

CASE REPORT

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# Relevance of bright spotty lesions in neuromyelitis optica spectrum disorders (NMOSD): a case series

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## Abstract

**Background:** Neuromyelitis optica (NMO), or neuromyelitis optica spectrum disorder (NMOSD), is an autoimmune CNS condition which often has a complex clinical course. Longitudinally extensive transverse myelitis (LETM) is an important and sensitive MRI finding but is not very specific to NMOSD and is seen in other causes of myelitis.

**Case presentations:** We report 11 NMO cases, all seen in women from 25 to 75 years at the time of diagnosis, with most above 65 years of age. All patients were seropositive for AQP4-IgG antibodies, and none had anti-MOG antibodies. Clinical presentations were diverse, the most common being paralytic and visual changes. In this study, 5 of the 11 seropositive NMO patients (45%) had bright spotty lesion (BSLs) on their MRI spine, as opposed to none (0%) in the control group. BSLs were defined as hyperintense foci of signal abnormality on T2-weighted images compared to the surrounding CSF. Treatment included symptomatic management and immunotherapy; timely management led to improvement in all the cases, with partial recovery seen in most (91%) and complete recovery seen only in one.

**Conclusions:** BSLs are a newly defined spinal MRI finding with high specificity, but low sensitivity for NMOSD. The absence of BSLs in the control group establishes its prolific role in distinguishing NMO from MS, ITM, MOGAD and other forms of myelitis. The main aim of this retrospective case-control study was to determine the diagnostic importance and specificity of bright spotty lesions (BSLs) in NMOSD and its ability to discriminate NMOSD from other causes of LETM.

**Keywords:** NMOSD, Bright spotty lesions, Longitudinally extensive transverse myelitis, Demyelinating diseases

## Background

Neuromyelitis optica (NMO) and neuromyelitis optica spectrum disorders ([NMOSD]; previously known as Devic's disease) are rare but severely disabling autoimmune inflammatory disorders of the central nervous system (CNS) characterized by complement-mediated destruction and subsequent demyelination of the optic nerve and spinal cord and resulting in multiple

neurologic deficits, including loss of vision, paralysis, and seizures [1–3]. Immunoglobulin G (IgG) autoantibodies that target the aquaporin-4 (AQP4) channel at the end-feet of astrocytes are highly specific for NMO and are a part of the revised NMO diagnostic criteria [2–4]. However, these antibodies (also called NMO-IgG antibodies) have limited sensitivity for NMOSD, and many NMO cases that demonstrate AQP4-IgG seronegativity are often misdiagnosed as multiple sclerosis (MS) due to several overlapping features between the two diseases [5, 6]. In addition, myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease (MOGAD) with positive serum MOG antibodies has been reported in a small number of patients with clinical characteristics

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of NMO; nearly all of these were AQP4–IgG-seronegative and were younger, less frequently female, and less likely to relapse compared with AQP4–IgG-seropositive patients [5]. These findings render the early identification of seronegative NMOSD cases highly consequential in avoiding misdiagnoses and potentially harmful treatments, as therapies such as those used to treat MS may worsen the clinical status of patients with NMOSD [5, 6]. Moreover, NMOSD causes severe and rapidly progressive disease, and a high degree of suspicion is key to their accurate diagnosis and timely intervention to prevent relapses, disabilities, and long-term neurologic complications [5].

Longitudinally extensive transverse myelitis (LETM), described as a T2 lesion of the spine extending  $\geq 3$  contiguous segments, has been one of the most consistent magnetic resonance imaging (MRI) features of NMOSD [3, 7, 8]. However, a new finding, called bright spotty lesions (BSLs), has been identified as a characteristic feature of NMOSD, thereby distinguishing it from MS and other etiologies of LETM [3, 9, 10]. BSLs, defined as hyperintense intramedullary lesions on axial T2-weighted images usually associated with T1 low signal, likely reflect intense damage to the spinal cord and are now reported to have higher specificity and sensitivity than LETM in diagnosing and discerning NMOSD against other causes of myelitis [2, 3, 11]. Both of these spinal MRI findings are crucial in differentiating seropositive and seronegative cases of NMO from multiple sclerosis (MS), MOGAD, spinal cord infarction (SCI), and other causes of myelitis [7].

In our study, we aim to particularly highlight the importance of BSLs in diagnosing NMOSD, its specificity in differentiating NMOSD from other demyelinating diseases, and its possible role as a prognostic factor for clinical outcomes.

A single-center retrospective study recruiting patients from the Department of Neurology within our hospital was performed between 08-01-2013 and 02-28-2022. We included 11 seropositive NMO cases with evidence of spinal attack from a total of 37 patients, all of whom met the revised 2015 International Panel for NMO Diagnosis (IPND) criteria and were finally selected based on the following: (1) age greater than 18 years; (2) laboratory-confirmed diagnosis of NMO (i.e., presence of AQP-4 IgG antibodies, anti-MOG antibodies, and/or oligoclonal bands); and (3) available MRI spine scans at the time of diagnosis with evident imaging findings [4]. All seronegative NMO cases were excluded. For comparison, we added a control group of 18 patients representing other causes of myelitis based on the inclusion criteria of: (1) age greater than 18 years; and (2) a confirmed diagnosis of multiple sclerosis (MS), idiopathic transverse

myelitis (TM), or neurosarcoidosis, with positive spinal cord lesions on imaging. No cases of MOGAD were included, since all patients with NMO were anti-MOG-Ab negative.

