THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Knowledge that will change your world

A Case of Fulminant, Recurrent, Tumefactive Demyelinating Lesions

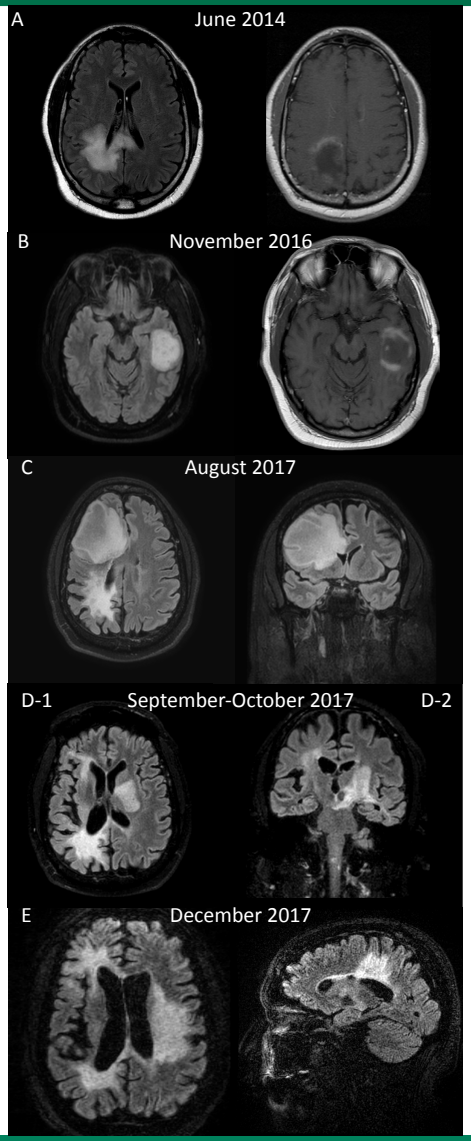
William A. Kilgo MD, Benjamin Jones MD, Khurram Bashir MD MPH

Introduction

Tumefactive demyelinating lesions (TDL) are rare, occurring in approximately 1-2/1000 cases of multiple sclerosis (Poser et al., 1992). Lesions typically seen in multiple sclerosis are ovoid, up to 1.5 cm in size and perpendicular to the long axis of the lateral ventricles. TDL are relatively large in size (>2cm) with associated mass effect, edema, and variable patterns of enhancement that often initially mimic malignancy or CNS infection. A large percentage of patients that present with TDLs go on to develop typical relapsing remitting multiple sclerosis. Here we present a patient with recurrent TDL that have followed a relapsing remitting course over a 4 year period.

Case Report

- 47 year-old African American man with a remote history of testicular carcinoma. He is otherwise healthy with no significant family history of cancer or autoimmune disease.
- In June 2014, he presented to a local neurosurgeon after developing forgetfulness and "bumping into walls." A brain MRI revealed a large right occipital lobe lesion (A) that was biopsied out of concern for malignancy given its radiographic appearance. Biopsy, however, revealed extensive perivascular lymphocytes, lipid laden macrophages, and reactive astrogliosis most consistent with inflammatory demyelination. Additional staining for the JC virus was negative as well. He was referred to the neuroimmunology clinic for further evaluation and treatment. He was treated with high dose IV steroids with incomplete response. This was followed by plasmapheresis and had substantial recovery with the exception of persistent hemianopsia.
- December 2014 - He developed new onset complex partial status epilepticus resulting in three hospital admissions, though these were subsequently well controlled with lacosamide. These seizures emanated from the right posterior occipital region. Imaging at that time (not shown) showed essentially stable findings as compared to previous studies.
- November 2016 - He developed acute confusion, behavioral change, and difficulty with word finding. Imaging at that time (B) showed a new left temporal lobe lesion. He was again treated with IV steroids and plasmapheresis with significant improvement.
- After this second event he began taking dimethyl fumarate for tumefactive multiple sclerosis. He remained stable on treatment and was able to return to work without restrictions.
- August 2017 - He developed uncharacteristic impulsivity, left hemiparesis, executive dysfunction, and dysfluent speech. Brain MRI (C) revealed a large right frontal lobe lesion. He was again admitted and treated with IV steroids and plasmapheresis, this time with moderate improvement.
- September/October 2017 - He presented again with depressed mental status, excessive drowsiness and new right hemiparesis. Repeat brain MRI (D-1) showed a new, enhancing lesion in the left basal ganglia along with improvement in the previous right frontal lesion. He was treated with IV steroids and plasmapheresis but continued to worsen. Steroid dosing was increased to twice daily and repeat MRI showed extension of the lesion into the midbrain and pons (D-2). At this point he began treatment with cyclophosphamide every 2 weeks and was discharged to rehabilitation. He showed modest improvement in mentation.
- December 2017 - After completing 3 cycles of bimonthly cyclophosphamide he continued to have worsening right hemiparesis, dysarthria, and drooling. Brain MRI (E) at this point revealed a new confluent T2 hyperintensity in the left corona radiata with associated enhancement. He was admitted again to receive IV steroids and plasmapheresis, however with incomplete response, rituximab was added. He has tolerated this treatment well, but with incomplete recovery.
- As of May 2018, he has remained clinically stable with monthly cyclophosphamide treatments. His clinical status has remained poor with little recovery after subsequent clinical attacks. He is globally aphasic and has severe right hemiparesis.



