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Disseminated Nannizziopsis obscura infection in a renal transplant patient- The first reported case

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ABSTRACT

This is a presentation of a case of disseminated fungal infection in a renal transplant patient with Nannizziopsis obscura, a species not previously reported as having caused disseminated disease in humans and not previously reported in the UK. The fungus was isolated from a intramuscular collection and from a lymph node. The patient responded well to a course of posaconazole.

1. Introduction

This is a presentation of a case of disseminated fungal infection in a renal transplant patient with *Nannizziopsis obscura*, a species not previously reported as having caused disseminated disease in humans and not previously reported in the UK.

A 34 year old African man on immunosuppressive medication for a renal transplant presented with back pain, a skin rash, fever and night sweats and imaging showed a soft tissue thoracic collection and subcarinal lymphadenopathy. The patient was initially suspected to have tuberculosis but subsequent culture of pus from the collection and tissue from the lymph node grew *Nannizziopsis obscura.*

There are only five previously reported cases of *Nannizziopsis* infection in humans, although infection with other *Nannizziopsis* species in reptiles is well described.

2. Case

A 34 year old African man from the Gambia presented to hospital in June 2015 with several weeks of fever, night sweats, cough and wheeze, together with increasingly severe back pain from what appeared to be a paraspinal abscess. He had a rash across his trunk and several pigmented skin lesions on his feet and legs, which had developed over six months (Figs. 1–5).

He had end stage renal failure of unknown cause with renal transplantation in 2008. Following an episode of antibody-mediated rejection in March 2014, his immunosuppressive regimen had been intensified such that at the time of presentation he was on tacrolimus 12 mg once daily, prednisolone 7.5 mg once daily and mycophenylate 1 g twice daily. He was HIV negative.

He had been resident in the UK for several years but regularly made visits to the Gambia, most recently in March 2015.

On the day of admission, Day 0, he had a raised CRP of 124 mg/L and a significantly elevated alkaline phosphatase of 1182 iu/L, of predominantly bone origin. A CT thorax on Day 0 demonstrated subcarinal lymphadenopathy causing compression of the right main bronchus and a few pulmonary nodules. MRI spine on Day 2 showed a loculated soft tissue collection at T6-T8 level with no spinal involvement.

The clinical suspicion was of tuberculosis, although pus from the paraspinal collection obtained on Day 8 was smear negative for acid-alcohol-fast bacilli. Pus grew a *Salmonella* species but this result went unnoticed at the time. No other microorganisms were isolated at this point, although the sample was not sent for mycological culture on this occasion. Scrapings from the skin rash showed fungal elements but the rash was thought to be pityriasis versicolor and so this was not investigated further at this point. The patient was commenced on standard anti-tuberculous therapy on Day 10. He was discharged from hospital on Day 24 and followed up in the TB clinic on Day 38.

By August, the back pain and paraspinal swelling had worsened. The patient was readmitted on Day 53 and a repeat CT thorax revealed a 13 cm by 6 cm collection in the thoracic musculature extending from T5 to T10. The subcarinal node and pulmonary nodules seen in June were still present, as was the rash on his trunk.

He underwent surgical drainage of the thoracic musculature collection on Day 55 and pus was examined microscopically and a few pseudohyphae or round fungal cells were seen. The sample was cultured on Sabouraud agar and incubated at 35 °C. White mould colonies grew following five days incubation (Fig. 6), and microscopy revealed club-shaped conidia borne on the sides of hyphae (Fig. 7) and cylindrical arthroconidia in chains (Fig. 8). DNA from the isolate was

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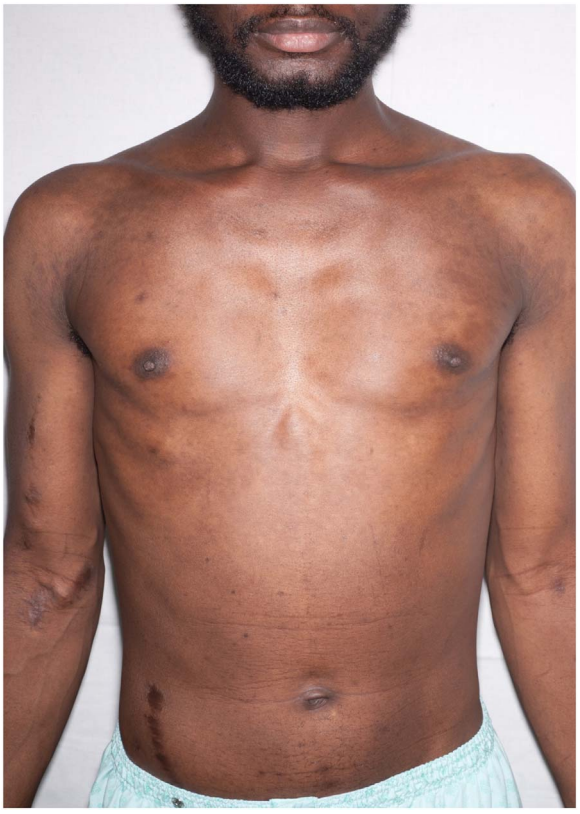

Fig. 1. Anterior view of truncal rash.

