INJ INTERNATIONAL NEUROUROLOGY JOURNAL

Case Of Toxoplasmic Encephalitis With Tuberculoma In Severely Immunocompromised Patients

Dr. Govind Shiddapur[1], *Dr. Vutukuru Kalyan Kumar Reddy[2] ,Dr. Nilesh Jagdale[3], Dr. Mohith Prakash Kondapalli[4], Dr. Adapa Sai Mounika[5], Dr. Sonali Agarwal[6]

[1]Professor, Department of General Medicine, Dr. D. Y. Patil Medical College, Hospital &Research Centre, D. Y. Patil Vidyapeeth, Pimpri, Pune – 411018.

[2]Resident, Department of General Medicine, Dr. D. Y. Patil Medical College, Hospital &Research Centre, D. Y. Patil Vidyapeeth, Pimpri, Pune – 411018.

[3]Assistant Professor, Department of General Medicine, Dr. D. Y. Patil Medical College, Hospital &Research Centre, D. Y. Patil Vidyapeeth, Pimpri, Pune – 411018.

[4]Resident, Department of General Medicine, Dr. D. Y. Patil Medical College, Hospital &Research Centre, D. Y. Patil Vidyapeeth, Pimpri, Pune – 411018.

[5]Resident, Department of General Medicine, Dr. D. Y. Patil Medical College, Hospital &Research Centre, D. Y. Patil Vidyapeeth, Pimpri, Pune – 411018.

[6]Resident, Department of General Medicine, Dr. D. Y. Patil Medical College, Hospital &Research Centre, D. Y. Patil Vidyapeeth, Pimpri, Pune – 411018.

Abstract

Toxoplasmosis is the most common central nervous system infection in patients with the acquired immunodeficiency syndrome (AIDS) who are not receiving appropriate prophylaxis. Toxoplasmosis is a principal opportunistic infection of the CNS in persons with AIDS. In immunocompromised hosts, the disease may be rapidly fatal if untreated. Cerebral tuberculoma is always considered in the differential diagnosis of solitary and large focal brain lesions in HIV-infected patients, particularly in tuberculosis endemic areas. Thus, accurate diagnosis and initiation of appropriate therapy are necessary to prevent fulminant infection. CT and MRI play an important role in early diagnosis and assist the clinician to provide effective management and prevent further complications

Key words: AIDS, CNS, CT, MRI, Toxoplasmosis

Introduction

Toxoplasmic encephalitis is a common presentation of Toxoplasma gondii infection of the central nervous system in the late stage in AIDS patients [1]. It has been shown to occur by reactivation of quiescent infection [2, 3] as a result of loss of cellular immunity. In the CNS, the predominant neuropathologic feature of TE is multifocal necrotizing encephalitis [4] which progresses to parenchymal abscesses with necrosis and surrounding inflammation [5]. This life threatening infection increases in frequency with severity of immune depression [1, 6] and has a variable worldwide seroprevalence [7].

In some high income settings with high seroprevalence, it has been estimated that in the absence of prophylaxis 30 to 40% of patients with AIDS will develop TE [8]. Like most CNS diseases in AIDS, diagnosis of TE is often difficult such that in clinical practice treatment of TE is usually initiated upon presumption based on clinical and radiological features as well as response to treatment [1, 9].

In toxoplasmosis, multiple ring-enhancing lesions (RELs) usually exist with oedema and mass effect with predilection for basal ganglia, and the frontal and parietal lobes [10]. Tuberculomas tend to involve the infratentorial compartment of brainstem and cerebellum, and involvement of the basal ganglia is usually due to vasculitic infarction instead of primary lesions [11]. There is no reliable way to exclude CNS tuberculosis, especially in an endemic country like India where the prevalence of CNS tuberculosis is comparable with that of toxoplasmosis [12]. Typically, patients with severe immune suppression (CD4 count <200/mm3) are at risk of infection with toxoplasma, cryptococcus and cytomegalovirus, whereas patients with moderate immune suppression (CD4 counts 200–500 cells/mm3) are at risk of tuberculous meningitis and PML.

