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Tumefactive demyelination: Clinical outcomes, lesion evolution and treatments

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Abstract

Objective: Large demyelinating lesions with possible mass effect (tumefactive multiple sclerosis or tumefactive demyelination) can be mistaken for tumour-like space-occupying lesions suggesting a malignant outcome.

Methods: We reviewed our own experience of multiple sclerosis subjects ($n = 28$) with tumefactive demyelination to determine the relationship between clinical outcomes and lesion evolution, clinical outcomes and their relationship to different therapies. Patients with central nervous system demyelinating disease were identified from our database over the last 10 years.

Results: No patient increased in extended disability status scale (EDSS). Overall, lesion regression was associated with improved EDSS. Lesion regression was also associated with therapy versus no therapy. No specific therapy or corticosteroid infusions improved EDSS over the long term. The absence of enhancement on follow up on magnetic resonance imaging portended lesion regression.

Conclusion: Tumefactive demyelination may predict a more benign overall course and is susceptible to traditional immunomodulatory treatments.

Keywords: Tumefactive, multiple sclerosis (MS), magnetic resonance imaging (MRI), extended disability status scale (EDSS)

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Introduction

Multiple sclerosis is an inflammatory disease of the central nervous system (CNS) whose aetiology and pathogenesis are still to be clarified.[1,2] Tumefactive demyelination or tumefactive multiple sclerosis are defined as demyelinating lesions (*c.* 2 cm or greater)[3] or lesions between 0.5 and 2 cm[4] with possible mass effect that can be mistaken for tumour-like space occupying lesions[3] and have a characteristic radiographic appearance.[5] The clinical and imaging spectrum has been outlined in several reviews over the years.[6–9] The clinical outcomes in general have been more benign than might be expected. The prevalence of tumefactive demyelination (not to be conflated with multiple sclerosis (MS) since not all tumefactive demyelination is MS) has not been formally evaluated but it is estimated to be approximately 1–2 per 1000 cases of MS[10] although others suggest an incidence as high as 1.4 to 8%.[4,11] Some investigators have suggested that tumefactive lesions are exquisitely sensitive to corticosteroids.[12] We reviewed our own experience of MS subjects diagnosed by MS Research Group (MSRG) physicians at UTHealth to determine the relationship between clinical outcomes (extended disability status scale (EDSS)) and tumefactive demyelination lesion evolution, tumefactive demyelination lesion evolution and clinical outcomes in relation to different therapeutic agents in MS patients and the effect of changes in Gd+ enhancement on decreasing lesion size. In particular we asked if these lesions were truly benign, if treatment was necessary, if corticosteroids were the best therapy for reducing tumefactive demyelinating lesions and whether any disease modifying therapy (DMT) showed increased beneficial effects on clinical outcomes over time.

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Material and methods

Human subjects

We asked the UTHealth School of Biomedical Informatics to query the Clinical Data Warehouse of our electronic medical record (Allscripts®) used in our clinical practice for the five UTHealth MSRG physicians that regularly see MS patients. The terms multiple sclerosis, tumefactive, the ICD-9 codes multiple sclerosis (340) (based on McDonald criteria 2010) or CNS demyelinating disease (341.9) were searched in the following ways: (a) patients seen with at least one note containing tumefactive (ICD9 codes not used); (b) patients evaluated with at least one note containing tumefactive and a relevant ICD9 code; or (c) patients treated with at least one note containing tumefactive, and at least one record with a relevant ICD9 code. We were able to retrieve 28 subjects who had been diagnosed by their physician with tumefactive demyelination from 2004 to 2014.

Clinical, MRI scanning and treatments

From the medical records, the patient's initial symptoms and EDSS at the time of diagnosis of tumefactive demyelination, magnetic resonance imaging (MRI) results contemporaneous with the above diagnosis and up to two subsequent MRIs during the period of observation, treatments if any initiated after the diagnosis of tumefactive demyelination and later, symptoms and EDSS at the end of the observation period were extracted from the clinical record (Table 1). We also determined increases or decreases if any in the overall size of lesions from the first to the last brain scan. Some subjects had more than three brain MRIs but we included only MRIs showing changes or the last scan available.