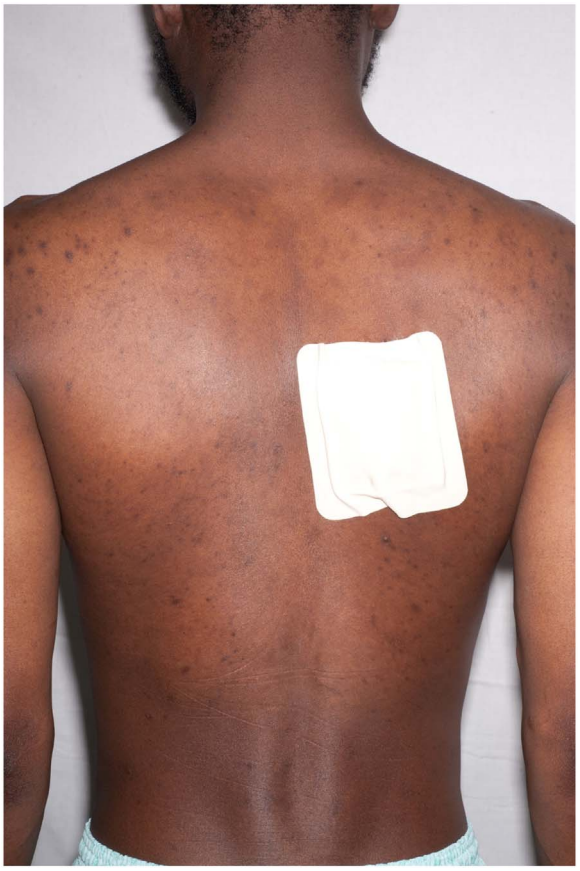

Fig. 2. Posterior view of truncal rash; dressing at site of thoracic collection drainage.

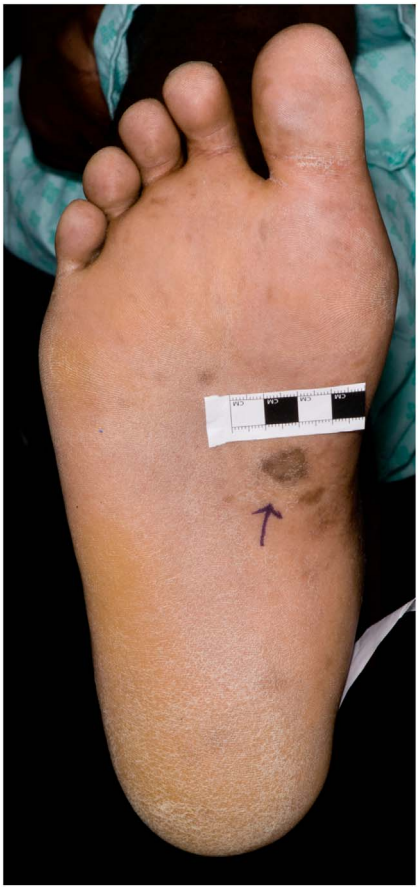

Fig. 3. Plantar lesions, right foot.

extracted, amplified and sequenced using universal fungal primers ITS5-F (5′- CCTTGTTACGACTTTTACTTCC-3′) and ITS4-R (5′-GCATATCAATAAGCGGAGGA-3′) [1]. A 787 nucleotide sequence was obtained with subsequent BLAST analysis identified closest alignment with *Nannizziopsis obscura* (100% identity, 100% query cover, 787/787) (accession KF466865.1). The fluid from this collection also grew *Salmonella enteritidis*.

The subcarinal node was biopsied under endobronchial ultrasound guidance on Day 64 and calcofluor staining revealed a mass of mycelium (Fig. 9). The sample was cultured on SAB agar at 35 °C and fine growth was observed after three days' incubation. Examination of colonies revealed similar colony morphology and microscopic appearance to the *Nannizziopsis spp*. isolated from the thoracic collection. Calcofluor staining of the lymph node tissue showed fungal hyphae.

Scrapings were taken from the truncal rash and fungal elements were seen on microscopy although fungal cultures were negative.

The isolates from the muscle collection and the lymph node were identical and also identified as *N. obscura*. An isolate was also sent for sensitivity testing to the Public Health England Mycology Reference Laboratory in Bristol and the results are shown in Table 1.

It was considered that he had disseminated *Nannizziopsis* infection with secondary infection of the thoracic musculature collection with *Salmonella enteritidis*. The tuberculosis treatment was stopped on Day 62 and he was treated with ciprofloxacin 500 mg twice daily for six weeks and posaconazole 300 mg once daily. He responded well with resolution of his main symptoms within a few weeks. The thoracic collection, skin rash and skin lesions improved and CRP and alkaline phosphatase levels had normalised by the beginning of September 2015, when he was reviewed in clinic on Day 86. The patient completed a total of ten months of posaconazole therapy and at the time of writing, seven months after the last dose, he has remained well with no evidence of