Severe primary cutaneous *Cryptococcus gattii* causing ulcerative cellulitis in an immunocompetent patient

Glorijoy Shi En Tan , Ravinder Singh, Tricia Yi Rui Chong, Pei Qi Su, Joyce Siong See Lee, Kevin Jian Hao Wong, Justina Wei Lynn Tan, Shawn Vasoo

Lancet Infect Dis 2019; 19: 1148

Department of Infectious Diseases (G S E Tan MBBS, S Vasoo MBBS), **Department of General Medicine** (R Singh MBChB), **Department of Orthopaedic Surgery** (K J H Wong MBBS), **and Department of Rheumatology, Allergy and Immunology** (J W L Tan MBBS), **Tan Tock Seng Hospital, Singapore; National Skin Centre, Singapore** (T Y R Chong MBBCh, P Q Su MBBS, J S S Lee MBBS); **and Infectious Disease Research Laboratory, National Centre for Infectious Diseases, Singapore** (S Vasoo)

Correspondence to: Dr Shawn Vasoo, National Centre for Infectious Diseases and Department of Infectious Diseases, Tan Tock Seng Hospital, 308442 Singapore
shawn_vasoo@ncid.sg

A 69-year-old man with chronic renal impairment and tophaceous gout, who had recently taken traditional Chinese medicines, presented to our hospital after 4 days of right forearm redness and swelling. A well demarcated, erythematous, indurated, mildly tender plaque was present, extending from the dorsum of the right hand to the elbow (figure). He had a white blood cell count of $8{\cdot}4\times10^9$ cells per L, haemoglobin concentration of 11·5 g/dL, platelet count of 146×10^9 per L, sodium concentration of 141 mmol/L, potassium concentration of 4·4 mmol/L, and creatinine concentration of 246 µmol/L.

He was given intravenous cefazolin, 2 g every 8 h, for presumed bacterial cellulitis. However, the rash progressed and blisters developed after 2 days (figure). A skin biopsy was done and a mucinous substance was observed. Histological results showed encapsulated yeast forms that stained positive with periodic acid-Schiff stain and Gomori methenamine silver stains, and mucoid capsules staining strongly with mucicarmine and Alcian blue (figure). Fungal cultures were positive for *Cryptococcus gattii*.

Blood fungal cultures, lumbar puncture, and unenhanced CT of the thorax, abdomen, and pelvis did not reveal disseminated disease. Serum cryptococcal antigen was positive at a titre of 1:320. The patient started oral fluconazole 400 mg daily, dose adjusted for his renal function.

Further assessment for an underlying immunodeficiency was negative for HIV, anti-IFN-γ, and anti-granulocyte-macrophage colony stimulating factor antibodies. His peripheral blood mononuclear cells responded appropriately to BCG with or without IFN-γ and IL-12 stimulation. He had normal lymphocyte subsets. His IgG, IgA, and IgM were low initially but recovered when traditional Chinese medicines were discontinued.

Despite being on antifungal therapy, the patient's wound worsened, developing ulcerations and myositis (figure). He required surgical debridement and intraoperative tissue also showed *C gattii*. He was treated for 5 days with intravenous liposomal amphotericin B 200 mg daily and transited back to oral fluconazole therapy 400 mg daily. After 6 months of antifungal therapy, the skin had just begun to re-epithelise (figure).

Severe ulcerative cryptoccocal cellulitis is unusual and can occur in apparently immuncompetent hosts. We believe the patient's renal disease and use of traditional Chinese medicines (suspected to be adulterated with steroids, although these medicines were unavailable for testing) might have contributed to this infection.

Contributions
GSET and SV wrote the manuscript. All authors were directly involved in the patient's care and critical appraisal of the manuscript.

Declaration of interests
We declare no competing interests.

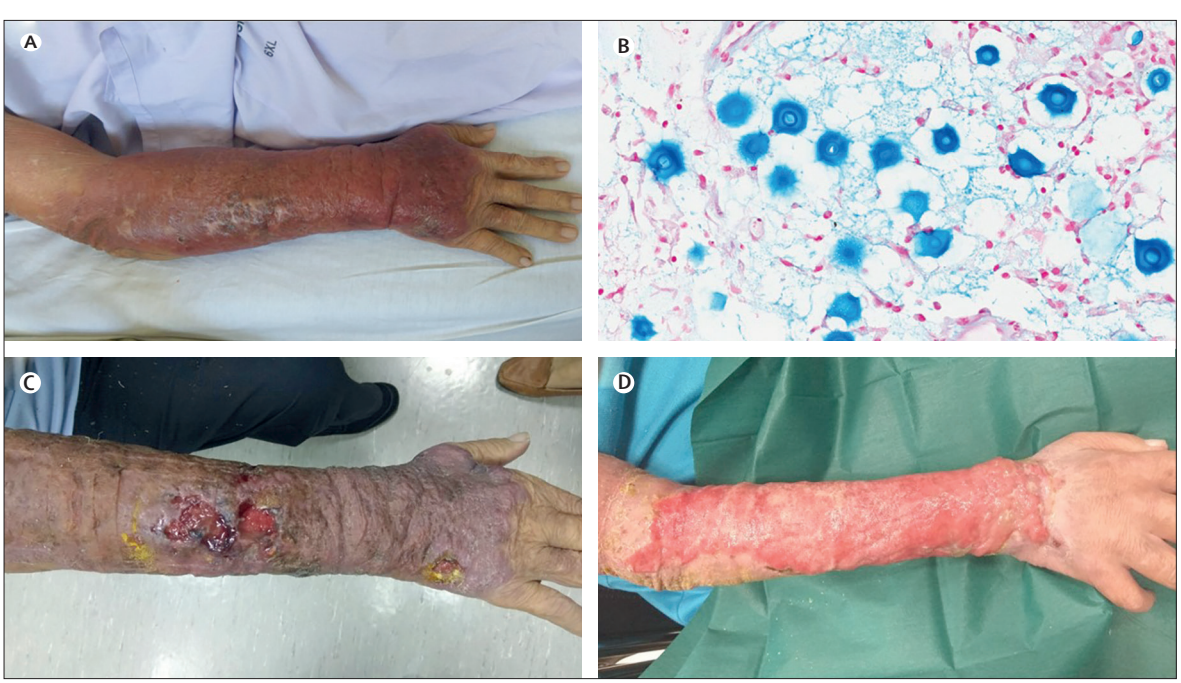

Figure: **Progression of ulcerative cellulitis**
(A) Initial presentation of erythematous and indurated skin. (B) Skin biopsy sample showing yeast forms with mucoid capsules, which stained strongly with Alcian blue (×400 magnification). (C) Progressive ulceration of the skin despite antifungal therapy. (D) Slow re-epithelisation of the skin after surgical debridement and 6 months of antifungal therapy.