From the eligible cases, we extracted information for each patient as available: age/sex, year of diagnosis, clinical presentation, serology status for NMO antibodies (and MOG antibodies for the control group), brain and spinal MRI imaging findings, treatment measures, and outcomes (Table 2 and Additional file 1: Table S1). Further details including, existing comorbidities, underlying risk factors for NMO, and a prior history of MS, TM, or spinal cord infarction (SCI), were also evaluated. Data regarding the control group was retrieved from our electronic health records (EHR) system using the Slicer Dicer self-service reporting tool, and all appropriate cases with a baseline spinal MRI were screened.

Laboratory testing included serological analysis for the presence of MOG and AQP4 antibodies and further grouping into seropositive and negative cases. The technique used to diagnose NMO was fluorescence-activated cell sorting (FACS) live cell-binding assay, done and obtained at MAYO Clinic. All patients underwent MRI imaging of the brain and cervico-dorsal spine. Scans were acquired variably on the Siemens MAGNETOM<sup>®</sup> Verio 3.0T (Germany) and Siemens MAGNETOM<sup>®</sup> Aera 1.5T (Germany) machines available at our center, and subsequent findings were studied in depth and determined through manual review by two separate neuroradiologists. Besides the MRI acquisition at initial diagnosis, we also reviewed the follow-up scans on subsequent attacks.

### Case presentations

We obtained the data of 11 individuals with seropositive NMO categorized in the cases group (Table 1). Similarly, the control group ( $n=18$ ) consisted of patients with alternative causes of myelitis, including MS ( $n=10$ ), idiopathic transverse myelitis (TM) [ $n=5$ ], and neurosarcoidosis ( $n=3$ ) (Table 1). Detailed information regarding age, gender, year of diagnosis, onset and presentation, relevant neuroimaging findings, seropositivity for NMO, treatment, and outcomes are described in Table 2 and Additional file 1: Table S1.

All cases of NMO were female, suggesting a sex predilection within this disease and in all age groups. Among these 11 cases, the mean age (range) was 60 (26–75) years at the time of diagnosis, wherein eight patients (72.72%) were older than 50, and only three patients (27.27%) were younger than 50, indicating a higher prevalence among the elderly (Table 1). The control group ( $n=18$ ) showed a contrasting demographic picture, with a mean age (range) of 43 (24–69) years and with 11 out of the 18 patients (61.1%) below 50 years and 7 (38.8%) above

**Table 1** General characteristics and comparison of patients in cases with NMO ( $n = 11$ ) and control arm ( $n = 18$ )

Variable	<i>n</i> (%)
Age ratio (Above and equal to 50: below 50)	
Cases group	8:3
Control Group	7:11
Gender (Female and Male ratio)	
Cases group	11:0
Control group	10:8
MRI spine findings—presence of bright spotty lesions	
Cases group	5(45.45%)
Control group	0
MRI spine findings—presence of LETM	
Cases group	10 (90.9%)
Control group	0
Presence of BSLs and LESCL in Cases Group (NMO) ( $n = 5$ )	
BSLs with LETM	4(80%)
BSLs without LETM	1(20%)
Seropositivity for NMO antibodies	
Cases Group	11(100%)
Control group	0
Recovery (Partial recovery: full recovery)	
Cases group	10:1
Control group	13:5

NMO: neuromyelitis optica; BSLs: bright spotty lesions, LETM: longitudinal extensive transverse myelitis

50 years of age. Moreover, in this cohort, the sex ratio was only slightly tilted towards the female population at 55.5% (compared to 44.4% for men) (Table 1).

Clinical manifestations between both groups were diverse and overlapped significantly (Table 2 and Additional file 1: Table S1). Some of the most common features included progressive unilateral or bilateral lower extremity weakness, hemiparesis, paresthesia, facial pain, and visual changes (such as blurring, unilateral and bilateral gradual loss of vision). One case progressed to hypoxic respiratory failure needing mechanical ventilation. Symptomatology and presentation appeared similar in patients with and without BSLs. All patients in the case group (100%) had seropositive confirmation of NMOSD, and all patients within the control group were NMO–IgG seronegative (Table 2 and Additional file 1: Table S1); none of the patients in the entire study had serum anti-MOG antibodies.

Immunotherapy was the mainstay of treatment in all cases, with other therapeutic regimens, including symptomatic management and supportive care (Table 2 and Additional file 1: Table S1). In the cases group ( $n = 11$ ), immunotherapy was delivered either as monotherapy ( $n = 6$ , 54.54%) or combination therapy ( $n = 5$ , 45.45%). Amongst the six patients managed with monotherapy,

rituximab was used in 3 cases (50%), satralizumab in two cases (33.33%), and eculizumab in one case (16.66%). Combination therapy included varying incorporations of rituximab, azathioprine, mycophenolate mofetil, IVIG, plasmapheresis (PLEX), oral prednisolone, and pulse oral steroids.

