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A severe transmissible Majocchi's granuloma in an immunocompetent returned traveler

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ABSTRACT

Severe dermatophyte infection is rare in immunocompetent adults. Recently cases have been described in travelers returning from South East Asia (Luchsinger et al., 2015) [1]. These may be sexually transmitted and can have permanent sequelae. We describe the first reported case of Majocchi's granuloma (MG) in an Australian returned traveler and its subsequent transmission via sexual contact. Both patients were successfully treated with systemic antifungals. MG should be considered in patients with severe rash after travel to South East Asia.

1. Introduction

MG is a rare cutaneous dermatophyte infection involving the hair follicle. *Trichophyton interdigitale* (previously *Trichophyton mentagrophytes var. interdigitale*), a causative organism, is thought to be transmitted sexually. We describe a case of severe MG from *Trichophyton interdigitale* infection occurring in a young immunocompetent returned traveler and further evidence for its sexual transmission.

Cutaneous dermatophyte infections are common and most of these infections are mild and respond to topical antifungal agents. MG is a rare infection that is mostly seen in immunocompromised patients or those treated with topical glucocorticoids [2]. Although *Trichophyton rubrum* is the most common causative organism, *Trichophyton interdigitale* is responsible for a significant proportion of MG [2]. Diagnosis may be difficult in patients in the absence of known risk factors for deep dermatophyte infection. Delays in diagnosing deep dermatophyte infection may lead to scarring, alopecia, and incapacitation secondary to severe pain.

A recent case series reported severe infection with *Trichophyton interdigitale* occurring in a number of immunocompetent adults in Germany, after travelling to South East Asia [1]. These cases appeared to be sexually transmitted. The infections resulted in severe pain, scarring and prolonged hospitalisation. In all cases systemic antifungal therapy was necessary to control the infection [1].

Sequence analysis of *Trichophyton interdigitale* cultures can assist in identifying the ecological origins of strains, which may inform on whether the source is anthrophilic or zoophilic. This can be important to inform clinical aspects such as treatment and also for source tracing [3].

2. Case report

A 25 year old male presented to his general practitioner (GP) on day +3 after symptom onset with a painful patchy rash on his groin. He had been in Thailand two weeks prior to symptom onset, day −14, and had a number of unprotected sexual exposures with local residents and tourists while abroad. He denied any animal exposure, ocean or creek bathing or travel to beaches during this time.

His GP remarked the appearance of superficial impetiginisation and he was prescribed oral cephalexin 500 mg four times daily and miconazole nitrate 2% with hydrocortisone 1% topically twice daily. From day +3 to day +18 he was seen by 3 more GP's from a separate practice and prescribed topical triamcinolone 0.02% and amoxicillin 875 mg with clavulanic acid 125 mg twice daily. During this period the rash spread to the suprapubic and inguinal regions. On day +14, after 11 days of therapy, his topical steroid was ceased and topical ketoconazole 2% shampoo was also prescribed. His symptoms worsened further after prescription of a course of oral flucloxacillin on day 16+ and he was referred to the emergency department of a tertiary hospital for evaluation on day +18.

On presentation to hospital the patient was febrile and had five annular granulomatous lesions in his suprapubic region, two lesions on his right leg with central eschar and purulent discharge (Fig. 1), bilateral inguinal lymphadenitis, a submental kerion and a level III neck kerion consistent with tinea barbae. Also of note were diffuse follicular associated pustules over the lateral buttocks and shins.

Bloods on day +18 revealed a leukocytosis with a neutrophilia.

