THE MRI FEATURES IN DIAGNOSING TUMEFACTIVE DEMYELINATING LESION
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ABSTRACT
Background: A demyelinating lesion can present as a space occupying lesion in Magnetic Resonance Imaging (MRI) brain. Lesions that have diameter greater than 2 cm is referred as tumefactive demyelinating lesion. These lesions can mimic a brain tumor, namely glioma or primary central nervous system lymphoma.

Case presentation: We present two female patients over 30 years old who presented with limb weakness. Their MRI demonstrated typical appearance of a solitary, incomplete rim enhancing lesion that involved the subcortical white matter with minimal mass effect. Also, the rim of enhancement opened to the grey matter. Due to their typical appearance, biopsy was not performed. The lesions in both patients reduced in size upon follow up after treatment commencement and currently recovering.

Conclusion: In this case report, we focus on discussing the MRI features of tumefactive demyelinating lesion and its main differentials, which are central nervous system lymphoma (CNSL) and glioma.

Keywords: Magnetic Resonance Imaging (MRI); Tumefactive demyelinating lesion (TDL); Open ring enhancement

INTRODUCTION
A demyelinating lesion can present as a space occupying lesion mimicking brain tumor (1). With a diameter greater than 2 cm, it is referred to as a tumefactive demyelinating lesion (TDL), which may have variable presentation. In this case report, we present two cases of TDL and discuss about the findings as well as differential diagnosis.

CASE PRESENTATION
Case 1
Madam B, 44 years old female with underlying diabetes mellitus, and previously activities of daily living (ADL) independent. She presented with aphasia, difficulty reading and expressing word for 5 months and progressive right sided body weakness for 2 months. The body weakness worsened and she became wheelchair bound. No history of fever, loss of appetite or weight loss. On examination, there was right sided homonymous hemianopia, reduced tone, power and sensation of the right upper and lower limbs. After thorough neurological examination, the provisional diagnosis was left parietal lobe syndrome with pyramidal sign; TRO inflammation / demyelinating syndrome. Her initial brain computed...
tomography (CT) scan reported lesion in the left parietal lobe. Her blood investigation and cerebral spinal fluid (CSF) study negative for infection. White cell count and inflammatory marker were not elevated and her CSF study is normal. Anti-Aquaporin 4 antibody is negative. Magnetic resonance imaging (MRI) of her brain showed ill-defined left parietal lobe white matter lesion measuring 4.5 cm in widest dimension, which demonstrated hypointensity on T1W, high signal intensity on T2W images with heterogeneity within and incomplete rim enhancement. No significant perilesional edema or mass effect detected. The overall features were suggestive of TDL with differential diagnosis of primary brain tumor. A repeated MRI brain with added advance MRI sequences which are magnetic resonance spectroscopy (MRS) was then performed. The findings show significant raised Choline and reduced NAA particularly at the center of the lesion which suggests neuronal loss. This helped in confirming that the lesion is demyelinating lesion. She was treated with methylprednisolone 1 g OD for 5 days, followed by 5 sessions of plasma exchange and is currently on two monthly intravenous (IV) cyclophosphamide 500 mg while awaiting for social welfare support for IV Rituximab. Her symptoms improved after the treatment. Two follow up MRI brain showed reduction in size of the lesion and resolution of the incomplete rim enhancement (Figure 1).

Case 2
Madam H, 38 years old female, no known medical illness, previously ADL independent. She complained of progressive right sided upper, then lower limb weakness. Subsequently, she required wheelchair for ambulation. On examination, there were increased tone and reflex and reduced power of the right upper and lower limbs. Sensations of her limbs were intact. Her blood investigation and CSF study does not favor infection. White cell count and inflammatory marker were not elevated and her CSF study is normal. Anti-Aquaporin 4 antibody is negative. CT brain and MRI brain showed left parietal intra-axial cystic lesion. The provisional differential diagnosis was neuroglial cyst and atypical supratentorial cystic astrocytoma. Repeat MRI brain showed left frontoparietal lesion measuring 4.5 cm in widest dimension. The lesion involved the subcortical white matter and cortex with minimal mass effect. The lesion had low signal on T1W images and high signal intensity on T2W images with peripheral incomplete rim enhancement. The overall findings were suggestive of TDL. She was treated with IV methylprednisolone 1 g for five days subsequently 1 session of plasma exchange and has completed 4th cycle of IV rituximab. Her symptoms improved after the treatment. Two follow up MRI brain showed reduction in size of the lesion and resolution of the incomplete rim enhancement (Figure 2).

DISCUSSION
TDL is a lesion with usual size greater than 2 cm diameter (2, 3). Solitary TDL is the most common initial MRI findings (3). It may exhibit mass effect, with or without perilesional edema and with or without contrast enhancement (1, 3). Subcortical white matter is commonly involved followed by the periventricular white matter and brainstem (1). The common location of TDL is supratentorial region especially frontal and parietal region (4). Smaller demyelinating lesion in between 0.5 to 2 cm may also demonstrate similar imaging findings (5).

It is a female predominant condition with female to male ratio of 2.3:1 (1, 6). The mean age of onset is in the third decade (3, 6, 7). In our case, both of the patients are female aged over thirty years old. The clinical presentation of TDL can be variable. The majority is pyramidal involvement such as limb weakness, hemiparesis or hemiplegia (3, 8). Other involvement includes sensory, brainstem, cerebellar, optic neuritis, visual field defects, dysfunction of the bowel or bladder, sexual dysfunction, acute cognitive changes, global aphasia, diplopia, and epileptic seizures (3, 8). Both of our patients had limb weakness. One of them initially presented with aphasia.