EDSS was extracted directly from clinical notes. MRI brain results including dimensions of lesions were taken from fluid-attenuated inversion recovery (FLAIR) sequences of MRI reports. In some cases, reports did not provide precise lesion dimension. If radiology reports did not exist, we looked through the available databases at Memorial Hermann Hospital and the 3 T Research Center. Dimensions were derived directly from these sources by the first author. Clinical outcomes were extracted from the last available clinical note contemporaneous to the last available brain MRI. Treatment regimens used between the first, second or third brain MRI available were tabulated. In one instance (subject #11) there were no dimensions provided for the lesion seen on the initial scan. However, over time the lesion size decreased. Although no dimensions are given for subject #25, there was decrease in the cerebellar component of the lesion by report. Results of brain biopsy and cerebrospinal fluid (CSF) examinations are included if performed and available. Brain biopsy was always confirmed by a neuropathologist. No patients were tested for AQP4 or MOG antibodies. We did not assume that patients lost to follow-up (LTFU) had good outcomes. The study was reviewed and approved by our Committee for the Protection of Human Subjects (HSC-MS-14-0815). The work described in our article was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

Statistics

Statistical analysis was performed using one-tailed Student's *t* test or log rank (Mantel-Cox method) (Prism 7, Version 7.0e, GraphPad Inc).

Results

Some 28 MS patients with the diagnosis tumefactive demyelination over the last 10 years were identified. All 28 presented with tumefactive demyelination. In our data base with of *c.* 3000 patients, we found 28/3000 (*c.* 1%) with tumefactive demyelination. Diagnosis of CNS demyelinating disease was based on findings consistent with the disease including lesions dissemination in time and space consistent with MS, CIS (clinically isolated syndrome) (tumefactive lesion without attaining McDonald criteria 2010), RIS (radiographically isolated syndrome) and/or biopsy proven demyelination or lesion regression consistent with demyelinating disease. Their age, sex, EDSS, CSF and biopsy results, CIS)/RIS diagnosis, results from MRIs, therapeutic interventions, lesion evolution and EDSS at the end of the observation period are outlined in Table 1. The period of observation that included serial MRI ranged from 3 to 94 months (mean $24.9 \pm$ SE 4.6 months). Average age was 39 years $\pm$ 1.88; 16 females:12 males. Average EDSS at the beginning of observation was 2.76 ± 0.38 and at the end 1.71 ± 0.39. None of the patients became clinically worse. The patients were not treated in some instances or treated with corticosteroids, adrenocorticotropin hormone (ACTH), interferon glatiramer acetate (IFN-β-1b sq), natalizumab (IFN-β-1a sq) and cyclophosphamide (IFN-β-1a IM), singly or in combination.

We assessed the relationship between changes in EDSS and lesion evolution over the entire

Table 1 EDSS, CSF and biopsy results, CIS/RIS diagnosis, results from MRIs, Rx interventions, lesion size (cm) and evolution.

