Candida famata central nervous system infection

To the Editor: This report aims to document possibly the first isolation of *Candida famata* as a cause of human central nervous system infection.

Yeasts and other medically important fungi cause various clinical conditions ranging from trivial infestations to serious life-threatening conditions. *Candida* species were demonstrated as being the causative agents of oral thrush from as early as 1839[1] and thereafter recognised as causing a multitude of infective disorders. With the advent of widespread oncological treatment in the early 1960s[1] and controlled iatrogenic immune suppression for various other reasons, *Candida* spp. once again arose as a formidable opportunistic human pathogen. Emerging yeast infections have been described with increasing frequency, with at least 17 species of the genus *Candida* now being recognised as potential human pathogens.[1] With further developments in medical intervention and the increasing population of patients with immune deficiencies, whether iatrogenic or acquired, such as HIV infection, the list of yeasts that can cause disease will continue to grow. The flagship of the genus *Candida*, namely *C. albicans*, is the most common species isolated from blood cultures and blood-associated infections[1] especially in the nosocomial setting. For new emerging yeast pathogens blood and catheter-associated infections are common,[1] although some species may cause infection at other sites. Yeast infections of the central nervous system caused by organisms other than *Cryptococcus* spp. are uncommon, with *Candida* and *Aspergillus* species being the only other noteworthy pathogens.[2] The emerging yeast *C. famata* has previously been described as a human pathogen, associated with eye[1] and intravenous catheter infections,[1] fungaemia[3,4] and peritonitis[5] respectively.

Case report

A 29-year-old man presented to a community hospital with a 3-week collateral history of feeling generally unwell. His main complaint was a severe relentless headache with occasional vomiting. At the time of admission he appeared neurologically suppressed, not responding well to vocal commands, but still responded briskly to painful stimuli. No further relevant history could be elicited bar that he had not travelled recently. Clinical examination revealed neck stiffness with both positive Kernig's and Brudzinski's signs but no other signs of pathology. A clinical diagnosis of bacterial meningitis was made and treatment was commenced with cefotaxime, administered intravenously.

Special investigations

A lumbar puncture performed shortly after admission revealed slightly turbid, xanthochromic cerebrospinal fluid (CSF). Biochemical investigation revealed CSF protein 28 580 mg/l (normal range 150 - 450 mg/l), CSF chloride 106 mmol/l (normal range 118 - 132 mmol/l) and CSF glucose 6.1 mmol/l (normal range 2.2 - 3.9 mmol/l). Microscopic analysis of the CSF sample revealed polymorphonuclear leucocytes (PMN) 5/µl (normal range 0 - 5/µl), lymphocytes 22/µl (normal range 0 - 10/µl),[6] with no overt micro-organisms observed. Cryptococcal and bacterial capsular antigen tests could not be performed due to clotting of the CSF sample. Syphilis serology was negative in the rapid plasma reagin (RPR), *Treponema pallidum* haemagglutination (TPHA) and fluorescent treponemal antibody absorption (FTA-abs) tests. HIV serology was positive with the standard battery of one screening enzyme-linked immunosorbent assay ELISA) and two confirmatory ELISAtests.

Case-isolate identification

The CSF sample was plated onto appropriate semisolid agar media according to standard microbiological operational procedures.[6] Within 72 hours positive growth was observed on both chocolate and blood agar plates. Subsequent Gram staining of the isolate revealed yeast cells, which were kept for further mycological analysis and identification. This isolate was inoculated onto the ID32C (Biomerieux SA, Marcy-l'Etoile, France) yeast identification system according to the manufacturer's instructions. Two separate identifications revealed *C. famata* with degrees of identification (specificity) as stated by the manufacturer, of 99.9% and 99.8% respectively. The use of the ID32C system has been proved previously to be the most accurate for the identification of infrequently isolated *Candida* species.[7] No other microorganisms including mycobacteria were isolated from this specimen.

Susceptibility testing

The case isolate was subjected to antifungal susceptibility testing employing the Fungitest micro-broth dilution kit (Biorad, Marnes la Coquette, France) according to the manufacturer's instructions. The *C. famata* strain was found to be sensitive to all antifungal agents tested including: 5-fluorocytosine, amphotericin B, miconazole, ketoconazole, itraconazole and fluconazole, which is similar to the findings of susceptibility studies published previously.[8]

Treatment

The patient's clinical condition improved slightly during hospitalisation to the extent that oral therapy with fluconazole could commence 8 days after admission with a stat oral dose of 400 mg fluconazole, followed by 200 mg administered twice

daily. Despite his initial recovery the patient's condition worsened and he died 12 days after admission.

Discussion

This case demonstrates that *C. famata* may act as a central nervous system pathogen in immune-compromised individuals.

A study conducted on mice previously treated with cortisone[9] demonstrated the organism's potential to invade the central nervous system under immune-compromising conditions. Of these infected animals, 50% were killed while this species proved non-pathogenic to normal mice with no gross pathology, microscopic lesions or positive tissue cultures at the end of the experiment.[9]

Our patient demonstrated a chronic clinical picture, with CSF special investigations supporting the diagnosis of meningitis caused by a fungal pathogen, with increased CSF lymphocytes, elevated CSF-protein and positive fungal culture being most suggestive. Fluconazole treatment for *C. famata* infections has reported mixed success,[4,5] with one case of successful treatment of catheter-associated fungaemia after administration of amphotericin B.[1] Successful therapy with fluconazole for yeast infections usually requires intravenous dosing, early commencement of therapy and an adequate dosage, this patient being a case in point, with delayed treatment and ineffective oral dosing probably leading to his death. The role of HIV as an immunosuppressive condition and possible co-factor for *C. famata* infection of the central nervous system could not be further investigated due to the death of the patient. *C. famata* is an uncommon human pathogen with few documented infectious conditions. The case presented shows the organism to be a possible novel pathogen in the human central nervous system. Failure to identify and recognise *C. famata* as a pathogen, combined with delayed therapy, especially when occurring in immune-compromised patients, may lead to unnecessary fatalities.

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Exclusive breast-feeding — a pipe dream?

To the Editor: In South Africa there is scepticism about the feasibility of exclusive breast-feeding (EBF) — despite success stories from Mexico, Bangladesh and Belarus.[1-3] We report on the steps taken to develop a breast-feeding counselling and support strategy, which supports EBF, in a rural subdistrict in KwaZulu-Natal, where mixed feeding was the norm. Prior research showed that traditional beliefs and concerns about milk sufficiency or infant satiety / health were the main reasons for mixed feeding.[4]

Between May and September 2000 we recruited matriculated women, living in the subdistrict, as breast-feeding counsellors (BCs). They were trained using the WHO / UNICEF breast-feeding counselling training course,[5] a 40-hour course with a strong counselling component. Knowledge before and after training was assessed using a tool developed by the study team. A field guide, containing information from the course and appropriate suggestions addressing traditional beliefs that hinder EBF, was developed as an *aide-mémoire* to facilitate quality, consistent breast-feeding counselling. All BCs were trained to use the field guide. BCs recruited pregnant or breast-feeding women at clinics, and visited them at home at least once a week. The involvement of influential family members during home visits was encouraged. During each home visit, using the listening and learning skills from the course,[5] BCs asked how feeding was going, whether additional feeds or fluids were given to the infant and reasons for these, and about breast health. They observed a breast feed, and then counselled the mother (and often the family) using 'building