radiographs revealed a periosteal reaction along the distal cortex of the left femur, with Codman's triangle just proximal to the metaphysis, including a sunburst appearance. Magnetic resonance imaging and a bone scan with non-enhanced computed tomography (CT) showed an aggressive lesion with peri-articular soft tissue swelling, a large knee joint effusion, marrow oedema and a pathological fracture (Figs 1 and 2). In addition to scintigraphy, the findings were highly suggestive of left knee septic arthritis and osteomyelitis of the left distal femur. Normal chest imaging and abdominal ultrasound investigations made osteosarcoma a less favourable diagnosis.

Intravenous (IV) cloxacillin 500 mg 6-hourly was commenced, while microbiological analysis from joint fluid aspiration observed scanty leucocytes and no organisms on Gram stain. Cytopathology showed scattered lymphocytes and neutrophils, with an absence of malignant cells. Tuberculosis culture and Xpert MTB/RIF Ultra, including bacterial culture, were negative. *Fusarium* species was isolated following standard operating procedural work-up in the mycology laboratory. The specimen was inoculated on blood agar plus gentamicin and Sabouraud dextrose agar plus chloramphenicol

plates and slopes, and incubated aerobically for 6 - 8 weeks at 34 - 36°C and 24 - 26°C, respectively. After 4 - 5 days, the macroscopic appearance comprised the growth of a fluffy white mould bearing an initial slightly pink centre, later becoming brownish-green, with a white periphery and light reverse (Fig. 3).

Microscopic morphological characteristics present on lactophenol cotton blue staining included septate hyphae with abundant hyaline small ovoid microconidia and typical canoe-shaped macroconidia (Fig. 4, panel A and B). A rapid test for HIV was negative and, apart from a raised erythrocyte sedimentation rate of 29 mm/h, blood laboratory investigations were within normal ranges.

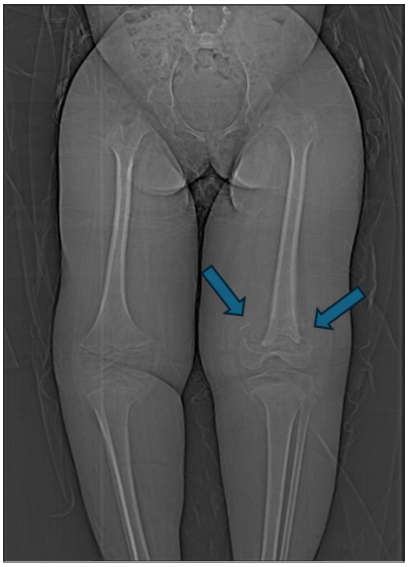

Fig. 1. Bone scan showing evidence of left knee septic arthritis and osteomyelitis.

Due to the unavailability of voriconazole at the time, monotherapy with IV amphotericin B deoxycholate at a dose of 1 mg/kg/day was initiated. Owing to persistent and worsening adverse effects (hypokalaemia and elevated urea and creatinine) despite adequate pre-hydration, this was stopped after a week, and IV liposomal amphotericin B at a dose of 5 mg/kg/day was subsequently prescribed, resulting in better tolerability. Orthopaedic clinical assessments noted satisfactory improvement, and did not recognise any indications for surgical intervention. Following 14 days of IV amphotericin B in total, the patient was switched to oral voriconazole at a dose of 9 mg/kg 12-hourly for 6 weeks, and discharged home. An outpatient review a month later noted a complete resolution of symptoms and return to prior functioning, and voriconazole was continued at the same dose for an additional month, for a total of 3 months of antifungal treatment. A work-up to exclude an inborn error of immunity was performed, including total immunoglobulins, B- and T-cell subsets, vaccine response assessment and neutrophil oxidative burst testing, all of which were within normal limits. The only abnormal finding was a mildly reduced absolute natural killer cell count of 60 cells/μL (reference: 100 - 400), which was considered clinically insignificant but recommended for repeat evaluation.