Appropriate management resulted in clinical improvement in 100% of the cases, and patient outcomes (partial versus full recovery) were further compared between both groups. Within the cases group, complete recovery was achieved only in one patient (9.09%) and partial recovery in the remaining 10 (90.9%) (Tables 1 and 2). On the other hand, the response to treatment was relatively better in the control arm, with complete recovery documented in 13 cases (72.2%) and partial recovery in five (27.7%) (Table 1 and Additional file 1: Table S1).

MRI imaging of the spine was available in all the patients, with additional imaging of the brain and orbits performed in the cases group. Longitudinally extensive transverse myelitis (LETM) (also known as longitudinally extensive spinal cord lesions), depicting myelitis in the form of abnormal T2 signal traversing at least three vertebral body segments in length, was seen in 10 (90.9%) out of the 11 confirmed NMOSD cases and was noticeably absent in all control group patients.

Furthermore, five patients in the cases group (out of the 11) demonstrated the characteristic bright spotty lesions (BSLs) on MRI of the spinal cord, consisting of marked T2 hyperintense foci of abnormal signals (similar to or higher than CSF signal) with corresponding T1 hypointense foci (as demonstrated in Figs. 1, 2, 3, 4, 5). Axial-BSLs and sagittal-BSLs were defined as above on axial T2-weighted images (T2WI) and sagittal T2WI, respectively [3]. Overall, the mean duration between the initial disease diagnosis and MRI acquisition for these cases was around 2.5 years. Out of these 5 NMO cases with BSLs, four (80%) also showed LETMs on MRI, while one patient (20%) did not. Most importantly, none of the patients in the control group ( $n = 18$ ) exhibited BSLs on spinal MRI. In a larger group outside the inclusion criteria, we recorded three cases of MOGAD, and none of them had BSLs on review of their MRI spine either.

## Conclusions

Neuromyelitis optica spectrum disorders (NMOSD) represent a range of complex diseases diagnosed through clinical examination, serologic testing for AQP4 (NMO)–IgG antibodies, and MRI imaging (with and without gadolinium) [2]. The presence of AQP4–IgG in the blood is the main pathogenic factor for NMO [6]. The International Panel for NMO Diagnosis (IPND) revised and developed the consensus diagnostic criteria for NMO in 2015 and defined the unifying term NMOSD using

**Table 2** Clinical demographics, characteristics and serum, CSF, MRI findings and outcomes of patients with NMO

Case	Age/gender	Year of diagnosis	Onset/presentation	Serum NMO	MRI results	Treatment	Outcomes
Case 1	75/F	2017	Progressive lower extremity weakness	Seropositive	MRI C spine: intramedullary hyperintensity with corresponding enhancement posteriorly at the T3 and T5/T6 level. MRI thoracic spine: evidence of transverse myelitis extending from the mid body of T4 down to about the T5–6 level MRI Brain: mild-to-moderate cortical and subcortical atrophy MRI orbit: NA	Eculizumab	Improved
Case 2	71/F	2016	Progressive lower extremity weakness, numbness below T1 dermatome	Seropositive	MRI C-spine: intramedullary hyperintensity with enhancing demyelinating plaque extending from the C7–T1 level. MRI T-spine: hyperintense cord lesion with enhancing demyelination plaques involving the upper thoracic spinal cord at the C7–T1 level and at the T6–T7 and T9–T10 levels, MRI brain: periventricular white matter hyperintensities MRI orbit: NA	Rituximab	Partially improved
Case 3	74/F	2011	numbness waist down	Seropositive	MRI C spine: intramedullary hyperintensity beginning at the level of C4 to T1, MRI T spine: hyperintensity and abnormal enhancement of the thoracic cord noted from the T1 through T6 level, MRI brain: subtle, nonspecific signal changes identified in the periventricular white matter, bilateral thalami, left cerebral peduncle and medulla MRI orbit: NA	Azathioprine and oral prednisone	Partially improved
Case 4	69/F	2008	Progressive lower Extremity weakness and band-like sensation in chest	Seropositive	MRI C spine: intramedullary hyperintensity beginning at the level of C4–C6, with diffuse cervical and cervico-thoracic cord atrophy noted MRI T spine: the mid-to-upper thoracic cord atrophy appears more severe with subtle cord signal changes T3–T5 MRI brain: abnormal hyperintense signal in the cervicomedullary junction with no mass effect or abnormal contrast enhancement MRI orbit: NA	Rituximab	Partially improved

