Longitudinally Extensive Transverse Myelitis Due to Toxoplasma: An Autopsy Study

Yareeda Sireesha, Megha S. Uppin[1], Komal Bohra, Rajesh Alugolu[2], Mathukumalli L. Neeharika, Angamuthu Kanikannan

Departments of Neurology, [1]Pathology and [2]Neurosurgery, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India

Abstract

Toxoplasma is an obligate intracellular parasite that remains asymptomatic in humans but, at times, can cause devastating disease. Here, we describe an autopsy study of a young immunocompetent gentleman with no comorbidities whose presentation was acute transverse myelitis. Magnetic resonance imaging spine showed longitudinally extensive spinal cord lesion (LESCL) that mimicked neuromyelitis optica with normal brain imaging at presentation. Investigations showed albuminocytological dissociation which prompted a course of parenteral steroid. However, the lesion relentlessly progressed to involve the brain stem and cerebrum leading to toxoplasmic encephalitis that terminated fatally. This report highlights that toxoplasma can present as LESCL and needs to be considered in the differential diagnosis of atypical myelitis.

Keywords: Autopsy study, immunocompetent adult, longitudinally extensive, myelitis, toxoplasma

Introduction

Longitudinally extensive transverse myelitis (LETM) refers to the involvement of spinal cord with contiguous extension over more than three vertebral segments on magnetic resonance imaging (MRI).[1] Neuromyelitis optica (NMO) and its spectrum disorder are the most common conditions presenting as LETM. Among the infectious causes, viral and bacterial infections are well known, while schistosomiasis is the only parasitic infestation causing myelitis that has been reported so far.[2]

Toxoplasma is an opportunistic protozoan that causes encephalitis or focal cerebral lesions predominantly in immunocompromised patients.[3] There are rare reports of this organism affecting the spinal cord in the setting of human immunodeficiency virus.[4] However, literature till date does not describe toxoplasma involving the spinal cord in immunocompetent individuals. This is unique as it is the first report of spinal toxoplasmosis confirmed by autopsy.

Case Report

A 35-year-old gentleman presented with pain in the neck and left upper limb of 10 days duration. He described it as paresthesia along medial aspect of the entire upper limb. MRI of spine showed hyperintensity in the cervical spine (C2–C6) with mild cord enlargement which was enhancing on contrast study. Brain imaging done at the same time was normal [Figure 1]. Possibilities considered were acute transverse myelitis and NMO based on MRI which showed a longitudinally extensive spinal cord lesion (LESCL). Serum biochemistry and hematological profile including erythrocyte sedimentation rate, CD4 counts, and complement levels were normal. Viral markers such as HIV, varicella-zoster virus, herpes simplex virus, cytomegalovirus, hepatitis B surface antigen, and hepatitis C virus were negative. Cerebrospinal fluid (CSF) analysis showed albuminocytological dissociation with two lymphocytes and significantly elevated protein of 232 mg/dl. CSF sugars were normal (76 mg/dl with corresponding blood glucose levels of 90 mg/dl). CSF Gram stain and Ziehl–Neelsen stain were negative and cultures were sterile. CSF angiotensin-converting enzyme, oligoclonal bands, and aquaporin-4 antibodies were negative. Based on the clinical presentation, imaging findings, and absence of cellular response in CSF, 1 g of intravenous

Address for correspondence: Dr. Angamuthu Meena Kanikannan, Department of Neurology, Nizam's Institute of Medical Sciences, Hyderabad - 500 082, Telangana, India.
E-mail: unit3nims@gmail.com

Access this article online

Quick Response Code:

Website: www.annalsofian.org

DOI: 10.4103/aian.AIAN_387_17

How to cite this article: Sireesha Y, Uppin MS, Bohra K, Alugolu R, Neeharika ML, Kanikannan A. Longitudinally extensive transverse myelitis due to toxoplasma: An autopsy study. Ann Indian Acad Neurol 2018;21:161-3.

