Tumefactive demyelinating lesion

Tumefactive demyelinating lesion (TDL) is defined as a solitary de-myelinating lesion greater than 2 cm, often reported as a rare variation of multiple sclerosis (MS).

It is a solitary cerebral demyelinating lesion clinically and radiologically mimicking brain tumors. It can occur in isolation or may be rarely associated with other demyelinating diseases. The underlying pathogenic mechanisms are unknown [1].

Epidemiology

It is most frequently encountered in women, usually young middle age (average onset at 37 years of age).

Unlike acute disseminated encephalomyelitis (ADEM), tumefactive demyelinating lesions are usually not post infective. Additionally, although patients with multiple sclerosis can develop large tumefactive demyelinating plaques (which have very similar appearances), patients who present with a solitary tumefactive demyelinating lesion infrequently go on to develop multiple sclerosis (MS) [2].

Clinical features

Patients present with symptoms atypical for multiple sclerosis such as focal neurologic deficits, seizures, and/or aphasia [3]

Most do not progress to multiple sclerosis [4].

Diagnosis

Tumefactive demyelinating lesions (TDLs), are a rare demyelinating pathological disease in the central neurological system, which have been proven to be a diagnostic dilemma to neurosurgeons. The clinical presentation and radiographic appearance of these lesions often results in their misdiagnosis as intracranial tumors, such as gliomas, which leads to unnecessary surgical resection and adjunct radiation [5].

When examined on magnetic resonance imaging (MRI) scans, TDLs have ill-defined borders, mass effect, perilesional edema, central necrosis, cystic degeneration, contrast enhancement and variable involvement of grey matter.

Unless specifically requested, pathological examination does not routinely include luxol fast blue staining, which can be used to detect demyelination. The presence of hypercellularity, atypical reactive astrocytes and mitotic figures can lead to an incorrect diagnosis of glial neoplasm. [6].

Differential diagnosis

The imaging spectrum can vary widely from small multifocal white matter lesions to confluent or extensive white matter involvement. Understanding the pathologic substrate is fundamental for understanding the radiologic manifestations, and a systematic approach to the radiologic findings, in correlation with clinical and laboratory data, is crucial for narrowing the differential diagnosis [7)]

General imaging differential considerations include:

high grade glioma (e.g. GBM): enhancement is usually a complete ring around central necrosis, prominent surrounding vasogenic oedema, may have non-enhancing tumour

CNS lymphoma vivid usually solid enhancement, without central non-enhancement (except sometimes in immunocompromised individuals)

Cerebral infective process: cerebritis or cerebral abscess: restricted diffusion prominent in central liquid component.

TDL is difficult to diagnose solely by magnetic resonance imaging (MRI) in patients with no history of MS. This is because the lesion often shows a ring enhancing lesion with perifocal edema on gadolinium MRI, thus mimicking glioblastoma multiforme (GBM) [8) 9)].

A delay in appropriate diagnoses can result in unnecessary invasive resections.

Clinicians should proceed with caution when considering invasive procedures with such lesions [10)].

11c methionine positron emission tomography is considered a possible diagnostic modality for demyelinating disease as it can appropriately reflect the pathological findings. MET PET will facilitate decision-making regarding surgery in patients with TDL [11)].

Proton magnetic resonance spectroscopy, diffusion-weighted axonography, and diffusion tensor tractography in a patient with tumefactive demyelination plaque (TDP) were evaluated for differential diagnosis from glioblastoma. The findings of glutamate and glutamine elevations on magnetic resonance spectroscopy and apparent tracts within the lesion on axonography and tractography were unlikely to represent glioblastoma, and were thus useful for the preoperative diagnosis of TDP [12)].

Treatment

Conservative medical management is often sufficient [13)].

Published data suggests that Fingolimod should not be used in TDL patients, mainly due to the possibility of more than just a chance association between TDLs and initiation of Fingolimod. The use of several new MS disease modifying therapy for the management of TDL remains to be studied. Further well-conducted research including multi-center trials is needed to explain several ambiguous aspects related to the etiology and management of TDL [14].