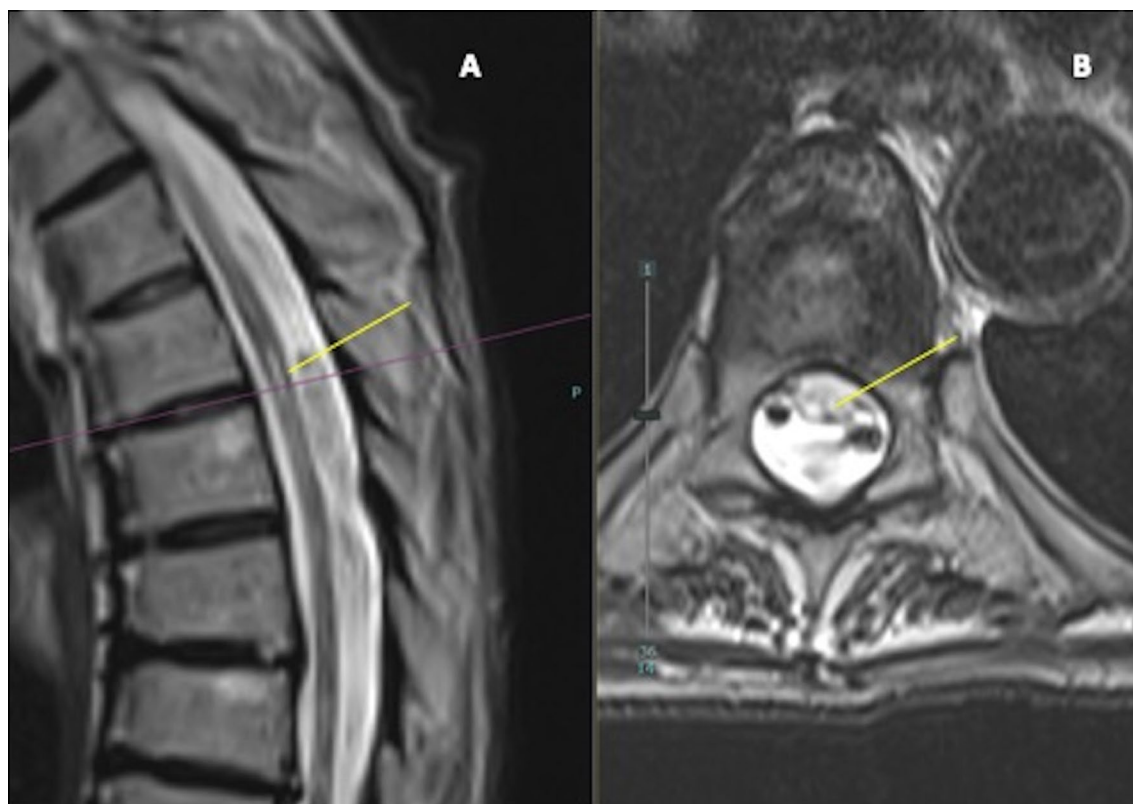
**Table 2** (continued)

Case	Age/gender	Year of diagnosis	Onset/presentation	Serum NMO	MRI results	Treatment	Outcomes
Case 5	64/F	2015	lower extremity weaknesses well as hypoxic respiratory failure requiring mechanical ventilation	Seropositive	MRI c spine: intramedullary hyperintensity beginning at the level of C2 to C7, no abnormal enhancement seen, MRI T spine: increased signal intensity in the mid to lower thoracic cord, MRI brain: no abnormal T2/FLAIR abnormality, MRI orbit: NA	Pulse oral steroids, plasmapheresis and rituximab	Partially improved
Case 6	35/F	2019	bilateral loss of vision left more than right	Seropositive	MRI C spine: multiple confluent T2 hyperintense cord lesions throughout the upper to mid cervical spine, some with patchy enhancement; MRI T spine: nonenhancing T2 hyperintense cord lesions, most prominently at T7 and T8; MRI brain and orbit: findings of bilateral optic neuritis and nonspecific periventricular white matter T2 hyperintensity along left lateral ventricle	Satralizumab	Partially improved
Case 7	69/F	1997	Progressive lower extremity weakness and right loss of vision	Seropositive	MRI c spine: intramedullary hyperintensity with corresponding enhancement at the level of C2–C3 to T4; MRI T spine: increased signal intensity in the mid to lower thoracic cord with enhancement at T5–T6; MRI brain with nonspecific white matter changes in frontal deep white matter, MRI orbit bilateral hyperintensity of optic nerve post chiasmatic segment and right optic nerve atrophy	Rituximab and IVIG	Partially improved
Case 8	26/F	2006	Bilateral loss of vision rt > lt; F/B bilateral arm and leg weakness	Seropositive	MRI C spine: intramedullary hyperintensity cord signal at C3 to C7 level, MRI T spine: cord signal again demonstrates abnormal T2 signal within the cord seems at the C7 level and extending inferiorly to the T7 level, MRI brain: bilateral optic nerve atrophy, otherwise, no acute intracranial process	Satralizumab	Partially improved

**Table 2** (continued)

Case	Age/gender	Year of diagnosis	Onset/presentation	Serum NMO	MRI results	Treatment	Outcomes
Case 9	36/F	2012	Progressive lower extremity weakness and paresthesia	Seropositive	MRI C spine: intramedullary hyperintensity cord signal at C2 to C6 level, MRI T spine: cord signal again demonstrates abnormal T2 signal within the cord seems at T6 level, MRI brain: unremarkable, MRI orbit: left optic nerve hyperintensity	PLEX, Pulse oral steroid and CellCept	Partially improved
Case 10	69/F	2005	Progressive lower extremity weakness and paresthesia	Seropositive	MRI C spine: unremarkable MRI T spine: cord signal again demonstrates abnormal T2 signal within the cord extending at T4 to T9 level MRI brain and orbit: hyperintensity along left optic nerve	Rituximab	Partially improved
Case 11	67/F	2008	Left blurry vision and left hemiparesis	Seropositive	MRI C spine: intramedullary longitudinal expansile T2 hyperintense cord lesion is currently noted from the C2 to C5 with abnormal enhancement MRI orbit: left optic nerve demonstrates abnormal signal changes MRI T spine: no cord lesion	Pulse oral steroid and PLEX	Partially improved

