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CASE REPORTS

Case Report on Cerebral Toxoplasmosis: An AIDS defining Disease

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Abstract:

Cerebral toxoplasmosis is an opportunistic infection of brain caused by Toxoplasma gondii*, which is a zoonotic intra-cellular parasite transmitted from cat and other feline animals. In immunocompetent person it causes mainly asymptomatic infection. But in case of immunocompromised people, reactivation of dormant organisms causes widespread dissemination producing focal or global cerebral symptoms. CD4+ lymphocytes provide the main defense against toxoplasmosis. So, in case of AIDS when CD4+ cell count falls below a critical level, predisposition to cerebral toxoplasmosis occurs giving it the title of an AIDS defining illness.*

Introduction:

Toxoplasmosis is a zoonotic, opportunistic infection caused by *Toxoplasma gondii*; which is an intracellular protozoan parasite-[1]. Cat, being the definitive host, serves as a natural reservoir[2]. But any animal or human can get infected by ingesting materials contaminated with oocyst or by consuming undercooked tissue of infected animals[2]. *Toxoplasma* seropositivity varies between different countries depending upon food habit, age, immunocompetency[3]. Spectrum of toxoplasmosis includes: cerebral toxoplasmosis, encephalitis, retino-choroiditis, congenital toxoplasmosis[2]. But cerebral toxoplasmosis is one of the AIDS defining illnesses[4]. It is the most common opportunistic infection of brain and its incidence increases significantly when CD4+ lymphocyte count fall[5]. Headache, confusion, lethargy, seizure, mass lesion, cranial nerve palsy, ataxia, psychomotor retardation, meningitis are features of cerebral toxoplasmosis[3]. Here, we describe a case history of an AIDS patient who subsequently developed cerebral toxoplasmosis.

Case Summary

Our patient was a 40-year-old Bangladeshi male, who was normotensive, non-diabetic, right- handed businessman. He was reasonably well 3 months ago when he developed vesicular rash over different parts of body including genitalia. For this, he was evaluated and screened for retroviral infection and tested positive for HIV. Then, he was started anti-retroviral therapy under the national guidance. His drug compliance was good. He had no history of blood transfusion, illicit drug misuse, needle sharing. He refused any extra-marital sexual relationship but gave history of sharing sharps in the men's saloon. He was smoker with 10 pack year history but non-alcoholic. He was married for 15 years with 3 children. None of his family members including spouse tested positive for HIV.

Two months ago, he developed gradual onset of weakness of right side of body starting from lower

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limb. Initially he had difficulty in walking and going upstairs, but gradually he noticed weakness of right upper limb wit difficulty in performing activities of daily living requiring help of others. He also noticed weakness of right side of face and deviation of angle of mouth towards left side and pouring of liquid from right side of mouth. He also complained of headache, nausea and occasional vomiting, which were more marked in the morning and aggravated by coughing, straining with associated visual disturbance. He had no history of convulsion or unconsciousness. He complained of low-grade fever for same duration with highest recorded temperature of 99°F and mild sweating. His fever was more marked over later part of the day but he had no cough, sputum production, diarrhea, abdominal pain, dysuria, oral ulceration or joint pain.

On examination, he was alert, oriented with normal vitals and no anaemia, jaundice, lymphadenopathy or thyromegaly. His higher cerebral function was intact with slurring of speech. He had weakness of right lower face with sparing of eye and forehead. Fundoscopy revealed bilateral papilledema with no other abnormality. He had no ophthalmoparesis or any other cranial nerve involvement. The patient had right sided spastic hemiparesis with muscle power of MRC grade 02 on the right side and normal on the left side. He had no cerebellar or sensory sign and no sign of meningeal irritation.

Our patient's hematology revealed mild anemia of microcytic hypochromic type, sedimentation rate 44mm in first hour, total count of 6500/µL, neutrophil 64% and lymphocyte 25% with no abnormal cells. Flow cytometry revealed absolute lymphocyte count was 1632/µL with CD4+ cell count 84cells/µL and CD4+:CD8+ ratio of 0.06 (normal 1.4-3.0). His renal function, liver function, chest x-ray, abdominal ultrasound revealed no abnormality. Hepatitis B and C virus screening were negative. TORCH panel revealed >400IU/ml test value for *Toxoplasma* IgG and 7.6AU/ml for IgM. He showed no current evidence of any other infection. Interferon gamma release assay to detect latent tuberculosis was negative.