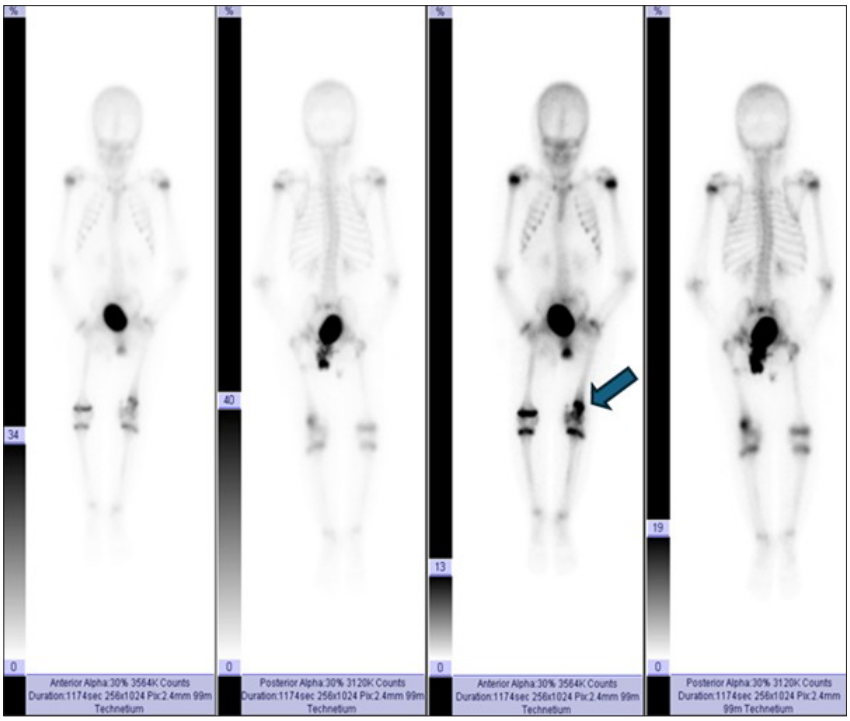

Fig. 2. Whole-body bone scintigraphy demonstrating increased radiotracer uptake in the left distal femur and proximal tibia.

Discussion

Fusarium is a growing opportunistic pathogen that primarily leads to invasive fungal infections in immuno-compromised patients, particularly those with neutropenia, severe T-cell immuno-deficiency, or those undergoing long-term corticosteroid therapy.[9,11,12] With a varying incidence across geographical regions, it is the second most common pathogenic mould after *Aspergillus* implicated in infection among those with haematological malignancies.[10,12,13]

In immunocompetent patients, it manifests more superficially, where tissue breakdown secondary to traumatic injury, severe burns, or foreign body are key risk factors.[12] In this regard, contributing elements to our case could be multifactorial, taking cognisance of the various potential scenarios: skin breach from the superficial burns may have resulted in organism colonisation and eventual infection; the bathtub fall onto the affected joint possibly created a direct contact portal of *Fusarium* species entry and infection nidus; or the knee bump from crawling around potentially contaminated surfaces may have been the traumatic inciting event that was unknown to the patient, given her sensorimotor impairment.[14]

Owing to static and dynamic changes of imbalanced bone modelling in children with spina bifida, an association between increased osteoporotic bone, atypical lower limb fractures and excessive periosteal reaction in this cohort of patients has been documented.[15] The left leg fracture >6 years ago may have predisposed the limb to future infectious insult, considering the uncertain history and lack of clinical information and management details surrounding that particular occurrence.[14]

Fusarium species is widely distributed in soil and plant debris, with *Fusarium solani* species complex most frequently involved in human pathogenicity, accounting for approximately two-thirds of all infections, followed by *Fusarium oxysporum* species complex.[9,10,13] Angioinvasion, direct tissue destruction, adherence to prosthetic material and the production of proteases and collagenases represent virulence factors from a pathophysiological perspective of invasive disease.[9]

Laboratory isolation of *Fusarium* species from an infected site constitutes a definitive diagnosis.[9,10] According to the European Society of Clinical Microbiology and Infectious Diseases and European Confederation of Medical Mycology joint guidelines, direct microscopy, culture and histopathology are recommended as essential

Fig. 3. Fusarium *species isolated in this case, cultured in Sabouraud dextrose agar plus chloramphenicol.*