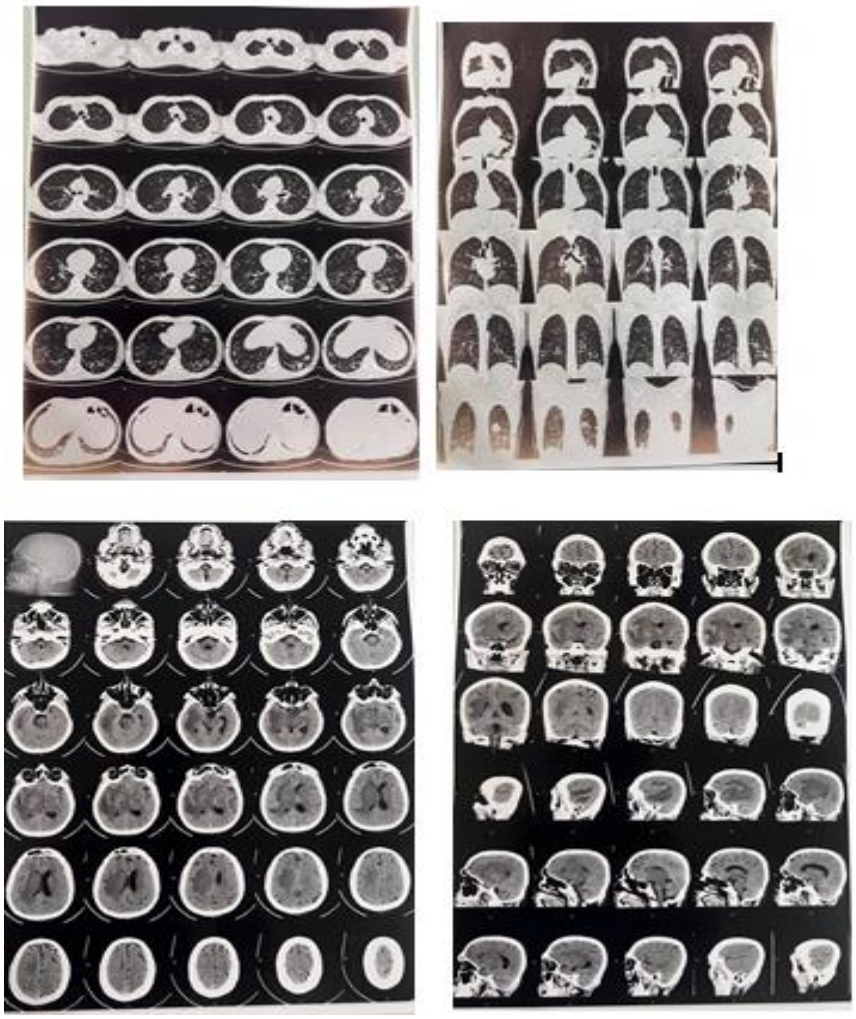
ISSN:2093-4777 | E-ISSN:2093-6931
DOI: 10.5123/inj.2023.4.inj17
Vol. 27 Iss. 4 (2023)

INJ INTERNATIONAL NEUROUROLOGY JOURNAL

Case Report

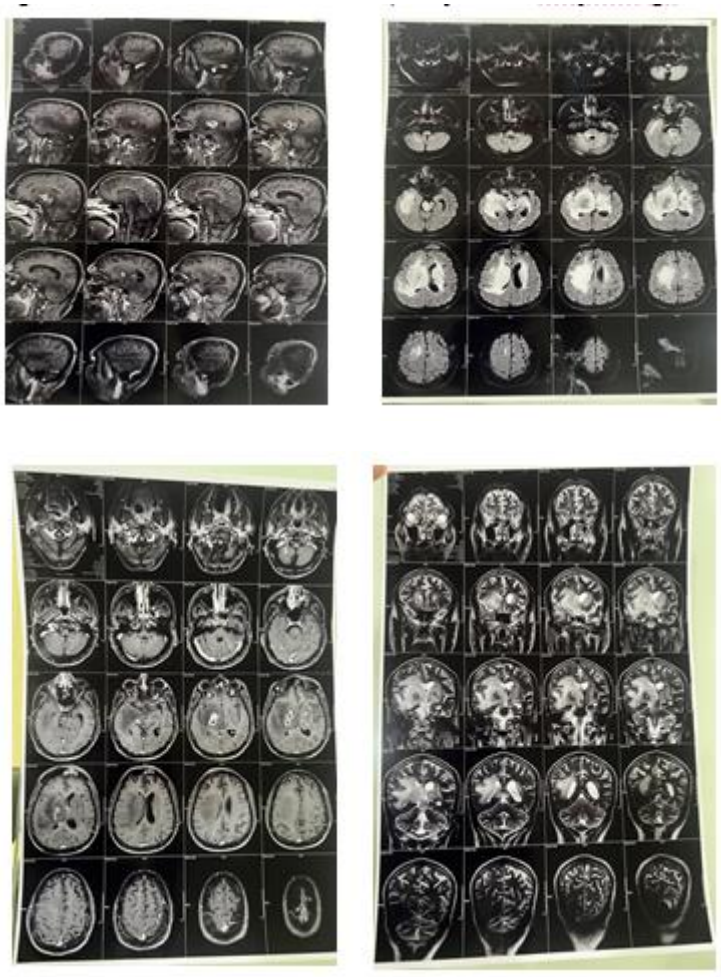
A 41-year-old male patient K/C/O PLHIV and K/C/O HBsAg positive patient presented with complaints of fever since last 4 days and altered sensorium since last 2 days. Fever which was high grade sudden in onset, intermittent in nature and associated with chills. Patient was confused, disoriented, irritable, and unable to identify the family members. There was no history of cough, cold, headache, vomiting, urinary complaints, and loss of consciousness or convulsions.

