TOXOPLASMA ENCEPHALITIS (TE): A REPORT ON THREE FATAL CASES

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Introduction

Toxoplasma gondii is a ubiquitous protozoan parasite. Humans are accidental dead end hosts, cat being the definitive host. Since the advent of AIDS, the impact of infection with this protozoan has been fully appreciated [1].

Toxoplasmosis and toxoplasma infection are two different terminologies, the former describes an active disease process whereas the latter is defined by the mere presence of viable organisms [2]. Chronic or latent infection is present in all those infected since the parasite resides in the cystic stage in some tissues without any clinical disease. Reactivation occurs in immunocompromised patients [3].

The parasite is acquired per-orally, transplacentally or rarely, parenterally in laboratory accidents, by transfusion, or from a transplanted organ. Individuals with HIV infection/AIDS frequently develop toxoplasmosis; the disease usually involves CNS and is often fatal [1]. Toxoplasma Encephalitis (TE) is the most common presentation of toxoplasmosis in AIDS patients [4]. About one third of the patients with AIDS who are latently infected with the parasite will develop TE [5]. Congenital infection is considered to occur only when primary infection is acquired during gestation [6]. Immunocompromised women who acquire the primary infection within 6-8 weeks before conceiving are an exception to the above [7]. The risk of infection to the fetus varies with the trimester of gestation when the mother becomes

infected, and increases with the period of gestation. We report below the 3 fatal cases of toxoplasmosis, including a case of congenital toxoplasmosis, to highlight the multiorgan disease, dominant CNS involvement and fatality caused therefrom, in the HIV infected group.

Fatal Case No.1

A 39-year-old male presented with dry cough and fever of 2 weeks and cervical lymphadenopathy of 4 weeks duration. FNAC of the lymph node showed evidence of tuberculosis. After one month of ATT, he developed eighth nerve palsy on the left side. CT scan of the brain revealed a large irregular ring enhancing lesion 3 cms in diameter in the left parietal region. Within a week after CT scan he developed signs of meningoencephalitis. A repeat CT scan revealed a space occupying lesion with compressed lateral ventricles, reported as tuberculoma of the brain. CSF showed raised proteins (80 mg/dL) with pleocytosis (20 lymphocytes/cmm). At this juncture, serum was tested for HIV and was positive for anti-HIV antibodies. Serum and CSF were strongly positive for toxoplasma IgG antibodies and borderline positive for IgM antibodies. He was put on therapy for toxoplasmosis and ATT was continued. He progressed to coma and died. Autopsy was not carried out.

Fatal Case No. 2

A 29 year male presented with cervical lymphadenopathy of 3 weeks duration. He was diagnosed as having tubercular lymphadenitis on FNAC and was put on ATT. A month after ATT was initiated he developed pain abdomen and was operated for a duodenal ulcer. Two weeks post surgery, he was readmitted with generalised lymphadenopathy and hepatosplenomegaly. Biopsy of the cervical lymph node showed atypical lymphoid hyperplasia. However ATT was continued. Patient's condition deteriorated, surgical wound did not heal and he lost considerable weight. History of multiple unprotected sexual exposures was elicited at this juncture. During his prolonged hospitalisation he developed right hemiparesis, jaundice, oral thrush, involuntary movements and seventh nerve palsy. Terminally, he had severe anaemia (Hb 6.8g/dL), a raised

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bilirubin of 3 mg/dL with mild elevation of serum transaminases. A clinical diagnosis of disseminated tuberculosis was made. His HIV status was explored and he tested positive. CSF showed raised protein (400 mg/dL). Glucose and cells were within normal limits (albumino-cytological dissociation). He developed generalised tonic-clonic seizures and succumbed to the respiratory failure.

At limited postmortem, the brain showed a greenish yellow hue on coronal sections with many softened areas in the central semiovale. Right fronto-parietal lobe showed well marked expansion of central white matter with atrophy of grey matter, compressing the right lateral ventricle. Greenish yellow gelatinous material was seen in the areas of softening. Histopathological sections from these areas showed cerebral oedema, areas of necrosis and many classical toxoplasma cysts containing bradyzoites in the areas of softening (Fig 1 and 2). Cerebellar grooving was seen. The cause of death was attributed to terminal brain stem injury due to raised intracranial tension and extensive infarction necrosis.

The serum separated from heart blood and CSF, both collected at postmortem tested positive for IgM antibodies to toxoplasma. In retrospect, the antemortem CSF sample (collected and preserved for biochemistry) also tested positive for IgM anti toxoplasma antibodies.

Fatal case No.3

A 3 month old male premature child born to HIV positive parents was brought to the hospital with cerebral palsy. The child had poor general condition, pyrexia, hepatosplenomegaly and microcephaly. Skull radiograph revealed periventricular calcifications in two foci. Fundoscopy was not contributory. In view of the above, serum was screened and was found to be positive for HIV and anti-toxoplasma IgM antibodies. The mother also tested positive for anti-toxoplasma IgG antibodies but negative for IgM antibodies. Treatment for toxoplasmosis was initiated, however the child succumbed.

Discussion

All 3 cases presented above exemplify the protean manifestations of toxoplasmosis in an immu-

nocompromised group, AIDS. Numerous studies have established that toxoplasmosis most commonly involves the brain in this group [8-9].

Both adult fatal cases had lymphadenopathy, diagnosed as tuberculosis on FNAC. All subsequent clinical chain of events were thus attributed to tuberculosis. It is documented that lymph node pathology in toxoplasmosis and tuberculosis could be similar in some respects [10]. Even the CNS lesions were taken as tubercular, although the presence of ring enhancing lesions in the first case should have pointed towards TE [8].

Autopsy findings in the second case were classical of TE, replete with multiple cysts containing numerous bradyzoites and conspicuous absence of inflammatory response [11]. CSF abnormalities in toxoplasma encephalitis (TE) in AIDS have been reported to be nonspecific in the form of mild mononuclear pleocytosis and mild to moderate increase in proteins which was found in all the cases.

The second adult and the child had systemic toxoplasmosis with liver and lung affected. Involvement of liver and lung have been documented in toxoplasmosis [12-13]. Congenital toxoplasmosis is the result of primary maternal infection during gestation, transmitted to the fetus either transplacentally or during birth. In the immunocompetent, infection acquired by the mother during first trimester infects 10-25 per cent of fetuses with very severe disease in infants. Approximately 65 per cent of fetuses are infected in third trimester, with mild or inapparent involvement at

Fig. 1 : photomicrograph showing cerebral oedema, focal necrosis and many toxoplasma cysts. (H & E stain, 100 X).

Fig. 2 : Photomicrograph showing bradyzoites within toxoplasma cysts. (H & E stain, 500 X).

birth [14]. The vertical transmission of toxoplasma infection is significantly more frequent in HIV infected when compared to non-HIV toxoplasma infected pregnant women. Further, infants with congenital toxoplasmosis born to HIV infected mothers are also infected with HIV suggesting that factors that predispose to vertical transmission of HIV also favour transmission of toxoplasma and vice-versa [8]. Congenital toxoplasmosis in the HIV infected infants appears to run a more rapid course, with multiorgan involvement as was seen in the child presented.

That there was a perfect setting for conjoint vertical transmission of HIV and toxoplasmosis in our case is unambiguous, albeit mere demonstration of anti-HIV antibodies in the infant cannot be sufficient to prove HIV transmission.

The cases presented drive us to conclude that toxoplasmosis and HIV should be considered in patients presenting with undiagnosed neurological syndrome. In fatal cases, autopsy would put us wiser on the pathogenesis and extent of dissemination of this notorious parasitic disease.

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