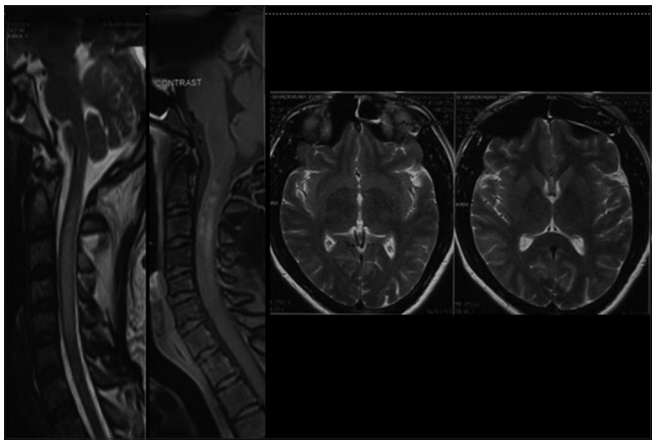

Figure 1: Magnetic resonance imaging of cervical spine showed longitudinal hyperintensity involving C1–C5 segments, with normal brain parenchyma

methylprednisolone was started with which his radicular pain responded. On the 2nd day, he developed high-grade fever without any localizing signs. Steroids were immediately stopped and antibiotics (cefoperazone–sulbactam) were started. However, there was a gradual drop in his sensorium which prompted a repeat imaging of brain and spine. This showed a new T2 and fluid-attenuated inversion recovery heterogeneous intensity lesion contiguously involving pons, midbrain, and thalamus [Figure 2] with mass effect. MR spectroscopy suggested increased lipid lactate peak suggestive of necrosis. Concurrent MRI spine showed no change in the previous spinal lesion. The patient continued to deteriorate with anisocoria, altered respiratory pattern, and refractory hypotension. Despite adequate cardiorespiratory support, the patient could not be revived. After obtaining informed consent from relatives, partial brain autopsy was performed within 2 h of death.

Pathological findings on postmortem

Gross examination of brain showed thin and transparent meninges without any basal exudates. The coronal sections showed extensive area of necrosis involving the entire brain stem and the right basal ganglia and periventricular white matter. The spinal cord cut surface showed small foci of necrosis which was in continuity with that of the necrosis in medulla [Figure 3].

Multiple sections taken from the necrotic foci in the brain and spinal cord showed large collections of neutrophils with necrosis. The meninges showed lymphocytic infiltrate. The parenchymal vessels showed complete destruction of the wall with perivascular histiocytes. Focal areas in the parenchyma showed microglial proliferation resembling pseudogranulomas. Within the necrosis, bradyzoites and tachyzoites of toxoplasma were identified [Figure 3]. Few cyst forms were also noted. The parasites were stained with anti-toxoplasma immunohistochemical antibody [Figure 4]. The sections from cervical cord also showed microabscesses with tachyzoites of toxoplasma. There was no evidence of

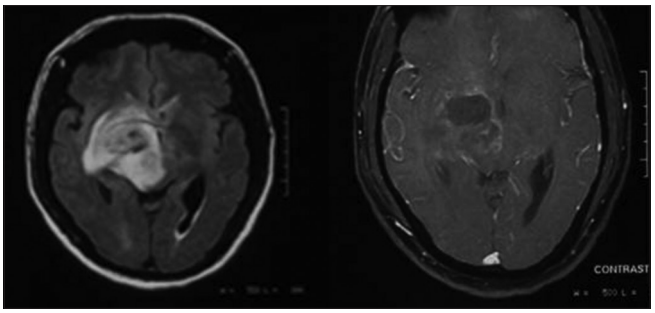

Figure 2: Magnetic resonance imaging brain-fluid-attenuated inversion recovery and contrast sequences showing heterogeneous lesion with surrounding edema in the region of basal ganglia, internal capsule, and midbrain. The margins of the lesion showed enhancement on contrast administration

demyelination. The gross and microscopic features were consistent with toxoplasmic myelitis and encephalitis.

