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Indian Journal of Pathology and Oncology

Journal homepage: www.ijpo.co.in

Case Report

Tumefactive demyelinating lesion mimicking glioma: A clino-radiopathological conundrum a rare case report and review of literature

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Abstract

A rare side effects of idiopathic inflammatory demyelinating disorders of the central nervous system (CNS) include tumefactive demyelinating lesions. Tumefactive demyelinating lesions have been described by several names in the literature, including pseudotumoral demyelinating lesions, tumefactive or tumorlike MS, and tumorlike demyelinating lesions, among other designations Because they can mimic tumors and abscesses and can be caused by a wide variety of illnesses, tumefactive demyelinating lesions pose a diagnostic difficulty. On imaging, tumefactive demyelination resembles primary brain neoplasms, frequently requiring a brain biopsy. Consequently, in order to make a diagnosis in these cases, brain biopsies are frequently performed, which raises morbidity and delays therapy.

Keywords: Tumefactive demyelinating lesions (TDL), Multiple sclerosis, Mass effect, Edema, Glioma.

Received: 11-11-2024; **Accepted:** 14-12-2024; **Available Online**: 15-03-2025

1. Introduction

Tumefactive demyelinating lesions are large demyelinating lesions that present with significant mass effect and surrounding edema. They are commonly associated with multiple sclerosis (MS). However, tumefactive demyelinating lesions are also seen in other conditions, such as clinically isolated syndrome (CIS), rare variants of MS, acute demyelinating encephalomyelitis (ADEM), acute hemorrhagic leukoencephalitis, Baló concentric sclerosis (BCS), myelinoclastic diffuse sclerosis (Schilder disease) and neuromyelitis optica spectrum disorder (NMOSD). The prevalence of TDL is estimated to be 1–3/1000 cases of MS with an annual incidence of 0.3/100,000.[2] Patient generally present at an median age of 30- 40 years. Females have slightly more predilection than males. Tumefactive demyelinating (TD) lesions are larger than those seen in typical MS (i.e >2 cm) and may occur in patients either with or without diagnosed MS. Tumefactive demyelinating lesions are commonly located in the cerebral hemispheric white matter, especially the frontal and parietal lobes, but can also be found elsewhere in the CNS.

2. Case Report

The 50-year-old male patient arrived at SVP hospital with the following main complaints: headaches for two to three years, unsteady walking for six months, irrelevant speech for three to four months and forgetfulness for one month, and appetite loss for two months. Vitals were steady upon assessment, and the CNS examination revealed nothing unusual. Radiological examination suggests bilateral symmetrical altered signal intensity areas with extensive vasogenic edema involving rostrum, genu, proximal body, splenium of corpus callosum, white matter of bilateral frontal and parietal lobe, caudate nucleus, anterior limb, genu of internal capsule and bilateral anterior thalamus. Possibility of tumefactive demyelination more likely. Remote possibility of neoplastic etiology to be ruled out (Figure 1). MR spectroscopy suggested evidence of elevated Choline (Cho) peak value, reduced NAA peak value with elevated Choline/Creatinine (Cho/Cr) ratio, Choline/

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https://doi.org/10.18231/j.ijpo.2025.012

NAA ratio and reduced NAA/Cr in the lesion in genu of corpus callosum as compared to normal white matter,- possibility of Neoplastic etiology more likely over demyelination. Patient did not came for further follow up.