21% of patients with TDL developed classical multiple sclerosis (MS) during follow-up (3). In our cases, both the patients had brain and whole spine MRI during their follow up but did not show new brain or spinal cord lesions.

As TDL is one of the mimicker of a CNS neoplasm such as glioma and CNS lymphoma (CNSL), there are few MRI features that help to differentiate them. Most of the TDL and CNSL
demonstrate hypointensity or mixed signal intensity relative to white matter on T1W images. Both TDL and CNSL also demonstrate hyperintensity or mixed signal intensity compared to grey matter on T2W images (9). In our cases, the lesions demonstrated T1W hypointensity as compared to white matter and T2W hyperintensity as compared to grey matter. On post contrast study, majority of TDL demonstrate incomplete rim enhancement as compared to CNSL and glioma (7, 9). Some authors commented that the enhancement is seen in active demyelination (10). The incomplete portion of the rim opens to the grey matter (2, 11). The part of the rim enhancement in the white matter represents the leading edge of demyelination while the non-enhancing center represents chronic phase (2). In both of our cases, the incomplete rim enhancement opened to the grey matter which matched the characteristic MRI findings of demyelination.

There are a few MRI features which are more commonly seen in TDL as compared to CNS glioma. One of it is area of T2W hyperintensity that does not show enhancement on post gadolinium image (12). In this case report, the T2W high signal intensity areas of both patients did not demonstrate enhancement on post gadolinium study.

Other than conventional MRI, MR perfusion is an advanced MRI technique that helps to differentiate TDL from other CNS neoplasm with similar conventional MRI features. In a study conducted by Cha et al, all TDLs had relative cerebral blood volume (rCBV) of less than 2 ml/100 g. Comparing with CNS neoplasm, there is statistically significant in the difference in mean rCBV between both TDL and CNS neoplasm in which higher rCBV is expected in neoplasm due to neovascularity (4, 13). In our case reports, MR perfusion was performed on the first case and her rCBV value is less than 2 ml/100 g which is not suggestive of CNS neoplasm.

With the emerging use of advanced MRI techniques, apparent diffusion coefficient (ADC) value and Magnetic Resonance Spectroscopy (MRS) were also used to differentiate TDL and CNS neoplasm.

The center of TDL which has myelin destruction and edema changes will have high ADC value while the periphery enhancing region of TDL has low ADC value. A threshold of $0.556 \times 10^{-3}$ mm$^2$/s has 81.3% sensitivity and 88.9% specificity in distinguishing TDL from primary CNS neoplasm (14). Study by Lu et al stated significant difference seen between PCNSL and TDL. The minimum value of ADC histogram (ADCmin) of TDL is $684 \pm 101 \times 10^{-6}$ mm$^2$/s while the ADCmin of PCNSL is lower, which is $563 \pm 90 \times 10^{-6}$ mm$^2$/s (14).

TDL will demonstrate increased choline (CHO) peak and decreased N-acetyl aspartate (NAA) peak with increased Cho/NAA ratio. A Cho/NAA ratio of greater than 1.72 or 1.73 favors high grade CNS neoplasm. Therefore, in adjunct to the findings in conventional MRI, this helps increase the confident in diagnosing TDL. Lactate peak and glutamate-glutamine peak may also see in TDL (4, 15).

Correlating the CT features of the TDL with the MR feature also plays a role. The enhancing component of TDL in MRI appears hypodense on CT scan. This finding is highly specific. Meanwhile, the enhancing component on MRI in CNSL and glioma mostly demonstrate either isodense or hyperdense on CT scan (9, 12). Unfortunately, the CT images of the patients were not available for correlation. The common sites of metastases are lungs, liver and bones (3). In the head and neck region, the nose and the paranasal sinuses is the commonest site for metastasis of RCC (3). However, primary tumor of the nasal and paranasal regions is still the commonest compared to metastatic disease.

CONCLUSION

In conclusion, although differentiating TDL from CNS tumor can be challenging for the reporting radiologist. However, the typical imaging features in TDL can increase confidence in diagnosing it. In these cases, the characteristic open rim enhancement where the enhancing rim signify the leading edge of demyelination and open to grey matter with supporting finding of T2W hyperintensity which does not enhance in post contrast study point toward TDL rather than other diagnosis such as CNSL and glioma. Other than conventional MRI findings, advanced MRI techniques such as MR perfusion and MRS serve as great adjuncts to the diagnosis of TDL. Together with the experience of the reporting radiologist, both patients are diagnosed with TDL in their initial MRI in our center. Biopsies were avoided and both patients responded to treatment and currently on regular follow up.
STATEMENT OF ETHICS
Written informed consent was obtained from the patients for publication of this case and any accompanying images.

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CONFLICT OF INTEREST
The authors declare that they have no conflict of interest.

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DATA AVAILABILITY STATEMENT
No additional data than the one presented in this article was used.

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FIGURE LEGENDS

Figure 1: MRI brain of case 1. (a) Initial MRI with left parietal lobe white matter lesion extending to subcortical U-fibers that shows high signal intensity on T2W (white arrow), low signal intensity on T1W and incomplete rim enhancement in post-gadolinium study (black arrow). Note that the high signal intensity area on T2W is not enhancing in post-gadolinium study. (b) Latest MRI done 5 months apart shows resolving lesion with no enhancement.
Figure 2: MRI brain of case 2. (a) Initial MRI shows left frontoparietal lobe lesion involving the subcortical white matter and cortex demonstrating high signal intensity on T2W (white arrow), low signal intensity on T1W and incomplete rim enhancement on post-gadolinium study (black arrow). The high signal intensity area on T2W does not enhance in post-gadolinium study. (b) Latest MRI in 4 months apart shows significantly smaller lesion with resolution of enhancement.