CT scan imaging of brain revealed large mixed density lesion in left basal ganglia area with perilesional hypodensity, ventriculomegaly and midline shifting. After contrast injection, the lesion showed circumscribed contrast enhancement. MRI of brain was also done. It showed rounded hypo-intense lesion on T1 weighted imaging and marginal hypo-intensity and central hyper-intensity

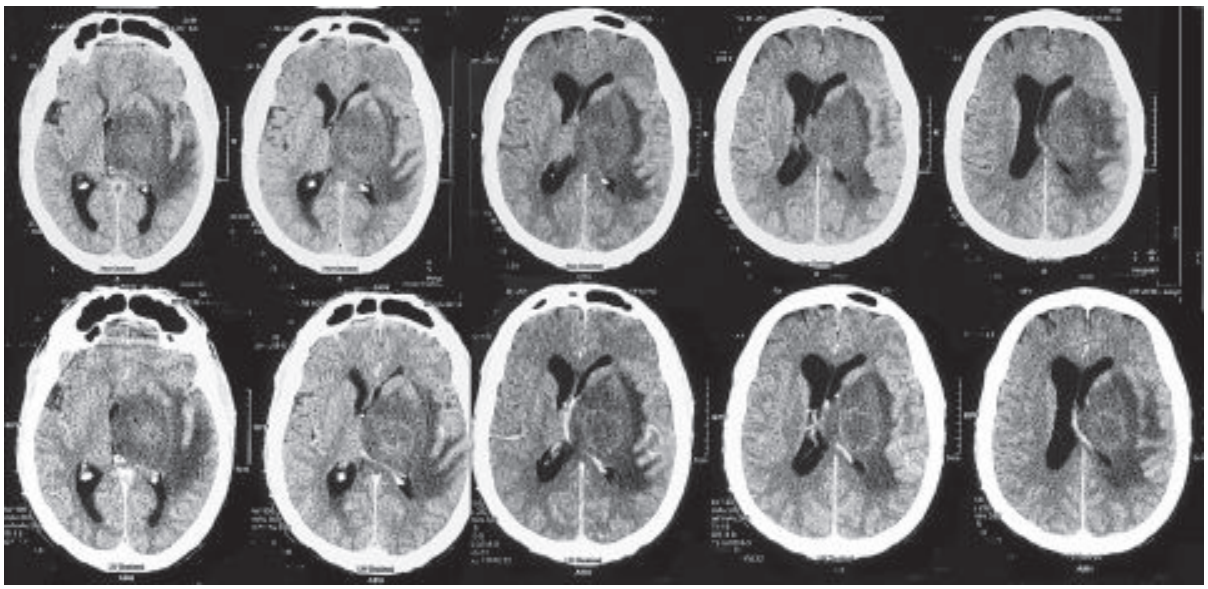

Fig.-1: *CT scan of brain of the patient. Upper row showing non-contrast image and lower row showing post contrast image.*