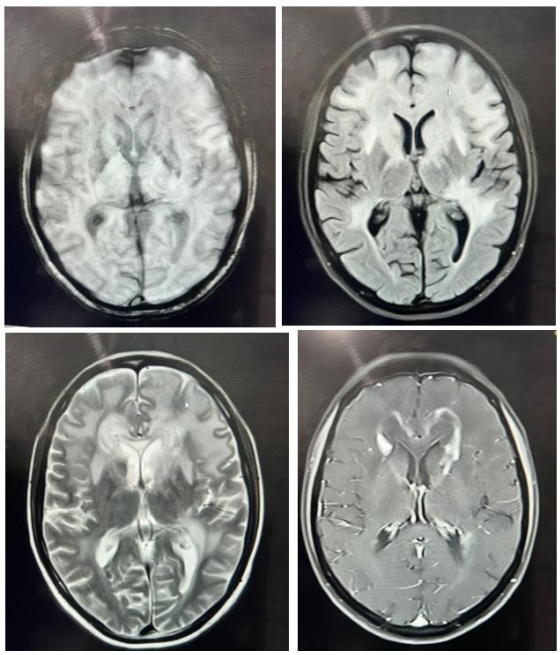

Figure 1: There is evidence of bilateral symmetrical altered signal intensity areas with extensive peripheral vasogenic edema involving rostrum, genu, proximal body & splenium of corpus callosum, white matter of bilateral frontal and parietal lobes, caudate nucleus, anterior limb and genu of internal capsules and bilateral anterior thalamus. It appears heterogeneously hyperintense on T2WI / FLAIR & hypointense on TWI, shows peripheral rim like diffusion restriction and post-contrast enhancement. No evidence of GRE blooming. No evidence of mass effect or midline shift noted

2.1. Intervention

Stereotactic biopsy was performed and tissue was sent for Histopathological examination at Histopathology Department at SVP hospital.

2.2. Gross examination

Specimen consists of multiple red soft tissue portions, total measuring 0.9 cm in aggregate.

2.3. Microscopic examination

Microscopic examination revealed normal brain parenchyma (**Figure 2**) along with reactive gliosis (**Figure 4**), macrophages (**Figure 3)** and perivascular lymphoid infiltrate (**Figure 5**). No evidence of neoplastic, vasculitis or granuloma was seen in received bits of tissue. Immunostains were advised and following Immunohistochemical stains were performed which was negative, ATRX (**Figure 6**) IDHR132H (Figure 7) was retained and Ki67 (Figure 9) was extremely low thus ruling out neoplastic etiology. CD 138 was positive highlighting macrophages (Figure 8).

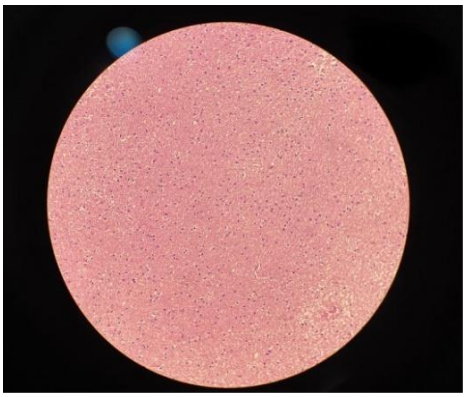

Figure 2: Image showing normal brain parenchyma (H&E stain, low 4x magnification)

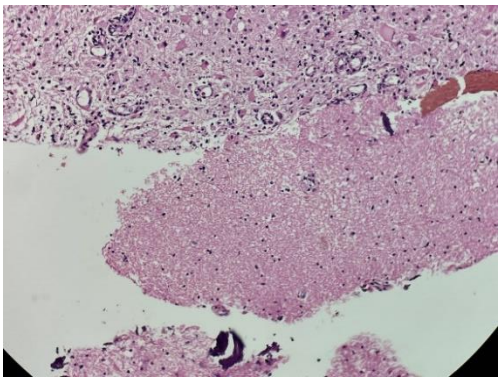

Figure 3: Image showing sharp demarcation between lesiona and normal brain (H&E stain, low 10x magnification)

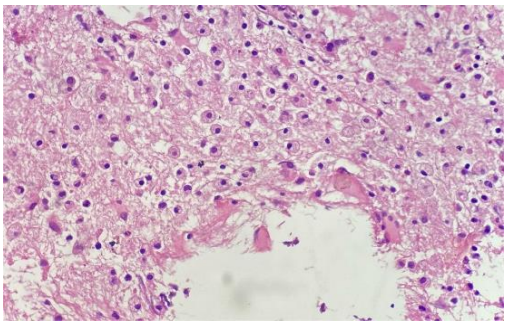

Figure 4: Image showing reactive gliosis highlighting gitter cells (H&E stain, low 10x magnification)

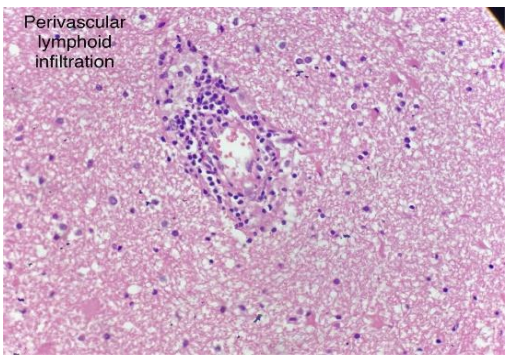

Figure 5: Image showing perivascular lymphoid infiltration (H&E stain, low 10x magnification)

