Diagnostic Microbiology & Infectious Disease 115 (2026) 117347

Contents lists available at ScienceDirect

Diagnostic Microbiology & Infectious Disease

journal homepage: www.elsevier.com/locate/diagmicrobio

Case Report

Cutaneous *Scedosporium* infection mimicking malignancy in a kidney transplant recipient: A case report

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ARTICLE INFO

Keywords:
Scedosporium
Cutaneous infection
Kidney transplantation
Voriconazole
Case report

ABSTRACT

Background: Cutaneous *Scedosporium* infection represents an extremely rare opportunistic fungal complication in solid-organ transplant recipients, often mimicking post-transplant skin malignancies due to chronic immunosuppression.

Case presentation: A 75-year-old woman, kidney transplanted in 2022 for IgA nephropathy on tacrolimus, mycophenolate, and prednisone, developed progressive firm nodular lesions on the left lower limb over two months. Punch biopsy revealed granulomatous inflammation with septate hyphae on Gomori-Grocott stain; culture confirmed *Scedosporium* spp. CT excluded dissemination.

Conclusion: Voriconazole (6 mg/kg loading dose, then 4 mg/kg maintenance dose) combined with surgical debridement, negative-pressure wound therapy, and skin grafting achieved complete healing at three months, with no recurrence at 12 months. Early biopsy is crucial to differentiate this rare entity from squamous cell carcinoma, enabling multidisciplinary success.

1. Introduction

Opportunistic fungal infections are significant complications in solid-organ transplant recipients due to chronic immunosuppression with agents such as tacrolimus, mycophenolate, and corticosteroids, but infections caused by *Scedosporium* spp. remain extremely rare and underrecognized in this population [1–3]. Cutaneous *Scedosporium* infection, in particular, is an uncommon clinical entity with very few reported cases worldwide, often presenting with nonspecific firm nodules that closely mimic more common post-transplant skin malignancies like squamous cell carcinoma, which is itself markedly increased in transplant recipients [4–5]. The rarity and clinical similarity to malignancy frequently delay diagnosis, posing a challenge for timely and effective management. Additionally, *Scedosporium* spp. exhibit intrinsic resistance to many widely used antifungal drugs, making treatment complex and outcomes uncertain.

This case report, adhering to CARE guidelines, documents one of the few detailed descriptions of cutaneous *Scedosporium* infection in a kidney transplant recipient, confirmed by histopathology and culture, and successfully managed through medical and surgical treatment. This report underscores the importance of heightened clinical suspicion and multidisciplinary care in recognizing and treating this rare but potentially serious infection, contributing valuable insight into its diagnosis and management in the transplant setting.

2. Case report

2.1. Patient information

A 75-year-old Italian woman underwent kidney transplantation in 2022 for IgA nephropathy. She received tacrolimus 10 mg/day, mycophenolate 1 g/day, and prednisone 5 mg/day. Comorbidities included hypertension, type 2 diabetes, atrial fibrillation, hypertensive cardiomyopathy, recurrent multidrug-resistant urinary tract infections, and prior cytomegalovirus reactivation. No family history of skin cancer or fungal infections noted. As past interventions she only had kydney

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https://doi.org/10.1016/j.diagmicrobio.2026.117347
Received 14 December 2025; Received in revised form 22 February 2026; Accepted 28 February 2026
Available online 1 March 2026

transplant with stable graft function pre-presentation.

2.2. Clinical findings

The patient presented with a two-month history of multiple firm, nodular lesions on the left lower limb, measuring 1-3 cm in diameter with irregular borders and progressive subcutaneous extension into the medial knee region (Supplementary Figure 1). The lesions were mildly painful on palpation but non-pruritic, without associated erythema, discharge, or systemic symptoms; she remained afebrile and hemodynamically stable. Physical examination revealed preserved distal pulses, no lymphadenopathy, and unremarkable laboratory findings including creatinine 1.4 mg/dL, normal liver enzymes, white blood cell count 6.2 $\times$ 10^3/μL, and negative blood cultures.

A contrast-enhanced CT scan of the left lower limb confirmed a contiguous subcutaneous lesion adjacent to the medial aspect of the knee without deeper fascial or osseous involvement (Supplementary Figure 2). In addition, contrast-enhanced CT imaging of the chest and abdomen was performed to assess for distant dissemination, showing no pulmonary nodules, consolidations, or visceral lesions suggestive of systemic *Scedosporium* infection.

2.3. Diagnostic assessment

Initially, an incisional biopsy of one representative lesion was performed with the primary aim of excluding malignancy, given the patient's history of kidney transplantation, chronic immunosuppression, and the clinical suspicion of post-transplant squamous cell carcinoma. Histopathological assessment revealed granulomatous inflammation containing slender septate hyphae highlighted by Gomori-Grocott methenamine silver staining (Fig. 1), and subsequent fungal culture grew *Scedosporium* spp., establishing the final diagnosis of localized cutaneous *Scedosporium* infection and ruling out squamous cell carcinoma as well as other infectious and lymphoproliferative differentials.