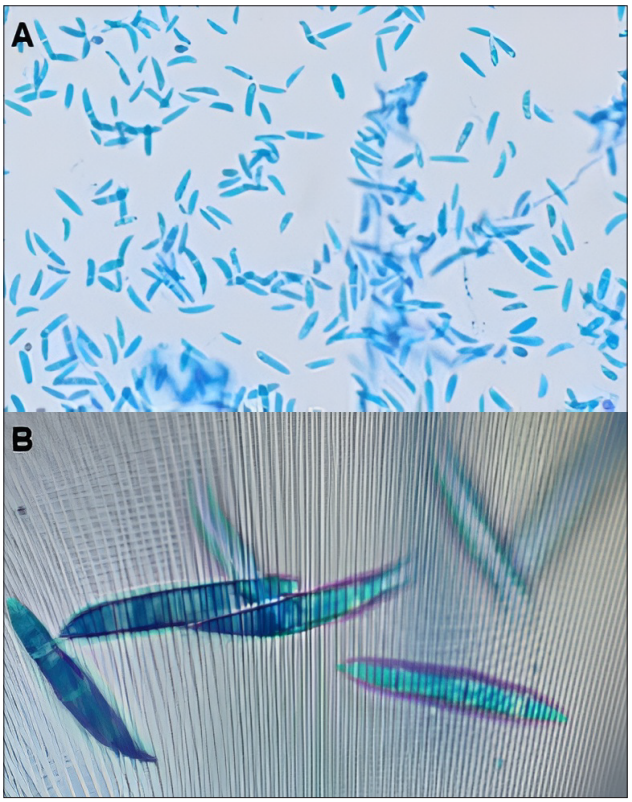

Fig. 4A and B. Lactophenol cotton blue stains in this case. Panel A: hyphae with macroconidia (10× magnification). Panel B: sickle-shaped macroconidia (40× magnification).

investigations in this regard, while CT scan is the imaging modality of choice in haematological patients.[10] Macroscopically, *Fusarium* grows rapidly on media without cyclohexamide, producing a lavender, pink, or grey-coloured cottony-textured surface and pale, cream, brown, or sometimes blue reverse.[2,9] Distinctive microscopic features of the genus *Fusarium*, as present in this case, include hyaline acute-branching septate hyphae with multicellular banana-shaped macroconidia and unicellular ovoid to cylindrical microconidia.[12] Molecular-based identification platforms such as polymerase chain reaction appear promising, and can be used for speciation by reference laboratories to supplement conventional tests.[9,10,16]

Fusarium infection of bone is unusual.[14] A literature review of osteomyelitis caused by *Fusarium* species performed by Hiebert *et al.*[8] identified 10 case reports from the preceding 40 years, with 4 cases occurring in healthy patients. A multicentre retrospective study of invasive fusariosis in intensive care units in France from 2002 to 2020 implicated arthritis (5%) and skin lesions (25%) in 55 patients meeting eligibility criteria.[17] During 2018 - 2023, *Fusarium* species was cultured in 92 patients in KwaZulu-Natal Province, SA, with 37% of specimens belonging to sterile sites (Prof. K Swe Swe-Han, personal communication). In immunocompetent hosts, an indolent presentation may occur, and organism introduction, usually a result of an open wound or penetrating injury, may precede overt infection by a year or longer.[14]

The ideal antimicrobial management for *Fusarium* infection is unknown, owing to the lack of clinical trials and insufficient data availability.[9,10,14] The relative *in vitro* resistance and high minimum inhibitory concentrations to many antifungals make therapy for invasive fusariosis a challenge.[9,13] The reversal of immunosuppression is recommended whenever possible, as mortality in these patients ranges between 50 and 80%, with host immune status being the single most important factor predicting outcome.[12] Optimal surgical source control along with early antifungal therapy is advocated for localised disease in order to halt progression; however, in our case, only a needle aspiration of the joint was performed.[10] Although epidemiological cutoff values have been investigated for *Fusarium* species, clinical breakpoints are yet to be established, precluding routine *in vitro* susceptibility testing.[9,18] Reports of anecdotal successes and the latest literature from published case reports incorporate various antifungal regimen recommendations, either as monotherapy or with combination agents.[8-10,12,14] Our patient was treated with antifungal therapy for 3 months without surgical intervention, from which marked symptom resolution and a satisfactory clinical outcome were achieved.

Teaching points

Clinicians should suspect fungal aetiology in similar scenarios, given the preceding clinical history and potential entry portals contributing to the pathophysiology, together with the absence of other positive laboratory findings.

Study limitations

Identification of *Fusarium* species was based on the presence of typical macro- and microscopic fungal morphological characteristics of the cultured isolate; further samples were unavailable for performing speciation or confirmatory testing.

Conclusion

This report provides insight into an unusual manifestation of joint- and bone-related *Fusarium* infection in a child. Owing to the rarity of this fungal species, there is a need to share further case studies and to pool data, thereby contributing to current literature in ascertaining best practise guidelines in the optimal management of *Fusarium*-related infection in children.

Data availability. N/a.

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Conflicts of interest. None.

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