Pt Age/sex	Sxs/EDSS/CSF/CIS-RIS	MRI #1 F/u (mos)-cm-location	Rx	MRI #2 F/u (mos - cm-location	Rx	MRI #3 F/u (mos) – cm-location	Rx/EDSS/lesion evolution
1. 42/M	Lt VF cut/EDSS=2.5	4 mos – 1.9 × 2.3 -Rt Pre Ft T2 hyper Gd+	none	8 mos – 2× 2 NC, Gd+	none	25 mos – 2.3 × 1.9 cm – Gd-	None/ EDSS=0 NC
2. 37/M	Lt Leg weak/ EDSS=3.5/◇	1 mos – 3.5 – Gd+ – Rt hemisphere	Steroids, IFN-β-1b sq	30 mos – 2.7 × 2.7 × 2.9 Gd+	NTZ	32 mos – 3 × 3.3 – Gd+	NTZ/ EDSS=3.5/ NC
3. 46/M	Dysarthria/ EDSS=2.0	4 mos – 1.5 & 1.3 × 1 – Rt occip Gd+	Steroids GA	39 mos – 1.1 × 0.9	GA	No 3rd scan	GA/ EDSS=0 ↓
4. 45/F	Hemiparesis/ EDSS=4/◇	0 mos – 2.7 – Rt Ft Gd+	Steroids	8 mos – 2.8 × 3.4 Gd+	IFN-β-1a sq 2/07	54 mos – New Lg – T2 JC & Sup Rt Ft	LTFU/ EDSS = ?/↑
5. 48/F	Wgt loss/EDSS=0/ /RIS	1 mos – 1.4 × 2 – Rt post parietal	ACTH	13 mos – 2.4 × 2.3 × 2.4	dexameth	24 mos – 2.2 × 1.9 × 2 -T1 hypo	ACTH/ EDSS=0↑
6. 46/F	Vertigo/EDSS=3/	3 mos – 2.5 × 1.2 × 1.4 – Rt dentate	none	6 mos – 2.5 × 1.2 × 1.4	none	10 mos – 2.5 × 1.2 × 1.4	None/ EDSS=0 NC
7. 33/F	Rt weakness/ EDSS=2/◇ *	1 mos – 3.9 × 2.3 – Lt parietal	IFN-β-1b sq	34 mos – 4.2 × 2.2	GA	No 3rd scan	GA/ EDSS=2/NC
8. 52/F	Tremors/EDSS=2/- /CIS	1 mos – 2 × 1.8 Lt Ft & 2.2 × 1.7 – post Lt Ft	steroids	4 mos – 4.3 × 4.2 × 3.6 & 2.5 × 2.5 × 2.7 Gd+	unknown	10 mos – 2.3 × 1.5 × 2.3 & 2.1 × 2.6 × 2.3 Gd+	LTFU/ ?/↑
9. 34/F	Headaches/EDSS=0/ /RIS	0 mos – 1.4 – Lt CR Gd+	none	1 mos – 1.6 x1.2 cm Gd-	none	3 mos – 1.4 cm Gd-	GA/ EDSS=0/NC
10. 47/F	Face numb/EDSS=2/ *	1 mos – 3 × 0.5 – Lt parietal Gd+	None	32 mos – 0.8 cm Gd-	none	62 mos – 1.3 cm Gd-	GA/EDSS=2↓↓
11. 27/M	Aphasia/ EDSS=4/◇/	0 mos – Lg – Lt par temp mesial Gd+	steroids	34 mos – 4.4 × 8.4 × 6.4 Gd+	CTX	45 mos – 1.1 cm Lt cerebellum	CTX/EDSS=3↓
12. 35/F	Lt face numb/EDSS=3.5/ *	9 mos – 6.5 × 3.2 × 3.5 – Rt Temp	Steroids GA	75 mos – Lg size – Rt temp	IFN-β-1a sq	80 mos – Lg size – Rt temp	IFN-β-1a sq/ EDSS=3.5 /NC
13. 23/F	Lt hand weak/ EDSS= 2.0	2 mos – 5.0 – Rt par Gd+	Steroids IFN-β-1a sq	12 mos – 1.1 × 1.0 – Rt parietal	IFN-β-1a sq	LTFU	IFN-β-1a sq/EDSS= 2.0/↓
14. 45/M	Leg stiffness/ EDSS=3.5	26 mos – 2.0 – Rt Ft Gd-	GA	46 mos – 0.5 – Rt Ft Gd-	GA	75 mos – 1.7 × 2.3 – Lt Front Gd-	GA/EDSS=3.0/↓-↑
Pt Age/sex	Sxs/EDSS/CSF/CIS-RIS	MRI #1 F/u (mos)-cm-location	Rx	MRI #2 F/u (mos - cm-location	Rx	MRI #3 F/u (mos) - cm-location	Rx/EDSS/lesion evolution
15. 32/M	Rt side weakness/ EDSS=2.5	9 mos 2.0 × 2.3 – Lt PV Gd-	IFN-β-1a sq	56 mos – 2.3 × 1.2 – Lt PV & 1.6 x1.0 RT PV	GA	80 mos – 2.5 Lt PV & 1.5 Rt PV- parietal	GA/EDSS = 1/↑
16. 59/M	Lt weakness/ EDSS=6/◇/CIS	1 mos 4.6 × 2.7 – Rt par	steroids	10 mos – Decreased in size	steroids	20 mos – Rt parietal resolved	Steroids/EDSS2.5/↓↓
17. 41/M	Lt field cut/EDSS=1/ CIS	0 mos > 5.5 – Rt occip	none	3 mos – 5.5 – Rt occip	IFN-β-1b sq	LTFU	IFN-β-1b sq/EDSS?↓
18. 20/M	Lt numbness/ EDSS=4/ ◇/CIS	0 mos 2.9 × 2.8 – Rt CSO Gd-	Steroids	1 mos – 6.4 × 5.9 × 6.7	Steroids	3 mos 2.8 × 3.3 Gd-	None/EDSS=4 /NC
19. 38/M	Dysarthria/ EDSS=2.5/◇	0 mos 4.7 × 3.0 – Lt PV to JC Gd+	GA	6 mos – 1.4 splenium	GA	50 mos resolved	GA/EDSS=0/↓↓
20. 34/F	Aphasia/EDSS=2.5	0 mos 2.5 Rt Ft -par Gd+	Steroids IFN-β-1b	3 mos – 2.5 Gd-	IFN-β-1b sq	LTFU	IFN-β-1b sq/EDSS=0/NC
21. 50/F	Seizures/EDSS=3.5/◇/CIS	0 mos Lg – Lt par	Steroids	LTFU			-
22. 50/F	Dysarthria/EDSS=2/CIS	1 mos 2.1 × 2.2 × 2.4 – Lt Par Gd+	None	11 mos – 2.7 Gd-	none	24 mos 2 × 1 × 0.5 Gd-	None/ EDSS=1.5/↓
23. 39/M	Numbness Lt/ EDSS=4/◇/CIS	0 mos 5.0 Rt -Temp Gd+	steroids	6 mos – 3.2 × 2.2 Gd+	steroids	16 mos 1.8 × 1.8 Gd-	None/EDSS = 2.5/?
24. 32/F	Lt field cut/EDSS=0/	0 mos 2.5 × 1.8 × 2.0 Lt -occip Gd+	IFN-β-1a sq	39 mos – Sig decreased	IFN-β-1a sq	42 mos New 1.5 Rt parietal	IFN-β-1a sq/ EDSS=0/↓-↑
25. 46/F	Foot drop/EDSS=7.5	1 mos Extensive entire pons post midbrain Gd+	Steroids CTX	2 mos – Gd+ pons/ Lt cerebellum	CTX	14 mos ↓cere les, pons/medulla unchanged	IFN-β-1a sq/ EDSS=7.5 NC
26. 29/F	Lt numbness/EDSS=1.5	0 mos 1.8 × 1.0 -Rt cereb ped	IFN-β-1a sq	12 mos – 0.5 × 0.8	CombiRx/ IFN-β-1a IM	42 mos resolved	IFN-β-1a sq/ EDSS=1/↓↓

