UNUSUAL PATHOGENS IN HIV POSITIVE CASES

A Report of Two Cases

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Introduction

The incidence of HIV infection is on the rise in the country as a whole as well as in the Armed Forces. It has been found that most patients who are tested positive for HIV fall into Group I (asymptomatic) or Group II (persistent generalised lymphadenopathy) PGL [1]. However, a small but significant number develop secondary opportunistic infections during the course of the illness and a rapidly fatal outcome. In our country, tuberculosis remains the most commonly encountered secondary infection. Unusual pathogens are, however, also surfacing. We report 2 cases of uncommon secondary infections in AIDS patients in India diagnosed at autopsy.

Case Report

Case No 1

A 31-year-old individual was found to be HIV positive during screening and transferred to a referral hospital. He developed tonic clonic seizures of sudden onset followed by unconsciousness. Eight days later he developed fever and right sided hemiparesis. No other significant past, personal or family history could be elicited.

Clinical examination revealed poor general condition. The patient had a temperature of 101.6 °F with a pulse rate of 98/minute. He was uncommunicative and responded only to painful stimuli by moving all 4 limbs. Meningeal signs were present. Plantar reflexes were extensor on both sides and deep tendon jerks were unremarkable.

CSF examination revealed a turbid fluid. Proteins were 160 mg/dl with increased globulin, sugar was 80 mg/dl (blood sugar was 112 mg/dl) and WBC's were 20/cu mm, predominantly lymphocytes. Haematological and biochemical parameters were within normal limits. Urine and CSF culture were sterile. Contrast enhanced CT scan of the brain revealed multiple hyperdense enhancing lesions with peripheral oedema.

A diagnosis of AIDS with tubercular meningitis was made and the patient was put on anti-tubercular treatment (ATT) with steroids and supportive therapy. However, he followed a rapid downhill course, with gastrointestinal bleeding and expired shortly thereafter.

At autopsy, the brain was found to weigh 1450 gm. The meninges were congested. Multiple foci of haemorrhagic necrosis affecting both the grey and white matter were found in both lobes including medial temporal lobes and orbital surface of the frontal lobe. The lungs were found to be congested. Other organs were unremarkable on gross examination.

Sections taken from the affected areas of the brain revealed acute haemorrhagic necrosis of grey and white matter accompanied by a predominantly chronic inflammatory cell infiltrate, and thrombosis and fibrinoid necrosis of parenchymal blood vessels. Perivascular cuffing was seen and inflammatory cells were present in the Virchow-Robin spaces and adjacent leptomeninges and Intranuclear Cowdry Type A inclusions could be seen within astrocytes and neurons (Fig 1). Sections taken from the cerebellum appeared normal. Sections from the lung showed moderate congestion. Histopathology of other organs was unremarkable.

A diagnosis of herpes simplex virus (HSV) encephalitis in an HIV positive patient was made, and confirmed by immunofluorescent studies. Brain sections and smears were tested for the presence of HSV-1 antigen by indirect immunofluorescence test and was found positive.

Case No 2

A 34-year-old individual was admitted to a referral hospital with a history of fever, weight loss, anorexia and weakness of one year duration. He also had intermittent bouts of loose motions.

Clinically he looked ill, had a temperature of 101°F and a pulse

Fig. 1 : Cowdry type A inclusion in the neuronal cell (arrow) H & E x 1000.

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Fig. 2: Yeast-like forms of *H.capsulatum* in imprint smears. Leishman-Giemsa x 1000.

rate of 100/minute. Bilateral axillary lymphadenopathy was present. The abdomen had a doughy feeling, organomegaly was present. Bilateral scattered crepitations and rhonchi were heard over the lungs. CNS and CVS examination were normal.

HIV-I antibody tested positive by ELISA and was subsequently confirmed by Western-blot test. Ultrasound scan (USS) of the abdomen revealed multiple loops of small gut matted together. Radiograph chest (PA view) revealed ill-defined non-homogeneous opacities in the RMZ, RLZ and LLZ. All other haematological, biochemical and serological tests were normal.

A diagnosis of HIV positivity with secondary tuberculosis of the abdomen was made and ATT with four-drug regimen was started. However, the individual showed a poor response and expired one-and-a-half months after initial admission.

At autopsy the abdominal cavity had ascitic fluid, and loops of small intestine were found matted together and to the colon with fibrinous adhesions. The mesentery was thickened, and mesenteric lymph nodes were matted and enlarged. All other organs were unremarkable on gross examination.

Imprint smears taken from the lymph nodes, stained by Gram's stain and Leishman-Giemsa stain, revealed a profusion of yeast like organisms (Fig 2). Swabs taken from the lymph nodes, lungs and ascitic fluid, were subjected to fungal and routine cultures.

Histological sections taken from the lymph nodes, intestines, spleen, kidneys and liver revealed proliferation of histiocytes stuffed with yeast-like organisms (Fig 3). The yeast cells had a central, lightly basophilic body surrounded by a clear zone or halo, which in turn was surrounded by a thin, poorly stained cell wall. A variable degree of associated lymphocytic inflammatory infiltrate was present. The native architecture of the lymph nodes and spleen was effaced, and that of other organs distorted in varying degrees. Morphologically, the organism appeared to be *Histoplasma capsulatum* (*H.capsulatum*) var. *capsulatum*. Fungal culture was done at room temperature and at 37°C. A dimorphic (yeast and mycelial forms) fungus was grown and confirmed morphologically to be *H.capsulatum* var. *capsulatum*.

Discussion

The AIDS pandemic has brought in its wake a number of secondary pathogens, mostly ubiquitous organisms of low pathogenicity under normal circum-

Fig. 3: Lymph node histiocytes stuffed with *H.capsulatum*. H & E x 400.

stances, which, however, are responsible for a significant morbidity and mortality in HIV positive cases. In our country, secondary infections are usually caused by *M.tuberculosis*. Our 2 patients had unusual secondary infections.

HSV has a global existence and infects humans of all ages. It is the most common culprit causing mild to severe forms of sporadic viral encephalitis, both HSV-1 and HSV-2 being implicated [1]. The incidence of HSV infection may approach 100 per cent in the general population, although most infections are latent. Host immunocompetence is an important factor in its aetiopathogenesis. In one series of AIDS patients studied, opportunistic viral infections were detected in 72 per cent of patients at autopsy. HSV was detected in 11 per cent of these cases, in contrast to cytomegalovirus which was detected in 66 per cent of the patients with viral infections [2]. Diagnosis of HSV infection may be made antemortem by detection of HSV-DNA in CSF by the polymerase chain reaction (PCR) [3]. In our case HSV infection was not diagnosed antemortem.

Disseminated histoplasmosis is a serious opportunistic infection in patients with AIDS, often seen as the first manifestation of the syndrome. However, cases are reported almost exclusively in patients who live in or have travelled to endemic areas (Central America and Central North America) and only rarely in patients from non-endemic areas [4-7]. It is still, however, a relatively uncommon pathogen in AIDS patients, even in endemic areas [8-11]. Diagnosis is often elusive and treatment difficult [12]. In India, *H.capsulatum* infection is known to occur in the North-East, but it is not recognized as an endemic area for this disease. To the best of our knowledge, no case of disseminated histo-

plasmosis has been previously documented in an AIDS patient in India.

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