F: female; NMO: neuromyelitis optica, PLEX: plasma exchange; MRI: magnetic resonance imaging



**Fig. 1** MRI sagittal T2 image (A) of the thoracic spine demonstrates an intramedullary mid-thoracic cord lesion (yellow arrow), with a corresponding focus that is as bright or brighter than CSF on the axial images (B) (yellow arrow)

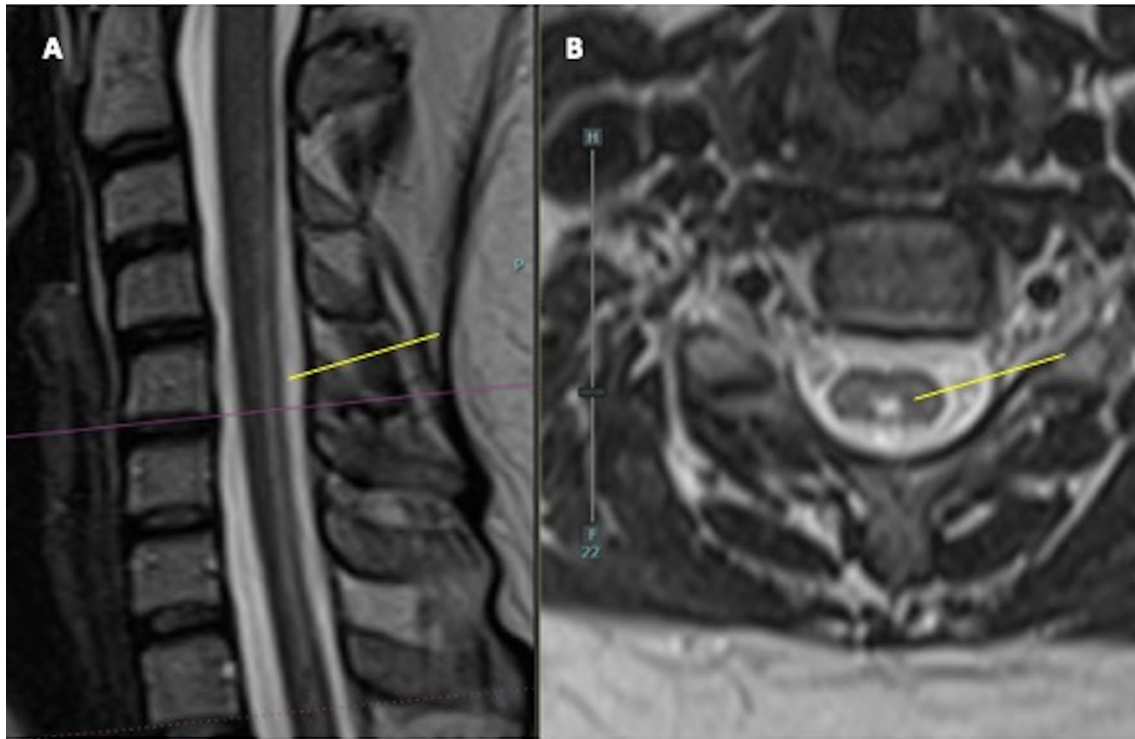
clinical and MRI characteristics, which was further stratified by serologic testing into NMOSD with AQP4–IgG positivity and NMOSD with negative or unknown AQP4–IgG status [2, 3, 12].

NMOSD often displays a relapsing–remitting course and typically presents with either monophasic or recurrent attacks of optic neuritis (ON) and transverse myelitis (TM), often leading to severe disability and occasionally life-threatening respiratory failure [12, 13]. Demographically, NMO is usually a disease seen in middle-aged women around 35–45 years of age (roughly a decade older than MS), but it can also occur in children and the elderly. It has a highly evident preponderance for females seen primarily among seropositive patients [5, 13]. These findings are clearly reflected in our study, since all the seropositive NMO cases were female, and most patients presented between 65 and 75 years of age (Tables 1 and 2). Moreover, the course and prognosis of NMOSD are variable, with some patients suffering chronic disabilities due to relapsing episodes [2]. Existing literature demonstrates that up to a quarter of patients fully recover with immunotherapy, supportive treatment, and rehabilitation, while less than 10% do not show any recovery [2];