(continued)

Table 1 Continued.

Pt Age/sex	Sxs/EDSS/CSF/CIS-RIS	MRI #1 F/u (mos)-cm-location	Rx	MRI #2 F/u (mos - cm-location	Rx	MRI #3 F/u (mos) – cm-location	Rx/EDSS/lesion evolution
27. 19/F	Lt leg clumsy/EDSS=3/ *	0 mos – Lt Par – 19 cc (BOD) Gd+	GA	6 mos – Decreased 5 cc (BOD) Gd-	GA	20 mos Unchanged	GA/ EDSS=0/↓
28. 44/m	Rt side clumsy/ EDSS=3.5/ *	0 mos -Lt temp 0.9 & Lt par 0.9 & 2.1 × 0.9 Lt PV	IFN-β-1a IM 4/03	25 mos – Lt temp resolved/ 1.6 × 1 & 0.8 × 0.9	IFN-β-1a IM	105 mos 2.2 × 0.8 & 1.1 × 1.0	IFN-β-1a IM/ EDSS=3.5/↓

All measurements are given in centimeters (cm). Lesions on the 2nd or 3rd scan are in the same location unless otherwise noted. In the last column the last available symptoms and EDSS are given at the end of the entire observation period. Lesion resolution or expansion was based on dimensions and not on presence or absence of gadolinium enhancement. If gadolinium enhancement is not mentioned, there was no gadolinium enhancement.