Patient was detected incidentally as HIV positive and was started on TLD regimen. History of hospital admission in view of breathlessness, abdominal pain, loose stools and weight loss of 30 kgs in 2 months was also present. HRCT was done S/O centrilobular nodules with tree in bud appearance in bilateral lung parenchyma in lower lobes and bronchoscopy was done; BAL CBNAAT came negative; BAL cultures s/o pneumocystis jirovecii pneumonia. Patient was started on ATT empirically (patient took it for 2 months and then stopped). Patient cd4 count was 71.



CT brain showed multiple (likely coalescing) target lesions in bilateral gangliocapsular, thalamic and right temporal periventricular white matter, with extensive perifocal oedema. Marked mass effect, with right lateral ventricular and third ventricular compression and contralateral left lateral ventricular dilatation; right subfalcine herniation with midline shift; and marked right uncal herniation with midbrain compression was present. In an immunocompromised patient, with low CD 4 count, above findings is likely s/o opportunistic infection with early abscess formation- likely tubercular or toxoplasmosis.

Lumbar puncture was done under all the aseptic precautions and CSF sample sent for routine microscopy. Elevated proteins, 40 cells/Lymphocytes were present. ADA was mildly increased. Differential diagnoses on the basis of these reports were tubercular meningitis, dengue meningoencephalitis,encephalitis, brain abscess. Initial treatment was given to the patient and patient was continued with antiepileptic and anti-oedema medications.
MRI brain revealed multiple coalescing ring enhancing lesions (RELs) in right lentiform nucleus, left lentiform nucleus, left thalamus and in inferior portion of right cerebellar hemisphere with moderate ill-defined peri-focal vasogenic oedema. Mass effect on right lateral ventricle and third ventricle with shift of midline structure towards left (6 mm) was there. Inferiorly oedema is extending in right cerebral peduncle, right half of midbrain, dorsal pons. On MR spectroscopy, there is decrease in NAA, increase in choline, increase in choline creatinine ratio and lactate inversion at 1.3. According to the signs, differential diagnosis needs consideration were Tuberculomas, Toxoplasmosis. Toxoplasmic IgG antibodies report revealed it reactive (>200).



Discussion

Toxoplasmosis is a disease caused by Toxoplasmosis gondii, an intracellular obligate protozoal parasite. T. gondii has three forms: the tachyzoite (the rapidly reproducing form), the bradyzoite (a slower reproducing form contained in tissue cysts), and the sporozoite (contained in oocysts) [13, 14].

Immunocompetent persons with an acute primary infection are usually asymptomatic. However, during the dormant phase of the disease, the organisms may be seen within the grey and white matter of the brain, skeletal muscle, heart, and alveolar lining of the lungs, mimicking Pneumocystis jirovecii infection [14, 15]. In immunosuppressed patients, especially patients with AIDS, the parasite can reactivate and cause disease, usually when the CD4 count falls below 100 cells/microL. In humans, toxoplasmosis is typically acquired through ingestion of infectious oocysts, usually from soil or cat litter contaminated with feline faeces, or undercooked meat from an infected animal.

The common presenting symptom of cerebral toxoplasmosis is headache, often accompanied by fever and altered mental status [16]. Individuals may also present with visual disturbances, seizures, cranial nerve abnormalities, and sensory disturbances. The common neurological signs include motor weakness and speech disturbances [15]. In individuals with AIDS, >95% of cases of Toxoplasma encephalitis (TE) are believed to be due to recrudescent infection. In most of these cases, encephalitis develops when the CD4+ T cell count falls below 100/μL. In immunocompromised hosts, the disease may be rapidly fatal if untreated. Thus, accurate diagnosis and initiation of appropriate therapy are necessary to prevent fulminant infection.

