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A rare demyelinating disease: Cause of acute hemiparesis in a young male

ABSTRACT

Demyelinating diseases of the central nervous system are frequently encountered pathological entities; multiple sclerosis (MS) being the most common. Atypical forms of demyelinating diseases such as tumefactive demyelination run an aggressive course, masquerade MS but without classical features of MS. These aggressive entities represent a diagnostic and therapeutic challenge for physicians. The manifestations of a demyelinating disease are protean. This case was fascinating for two reasons: the diagnostic challenge it posed in the face of different etiologies of a demyelinating disease and the rapid response to plasma exchange and rituximab therapy in the acute phase of the disease.

Keywords: Tumefactive demyelinating disease, Magnetic resource imaging, Plasma exchange

INTRODUCTION

Tumefactive lesions are an atypical presentation of demyelinating disease and can pose a diagnostic challenge in patients. On magnetic resonance (MR) imaging, tumefaction is exemplified by a plaque size ≥2 cm with mass effect, edema, or ring enhancement.[1] TDD is known for having varying clinical and radiologic features that resemble multiple sclerosis (MS), neoplastic, infectious, or inflammatory process.[2] It is a rare variant with only 1 out of 1000 MS cases and has a prevalence of a few cases per million inhabitants a year.[2,3] The clinical presentation is correlated to the area and degree of the brain involved, and this can lead to multitude of signs and symptoms, which include: Headache, cognitive abnormalities, mental confusion, seizures, aphasia, and apraxia. They typically appear hypointense on T1 and hyperintense on T2-weighted images with mild post-contrast enhancement with gadolinium.[4,5]

TDD could present as a monophasic illness or can be notorious to several relapses and recurrences. It usually represents a unique form of isolated atypical demyelinating disease, without salient radiological features of MS.[6]

Here, we report a middle-aged gentleman who had presented with acute weakness of all four limbs and difficulty in speech preceded by a bout of dizziness, who had a battery of tests and an extensive workup done for several causes which, in turn, led to the diagnosis and treatment for tumefactive demyelinating disease (TDD).

CASE REPORT

A 42-year-old man presented to our facility with a ten-day history of progressive weakness of bilateral upper and lower limbs along with slurred speech. He was referred to us from a small hospital where he was admitted for four days with a concern for an ill-defined small focused mass in the left parietal white matter region and right brachium pontis on D1W and ADC drop images which was suspicious of inflammatory etiology [Figure 1]. He received high doses of steroids for five days which provided no relief, hence he was bought here. On history, he exclaimed that the symptoms began with dizziness and slight weakness of the left arm and leg, followed by slurring and staccato speech the next day. The weakness then progressed to right arm and leg, rendering him completely unable to move his right side accompanied by slight numbness and tingling in his feet and worsening speech. The patient did not report any preceding illness, travel history, or vaccine administration. He was reported negative for COVID-19. He denied seizures, headaches, visual loss, hearing loss, photophobia, cough, breathlessness, back pain, fever, joint pains, rashes anywhere on the body, gastrointestinal involvement, bowel, and bladder involvement. There was no history of Lhermitte's symptoms or Uhthoff phenomenon. There was no significant past or medical history. Neurological examination revealed reduced muscle power of 4/5 on left extremities and 1/5 on right extremities. His speech was slow, labored, and jerky. Words were pronounced with irregular force and speed with unintelligible pauses. Nystagmus was elicited upon looking toward the right. There was a reduced sensation to light touch, crude touch, and pain on the right arm and leg,

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more pronounced below the knees. Proprioception and vibration of both sides were impaired more on the right extremity than the left. Reflexes were intact and plantar reflexes showed flexor response bilaterally. No cranial nerve deficits and autonomic dysfunction were found. Expanded Disability Status Scale (EDSS) Score of the patient at admission was 8.5.

The initial diagnostic evaluation included visual evoked potential, somatosensory evoked potential, which were unremarkable. Blood reports revealed high sugars and he was diagnosed with Type 2 diabetes mellitus in the hospital. However, sequential MRI scans of the brain in our hospital on Diffuse weighted and ADC maps along with FLAIR axial and post-contrast T1 coronal images revealed lesion in the left parietal periventricular white matter which has moderately increased in size and shows peripheral restricted diffusion and incomplete post-contrast enhancement. New focal lesions are shown in left occipital white matter and right and central part of pons with lesion in the right brachium pontis showing moderate resolution of restricted diffusion [Figures 2-4]. MRI of the spine revealed no significant abnormality.

Workup for metastatic, inflammatory, vasculitis, and autoimmune causes was initiated with CT of the chest, cerebrospinal fluid (CSF) analysis, vasculitis workup, and anti-nuclear antibody. All studies proved to be negative. CSF workup for neuromyelitis optica (NMO) and oligoclonal bands for MS was negative. CSF routine yielded normal protein and leucocytes count and an elevated IgG with raised CSF-IgG index.