Case series

The clinical and radiographic features of 14 patients with cerebral TDLs who underwent surgical treatment between January 2004 and January 2009 were reviewed and analyzed. The surgical methods used included biopsy and resection, while steroid therapy was indicated when TDLs were confirmed by histopathological analysis. The patients were followed-up and the outcomes were evaluated using the Karnofsky performance scale (KPS). The main clinical presentations included: Hemiplegia (8 cases), increased intracranial pressure (4 cases) and seizures (general in 1 case; partial in 3 cases). On magnetic resonance imaging scans, 12/14 TDL cases demonstrated an isolated local subcortical mass and 6/14 cases (42.9%) demonstrated enhancing veins coursing undistorted through the lesion. The postoperative complications included: Hemiplegia (2 cases) and mortality (1 case). A total of 9 cases underwent microsurgical total resection, and 5 cases received stereotactic biopsy that was followed with high-dose methylprednisolone therapy. The follow-up study demonstrated that 2 cases presented recurrence with multiple sclerosis and the KPS scores for 13/14 patients (92.9%) were ≥80. In conclusion, the clinical and radiographic features of TDLs may help to establish the correct diagnosis prior to surgery, in order to avoid unnecessary resection or adjunctive therapy. Using steroid therapy, the majority of patients with TDLs appeared to achieve satisfactory prognosis [15].

Fallah et al. present 3 cases

Case 1: A 50-year-old woman who presented with a 3-day history of headaches and generalized tonic-clonic seizures. Physical examination did not reveal a focal point of her seizure. A computed tomography (CT) scan of the patient’s head revealed a large right frontal ring enhancing lesion with central necrosis, peritumoral edema and a mild midline shift. This presentation was most consistent with a malignant brain tumour. The patient underwent surgery for resection of the lesion. Postoperative pathology indicated an extensive inflammatory cell reaction, both acute and chronic, with focal necrosis predominantly through the white matter areas. Luxol fast blue staining showed an absence of myelin. A diagnosis of acute disseminated encephalomyelitis was made.

Patient 2 was a 43-year-old woman who presented with a 4-day history of left facial droop and left arm weakness that was more pronounced distally. Physical examination confirmed these symptoms, including gait ataxia. Her medical history included a diagnosis of MS 3 years ago when she had transverse myelitis. Magnetic resonance images obtained 3 years earlier showed transverse myelitis from T4 to T7 with unremarkable intracranial pathology. A new CT scan of her head showed a large solitary right frontal hypodense white-matter lesion. It was unclear whether this represented a tumefactive multiple sclerotic lesion or a low-grade cystic neoplasm. The patient underwent a stereotactic biopsy to determine the nature of the lesion. The diagnosis of MS was confirmed by biopsy

Patient 3 was a previously healthy 35-year-old woman who presented with new-onset generalized tonic-clonic seizures and headaches. Magnetic resonance imaging scans showed a large right frontal

mass with surrounding edema and a mild midline shift. The patient underwent a diagnostic stereotactic brain biopsy. Low-grade glioma and reactive gliosis were among the likely differential diagnoses. Permanent section showed a demyelinating lesion. In retrospect, the appearance of the mass was similar to that seen in Balo concentric sclerosis in which there are large regions of alternating zones of demyelinated and myelinated white matter [16].

Case reports

A 54-year-old healthy woman complained of headache 1 month before admission. She developed a decline in cognitive function, decreased attention, and executive function disorder 10 days before admission. Gadolinium MRI showed a ring-shape enhancement accompanied with massive brain edema in the left frontal lobe. This suggested GBM, but 11c methionine positron emission tomography (MET PET), surprisingly, showed no uptake with a tumor to normal brain ratio of 1.18. Accordingly, they eliminated GBM and suspected brain abscess because diffusion-weighted images showed high signal intensity in the lesion. Although they performed drainage, they could not demonstrate the presence of pus. Pathological analysis of a specimen obtained by needle biopsy revealed broad necrosis and a small number of inflammatory cells. They therefore prescribed steroid therapy, by which symptoms gradually improved. No relapse occurred for 2 years. They finally diagnosed the patient as having TDL.

MET PET is considered a possible diagnostic modality for demyelinating disease as it can appropriately reflect the pathological findings. MET PET will facilitate decision-making regarding surgery in patients with TDL [17].