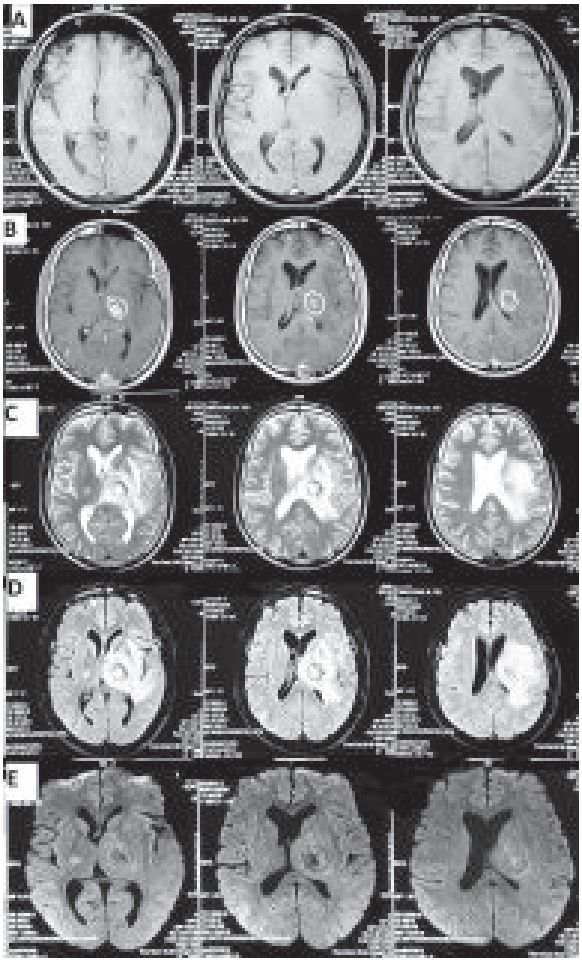

Fig.-2: *MRI of brain of the patient. A: T1 weighted image, B: T1 post contrast, C: T2 weighted image, D: T2 FLAIR image, E: Diffusion weighted image*

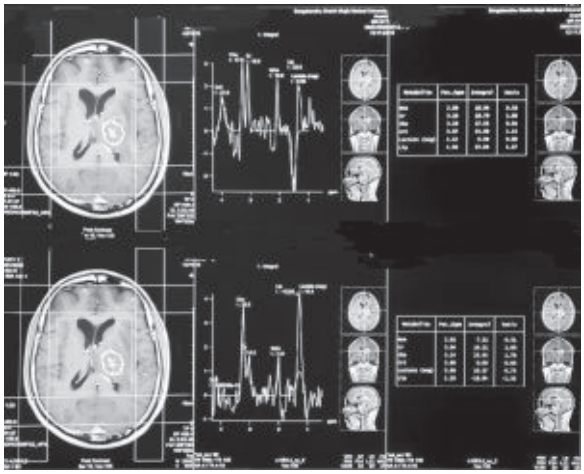

Fig.-3: *MRS of brain of the patient.*

on T2 weighted imaging in left thalamo-ganglionic area. There was surrounding vasogenic edema and mild restriction of diffusion on DWI sequence. Post gadolinium injection showed marginal enhancement with multiple tiny areas of similar lesion in both cerebral and cerebellar hemispheres. Left lateral ventricle was effaced. Spectroscopic analysis revealed increased choline peak indicating increased membrane synthesis and/or increased number of cells; increased choline/creatine ratio (1.89). NAA peak was suppressed at 2.0ppm indicating neuronal degradation and depressed NAA/creatine ratio and increased lipid and lactate peak. We did not perform lumbar puncture as it was contra-indicated.

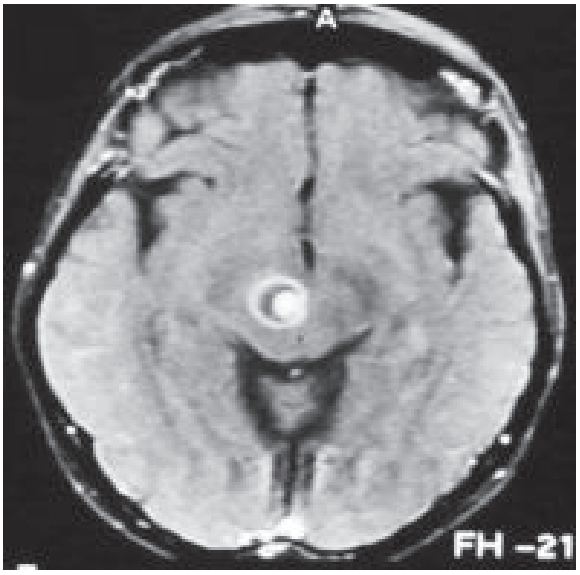

Fig.-4: *Axial T1WI post contrast image[9] of brain showing 'eccentric target sign'.*

The patient continued on anti-retroviral therapy. After thorough work-up, we considered co-trimoxazole (480mg) two tabs twice daily with injectable dexamethasone which was tapered subsequently. Patient showed good response with no adverse effect, so co-trimoxazole was continued for two months. At follow-up the patient had some residual weakness but could walk without support and perform his activities of daily living independently.

Discussion:

Toxoplasma gondi is an intracellular protozoa found worldwide. Human gets infected by taking cyst in

under-cooked meat of infected animal or contaminated vegetables or direct contact with cat feces[6]. Cat is the definitive host. It has 3 developing forms: sporozoites in oocyst, slowly proliferating bradyzoites in tissue-cyst and rapidly growing tachyzoites[2]. Crescentic tachyzoites are responsible for acute infection[2].