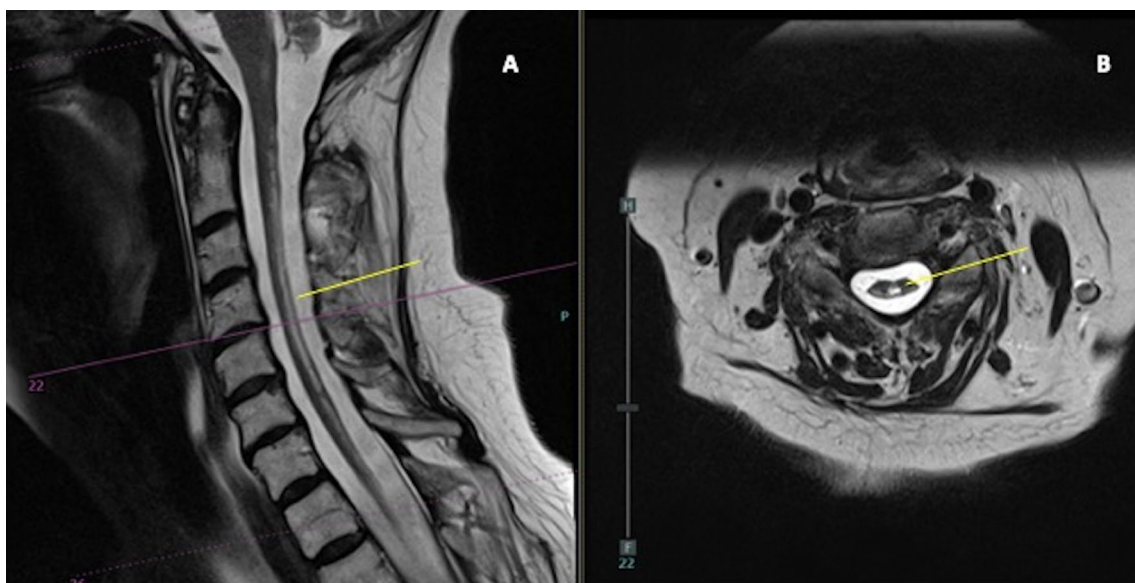
this is reproduced in our analysis, where partial recovery was seen in 90% of the cases in our study and only one patient gained a full recovery (Tables 1 and 2).

MRI is the most crucial imaging technique in the differential diagnosis of NMOSD and should always include imaging of the entire CNS (cranial and spinal cord MRI), irrespective of the presenting signs and symptoms [14]. MR imaging clues to the diagnosis of NMOSD are longitudinally extensive lesions of the optic nerve (more than half the length) and spinal cord (three or more vertebral segments, which differ from MS, demonstrated by short, multiple lesions, bilateral optic nerve lesions and lesions of the optic chiasma) [14, 15]. Of note, an LETM (or LESCL) MRI pattern may occur in patients with various other demyelinating and CNS inflammatory disorders, including MS, MOGAD, and acute disseminated encephalomyelitis (ADEM), or in certain infections, neoplastic and paraneoplastic diseases [11]. Co-existing features, such as cervico-medullary junction involvement, a higher cord expansion ratio, BSLs, and female sex are highly indicative of AQP4-antibody seropositivity in patients with LETM and may further predict a diagnosis of NMOSD [16].



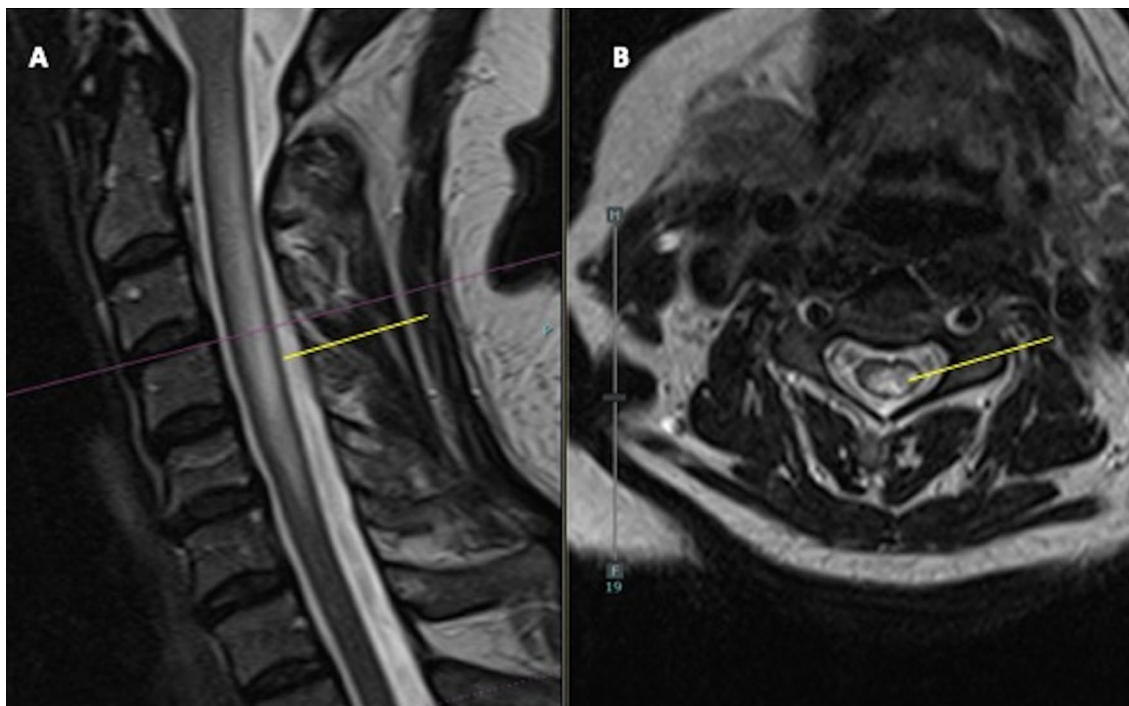


**Fig. 2** MRI sagittal T2 image (A) of the cervical spine demonstrates longitudinally extensive T2 hyperintense cord lesions (yellow arrow), with corresponding foci that are as bright or brighter than CSF on the axial images (B) (yellow arrow)