No patients were tested for AQP4 or MOG antibodies.

BOD = burden of disease.

Cere = cerebellum.

CIS = tumefactive lesion without attaining McDonald criteria 2010.

CR = corona radiata.

CSO = centrum semiovale.

CTX = cyclophosphamide.

EDSS = Expanded Disability Status Scale.

Ft = frontal.

GA = glatiramer acetate.

JC = juxtacortical.

Lg = large.

LTFU = lost to follow-up.

NTZ = natalizumab

NC = no change.

Occip = occipital.

Par = parietal.

Post = posterior.

PV = periventricular.

RIS = radiographically isolated syndrome.

Rt – right

Lt – left

Sup = superior.

Sxs = symptoms

↓ = decreasing tumefactive lesion size

↑= increasing tumefactive lesion size

↓-↑= decreasing tumefactive lesion size followed by increasing lesion size.

◇ Biopsy proven

* = CSF + for OCBs or elevated IgG index; neg CSF = -.

Table 2. Relationship between changes in expanded disability status scale (EDSS) score and lesion evolution.

		Δ EDSS=0		↓EDSS		Total	
	↑EDSS	F/U < 1 yr	F/U > 1 yr	F/U < 1 yr	F/U > 1 yr	F/U < 1 yr	F/U > 1 yr
MRI appearance							
No change	**0**	6	4	3	1	9	5
↓ dimension	**0**	2	2	8	7	10	9
↑ dimension	**0**	2	1	1	0	3	1
↓-↑dimension	**0**	2	1	0	0	2	1
	0	12	8	12	8	24	16

EDSS scores are compared between the time of the tumefactive lesion and the last available clinical examination.
Better clinical outcome –
↓ dimension v. no change; ↑ dimension or ↓-↑ dimension in all patients ($p < 0.005$); for patients followed >1 year ($p < 0.02$).

Table 3. Lesion evolution after each MRI brain scan in relation to different therapeutic agents.

	Lesion evolution						Total Rx	
	No change (NC)		↓dimension		↑dimension			
Agent	F/U <1 yr	F/U >1 yr	F/U <1 yr	F/U >1 yr	F/U <1 yr	F/U >1 yr	F/U <1 yr	F/U >1 yr
None	8	3	5	4	0	0	13	7
Steroids	5	3	7	7	2	1	14	11
ACTH	0	0	0	0	1	1	1	1
IFN-β-1b sq	2	2	0	0	0	0	2	2
GA	3	2	5	4	1	0	9	6
CTX	2	2	1	1	0	0	3	3
IFN-β-1a sq	1	2	3	2	3	2	7	6
NTZ	1	2	0	0	0	0	1	2
IFN-β-1a IM	0	0	0	0	1	1	0	0
TOTAL	22	16	21	18	8	5	43	39

Assessment of outcome was made from the first brain scan until the last brain scan. All agents taken by individual subjects were included during the time after the first scan and before the second or third MRI brain scan. Some subjects use multiple agents during the same interval, so the total number of agents is greater than the number of intervals between brain scans. ACTH = 5 days 80 IU sq × 5 days; steroids solumedrol 1 gm IV × 5 days; IFN-β-1a sq, glatiramer acetate, IFN-β-1a sq, natalizumab, and IFN-β-1a IM were given at standard periodic dosages during the intervals between MR scans; cyclophosphamide 800 mg/m^2 IV monthly.
There was a significant difference between treatment (14/18, 78%) v. no treatment (4/18, 22%) favouring treatment for decreasing lesion size for patients followed for more than 1 year ($p < 0.02$).

observation period for all subjects and separately for subjects followed for at least 1 year (Table 2). Although our database is relatively limited by total time of observation (*c.* 25 months), EDSS did not increase over time in any of our subjects regardless of length of observation. In general, subjects with decreasing size of their tumefactive lesions (80%, 8/10) had decreased EDSS compared to those individuals who had no change in lesion size (33%, 3/9), increasing lesion size (50%, 1/2) or decreasing lesion size followed by increasing lesion size (0/2, none) for all patients. Subjects followed for a year or more also had decreased EDSS with decreasing size of their tumefactive lesions (78%, 7/9). There was no relation between the presence of an active CSF ($n = 4$) (CSF + for OCB (oligoclonal bands) or elevated IgG index) and changes in EDSS.