On plain CT images, cerebral toxoplasmosis usually appears as multiple hypoattenuating or isoattenuating lesions representing abscesses with surrounding vasogenic oedema and mass effect. Solitary lesions are very rare but have been reported [17]. Calcifications are usually rare but can be seen after therapy with antitoxoplasmic agents. However, calcifications are very commonly seen in congenital toxoplasmosis [18]. On contrast-enhanced CT, the lesions show either a thin, smooth, or ill-defined rim of enhancement or a solid, eccentric nodular enhancement. At times, no obvious enhancement has been observed [19].

On MRI, cerebral toxoplasmosis appears as hypointense lesions on T1-weighted images and may show peripheral hyperintensity (which helps to differentiate it from CNS lymphoma). The lesions on T2 and FLAIR images have high or mixed signal intensity. On contrast-enhanced T1-weighted images, the lesions show rim like enhancement with surrounding hypointense areas (representing oedema) [19]

It was challenging to diagnose cerebral toxoplasmosis based on MRI findings, because, on cranial imaging, it is very similar to central nervous system (CNS) lymphoma, primary and metastatic CNS tumors, or other intracranial infections like tuberculoma or abscesses [20]. On brain-MRI, our patient presented multiple coalescing ring enhancing lesions (RELs) in right lentiform nucleus, left lentiform nucleus, left thalamus and in inferior portion of right cerebellar hemisphere with moderate ill-defined peri-focal vasogenic edema.

Tuberculosis in HIV-infected patients has a high frequency of extrapulmonary manifestations. In patients with advanced immunodeficiency (defined by CD4+ cell counts 200/μL) 50% of patients with tuberculosis have extrapulmonary manifestations [21]. Cerebral manifestations are present in 15% of patients with extrapulmonary tuberculosis [22]. Primary solitary cerebellar granulomas have been reported in only a few cases of HIV-infected patients [23]. This case report indicates that differential diagnosis of brain lesions in HIV infected patients must include tuberculoma.

There were specific points which lead to differential diagnosis of toxoplasmosis and tuberculoma like the patient had a CD4 count <100 cells/microL, a positive T. gondii IgG antibody, brain imaging (preferably magnetic resonance imaging) that demonstrated a typical radiographic appearance (e.g. multiple ring-enhancing lesions), and on MR spectroscopy there was decrease in NAA, increase in choline, increase in choline creatinine ratio and lactate inversion at 1.3.

The treatment of toxoplasmosis in patients with HIV includes antimicrobial therapy directed against T. gondii as well as antiretroviral therapy (ART) for immune recovery. Primary Prophylaxis is patients with AIDS should be treated for acute toxoplasmosis; in immunocompromised patients, toxoplasmosis is rapidly fatal if untreated. AIDS patients who are seropositive for T. gondii and who have a CD4+ T lymphocyte count of <100/μL should receive prophylaxis against TE.

Secondary Prophylaxis is individuals who have completed initial therapy for TE should receive treatment indefinitely unless immune reconstitution, with a CD4+ T-cell count of >200/μL, occurs as a consequence of combined ART (cART). Combination therapy with pyrimethamine plus sulfadiazine plus leucovorin is effective for this purpose. An alternative to sulfadiazine in this regimen is clindamycin or TMP-SMX.

Long-Term Maintenance Therapy is patients receiving secondary prophylaxis for TE are at low risk for recurrence when they have completed initial therapy for TE, remain asymptomatic, and have evidence of restored immune function. Individuals with HIV infection should have a CD4+ T lymphocyte count of >200/μL for at least 6 months after cART. A repeat MRI brain scan is recommended. Secondary prophylaxis should be reintroduced if the CD4+ T lymphocyte count decreases to <200/μL.

ISSN:2093-4777 | E-ISSN:2093-6931
DOI: 10.5123/inj.2023.4.inj17
Vol. 27 Iss. 4 (2023)

Conclusion

CNS toxoplasmosis should be considered as an important differential diagnosis in immunocompromised patients with neurological findings and unknown etiology. Cerebral tuberculoma is always considered in the differential diagnosis of solitary and large focal brain lesions in HIV-infected patients, particularly in tuberculosis endemic areas. CT and MRI play an important role in early diagnosis and assist the clinician to provide effective management and prevent further complications. This case report will help physicians in making a proper differential diagnosis and in starting the appropriate treatment in HIV patients with intracerebral mass lesions without wasting time.