Based on the acute onset and rapid progression of the disease, clinical, radiological, and biochemical analysis a diagnosis of TDD was made. Given unresponsiveness to corticosteroid treatment, the patient was started on a 5-day course of plasma exchange for 3–4 h followed by two infusions of 500 mg rituximab after a week. Thereafter, he also underwent active physiotherapy (land and aqua) and speech therapy. He displayed dramatic response to treatment with a return of normal speech and regaining of muscle power to 3/5 on left extremities. He was monitored for a few days and subsequently discharged. The patient was not put on any disease-modifying therapies such as interferon, natalizumab, glatiramer, and fingolimod.

After a 3 month follow-up, patient had improved remarkably neurologically with normal speech and limb power grading of 5/5 on all limbs. EDSS score upon 3 months follow up was 3.

MRI FLAIR axial images on follow-up revealed moderate resolution of white matter and pontine lesions [Figure 5].

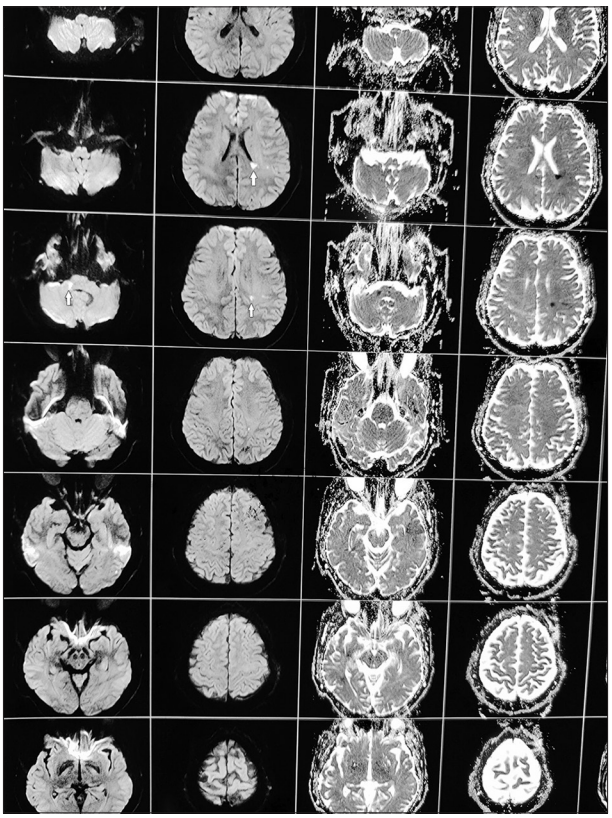

Figure 1: MRI reveals small focus area of restricted diffusion with corresponding ADC drop on right brachium pontis and left parietal periventricular white matter

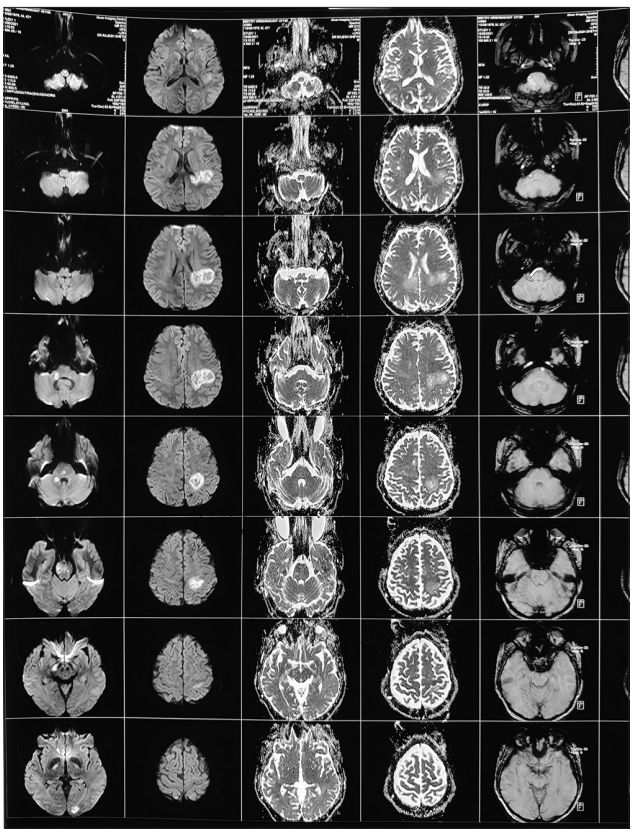

Figure 2: Diffuse weighted and ADC maps reveal lesion in the left parietal periventricular white matter which has moderately increased in size and shows peripheral restricted diffusion New focal lesions are shown in left occipital white matter and right and central part of pons with a lesion in the right brachium pontis showing moderate resolution of restricted diffusion

