# Cutaneous *Microsphaeropsis arundinis* infection in renal transplant recipients—A report of 2 cases and review of the literature

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## INTRODUCTION

*Microsphaeropsis arundinis* is a dematiaceous mold of the coelomycetes class that is emerging as a cause of opportunistic cutaneous infections in immunocompromised hosts.[1,2] *M arundinis* typically inhabits plant hosts and is ubiquitous in soil and fresh water.[3]

## CASE REPORTS

### Case 1

A 69-year-old Filipino woman presented with a 6-month history of an asymptomatic scar-like plaque on the dorsum of the right hand. It started as a laceration while gardening and developed into a crusted plaque. Her medical history was clinically significant for renal transplantation secondary to renal failure of unknown cause in 2014 necessitating immunosuppression with prednisone, tacrolimus, and mycophenolate mofetil. Other medical history included type 2 diabetes mellitus, asthma, and hyperlipidemia. She was also receiving valganciclovir, calcitriol, pantoprazole, gliclazide, insulin, atorvastatin, and budesonide inhaler.

On examination, she had a solitary linear hyperkeratotic plaque on the right dorsal hand overlying the second metacarpophalangeal joint (Fig 1). There was no regional lymphadenopathy. Investigations found a full blood count with decreased white cell count, neutrophil count, and hemoglobin, consistent with baseline for this patient. Electrolytes showed stable hyponatremia and slightly elevated creatinine and urea; all else was within normal range. Liver function results were unremarkable.

*Abbreviation used:*

DiPAS: periodic acid—Schiff with diastase

A punch biopsy specimen was sent for histology and microbiology including mycobacterial and fungal cultures. Histopathology with hemotoxylin-eosin staining showed hyperkeratosis and parakeratosis of the stratum corneum with neutrophilic infiltration. There was acanthosis of the epidermis, and a jagged interface with the underlying dermis (pseudoepitheliomatous hyperplasia) (Fig 2). Dense granulomatous inflammation was present in the papillary dermis composed of epithelioid histiocytes with intermingled neutrophils. Numerous fungal elements were highlighted with periodic acid—Schiff with diastase (DiPAS) and methenamine silver staining including yeast forms and occasional septate pseudohyphae (Fig 3). These were seen within the dermis and also in the stratum corneum. Fungal culture was positive for *M arundinis*. Bacterial culture was positive for coagulase negative *Staphylococcus*.

The patient was started on a 6-month course of oral itraconazole. After 1 month of therapy she reported substantial reduction in lesion size.

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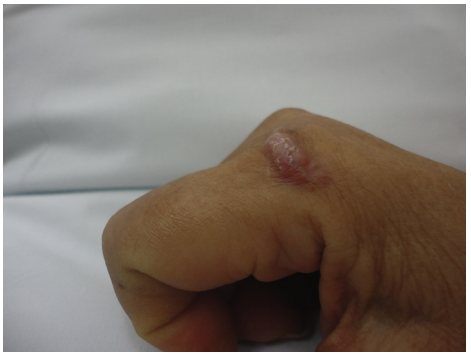

**Fig 1.** Single linear hyperkeratotic plaque overlying the second metacarpophalangeal joint.

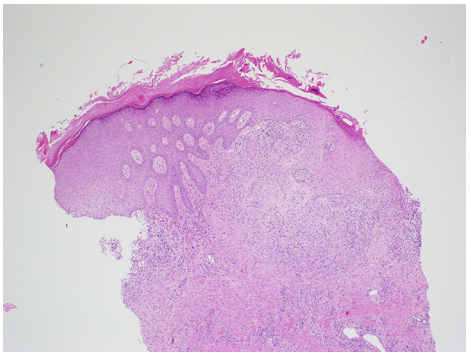

**Fig 2.** Pseudoepitheliomatous hyperplasia.

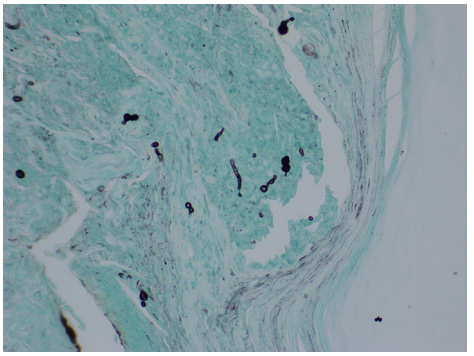

**Fig 3.** Methenamine silver stain highlights the fungal hyphae and spores.

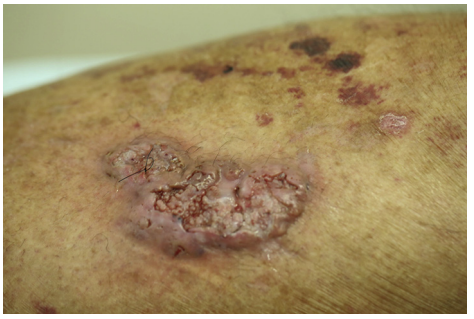

**Fig 4.** Friable exophytic plaque with central ulcer on the leg.

### Case 2

A 65 year-old-man presented with a 12-month history of nodules on his legs and dorsum fifth left toe. His medical history was significant for renal transplantation secondary to diabetic nephropathy in 2014 for which he was on prednisone, tacrolimus, and azathioprine. Other medical history included type 2 diabetes mellitus, hypertension, peptic ulcer disease, nonmelanoma skin cancers, and aortic valve stenosis. He was also receiving insulin, amlodipine, sodium bicarbonate, darbepoetin, and magnesium.