References

1. Luft BJ, Remington JS: Clinical infectious diseases: an official publication of the infectious diseases society of America. Toxoplasmic encephalitis in AIDS. 1992, 15 (2): 211-222.
2. Saadatnia G, Golkar M: A review on human toxoplasmosis. Scand J Infect Dis. 2012, 44 (11): 805-814.
3. Goncharov DB, Gubareva EV, Kobets NV, Domonova EA, Ievleva ES: Toxoplasmosis in HIV infection: invasion reactivation criteria. Zh Mikrobiol Epidemiol Immunobiol. 2012, 4 (88): 92-p. 92
4. Mamidi A, DeSimone JA, Pomerantz RJ: Central nervous system infections in individuals with HIV-1 infection. J Neurovirol. 2002, 8 (3): 158-167.
5. Skiest DJ, Erdman W, Chang WE, Oz OK, Ware A, Fleckenstein J: SPECT thallium- 201 combined with toxoplasma serology for the presumptive diagnosis of focal central nervous system mass lesions in patients with AIDS. J Infect. 2000, 40 (3): 274-281.
6. Nascimento LV, Stollar F, Tavares LB, Cavasini CE, Maia IL, Cordeiro JA: Risk factors for toxoplasmic encephalitis in HIV-infected patients: a case–control study in brazil. Ann Trop Med Parasitol. 2001, 95 (6): 587-593.
7. Chiang TY, Hsieh HH, Kuo MC, Chiu KT, Lin WC, Fan CK: Seroepidemiology of toxoplasma gondii infection among healthy blood donors in Taiwan. PLoS One. 2012, 7 (10): e48139-10.1371/journal.pone.0048139.
8. Leport C, Ambroise-Thomas P, Bazin C, Chene G, Derouin F, Katlama C: Risk factors of the occurrence of cerebral toxoplasmosis in patients with HIV infection. Definition of indications of primary prevention. Proposals of the toxoplasmosis and other protozoan infections group. Coordinated action N.5 - 1996 February. Presse Med. 1996, 25 (11): 519-520.
9. Cohen BA: Neurologic manifestations of toxoplasmosis in AIDS. Semin Neurol. 1999, 19 (2): 201-211.
10. Berger JR. Mass lesions of the brain in AIDS: the dilemmas of distinguishing toxoplasmosis from primary CNS lymphoma. AJNR Am J Neuroradiol 2003;24:554.
11. Sanei Taheri M, Karimi MA, Haghighatkhah H, et al. Central nervous system tuberculosis: an imaging-focused review of a reemerging disease. Radiol Res Pract 2015;2015:1–8.
12. Lanjewar DN, Jain PP, Shetty CR. Profile of central nervous system pathology in patients with AIDS: an autopsy study from India. AIDS 1998;12:309–13.
13. Alice B, Smith, Smirniotopoulos James G., MD, Rushing Elisabeth J., COL, MC, USA Central nervous system infections associated with human immunodeficiency virus infection: Radiologic-pathologic correlation. Radiographics. November-December 2008
14. Khan Ali Nawaz, MBBS, FRCS, FRCP, FRCR, Smirniotopoulos James G. Imaging in CNS toxoplasmosis. Medscape. June 11 2013
15. Lee Gregory Tse, MD, Antelo Fernando, MD, Mlikotic Anton A., MD Cerebral toxoplasmosis. Radiographics. July-August 2009
16. Porter SB, Sande MA. Toxoplasmosis of the central nervous system in the acquired immunodeficiency syndrome. N Engl J Med. 1992;327(23):1643–1648.
17. Vastava P.B., Pradhan S., Jha S., Prasad K.N., Kumar S., Gupta R.K., MRI Features of toxoplasma encephalitis in the immunocompetent host. Neuroradiology. 2002 Oct;44(10):834–838.
18. Grossman RI, Yousem DM. Neuroradiology: the requisites. 2nd ed. Mosby, Elsevier Inc.; Philadelphia, Pa: 2003. p. 224. 223.
19. Osborn AG, Blaser SI, Salzman KL. Diagnostic imaging: brain. Amirsys; Salt Lake City, Utah: 2004. pp. 70–73.
20. Kumar GG, Mahadevan A, Guruprasad AS, Kovoor JM, Satishchandra P, Nath A, et al. Eccentric target sign in cerebral toxoplasmosis : neuropathological correlate to the imaging feature. J Magn Reson Imaging. 2010;31:1469–1472.
21. Murray, j. F.: Cursed duet: HIV Infection and tuberculosis. Respiration. 1990;57:210-220

22. Leonard, j. M. and R. M. Des Pres: Tuberculous meningitis. In: Scheid, W. M. and B. Wispelwey, eds. Infectious Disease Clinics of North America: Meningitis. Philadelphia: W. B. Saunders Co. 1990;4:769-787
23. Malasky, C. and L. B. Reichman: Long-term folIo-up of tuberculoma of the brain in an AIDS patient. Chest. 1990;101(1):278-279..