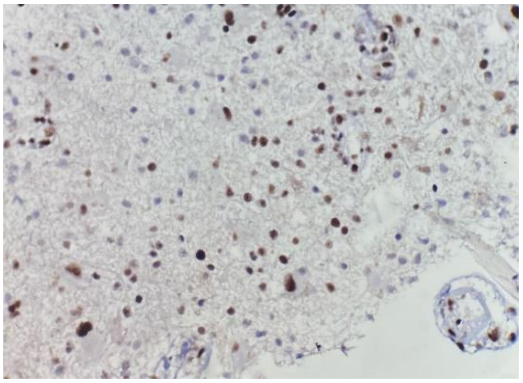

Figure 6: Image showing Immunostain ATRX which is retained (IHC, low 10x magnification)

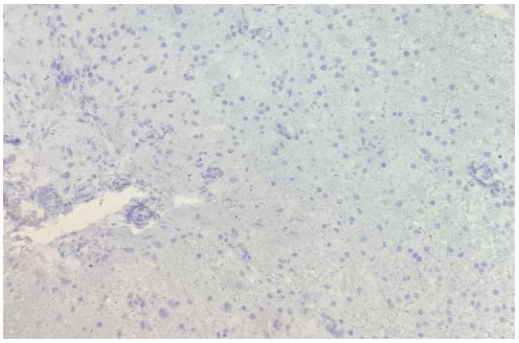

Figure 7: Image showing Immunostain IDH1 R132H which is negative (IHC, low 10x magnification)

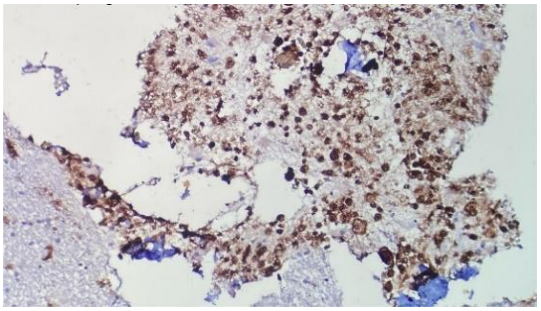

Figure 8: Image show CD163 highlighting macrophages (IHC, low 10x magnification)

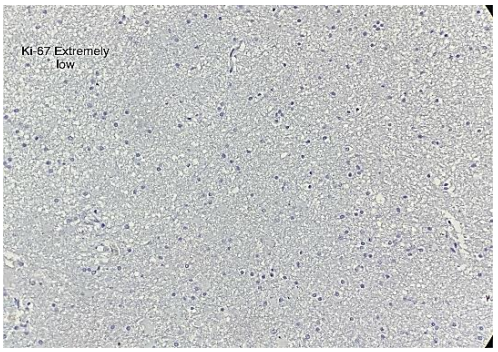

Figure 9: Image show extremely low Ki67 indicating low mitotic activity (IHC, low 10x magnification)

3. Discussion

"Kepes et al. coined the term "tumefactive demyelinating lesion" (TDL) in 1993. The incidence of TDL has been reported to be 0.3 cases per 100,000 per year.[7] Approximately 15 cases have been reported from the Indian subcontinent.[13] Several recent cohort studies reported a wide range of tumefactive demyelination prevalence among patients with MS, ranging between 1.4% (10 of 711 patients) and 8.2% (24 of 293 patients).[16,17] Female preponderance is slightly higher than males.[8] Particularly in the second or third decade of life. Tumefactive demyelinating lesions have been described by several names in the literature, including pseudotumoral demyelinating lesions, tumefactive or tumorlike MS, and tumorlike demyelinating lesions, among other designations.[5] These terms have often been used interchangeably, which may in part reflect both the diagnostic challenge of tumefactive demyelination and its elusive relationship to associated conditions, many of which have overlapping features with each other. Efforts are underway to clarify the interrelationship between tumefactive demyelination, MS, and atypical demyelinating disease processes that were previously considered subtypes of MS.[6] TDL may be defined as pseudotumoural demyelinating lesions in radiological terms because they are greater than 2 cm in dimension. Though smaller lesions between 0.5 and 2 cm may also show similar MRI characteristics and clinical evolution. Although majority of TDL patients have non-specific clinical characteristics. Acute onset weakness with flare-ups and remissions is the most typical manifestation. The following traits may be useful in favoring TDL even though there are no pathognomonic imaging signals to indicate a TDL these are following characteristics which may be helpful in favouring TDL over a neoplasm or abscess. TDLs are typically well-defined supratentorial lesions that preferentially affect the frontal and parietal lobes.[10,12] These neuroimaging features mimic closely with that of glial neoplasm or even a persistant abscess.[15] This misdiagnosis can lead to unintentional surgery or radiotherapy.[11,13] MR spectroscopic metabolic information can also aid in distinguishing gliomas from Tumefactive demyelinating Lesion, because elevation of glutamic glutamate is seldom seen in gliomas.[14] The spectrum of MOG antibody-related encephalomyelitis has been enriched during the last years to include cases with presentation of TDL the spectrum."