Table 4. Changes in expanded disability status scale (EDSS) score in relation to different therapeutic agents.

		Δ EDSS=0		↓EDSS		Total	
	↑EDSS	F/U < 1 yr	F/U > 1 yr	F/U < 1 yr	F/U > 1 yr	F/U < 1 yr	F/U > 1 yr
Agent							
None	0	2	1	4[a]	2[b]	6[a]	3[b]
Steroids	0	6	4	5[c]	3[d]	11[c]	7[d]
ACTH	0	1	1	0	0	1	1
IFN-β-1b sq	0	3	3	1	0	4	3
GA	0	3	3	4[e]	0[f]	7[e]	3[f]
CTX	0	1	1	1	1	2	2
IFN-β-1a sq	0	3	2	2	1	5	3
NTZ	0	1	1	0	0	1	1
IFN-β-1a IM	0	1	1	1	1	2	2
TOTAL	0	23	16	9	8	32	25

EDSS are compared between the time of the tumefactive lesion and the last available clinical examination. All agents taken by individual subjects were included during the time of observation. Some subjects used multiple agents between brain scans so the total number of agents is greater than the number of subjects.
[a]no Rx and ↓EDSS all
[b]no Rx and ↓EDSS > 1 yr
[c]corticosteroid and ↓EDSS all
[d]corticosteroid and ↓EDSS > 1 yr
[e]other Rx and ↓EDSS
[f]other Rx and ↓EDSS > 1 yr

With regard to lesion regression and the relationship to different therapeutic agents (Table 3), corticosteroids were associated with regression of only half the tumefactive lesions (50%, 7/14, overall; 63%, 7/11, followed for >1 yr). However, corticosteroid use was also associated with no change in lesion size (36%, 5/14 ; 27%, 3/11) and also increase in lesion dimensions (14%, 2/14; 9%, 1/11). Subjects that received no specific therapy had variable lesion outcomes; decreased lesion size (38%, 5/13; 42%, 4/7), no change (62%, 8/13; 42%, 3/7). The only disease modifying agent that seemed to be associated with subsequent lesion size regression was glatiramer acetate (GA) (56%, 5/9; 66%, 4/6) while only one lesion showed enlargement. This despite treatment in larger lesions (GA treated 22.75 ml ± 34 SD v. other treatments 4.5 ml ± 3.25 SD) and GA's presumed delayed onset of activity. However, our study is underpowered to establish a clear beneficial relationship for GA. There was a significant difference between treatment (Table 3, all active Rx) and no treatment favouring treatment for decreasing lesion size for patients followed for more than 1 year (78% v. 22%). Incidentally, there was no relation between the seven biopsy-proven demyelinating disease and outcome – four subjects had decreased lesion size, three showed no change in lesion dimensions and one had increase in lesion size.

When we compared changes in EDSS in relation to different therapeutic agents (Table 4), no therapy was associated with subsequent clinical improvement in 66% (4/6) of cases (66%, 2/3 followed for >1 yr). Corticosteroid use was followed by clinical improvement in 45% (5/11) of cases (42%, 3/7 followed for >1 yr) while use of other therapeutic agents trailed behind GA with an associated transient improvement in 57% (4/7) that was not sustained (0%, 0/3 followed for >1 yr). There were no statistically significant different effects of one agent compared to another.

We next asked about the effect of changes in gadolinium enhancement on lesion resolution (Table 5). The majority of lesions showing a decrease in lesion size changed from initial enhancing to subsequent non-enhancing (72%, 8/11; 75%, 6/8). Those lesions showing no enhancement throughout observation showed decreased (27%, 3/11; 25%, 2/8), no change (60%, 6/10; 40%, 2/5), or increased (50%, 3/6; 40%, 2/5) lesion size. There was a trend for lesions converting from Gd+ to Gd- with decreasing lesion size in all patients and for patients followed for more than a year ($p < 0.10$).