Prevalence of toxoplasmosis averages 25-30% in the world[5]. But it varies between regions, depending upon food habits, age, immune-competency and proximity to cats[3]. Highest rates of infection are reported in South-America (42-72%) and Asia (40%)[5]. It is the most frequent opportunistic infection of brain and its incidence rises rapidly when CD4+ lymphocyte count falls below 100cells/μL[5].

In immune-competent person *Toxoplasma* infection may be asymptomatic or cause mononeucleosis like syndrome, fever, lymphadenopathy, splenomegaly, malaise, myalgia etc[2]. But as the immune system cannot completely clear the organism; latent phase remains dormant in brain, skeletal muscle and heart[6]. When immune system becomes incompetent, reactivation of these dormant organisms occurs with dissemination to brain, lungs, lymph nodes, gastro-intestinal tract, muscle[5]. Toxoplasma can infect all cell types of brain cells[2]. The CD4+ cells release interferon gamma that prevents proliferation of cyst; so when CD4+ cell count falls, spread of infection hastens[2]. This spread is serologically evidenced by increase of IgG against Toxoplasma with minimal or no increase of IgM[7].

PCR for Toxoplasma can be done from CSF with specificity of 100% but low sensitivity (50%)[2]. Diagnostic criteria[8] includes:

1. HIV-infected patients with CD4 levels <200/μL
2. Neurological deficit
3. Brain imaging showing ring-enhancing lesion
4. Serological evidence of *Toxoplasma* antibody (IgM and IgG)

Empirical therapy may be started when 3 out of 4 criteria are fulfilled[8].

Differential diagnoses are many, which include CNS lymphoma, tuberculosis, aspergillosis, progressive multifocal leuco-encephalopathy, cryptococcosis, bacterial abscess etc[6]. Lymphoma is more locally infiltrative, periventricular, butterfly like pattern can be seen with diffuse contrast enhancement[6]. CNS tuberculoma is seen in T2 weighted imaging as hypointense center with surrounding iso-intense capsule, more tendency to involve basal ganglia and cisternal enhancement on contrast injection[6]. In AIDS patients, CNS tuberculoma mainly occurs with CD4+ count of <200cells/μL[6], CNS lymphoma in CD4+ count of <50cells/μL[6], whereas cerebral toxoplasmosis mainly occurs with CD4+ count of <100cells/μL[9].

Cerebral toxoplasmosis is seen as multiple hypo-dense lesions with vasogenic edema and mass effect on CT scan with propensity to affect the basal ganglia, cortico-medullary junction, white matter and periventricular region[6]. After contrast injection ring enhancing lesion can be seen in basal ganglia (48%), frontal lobe (37%), parietal lobe (37%), temporal lobe (18%) and brainstem/cerebellum (5-15%)[1]. Calcification is rare, but may follow successful therapy[6]. On MRI T1WI shows hypo-intensity with occasional peripheral hyper-intensity which may differentiate toxoplasmosis from lymphoma[6]. Hyper-intensity is also seen in T2WI, FLAIR and on DWI sequence peripheral restricted diffusion may be seen when hemorrhage occurs within capsule but no diffusion restriction occurs within central portion[6]. There are two signs with high specificity but less sensitivity. 'Eccentric target sign' (seen in <30% cases)[1,9] and 'concentric target sign'[1].

There are multiple treatment options like, sulfadiazine+ pyrimethamine, co-trimoxazole, clindamycin[6]. A meta-analysis[10] revealed that co-trimoxazole is the preffered treatment choice. It has less adverse effects, good posology, less cost and more accessibility[9]. Folinic acid is added with pyrimethamine therapy to prevent hematologic toxicity[6] as folic acid decrease the efficacy of therapy[7]. Duration therapy should be 6 weeks followed by maintenance therapy for 12 months to prevent relapse[6]. Ninety percent patients respond to initial therapy with clinical and radiological

improvement within 14 days[2]. Poor prognostic factors include: decreased level of consciousness, fever, multiple lesion, lymphocyte count <24%, long duration of AIDS, Kaposi's sarcoma, *Pneumocystis jiroveci* pneumonia infection[11].

Conclusion:

Cerebral toxoplasmosis is still one of the main causes of death and disability in AIDS patients. So, in any AIDS patients with cerebral involvement, toxoplasmosis should be considered in the differentials as it can be easily treated to prevent mortality.

Conflict of interest

The authors have no conflict of interest.

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