CSF Findings

Date	WBC Count	Protein	Glucose	MS Profile
June 2014	0	37	116	Normal
December 2014	3	52	66	Normal
August 2017	3	153	70	_____
September 2017	1	87	96	5 OCBs IgG Index 1.03

Discussion

TDLs are relatively rare as noted before, and have largely been studied via case reports, case series, and via retrospective analyses at large academic medical centers. There have been relatively few reported cases of recurrent tumefactive lesions in a relapsing course such as is seen in our patient. In most patients with TDLs that go on to develop clinically definite multiple sclerosis, the lesions that follow the TDL are more typical in appearance for demyelinating disease and behave like relapsing remitting multiple sclerosis. Our literature search yielded three other detailed reported cases in adults with TDLs following a relapsing remitting course. A 2012 review of a cohort of patients with or without known multiple sclerosis who had TDLs showed recurrence in 9 of 54 (16.7%). Another 2017 retrospective review of pathologically confirmed cases of TDLs noted recurrence of TDLs in 3 of 29 (10.3%) patients, all of whom initially presented with solitary TDLs.

Throughout treatment, extensive work-up for alternative causes was negative, including CSF JC PCR. His CSF findings were unimpressive at the onset of symptoms in 2014. By August 2017 with the third clinical attack, he had marked protein elevation. Interestingly, he did not develop CSF oligoclonal banding or an increased IgG index on repeat CSF testing until September 2017. The absence of CSF oligoclonal banding has in the past been suggested to be a favorable prognostic factor against recurrence of further demyelination, though more recent papers have noted recurrence of demyelination in patients with initially normal CSF.

Management in this case required extensive immunosuppressive therapy with multiple rounds of high dose steroids, plasmapheresis, rituximab and cyclophosphamide. Choosing a maintenance disease modifying drug in the tumefactive population has proven difficult, with emerging case reports of TDLs following fingolimod discontinuation and initiation . A case published last year noted the occurrence of a TDL four months after initiation of alemtuzumab. Our patient was placed on dimethyl fumarate following his second attack in November 2016 until his third attack in August 2017, so it is unclear as to whether disease recurrence is related.

While a presentation such as the one seen in our patient is uncommon, the most likely outcome for a patient with a TDL is to go on to develop clinically definite multiple sclerosis with typical demyelinating lesions. Early treatment should be considered in patients with TDLs. Primary central nervous system lymphoma and high grade gliomas should be ruled out in lesions that cross the corpus callosum such as in our patient. Our hope is that this case adds evidence to the body of literature for treatment of aggressive demyelinating disease.

References

1. Selkirk, S. Shi, J. Relapsing-remitting tumefactive multiple sclerosis. Multiple Sclerosis. 2005; 11: 731-734
2. Turnbull H, Karsan N, Hogg F, et al. A case of relapsing-remitting tumefactive multiple sclerosis. J Neurol Neurosurg Psychiatry 2012;83:A20-A21.
3. Tremblay, et al. Clinical and imaging correlation in patients with pathologically confirmed tumefactive demyelinating lesions. Journal of the Neurological Sciences. 2017; 381:83-87.
4. Luchinetti, et al.Clinical and radiographic spectrum of pathologically confirmed tumefactive multiple sclerosis. Brain. 2008; 131: 1759-1775
5. Altintas, A, et al. Clinical and radiological characteristics of tumefactive demyelinating lesions: follow-up study. *Multiple Sclerosis Journal.* 2012; 18:10: 1448-1453
6. Zeydan, B. Recurrence of tumefactive demyelinating lesions: case report. Controversies in Neurology: Abstract presentation. April 11-14, 2013, Istanbul, Turkey.
7. Barton, et al. Tumefactive demyelination following treatment for relapsing multiple sclerosis with alemtuzumab. Neurology. 88(10):1004-1006, March 07, 2017.

UAB MULTIPLE SCLEROSIS CENTER

uab.edu