In vitro antifungal susceptibility testing (AST) of the isolate was not performed, and treatment was guided by current evidence supporting voriconazole as first-line therapy for these infections.

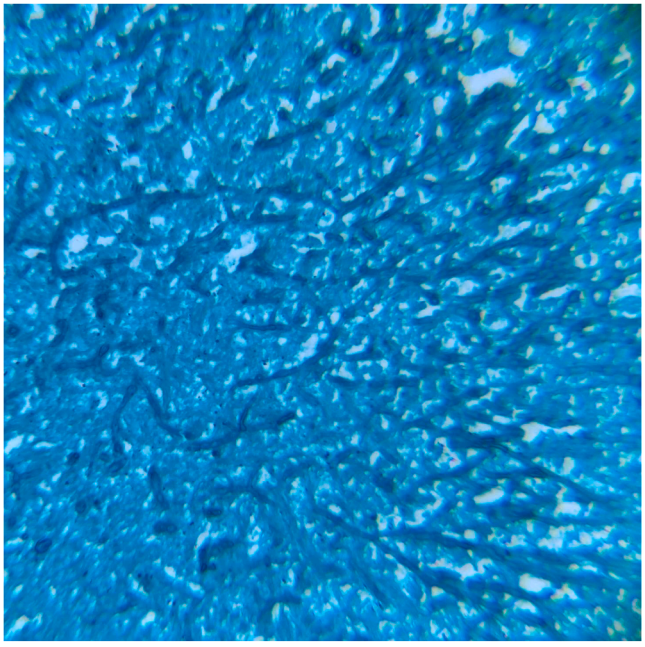

Fig. 1. Zoomed-in histological section stained with Gomori–Grocott methenamine silver showing slender, septate hyphae with acute-angle branching, morphologically consistent with *Scedosporium* spp.

2.4. Therapeutic interventions

Therapeutic interventions comprised systemic voriconazole, administered as a 6 mg kg^{-1} intravenous loading dose every 12 hours on day 1, followed by 4 mg kg^{-1} every 12 hours, with therapeutic drug monitoring performed to maintain appropriate drug exposure throughout the six-month treatment course, in association with a careful reduction of immunosuppression by lowering tacrolimus dosage. Tacrolimus trough levels were monitored closely, and the dose was titrated to maintain concentrations in the range of approximately 4-6 ng/mL, to balance the increased exposure expected with voriconazole co-administration against the need to preserve renal allograft function. In parallel, the patient underwent wide surgical excision and debridement of the affected areas, after which negative-pressure wound therapy was applied at 125 mmHg to promote granulation tissue formation and control local infection, followed by split-thickness skin grafting to achieve definitive wound closure.

2.5. Outcomes

Clinical and laboratory outcomes were favorable, complete wound healing with good graft take was documented three months after surgery, and renal allograft function remained stable, with serum creatinine of 1.3 mg/dL and no evidence of voriconazole-related toxicity. At 12-month follow-up, there was no local recurrence of cutaneous lesions or radiological or clinical evidence of systemic dissemination, confirming the effectiveness and tolerability of the combined antifungal, surgical, and immunosuppression-modulating strategy in this high-risk transplant recipient. Given the absence of relapse after one year and the localization of disease at diagnosis, the long-term prognosis is considered favorable, although continued clinical and radiological surveillance remains warranted because of the patient's persistent immunosuppressed state.

3. Discussion

Cutaneous *Scedosporium* infection is an exceptionally rare complication in solid-organ transplant recipients, who are nonetheless a high-risk group for emerging molds because of prolonged and often intensified immunosuppression [6–8]. Primary cutaneous fungal infections in this setting frequently present with non-specific papules, plaques, ulcers, or nodules, requiring a high index of suspicion and early biopsy to avoid diagnostic delay [4]. In parallel, solid-organ transplant recipients face a dramatically elevated risk of cutaneous squamous cell carcinoma, estimated up to 65-250 times higher than in the general population, so new nodular or hyperkeratotic lesions are commonly approached as potential malignancies [9–10]. In the present case, this background justified the initial suspicion of post-transplant squamous cell carcinoma and the decision to perform an incisional biopsy, which ultimately revealed a fungal etiology rather than neoplastic disease.

Histopathology is crucial to distinguish cutaneous *Scedosporium* infection from skin cancer and other infections. *Scedosporium* spp. typically appear as slender septate hyphae with acute-angle branching on Gomori-Grocott methenamine silver staining and are often indistinguishable morphologically from *Aspergillus* spp., making culture or molecular identification essential for definitive diagnosis [11–12]. Other hyaline septate molds, including *Fusarium* spp. and related genera, may show overlapping histological features, so the differential diagnosis of septate, acutely branching hyphae in tissue requires integration of morphology with culture characteristics and, where available, molecular assays. In our case, the observation of septate hyphae with acute-angle branching prompted consideration of *Aspergillus, Fusarium*, and other hyaline molds, but growth of *Scedosporium* spp. in culture allowed definitive attribution of the infection to this genus.