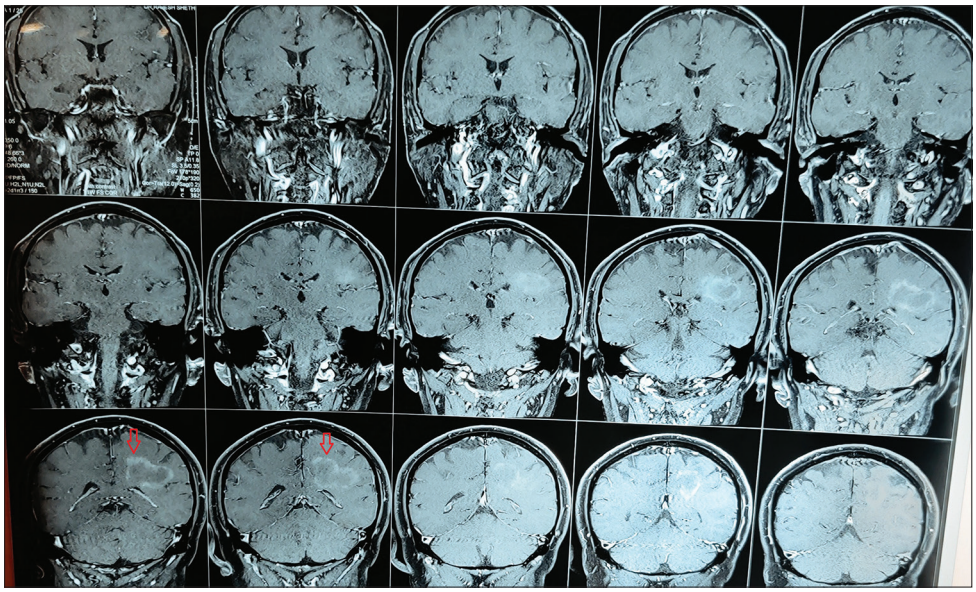

Figure 3: Post-contrast T1 coronal image reveals lesion in the left parietal periventricular white matter with incomplete post-contrast enhancement

DISCUSSION

Tumefactive lesions pose a diagnostic challenge for clinicians. Herein we presented an extremely rare case of tumefactive demyelinating lesion with pertinent findings on MRI, with atypical tumor-like features (homogenous enhancement, mass effect, and expansion in the same anatomical site), with refractory response to doses of heavy steroids but remarkable recovery after five cycles of plasma exchange and rituximab administration and finally, with a good outcome. CSF analysis along with imaging play an important diagnostic role to help distinguish TMS lesions from other pathologies. The positive CSF for serum IgG and IgG index in tumefactive lesions is indicative of chronic inflammation[6] in addition to the absence of oligoclonal bands in patients diagnosed with TDD[7,8] has been reported in the literature. This case is supportive of both the above findings. Broader literature also suggests that tumefactive disease is characterized by hypointense lesion on T1 and hyperintense on T2 weighted images with mild post-contrast enhancement with gadolinium[4,5] which is seen in our case as well.

Differential diagnosis includes causes of these demyelinating lesions such as multifocal brain tumors, inflammatory disorders, infectious, metabolic, and vascular causes. Demyelinating disorders such as acute disseminated encephalomyelitis, Balo's concentric sclerosis, Schilder's diffuse sclerosis were also considered. MS and NMO were unlikely at the forefront of possible etiologies because of salient MRI picture seen in MS and negative MOG, AQP-4 antibody titer, and absence of oligoclonal bands in blood and CSF. Infective causes such as Behcet's disease, Whipple's, and progressive multifocal leukoencephalopathy were also considered but the absence of pathognomic clinical features and MRI findings dismissed the possibility. Neoplasms, gliomas, and abscess were also ruled out on subsequent MRI neuroimaging films. Other potential etiologies also include Sarcoidosis and Collagen vascular diseases.

Balo's concentric sclerosis has a typical feature on MRI seen as concentric rings in T2WI and T1WI contrast and histologically, it reveals alternating layers of myelin loss and myelin preservation or remyelination.[9,10] Schilder's diffuse sclerosis which is infrequently seen in children has MRI findings of two large lesions, often bilateral involving the centrum semiovale with no significant peripheral edema.[11] The MRI appearance in our patient showed divergent findings. ADEM is another fulminant demyelinating disease that attains rapid remission after progressing over days. It occurs due to an autoimmune response following an immunization or infection source, predominantly occurs in younger age groups. On imaging, its lesions predominantly extend into the grey matter.[12] In our case, patient was an older adult with no history of any infection or vaccination.