A patient with unilateral weakness and radiologic findings that were concerning for a high-grade glioma. Peripheral studies were equivocal. The decision was made to proceed with a stereotactic biopsy, yielding a definitive diagnosis of tumefactive demyelinating lesion (TDL). The patient responded robustly to medical management and made a full clinical recovery. While TDLs and gliomas may look radiologically identical during acute demyelinating episodes, unlike gliomas, TDLs will demonstrate evolvement over serial imaging and robust clinical response to high dose steroids. Clinicians should proceed with caution when considering invasive procedures with such lesions. Conservative medical management is often sufficient as seen in this patient. This case highlights the importance of timely diagnosis and management of TDLs [18].

5-aminolevulinic acid fluorescence in tumefactive demyelinating lesion [19].

A 60-year old man who was diagnosed as having tumefactive demyelination on a stereotactic biopsy. At autopsy, however, the lesion revealed a grade IV glioblastoma. The myelin loss along the periphery of the lesion was erroneously interpreted as TD during the histopathological examination. Gupta et al. described the imaging, the biopsy, and the autopsy findings of this instructive case. It is pertinent to recognize its histology to prevent a misdiagnosis [20].

Kebir et al. presents the case of a patient with a large contrast-enhanced frontal brain lesion, who was initially diagnosed with tumefactive multiple sclerosis. Following the progression of the brain lesion, an 18F-fluoroethyl-L-tyrosine positron emission tomography (18F-FET PET) was performed, revealing markedly elevated static 18F-FET uptake parameters along with time activity-curves consistent with glioma. Subsequently, a biopsy was undertaken, which confirmed the presence of anaplastic oligoastrocytoma. This case illustrates that 18F-FET PET may provide useful diagnostic information in cases where distinction between neoplastic and demyelinating inflammatory CNS lesions is challenging. However, further systematic and prospective analyses are warranted to explore the value of this method in this setting [21)].

Baló's concentric sclerosis (BCS) and tumefactive demyelination (TD) are considered atypical forms of multiple sclerosis (MS). Baló lesions are characterized by concentric rings corresponding to alternating bands of demyelination and relatively preserved myelin (Hu and Lucchinetti, 2009). Tumefactive lesions are pseudotumoural demyelinating lesions of >2 cm and may have an open ring-enhancing magnetic resonance imaging appearance (Hu and Lucchinetti, 2009; Lucchinetti et al., 2008; Altintas et al., 2012). We present a patient who developed limb weakness and focal seizures secondary to a lesion radiologically and histopathologically consistent with BCS who, six months later, developed a tumefactive demyelinating lesion. This is the first description of BCS and TD occurring in the same patient and is particularly notable because of the lack of any other more typical demyelinating lesions on the MRIs. The nature of BCS and TD in relation to more typical multiple sclerosis is discussed [22)].

Javalkar et al. present a patient with a history of headache, ataxia and sensory disturbances in the lower extremities. A cranial MRI scan showed a large frontal lesion with mass effect, midline shift and with open ring enhancement. These findings are characteristics of tumefactive multiple sclerosis. Such lesions can be confused with neoplasms and abscesses. Open ring enhancement may help in differentiating atypical demyelination from a neoplasm or an abscess [23)].

A 37-year-old Asian man complaining of mild left leg motor weakness visited our clinic. Magnetic resonance imaging demonstrated high-signal lesions in bilateral occipital forceps majors, the left caudate head, and the left semicentral ovale on fluid-attenuated inversion recovery and T2-weighted imaging, and these lesions were enhanced by gadolinium-dimeglumin. Tumefactive multiple sclerosis was suspected because the enhancement indistinctly extended along the corpus callosum on magnetic resonance imaging and scintigraphy showed a low malignancy of the lesions. But oligoclonal bands were not detected in cerebrospinal fluid. In a few days, his symptoms fulminantly deteriorated with mental confusion and left hemiparesis, and steroid pulse therapy was performed. In spite of the treatment, follow-up magnetic resonance imaging showed enlargement of the lesions. Therefore, emergent biopsy was performed and finally led to the diagnosis of demyelinating disease. The enhanced lesion on magnetic resonance imaging disappeared after one month of prednisolone treatment, but mild disorientation and left hemiparesis remained as sequelae.

Fulminant aggravation of the disease can cause irreversible neurological deficits. Thus, an early decision to perform a biopsy is necessary for exact diagnosis and appropriate treatment if radiological studies and cerebrospinal fluid examinations cannot rule out the possibility of brain tumors [24)].

Shalmon et al. present 2 cases of giant tumefactive lesions, proven by brain biopsy to be of demyelinating nature [25].

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