Tubercular Rhombencephalitis: A Clinical Challenge

Sir,

Rhombencephalitis is described as an inflammatory disease affecting the hindbrain. It is important to know its clinical presentation and etiology; therefore, it can be treated early.

A 20-year-old male presented in outpatient department with 3 days history of double vision, while looking toward distant objects. He denied any history of fever, headache, vomiting, vertigo, blurring of vision, altered sensorium, and limb weakness. In addition, there was no history of weight loss, malar rash, joint pain, alopecia, and oral ulcers. Neurological examination showed left sixth nerve palsy with bilateral gaze revoked nystagmus. Rest of the central nervous system (CNS) and systemic examination was normal. Magnetic resonance imaging (MRI) of brain showed hyperintensity in bilateral internal capsule, and homogeneous diffuse hyperintensity in midbrain, pons, medulla, and left side of cerebellum without contrast enhancement [Figure 1a-c]. Hence, with this acute manifestation and neuroimaging finding, the possibilities of demyelinating disorders like neuromyelitis optica (NMO), myelin oligodendrocyte glycoprotein (MOG), and multiple sclerosis, and autoimmune conditions like systemic lupus erythematosus, Behcet's disease, sarcoidosis, and paraneoplastic etiology were considered.

He was admitted and routine blood investigations including complete blood count, erythrocyte sedimentation rate, kidney function test, liver function test, serum calcium, and angiotensin-converting enzyme level were normal. Human immunodeficiency virus test was nonreactive. His serum antinuclear antibodies and antinuclear antibodies 3 profile, anti-NMO, anti-MOG, oligoclonal bands and paraneoplastic panel [anti-amphiphysin, anti-CV2, anti-PNMA2 (Ma2/Ta), anti-Ri, anti-Yo, anti- Hu, anti-GAD, anti-titin, anti-recoverin, SOX1, Zic4, and anti-Tr] were negative. Pathergy test was negative. Visual evoked potential was normal.

Further, MRI spine was done to look for cord lesion, but only significant finding was pretracheal and paratracheal lymph nodes [Figure 1g]. Computer tomography of chest showed necrotic mediastinal lymphadenopathy. Cerebrospinal fluid examination (CSF) revealed cell count of 32/μL, lymphocytic predominant (98%), protein 88.6 mg/dL, glucose 55.5 mg/dL; negative for Ziehl-Neelsen, India ink, and Gram stain. CSF Gene expert for tuberculosis and BioFire FilmArray (*Escherichia coli*, *Haemophilus influenzae*, *Neisseria meningitidis*, *Listeria monocytogenes*, *Streptococcus agalactiae*, *Streptococcus pneumoniae*, Cytomegalovirus, Enterovirus, Herpes simplex virus 1 and 2, Human Herpesvirus-6, Varicella-zoster virus, and *Cryptococcal neoformans/gattii*) for Meningitis/ Encephalitis panel was negative. CSF did not show any malignant cells and oligoclonal bands were in a normal range. Therefore, we narrow down our possibility to sarcoidosis and paraneoplastic.

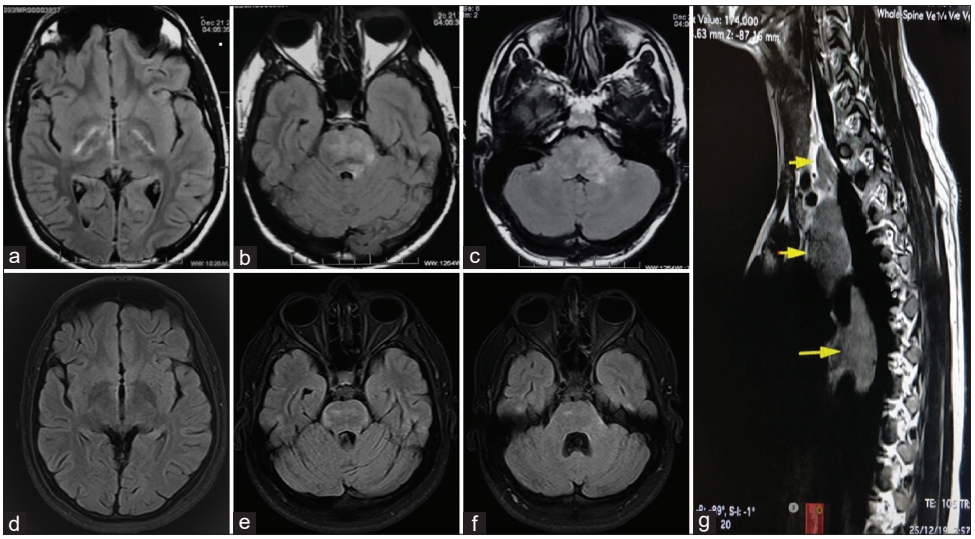

Figure 1: MRI Brain: T2-weighted fluid-attenuated inversion recovery sequences showing hyperintensity in bilateral internal capsule, pons, and left side of cerebellum before (a, b, c) and after (d, e, f) antitubercular treatment. MRI Spine: Pretracheal and paratracheal lymph nodes (g)