As mentioned above, the absence of oligoclonal bands in patients diagnosed with Tumefaction has been reported in literature, with definitive diagnosis relying on biopsy in these patients.[13] A biopsy is ultimately diagnostic but is usually considered the last line because it leads to high morbidity and is indicated only when other imaging modalities are unclear. Sequential imaging and response to plasma exchange and rituximab therapy eliminated our patient's need for a biopsy.

Treatment options for tumefactive demyelination are similar to prototypic MS, with corticosteroids being effective. However, one case report showed that plasma exchange therapy was effective in a patient with corticosteroid-resistant tumefactive demyelination.[13] Our case exemplifies

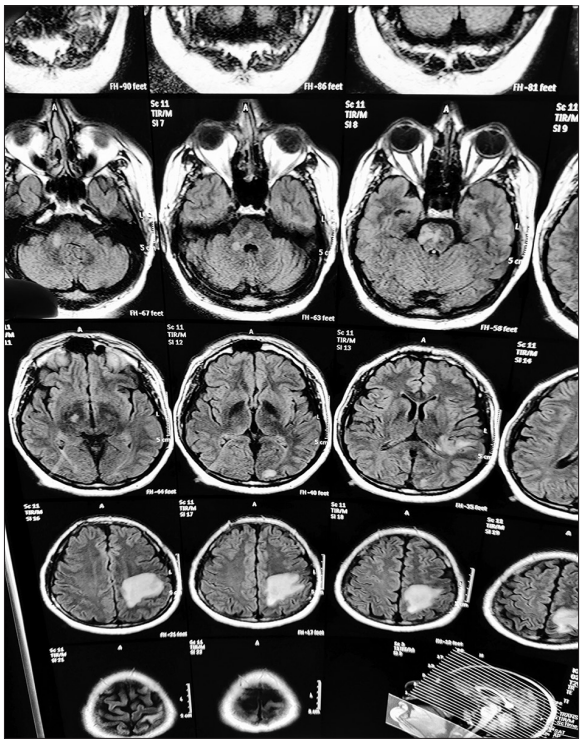

Figure 4: FLAIR axial image reveals hyperintense lesion in the temporal lobe extending into the occipital region with mass effect on the adjacent lateral ventricle

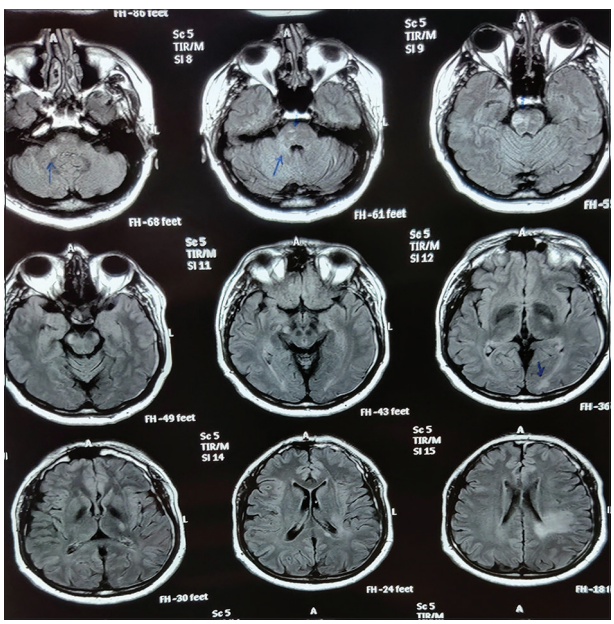

Figure 5: Post recovery FLAIR axial images show moderate resolution of lesion in left parietal, left occipital white matter, pons and brachium pontis

tumefactive demyelination responsive to plasma exchange followed by rituximab which was unresponsive to steroid therapy. We were also reluctant on prescribing corticosteroids due to their inherent risk of driving up blood sugars of the patient.

Our case had the following limitations; follow-up of the patient was limited to a 3-month period which is brief to estimate the prognosis and anticipate chances of future relapses as Demyelinating diseases stand a fair chance to recur in the future. Second, we could not account nor prognosticate if TDD is a unique form of CNS demyelinating disease or part of spectrum of MS. This particular limitation is highly debatable.

CONCLUSION

TDD is a rare variant that can take a progressive and fulminant course, as in this case. The importance of sequential films of MRI in reaching a precise diagnosis is indisputable. Thus, an early decision for an exact diagnosis and appropriate treatment is the foremost priority. Our findings also suggest that rituximab administration can be considered a treatment option for an acute-phase TDD which is refractory to conventional therapy of corticosteroids.

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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