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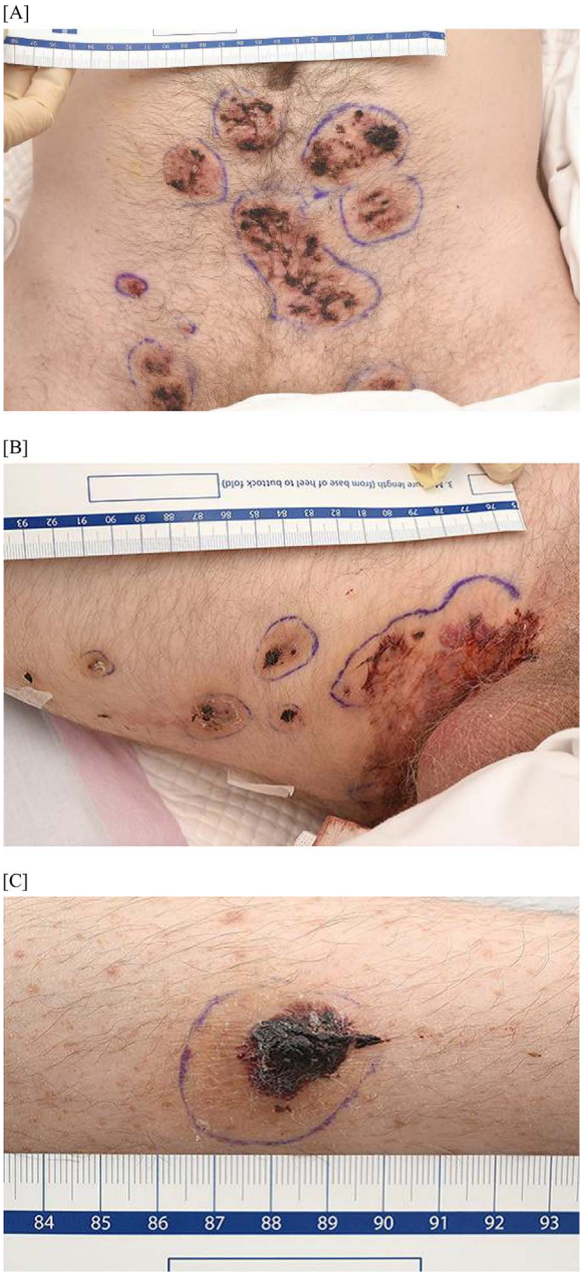

Fig. 1. (A) Cutaneous abdominal lesions on presentation to hospital with associated inguinal lymphadenitis; (B) Spread of lesions to inguinal region; (C) A lesion on the anterior shin with associated patchy follicle associated pustules.

Liver function tests were mildly deranged and a liver ultrasound was normal. Biopsies were taken and he was treated with intravenous flucloxacillin 1 g every 6 h. Histology of the lesions from a punch biopsy on day +21 showed dense periadnexal mixed inflammatory infiltrate as well as dense superficial and deep perivascular lymphocytic infiltrates in the dermis. The follicular lumen was distended by keratin, squames and inflammatory cells.

Doxycycline was added for possible Donovanosis on day +20. The lesions became progressively more painful on day +25, to the point that the patient could hardly mobilize and an area of indurated, tender cellulitis extended into the perineum and natal cleft. This prompted the consideration of a diagnosis of necrotising fasciitis and a computed tomography (CT) scan of the pelvis was ordered. At this point Lincomycin 600 mg every 8 h was added. Results of the CT scan showed soft tissue inflammation of the abdominal and inguinal regions as well as subcutaneous fat stranding in the inguinal region without signs of tissue necrosis. Fungal cultures identified *Trichophyton interdigitale* and a diagnosis of MG was made on day +28.

Culture was submitted to whole genome sequencing using Nextera XT library preparation on an Illumina NextSeq. 500. A *de novo* assembly was performed in CLC Genomics Workbench V7 and is available at the European Nucleotide Archive (ENA) in project PRJEB19281 http://www.ebi.ac.uk/ena/data/view/PRJEB19281. Identification as *Trichophyton interdigitale* was confirmed by a Kmer search on fastq reads using KmerFinder 2.0 (https://cge.cbs.dtu.dk/services/KmerFinder/).