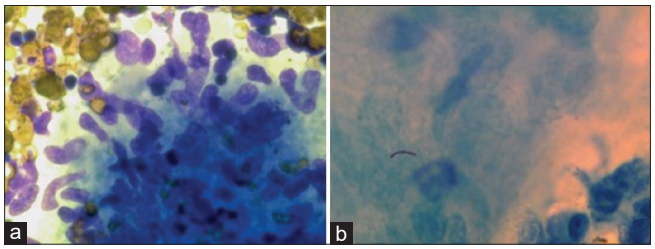

Figure 2: Multiple epithelioid cell granulomas with reactive lymphoid cells (a) and Ziehl-Neelsen stain positive (b)

Fine-needle aspiration cytology of mediastinal lymph node revealed multiple epithelioid cell granulomas with reactive lymphoid cells, positive for Ziehl-Neelsen stain [Figure 2a and b]. Diagnosis of tubercular rhombencephalitis was made. Antitubercular drugs were initiated [tablets rifampicin 450 mg, isoniazid 300 mg, pyrazinamide 750 mg, ethambutol 800 mg (all tablets once daily)]. In addition, pulse therapy of methylprednisolone 1 g/day was given for 3 days, after which tablet Dexamethasone 4 mg thrice daily was given, with tapering off the dose over 1 month.

At the end of 2 months, his diplopia completely improved. His neuroimaging 7 months after presentation showed near total improvement in lesion size [Figure 1d-f].

Discussion

In 1951, Bickerstaff and Cloake initially used the term "Rhombencephalitis".[1] It is defined as an inflammatory disease affecting the hindbrain, which includes both brainstem and cerebellum. It has a wide variety of etiologies, including demyelinating diseases like multiple sclerosis, autoimmune disease like Bechet's disease and systemic lupus erythematosus, infectious diseases like listeriosis, tuberculosis, mycobacterium avium complex, Brucella, Borrelia, Pneumococcal infections, Cytomegalovirus, Epstein Barr virus, Enterovirus, West Nile fever virus, Adenovirus and JC virus, paraneoplastic syndrome associated with anti-Yo and anti-Tr antibodies, malignancy like lymphoma, and relapsing polychondritis.[2-8] But majority of cases has unknown etiology.[2] Moragas *et al*. (2011) published a largest series of rhombencephalitis in which tuberculosis comprises ~ 2% of all cases.[2]

Intracranial tuberculosis is broadly divided into two types: First, meningeal pattern like leptomeningitis and pachymeningitis, and second pattern as parenchymal lesions like tuberculoma, cerebritis, abscess, rhombencephalitis, and encephalopathy.[9] CNS tuberculosis usually presented with chronic symptoms like fever, cough, weight loss, neck pain and symptoms of raised intracranial hypertension like headache, vomiting, focal deficits, and altered sensorium. Classical MRI findings of CNS tuberculosis include ring-enhancing tuberculoma, meningeal enhancement, basal exudates, obstructive hydrocephalus, or vasculitic infarcts. Our patient manifests with a noticeably short history, i.e., 3 days of diplopia without any other above clinical manifestation, and with unusual hyperintensity of internal capsule and diffuse hyperintensity in brain steam and cerebellum without contrast enhancement. He showed excellent response both clinically and radiologically to antitubercular drugs and steroids.

Clinicians should always have a high degree of suspicion of tuberculosis while evaluating a patient of rhombencephalitis even if patient presented with a short history. Always search thoroughly for other sites to confirm the diagnosis, so that timely treatment is possible.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients

understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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References

1. Bickerstaff ER, Cloake PCP. Mesencephalitis and rhombencephalitis. Br Med J 1951;2:77-81.
2. Moragas M, Martínez-Yélamos S, Majós C, Fernández-Viladrich P, Rubio F, Arbizu T. Rhombencephalitis: A series of 97 patients. Medicine (Baltimore) 2011;90:256-61.
3. Duong M, Piroth L, Chavanet P, Comvernoux A, Grappin M, Portier H. A case of rhombencephalitis with isolation of cytomegalovirus and Mycobacterium avium complex in a woman with AIDS. AIDS 1994;8:1356-7.
4. Arai Y, Kohno S, Takahashi Y, Miyajima Y, Tsutusi Y. Autopsy case of Neuro-Behcet's disease with multifocal neutrophilic perivascular inflammation. Neuropathology 2006;26:579-85.
5. Kuntzer T, Bobousslavsky J, Miklossy J, Steck AF, Janzer R, Regli F. Borrelia rhombencephalomyelopathy. Arch Neurol 1991;48:832-936.
6. Fu YC, Chi CS, Chiu YT, Hsu SL, Hwang B, Jan SL, *et al*. Cardiac complications of enterovirus rhombencephalitis. Arch Dis Child 2004;89:368-73.
7. Nichter CA, Pavlakis SG, Shaikh U, Cherian KA, Dobrosyzcki J, Porricolo ME, *et al*. Rhombencephalitis caused by West Nile fever virus. Neurology 2000;55:153.
8. Zagardo MT, Shanholtz CB, Zoarski GH, Rothman MI. Rhombencephalitis caused by adenovirus: MR imaging appearance. Am J Neuroradiol 1998;19:1901-3.
9. Khatri GD, Krishnan V, Antil N, Saigal G. Magnetic resonance imaging spectrum of intracranial tubercular lesions: One disease, many faces. Pol J Radiol 2018;83:524-35.

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