Table 5. The effect of changes in gadolinium enhancement on tumefactive lesion resolution.

	Gd+ → Gd-		Gd+ → Gd+		Gd− → Gd+		Gd- → Gd-		Total lesions	
Δ lesion size	F/U <1 yr	F/U > 1 yr	F/U <1 yr	F/U > 1 yr	F/U <1 yr	F/U > 1 yr	F/U <1 yr	F/U > 1 yr	F/U <1 yr	F/U > 1 yr
No change	3	2	1	1	0	0	6[e]	2[f]	10[e]	5[f]
↓	8[a]	6[b]	0	0	0	0	3[c]	2[d]	11[a,c]	8[b,d]
↑	2	2	0	0	1	1	3[g]	2[h]	6[g]	5[h]

The initial brain scans (MRI#1) were either enhancing (Gd+) or non-enhancing (Gd-). The initial brain scan (MRI#1) was compared to the final brain scan (MRI#2 or MRI#3) for presence or absence of enhancement.
[a]Gd+ → Gd- decreasing lesion size all
[b]Gd+ → Gd- decreasing lesion size >1 yr
[c]Gd− → Gd- decreasing lesion size all
[d]Gd− → Gd- decreasing lesion size >1 yr
[e]Gd− → Gd- NC lesion size all
[f]Gd− → Gd- NC lesion size all >1 yr
[g]Gd− → Gd- decreasing lesion size all
[h]Gd− → Gd- decreasing lesion size >1 yr

Discussion

The review of our clinical database identified 28 MS patients who were diagnosed with tumefactive demyelination by our MS neurologists. The mean period of observation was 25 months (>2 years). The most compelling finding is that clinical improvement over the time of observation was associated with decreased size of the tumefactive lesions in the short term and in patients followed for >1 year. No patients increased their EDSS. Treatment was linked with decreasing lesion size for patients followed for more than 1 year. Corticosteroid infusions also decreased EDSS. The disease modifying compound GA did show short-term but no longer-term beneficial clinical effects compared to the other disease modifying agents. Finally, there was a trend for decrease in lesion size in subjects with Gd+ lesions at presentation and subsequent absence of enhancement on follow up. Our conclusions are supported by a lack of an apparent treatment bias between conservative and aggressive therapies since cyclophosphamide (CTX) and natalizumab were only used in three patients and patients not given treatment did not have significantly smaller lesions compared to patients given any therapy (data not shown).

There is a dearth of information on untreated tumefactive demyelination lesions in the literature. In most reports, patients were treated with corticosteroids. Our finding that patients in our cohort do well overall conforms to previous experience.[8] We found that treatment with different immunomodulators is advantageous. Moreover, patients with tumefactive lesions may have a better prognosis compared to MS patients without such lesions.[7,8]

Steroids do have beneficial effects in reducing lesion size[12] and resolving clinical disease[13–15] although steroid responsiveness is not universal.[16–18] Only half of our steroid treated patients had reduction in lesion size. In one large series, 75% of lesions resolved over 4 months.[19] However, the response to steroids was incomplete, as 38.5% of the patients had residual neurological deficits and 8% did not improve at all.[19] Tumefactive lesions are not exquisitely sensitive to steroids and steroids do not have a universal beneficial effect. Cyclophosphamide has also shown therapeutic benefits.[20]

There is little if any comment on the effect of disease modifying therapy on the evolution of tumefactive lesions in the existing literature although we had no patients using fingolimod as a DMT.[11,21] Therefore, our cohort of tumefactive MS may predict a more benign overall course and be susceptible to traditional immunomodulatory treatments. Our data buttresses other investigators about prognosis in tumefactive demyelination not being different compared to typical MS.[22] The underlying biochemical pathways responsible for large lesion devolution or regression might be a way to study repair mechanisms using tumefactive demyelination subsets prone to milder disease.

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Authors' contributions

The corresponding author takes responsibility for the writing of the manuscript. The other authors provided patient information and reviewed the manuscript.

Availability of data and materials

Not applicable.

Conflicts of interests

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