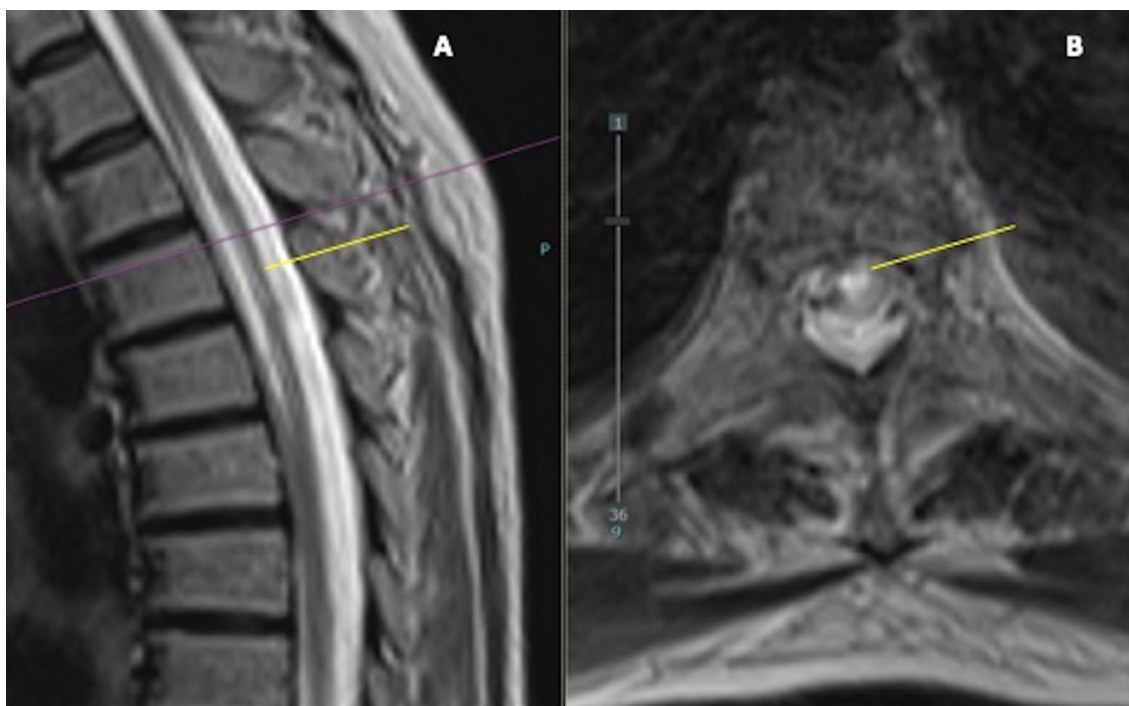


**Fig. 3** MRI sagittal T2 image (A) of the cervical spine demonstrates longitudinally extensive T2 hyperintense cord lesions (yellow arrow), with corresponding foci that are as bright or brighter than CSF on the axial images (B) (yellow arrow)





**Fig. 4** MRI sagittal T2 image (A) of the cervical spine demonstrates longitudinally extensive T2 hyperintense cord lesions (yellow arrow), with corresponding foci that are as bright or brighter than CSF on the axial images (B) (yellow arrow)



**Fig. 5** MRI sagittal T2 image (A) of the thoracic spine demonstrate a longitudinal extensive intramedullary mid-thoracic cord lesion (yellow arrow), with a corresponding focus that is as bright or brighter than CSF on the axial images (B) (yellow arrow)

Bright spotty lesions (BSLs) are characterized as intramedullary and markedly hyperintense lesions on axial T2-weighted images (T2WI) without flow void effects, with either a higher or equal signal intensity to the surrounding CSF. They have recently been described as the most striking NMO spinal MRI finding compared to MS and are highly specific for NMO, helping to distinguish NMOSD from other etiologies of LETM and CNS inflammatory disorders, such as MS, MOGAD, neurosarcoidosis, and transverse myelitis (TM) [2, 17]. The pathophysiology of BSLs remains unknown, but they likely correspond to transient necrotic areas with cystic inflammatory lesions due to astrocytic impairment associated with the loss of AQP-4. These lesions are not as hypointense as CSF on the T1-weighted images, distinguishing bright spotty lesions from syringomyelia, and the axial T2W sequence is an essential MRI series to evaluate BSLs [13].

NMO was historically understood as a variant of MS, and since their clinical manifestations and radiologic findings often co-occur, the disease is frequently misidentified as MS. Similarly, the distinction of NMO from spinal cord infarction (SCI) is also necessary, as these disease processes may be misdiagnosed clinically and on imaging. However, with proper evaluation, these conditions can be distinguished from NMOSD based on their clinical, radiological, and spinal fluid analyses [14]. More specifically, NMOSD patients typically present with highly characteristic BSLs, compared to patients with SCI and MS [18]. Moreover, MOGAD, now considered a distinct disease entity from NMOSD, was initially believed to be a part of AQP4-IgG-negative NMOSD due to the presence of anti-MOG antibodies in a subset of seronegative NMOSD patients [19]. LETM is a classical spinal MRI feature of MOGAD, but BSLs, on the other hand, are rarely seen in MOG-IgG myelitis and are more representative of AQP4-IgG myelitis. BSLs, in fact, are crucial for the differentiation of MOGAD from NMOSD during the acute phase [20]. This was depicted in a review by Kim et al. in which none of the 49 MOG-IgG myelitis patients exhibited BSLs, while 30% of patients with AQP4-IgG myelitis had BSLs in the acute phase when the original definition of BSL was applied [19]. Likewise, none of the NMO cases in our study had anti-MOG antibodies, and conversely, out of the three AQP4-seronegative MOGAD patients, none showed BSLs on spinal imaging (Table 2).