On examination, there were 3 ulcerated exophytic plaques on the right medial calf, left posterior calf, and left fifth toe, in a sporotrichoid distribution (Fig 4). The tissue was friable and discharged serous fluid. There was no lymphadenopathy or hepatosplenomegaly.

Three incisional biopsies found an epidermis that was markedly hyperplastic with pseudoepitheliomatous hyperplasia with keratoacanthoma-like changes overlying suppurative granulomatous inflammation and abscess formation within the dermis. Alcian blue periodic acid–Schiff stain showed numerous fungal elements (septate pseudohyphae and yeast-like structures) within the inflamed dermis. Panfungal nucleic acid detection was performed detecting *M arundinis* DNA by polymerase chain reaction and DNA sequencing.

In consultation with his renal physician and the infectious diseases team, the patient was started on voriconazole for a total of 6 months with clinical improvement of the lesions. During this time, the patient was also placed on a reduced dose of tacrolimus, and weekly serum tacrolimus levels were measured, as voriconazole is known to interfere with tacrolimus metabolism and precipitate its toxicity.[4]

## DISCUSSION

*M arundinis* is a rare fungal infection in human hosts, and there have only been 8 previously described cases in the literature.[1-3,5] Five of the cases have been reported in Australia,[1,3] 2 in Japan,[5] and one in the United States.[2] All cases described have been in immunosuppressed patients including 4 renal transplant patients[1,2] and 4 patients receiving long-term corticosteroids, including 2 patients with chronic kidney disease,[3] 1 patient with systemic lupus erythematosus and autoimmune hepatitis, and another patient with recalcitrant temporal arteritis.[3] Similarly, both the cases described in our cases

series were postrenal transplant recipients on long-term immunosuppression to prevent organ rejection.

Clinical presentation of *M arundinis* is described in the literature as a crusted indurated plaque that can be mistaken for other conditions such as squamous cell carcinoma. Furthermore, if only a superficial shave biopsy is performed, the histology of pseudoepitheliomatous hyperplasia can also mimic a squamous cell carcinoma as the underlying granulomatous, and suppurative inflammation may not be sampled.[2] In our cases, differential diagnoses included squamous cell carcinoma, infectious etiology, atypical keloid, reactive perforating collagenosis, or perforating granuloma annulare. *M arundinis* infection has been reported with sporotrichoid spread, supporting lymphatic dissemination,[2,5] consistent with the presentation of our second case. In contrast, the first patient presented with a single lesion on the dorsum of the right hand after injury, suggestive of a keloid. As Coelomycetes are implanted into human skin through trauma, the dorsal hands and feet are often involved.[1,5]

Diagnosis is made when histopathologic examination finds granulomatous inflammation[1] and positive fungal staining with special stains such as the DiPAS and methenamine silver staining (used in our case), highlighting fungal elements such as spores and septate pseudohyphae. Fungal culture and DNA sequencing are then used to identify the fungal isolate.[1]

Previous treatments described for *M arundinis* infection include surgical excision, thermotherapy, and antifungal medications including terbinafine, amphotericin, and the azole antifungals such as itraconazole, posaconazole, and voriconazole.[1,5] Prolonged treatment is generally required, particularly with the azole antifungals, with previous patients requiring a minimum of 3 months treatment on terbinafine[3] or 6 to 12 of months therapy with the azole antifungals itraconazole, posaconazole, or voriconazole.[1-3] The infectious diseases physicians prescribed for our patients a total of 6 months therapy with oral itraconazole and voriconazole, respectively, for resolution of their lesions. Caution should be exercised with voriconazole, which has been associated with several dermatologic complications including photosensitivity and an association between long-term voriconazole exposure and the increased risk for nonmelanoma skin cancers in studies in lung and hematopoietic cell transplant recipients.[6-10]

*M arundinis* is an emerging cause of opportunistic skin infections in immunocompromised patients, and it is important for clinicians to recognize presentations of this unusual fungus. Prolonged therapy with oral azole antifungals seems to be an effective treatment for this infection; however, caution must be exercised when prescribing, given numerous potential interactions with immunosuppressant medication.[4]

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