"To reach a definitive diagnosis in the majority of TDL cases, either neuronavigation or stereotactic biopsy are performed. In these situations, the best location for a biopsy is a tiny, hypointense area in the ring region's wall, which is the border between remyelination and demyelination. Therefore, even a small change in the biopsy location within the same lesion can result in a tissue diagnosis that is incorrect. Cell type identification may benefit by intraoperative squash preparations made from TDL.[11] Clusters of foamy macrophages and lymphocytic infiltration should raise suspicions of TDL if they are observed in large quantities in the squash smears. However, analyzing these squash preparations can be quite challenging and misleading. If samples are taken from the cystic or necrotic areas, similar results may also be observed in inflammatory lesions, high-

grade gliomas, or metastases.[19] Smears of macrophages may be mistaken for carcinomatous or oligodendroglial cells."

Reactive gliosis, perivascular lymphocytic infiltration, and foamy macrophages are the hallmark histological features.[18] Numerous biopsy lesions can have characteristics similar to those of TDL. Active TDLs consist of areas of demyelination with relative axonal sparing, inflammatory infiltrates mainly by myelin-containing foamy macrophages, perivascular lymphocytes, and reactive astrocytes that may contain multiple nuclei (Creutzfeldt–Peters cells). Differential diagnosis includes neoplasms (glial tumors, primary CNS lymphoma), metastasis, brain abscess, granulomatous disease, and vasculitis.[9] Creutzfeldt-Peters cells are reactive astrocytes with fragmented nuclear inclusions that can be seen in tumefactive demyelination, but can also be found among neoplastic glial cells in glioblastomas.[20] A primary CNS lymphoma may be mistaken for extensive perivascular lymphocytic infiltrates in TDL. A cerebral infarct may also exhibit foamy macrophages collections, necrosis and perivascular inflammatory infiltration. Progressive multifocal leukoencephalopathy (PML), which is characterized by demyelinating lesions is another lesion that closely resembles TDL.[11] Because both infections and vasculitis with infarcts can include perivascular inflammatory infiltrates, they can infrequently mimic TDL. TDL can also be diagnosed with the use of immunostaining such as Luxol Fast Blue, CD 163, GFAP, Ki67, CD 3 can be used to rule out neoplastic etiology.[18] Similarly grams stain, fungal-specific stains can rule out any infectious cause. A biopsy study by itself, though, may be deceptive. To diagnose TDL, all histology results should be compared to clinical, imaging, microbiological culture, and other laboratory tests.

4. Conclusion

It is quite difficult to diagnose TDL accurately. A remarkable full clinical recovery would be encouraged by early therapy for these patients. When making a differential diagnosis for a single space-occupying lesion, the neurologist, neurosurgeon, and neuropathologist should be aware of this non-neoplastic entity. Despite only providing a little amount of tissue, stereotactic biopsy strongly resembles astrocytoma or oligodendroglioma due to hypercellularity in sections stained with hematoxylin and eosin. The neuropathologist's dilemma can be resolved by the presence of a perivascular lymphocytic inflammatory infiltration, perivenular macrophage collection, and careful application of immunohistochemistry. The contribution of a neuropathologist is of the utmost importance for diagnosis of TDL that presents atypically or when the diagnosis is not appreciated radiologically.

5. Source of Funding

None.

6. Conflict of Interest

None.

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Cite this article: Gandhi SP, Gandhi M, Damor D, Parmar D, Shah C, Jagrit N. Tumefactive demyelinating lesion mimicking glioma: A clino-radiopathological conundrum a rare case report and review of literature. *Indian J Pathol Oncol*. 2025;12(1):59–63.