Another study by Sylvain Rabasté et al. reported that the specificity of axial-BSLs for AQP4 + NMOSD patients was 94.0% (95% CI (3)). The sensitivity was 40.0% (95% CI (3)), and in the multivariable analysis, the only MRI feature associated with AQP4-IgG positivity was the presence of axial-BSLs (OR: 9.2, 95% CI (3);  $p=0.022$ ) (3). In

a parallel investigation by Yonezu et al. BSLs were more frequently observed in patients with NMO (54%) than in those with MS (3%;  $p<0.01$ ). LETM was found in 67% of NMO patients, and BSLs were seen in 63% of the patients without LETM. BSLs or LETM were documented in 88% of the NMO patients [9, 10]. Remarkably, out of 11 seropositive NMO cases in our study, LETM was discovered in 90.9%, BSLs in 80%, and BSLs without LETM in 20% of patients (Tables 1 and 2). Analogizing the case and control groups, we could confidently hypothesize that BSLs were more specifically seen with NMOSD, as opposed to MS, idiopathic TM, and neurosarcoidosis, since none of these cases revealed BSLs on spinal imaging (Table 1 and Additional file 1: Table S1). In addition, AQP4-IgG antibodies, routinely present during an acute NMO attack, have disappeared over time in many instances, potentially yielding the diagnosis of NMO challenging in these cases. Hence, BSLs are of significant value in providing a timely and accurate diagnosis of NMOSD, especially in those who are AQP4 IgG-seronegative, where the diagnosis is ambiguous.

In summary, NMOSD are considered rare disorders as they have often been misdiagnosed as (or considered a variant of) MS, with some overlapping clinical, laboratory, and imaging features with MS and MOGAD. Our study investigates and highlights the importance of a striking new spinal imaging finding called 'Bright Spotty Lesions' (BSLs) for the early detection of NMOSD and to help distinguish NMOSD from other forms of myelitis (mainly MS). Patients with NMOSD in this study were found to have a higher number of BSLs and T1 dark lesions on MRI as opposed to patients with MS. We conclude that axial-BSLs are a highly useful and reliable marker in diagnosing and discriminating seropositive NMOSD patients from potential mimickers on imaging (such as cord infarcts), and from other neuroinflammatory causes of myelitis, including MS, transverse myelitis (TM), neurosarcoidosis, and MOGAD. BSLs have much greater specificity than LETM and can be used in combination with LETM to help differentiate patients with NMOSD from those with MS with a higher sensitivity than LETM alone. However, despite the high specificity, they also demonstrated a low sensitivity (45%) for NMOSD. Moreover, this study exclusively involves the original data of a single center with a limited number of cases, which establishes the need for future multicenter studies (with a larger sample size) on BSLs to corroborate our findings and validate the neurodiagnostic relevance of BSLs in NMOSD and the differential diagnosis of CNS inflammatory disorders.

## Abbreviations

NMO: Neuromyelitis optica; NMOSD: Neuromyelitis optica spectrum disorders; LETM: Longitudinally extensive transverse myelitis; LESCL: Longitudinally extensive spinal cord lesions; AQP4-IgG: Aquaporin-4 antibodies; BSLs: Bright spotty lesion; MS: Multiple sclerosis; MOG: Myelin oligodendrocyte glycoprotein; MOGAD: Myelin oligodendrocyte glycoprotein antibody disorder; TM: Transverse myelitis; IVIG: Intravenous immunoglobulin; IVMP: Intravenous methylprednisolone; PLEX: Plasma exchange/Plasmapheresis; CNS: Central nervous system; SCL: Spinal cord infarction; MRI: Magnetic resonance imaging; CSF: Cerebrospinal fluid; FACS: Fluorescence-activated cell sorting; ON: Optic neuritis; ADEM: Acute disseminated encephalomyelitis.

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s41983-022-00601-7>.

**Additional file 1: Table S1.** Spectrum of demyelinating disease including multiple sclerosis, idiopathic transverse myelitis and neurosarcoidosis.

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## Disclosures

Joe Joseph, Parissa Feizi, Shreya R Pasham, Lalit Nirwan, Kanika Sharma, Samiksha Srivastava, Shruti Jaiswal, Shitiz Sriwastava: reports no disclosure.

## Author contributions

Conceptualization: SS. Drafting the manuscript: JJ, PF, ME, LN, SP, KS, SS, SJ, SS. Editing and final draft: SS. All authors read and approved the final manuscript.

## Funding

NonE.

## Availability of data and materials

This will be provided on request.

## Code availability

Not applicable.

## Declarations

### Ethics approval and consent to participate

Institutional Review Board at West Virginia University authorized the publication of case report, under IRB protocol number: 2003947403.

### Consent for publication

Informed consent waived as this study was conducted under approval of West Virginia University IRB; IRB protocol number: 2003947403.

### Competing interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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