Several series of transplant patients with primary cutaneous fungal infections, including *Scedosporium apiospermum*, emphasize the

importance of combined clinical, histopathologic, and microbiologic assessment to document localized disease and rule out dissemination [4–5]. In this case, the absence of vascular invasion on histology and the lack of radiological signs of systemic spread supported localized cutaneous *Scedosporium* infection and a potentially favorable prognosis with timely treatment. The choice to image the chest and abdomen was guided by the recognized predilection of *Scedosporium* spp. for pulmonary involvement and the potential for subsequent hematogenous spread to other organs, including the central nervous system, particularly in immunocompromised hosts and transplant recipients [13–15].

In our case, the isolate was reported as *Scedosporium* spp., identified by MALDI-TOF MS, supported by conventional culture and morphology, while species-level identification (for example, *Scedosporium apiospermum* versus *Lomentospora prolificans*) was not available because advanced techniques such Next Generation Sequencing were not routinely implemented in our laboratory at the time of diagnosis. This represents a limitation, since different members of the *Scedosporium/Lomentospora* complex display distinct antifungal susceptibility patterns and prognoses, and more precise speciation could potentially refine risk assessment and therapeutic decision-making in similar cases.

A further limitation is the absence of isolate-specific antifungal susceptibility data in our case. Nevertheless, the choice of voriconazole was consistent with published data identifying it as the preferred agent for most *Scedosporium* infections.

Management of *Scedosporium* infections is challenging because these molds exhibit intrinsic resistance to many conventional antifungal agents, particularly amphotericin B and, variably, echinocandins [16–17]. Voriconazole is considered the drug of choice, with large series reporting overall response rates of approximately 57-61% across all infection sites and up to 90% success in skin and subcutaneous infections when therapy is prolonged [18]. In the present patient, voriconazole was administered with therapeutic drug monitoring over six months, combined with careful reduction of calcineurin inhibitor exposure, reflecting recommendations to balance antifungal efficacy with preservation of allograft function. In practice, this required stepwise tacrolimus dose reduction with frequent trough monitoring, aiming for lower but still therapeutic levels in a stable kidney transplant recipient, and illustrates the broader need to individualize immunosuppression when potent azoles are introduced in order to avoid both rejection and drug-related nephrotoxicity. Aggressive local surgical management using wide excision and debridement, followed by negative-pressure wound therapy and split-thickness skin grafting, is in line with previous reports where cure was achieved through debridement plus systemic antifungals and adjustment of immunosuppression. In our patient, the decision to continue voriconazole for six months reflected the need for prolonged therapy described in series of scedosporiosis [19–21], in which median treatment durations for skin and soft-tissue infections often extend over several months, and successful outcomes are associated with extended courses of therapy, particularly in immunocompromised hosts. The duration was individualized rather than protocol-driven, and treatment was maintained until complete wound epithelialization, absence of radiological evidence of progression, and stable renal allograft function were achieved, with therapeutic drug monitoring used to ensure adequate systemic exposure throughout the course.

The favorable outcome observed, complete wound healing by three months, stable renal allograft function, and absence of recurrence or dissemination after 12 months, illustrates the potential for cure in localized cutaneous *Scedosporium* infection when diagnosis is timely and a multidisciplinary strategy is adopted. This contrasts with disseminated *Scedosporium* infections in transplant recipients, which carry high mortality rates approaching 50-80% despite therapy, highlighting the importance of early recognition at a localized stage [5,22]. From a practical standpoint, any new or atypical cutaneous nodule in a transplant recipient, particularly one that does not display classic features of actinic damage or keratinocytic neoplasia, should prompt low threshold for biopsy and consideration of opportunistic fungal disease in the differential diagnosis. This case reinforces the need for close collaboration among dermatologists, infectious disease specialists, transplant physicians, and plastic surgeons to optimize outcomes in rare but severe opportunistic infections in immunosuppressed hosts.

4. Conclusions

Cutaneous *Scedosporium* infection should be considered in the differential diagnosis of atypical nodular skin lesions in solid-organ transplant recipients, prompting early incisional biopsy with combined histopathological and microbiological assessment to distinguish fungal disease from malignancy and guide management. Localized cutaneous *Scedosporium* infection can be cured with multidisciplinary care integrating optimized voriconazole therapy, careful immunosuppression modulation, and aggressive surgical source control, achieving complete healing without compromising renal allograft function. Absence of recurrence at 12 months supports a favorable long-term prognosis with ongoing surveillance.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

CRediT authorship contribution statement

Martin Iurilli: Writing – original draft, Project administration, Methodology, Investigation, Data curation, Conceptualization. **Luigi Bonat Guarini:** Writing – original draft, Investigation, Data curation, Conceptualization. **Stefano Di Bella:** Writing – review & editing, Validation, Supervision, Project administration, Methodology. **Verena Zerbato:** Writing – review & editing, Validation, Investigation. **Giovanni Papa:** Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors wish to thank Dr. Davide Rozze from the Pathology Unit of the Azienda Sanitaria Universitaria Giuliano Isontina (ASUGI) for his valuable contribution.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.diagmicrobio.2026.117347.

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