Discussion

Toxoplasma gondii is an intracellular protozoan that exists as dormant bradyzoites, active tachyzoites and sporozoites contained in an oocyst.[5] Toxoplasmosis is mostly seen in immunosuppressed individuals in the setting of acquired immunodeficiency syndrome with a CD4 of <100/mm^3.[6]

This is the first report of toxoplasmic myelitis in an immunocompetent host. A study from French Guiana reported 16 cases of severe primary toxoplasmosis in immunocompetent individuals. They had nonspecific syndrome with predominant pulmonary localization.[7] None of them had spinal cord involvement. This is the first report of spinal toxoplasmosis mimicking NMO and confirmed at autopsy.

The differences in the pathology of the involvement of brain and spinal cord were studied in a murine model with experimental chronic toxoplasma infection. They found alterations in pathogenesis at a functional level in spinal cord neurons with no structural differences to that of brain involvement.[8]

The mimicker of central nervous system toxoplasmosis is pyogenic abscess which shows diffusion restriction with low apparent diffusion coefficient (ADC) value, unlike toxoplasma where the ADC values are very high.[9]

Large solitary lesions in the brain of >2 cm, with mass effect, mimicking a neoplasm should prompt a consideration of tumefactive demyelination. There are only few case reports of tumefactive demyelination affecting the spine, unlike the brain.[10]

In our case, although there was LESCL, the patient did not respond to steroids and further developed high-grade fever, which were clues for a nondemyelinating pathology.

The contribution of methylprednisolone to the pathogenesis of our case was contemplated, and a literature review was done. A single report showed reactivation of cerebral

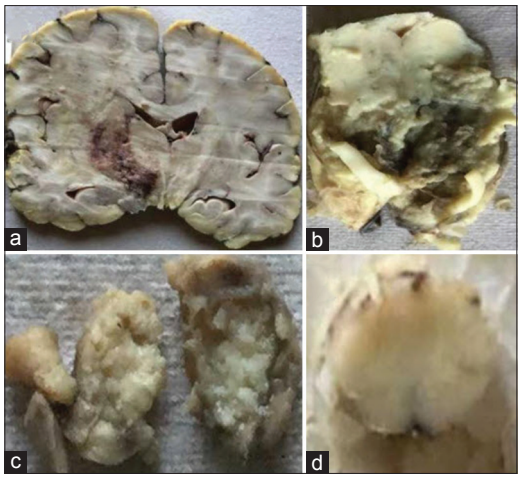

Figure 3: Gross examination of brain showing (a) large area of necrosis involving the right basal ganglia extending to periventricular white matter, (b) completely necrotic midbrain and (c) pituitary gland, (d) a small focus of necrosis with spinal cord

toxoplasmosis after intravenous methylprednisolone in an systemic lupus erythematosus patient.[11] Although our patient received steroids after worsening neurologically, autopsy showed several toxoplasma cysts in the spinal sections, suggesting that he had toxoplasmic myelitis at the onset and not steroid-induced reactivation of a dormant disease.

Why is it that immunocompetent individuals are at times susceptible to toxoplasmosis? The "strain hypothesis" explains the relationship between *Toxoplasma gondii* genotype and severe form of disease in immunocompetent individuals.[12] Virulent strains containing type 1 alleles or atypical alleles are associated with predilection to affect the brain and end up fatally.

