



RARE CASE OF CHRONIC MENINGITIS BY CRYPTOCOCCUS NEOFORMANS VAR. GRUBII IN AN IMMUNOCOMPETENT HOST

Microbiology

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ABSTRACT

Cryptococcosis is the opportunistic infection usually seen in immunocompromised individuals. Among HIV seropositive subjects cryptococcal meningitis is the second most common cause of opportunistic neuro-infection but at times it occurs in non-HIV patients who are immunodeficient due to chronic glucocorticoid use, organ transplantation, malignancy as well as sarcoidosis. We present a fatal case of *Cryptococcus grubii* meningitis in a 54-year-old HIV-negative male patient with a past history of pulmonary tuberculosis.

KEYWORDS

INTRODUCTION

Cryptococcosis is the infection caused by *Cryptococcus neoformans* (*C. neoformans*). It has received major attention as one of the common complications in HIV⁺ individuals and AIDS patients with an estimated 120 cases per 1000 HIV infected individuals per year. (1) After inhalation from environmental sources, this organism enters into human body through lungs and spreads to the central nervous system. (2) These infections are mainly due to the three varieties of *C. neoformans* which are based upon biochemical differences. They are *C. neoformans var. grubii* (serotype A), *C. neoformans var. neoformans* (serotype D) and *C. neoformans var. gattii* (serotype Band C). (3, 4) Among all fungi causing meningitis, *Cryptococcus neoformans* is the commonest one. (5) *C. neoformans var. grubii* is an opportunistic pathogen of immunocompromised patients, with HIV infection, corticosteroid therapy and hematological malignancies identified as major risk factors. However here we report a rare case from Uttarakhand of isolating *C. neoformans var. grubii* from an immunocompetent individual who finally succumbed to his illness.

CASE DESCRIPTION:

A 54-year-old male resident of Pauri Garhwal was brought to emergency department of a tertiary care teaching hospital of Rishikesh, Uttarakhand with chief complaints of fever, difficulty in breathing and headache since last 16 days. He had continuous low-grade fever for 8 days along with few episodes of vomiting. The headache was moderately severe in nature and was associated with altered sensorium for the last five days. He was diagnosed as a case of pulmonary tuberculosis six years ago during his stay in Mumbai, where he was initiated on ATT (Anti-tubercular therapy). On examination, the patient was febrile and unconscious with a Glasgow coma scale of E¹M¹V¹. Neck rigidity and Kernig's sign were positive. Pupillary response was bilaterally sluggish and plantars were equivocal. All deep tendon reflexes were diminished. Examination of other systems revealed no obvious abnormality. Laboratory investigations revealed raised total leukocyte count (15,000/mm³) with 90% neutrophils. Serum electrolytes, renal function tests and liver functional tests were within normal limits. A CT-scan head was done which revealed pontine infarct with capsule-ganglionic infarct. Serology for HIV was found to be non-reactive. Examination of cerebrospinal fluid (CSF) examination showed an opalescent fluid, with mild pleocytosis (90 WBCs per mm³ with predominantly lymphocytes), low glucose (20 mg/dl) and increased protein level (244mg/dl). Microscopy revealed occasional mononuclear cells and Gram stain revealed gram-positive yeast budding cells. AFB was negative. Wet mount and India ink preparation showed characteristic predominant round budding yeast cells ranging from 5-20 µm in size

with distinct halo of capsules around yeast cells. Culture on Sabouraud's dextrose agar (SDA) with antibiotics yielded highly mucoid, cream colored colonies of yeast after five days of incubation at 37°C which also revealed capsule on India ink. For further identification Rapid urease test was performed which gave a positive reaction (pink color). Additionally, matrix-assisted laser desorption/ionization time of flight mass spectrometry (MALDI-TOF-MS) (Bruker Biotyper Microflex, Massachusetts) confirmed the isolate identification as *Cryptococcus neoformans var. grubii* with a confidence interval of 2.43. Treatment was started on aggressive basis with Amphotericin B at 1mg/kg per day as an intravenous infusion. After two days of treatment the patient succumbed to infection on 4th treatment day.

DISCUSSION:

Before the AIDS epidemic, it was found that at least 80% of clinical isolates worldwide were *C. neoformans* serotype A (*var. grubii*). It is a capsulated fungus that reproduces by budding and has a worldwide distribution causing disease not only in immunocompromised but also in the immunocompetent. The organism has a special predilection to infect the central nervous system (CNS) (neurotropism) probably due to (i) presence of receptors specific for some ligand on the yeast and (ii) increased dopamine levels in CNS allows melanin production by the phenoloxidase in the yeast contributing to increased fungal virulence. (6, 7) As a consequence, meningitis is seen to be the commonest manifestation. Most present with signs and symptoms of subacute meningitis, such as headache, fever, cranial nerve palsies, lethargy, coma, or memory loss over several weeks. It is the second most common CNS fungal pathogen causing lethal infections in immunocompromised patients, particularly with AIDS. (8) However in our case, the patient was immunocompetent and majority of the infections in such individuals are caused by *Cryptococcus neoformans var. gattii*. (9) The use of MALDI-TOF additionally enabled us to rapidly identify the variant of *Cryptococcus* giving us a better epidemiological profile of the types/variants of *Cryptococcus* prevalent in this geographical region. Early identification helped us to initiate the treatment on an urgent basis, but despite having a good prognosis in immunocompetent hosts, this patient succumbed to his illness.

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