The ITS regions 1 and 2 were identified from the *de novo* assembly and aligned to ITS sequences representing all known *Trichophyton interdigitale* types [3,4]. The ITS regions were determined to be 100% identical to the type IV-variant found in RCPF-1640, a strain causing tinea corporis. In the literature type IV strains have been reported to be associated with zoophilic sources [4].

Oral terbinafine 250 mg twice daily was commenced on day +28 and a 5 day course of flucloxacillin 500 mg every 6 h was given to treat bacterial superinfection of the left thigh. The patient had residual pain and inflammation at day +140 and the terbinafine was reduced to 250 mg daily, at which time itraconazole 50 mg daily was added to his therapy. By day +196, after 6 months of treatment all signs of infection had resolved but the patient was left with alopecia and scarring over the affected areas.

An intimate contact of the index patient's also presented with a similar painful fungal-looking rash two weeks after their last sexual encounter. This was confirmed to be *Trichophyton interdigitale* by fungal culture and likely reflects an instance of sexual transmission. This case was successfully treated with 6 weeks of oral terbinafine 250 mg daily.

3. Discussion

This report describes the first published case of MG secondary to *Trichophyton interdigitale* in an immunocompetent person returning from travel in South East Asia and its likely sexual transmission within Australia.

Despite recent advancements in molecular diagnostics, rapid and reliable molecular methods to diagnose *Trichophyton interdigitale* infections are not widely available [5,6]. A systemically unwell patient with a worsening rash despite topical antifungals can pose a difficult diagnostic challenge, especially considering fungal cultures and sensitivities can take many days to become positive. Delay in diagnosis and effective treatment may result in longer hospitalisation, incorrect treatments, scarring and avoidable pain and anxiety to the patient. If severe or rapidly progressive, such as in this presentation, symptoms may also raise concern for necrotising soft tissue infection and could lead to unnecessary radiation exposure or surgical intervention.

This case supports the notion that travel to South East Asia and sexual activity may be important risk factors for severe infection with *Trichophyton interdigitale*. The detection of a similar painful fungal lesion in another young immunocompetent female after sexual contact adds further evidence that this infection is transmitted by close body contact. Patients should be advised to abstain from such activity until symptoms have resolved. Clinicians should consider voluntary contact tracing for immunocompetent patients with confirmed severe *Trichophyton interdigitale* infections. In some reports of MG the affected persons have practiced shaving of the affected area; this has been proposed as a risk factor for infection [7], although it was absent in this case.

Apparent fungal infection in the returned traveler should prompt consideration of early biopsy and regular review to assess the efficacy of treatment. Poor response to therapy or systemic features should trigger referral for specialist evaluation.

There are no consensus guidelines for the treatment of MG. We describe the successful use of both itraconazole and terbinafine in combination after failure of monotherapy with terbinafine. This combination has been demonstrated to act synergistically in the treatment

of other fungal infections [8].

Genomic analysis of the fungal culture from the index patient not only confirmed the culture identification, but also allowed the ITS sequence type to be extrapolated. The ITS type is used to determine the anthropophilic or zoophilic origins of *Trichophyton interdigitale*, which in this case was a type IV variant, a type reported as having zoophilic origins. Despite this, the isolate seems to have spread in an anthropophilic fashion.

The sequencing and subsequent publication of genomic sequence is an important contribution for further genomic and functional characterisation of *Trichophyton interdigitale* isolates associated with a severe phenotype. This may yield insights into the pathophysiology of this organism and the mechanisms of its wide variation in pathogenicity.

Clinicians should be aware of the potential for severe dermatophyte infection in patients who have recently returned from South East Asia. Sexual activity appears to be a major risk factor for acquisition and transmission of such infections. Severe infections associated with systemic symptoms or failure of topical therapy may require prolonged courses of systemic antifungals either as monotherapy or in combination. Early specialist referral and contact tracing may aid with diagnosis. Treatment of such infections should be based on systemic antifungal therapy. Prolonged courses of combined antifungals may be required in some cases.

Conflict of interest

There are none.

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