Conclusion

Spinal toxoplasmosis is a treatable cause of myelitis that needs to be considered in patients with atypical course of transverse myelitis or nonresponsiveness to steroid therapy. The presence of fever might be a clue. Host immune responses and parasitic genotypic variability are factors that predict susceptibility and severity in immunocompetent individuals and offer a scope for future research.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient's relatives have given their consent for the patient's images and other clinical information to be reported in the journal. The patient's relatives understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

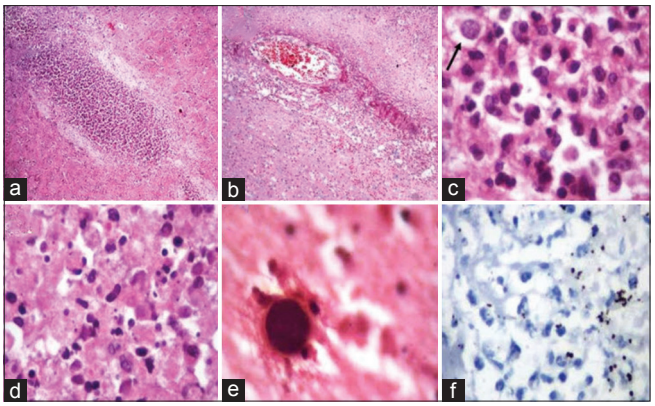

Figure 4: Microscopic sections from brain showing (a) necrosis with collections of neutrophils (H and E, ×40), (b) vessel wall necrosis with perivascular aggregates of histiocytes (H and E, ×40), (c) bradyzoites of toxoplasma (arrowhead) (H and E, ×40), (d) histiocytes with intracytoplasmic tachyzoites (H and E, ×100), (e) toxoplasma cyst, and (f) immunohistochemical positivity of tachyzoites for toxoplasma antibody

Conflicts of interest

There are no conflicts of interest.

References

1. Pandit L. Neuromyelitis optica spectrum disorders: An update. Ann Indian Acad Neurol 2015;18:S11-5.
2. Kitley JL, Leite MI, George JS, Palace JA. The differential diagnosis of longitudinally extensive transverse myelitis. Mult Scler 2012;18:271-85.
3. Luft BJ, Remington JS. AIDS commentary. Toxoplasmic encephalitis. J Infect Dis 1988;157:1-6.
4. García-García C, Castillo-Álvarez F, Azcona-Gutiérrez JM, Herraiz MJ, Ibarra V, Oteo JA, *et al.* Spinal cord toxoplasmosis in human immunodeficiency virus infection/acquired immunodeficiency syndrome. Infect Dis (Lond) 2015;47:277-82.
5. Smith AB, Smirniotopoulos JG, Rushing EJ. From the archives of the AFIP: Central nervous system infections associated with human immunodeficiency virus infection: Radiologic-pathologic correlation. Radiographics 2008;28:2033-58.
6. Taila AK, Hingwe AS, Johnson LE. Toxoplasmosis in a patient who was immunocompetent: A case report. J Med Case Rep 2011;5:16.
7. Carme B, Bissuel F, Ajzenberg D, Bouyne R, Aznar C, Demar M, *et al.* Severe acquired toxoplasmosis in immunocompetent adult patients in French Guiana. J Clin Microbiol 2002;40:4037-44.
8. Möhle L, Parlog A, Pahnke J, Dunay IR. Spinal cord pathology in chronic experimental *Toxoplasma gondii* infection. Eur J Microbiol Immunol (Bp) 2014;4:65-75.
9. Chong-Han CH, Cortez SC, Tung GA. Diffusion-weighted MRI of cerebral toxoplasma abscess. AJR Am J Roentgenol 2003;181:1711-4.
10. Kantorová E, Marcinek J, Zeleňák K, Kantor K, Michalik J, Sivák Š, *et al.* Tumefactive demyelination of the spinal cord: A case report. Spinal Cord 2015;53:877-80.
11. Pagalavan L, Kan FK. Cerebral toxoplasmosis in systemic lupus erythematosus following intravenous methylprednisolone. Med J Malaysia 2011;66:68-70.
12. Xiao J, Yolken RH. Strain hypothesis of *Toxoplasma gondii* infection on the outcome of human diseases. Acta Physiol (Oxf) 2015;213:828-45.