CASE REPORTS

Mimics of Optic Neuritis in Neuromyelitis Optica Spectrum Disorder: A Case Report

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ABSTRACT

The optic nerve can be involved in a myriad of pathologies underscoring the importance of ruling out both surgical as well as medical causes. Often, it is the temporal profile, clinical presentation and imaging that helps to establish the final diagnosis. Neuromyelitis optica spectrum disorder (NMOSD) is an inflammatory demyelinating disorder involving the optic nerves and the spinal cord, which if promptly and adequately managed, may yield gratifying outcomes. We report an unusual presentation of NMOSD, mimicking a compressive optic neuropathy. A comprehensive review of the history, extensive investigations including brain and spinal cord imaging, and positive anti-aquaporin 4 antibodies helped in the definitive management.

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Neuromyelitis optica; optic nerve; tuberculum sellae meningioma; radiation-induced optic neuropathy

Introduction

Neuromyelitis optica spectrum disorder (NMOSD), also known as Devic's disease, is an inflammatory demyelinating disorder of the central nervous system (CNS) characterised by recurrent attacks of optic neuritis (ON) and longitudinally extensive transverse myelitis (LETM), distinct from multiple sclerosis. The discovery of neuromyelitis optica immunoglobulin/anti-aquaporin 4 antibody (AQP4-IgG) with a high specificity and sensitivity of 91% and 98%, respectively,¹ has led to a revolution in the diagnosis of NMOSD. We present a case of recurrent optic neuropathy, where the first episode of vision loss was considered compressive and attributed to a tuberculum sellae meningioma (TSM) and the second episode to radiation-induced optic neuropathy. The patient eventually tested positive for AQP4-IgG antibody, underscoring the need for a high index of suspicion for NMOSD.

Case presentation

A 51-year-old woman, with no prior comorbidities, presented to the Neuro-ophthalmology outpatient services with a history of three episodes of visual loss.

The first episode was six years prior to her current presentation to us, when she developed visual

loss in the right eye, which progressed to counting fingers close to her face over a period of three to four days. There was no pain on eye movement abnormalities, no local symptoms and no other systemic complaints. Gadolinium-enhanced brain magnetic resonance imaging (Gd-MRI) of the brain was suggestive of a TSM in close proximity to the right optic nerve ([Figure 1a](#)). She did not consent to surgical excision of the tumour and was treated with gamma knife radiosurgery (18 Gy @50% iso-dose prescription) followed by oral corticosteroids for a week. The optic apparatus was preserved from 8 Gy radiation exposure. Her vision gradually improved to 6/6 in the right eye over a period of one month and she remained asymptomatic for around four years.

The second episode occurred four years after the first episode, when she presented with a second episode of subacute onset painless vision loss, this time in the left eye. The visual loss progressed to no perception of light over the course of two days. Gd-MRI brain was suggestive of a shrunken TSM ([Figure 1b](#)) with no compression of the optic apparatus. In view of the temporal sequence and previous irradiation, radiation-induced optic neuropathy was the perceived diagnosis and she received steroids (intravenous methylprednisolone 1 g daily for three days) and anti-vascular endothelial growth

Figure 1. (a) Gadolinium-enhanced magnetic resonance imaging (Gd-MRI) of the brain showing a tuberculum sellae meningioma (arrowed), just anterior to the optic chiasm, abutting the right optic nerve. Follow-up Gd-MRI four years (b) and five years and 10 months later (c) showing residual sellae meningioma (arrowed) with no signs of optic nerve compression.

Figure 2. Fundus photographs showing bilateral secondary optic atrophy with optic disc pallor; (a) – right and (b) – left.

factor (anti-VEGF injections 5 mg/kg). There was mild improvement in her vision over six to seven months. She could count finger at 6 m distance but never regained complete vision in left eye.

The third episode occurred one year and ten months after the second episode (two months prior to presentation to our Neuro-ophthalmology services). She presented with subacute onset, painless, progressive vision loss in her right eye over two days. Her general physical and systemic examination was normal. Her visual acuity was only perception of light in the right eye and 6/18 in the left eye. Her visual fields in the right eye were severely depressed and in the left eye showed a temporal hemianopia. On indirect fundus examination, bilateral secondary optic disc atrophy was present (Figure 2). Gd-MRI of her brain was suggestive of residual TSM with no evidence of compression of the optic nerves and her spine imaging

was normal (Figure 1c). Hence, she was referred to our Neuro-ophthalmology clinic.

In the view of the recurrent episodes of subacute-acute visual loss, her AQP4-IgG antibody testing was done by indirect immunofluorescence, which was positive at 1:10 sample dilution. Other investigations including a full blood count, renal and liver function tests, thyroid function tests, serum electrolytes, serum vitamin B₁₂ levels, serum erythrocyte sedimentation rate, C-reactive protein, anti-nuclear antibody, anti-neutrophil cytoplasmic antibodies and cerebrospinal fluid analysis were normal. She was started on immuno-modulation including a course of intravenous high-dose corticosteroids followed by oral tapering over a period of eight weeks. In addition, she was started on oral mycophenolate mofetil (2 g/day). Her visual acuity on two months' follow-up was 6/24 in the right eye and 6/6 in the left eye.

Discussion

NMOSD is a severe autoimmune inflammatory disorder of the CNS, presenting as a monophasic or relapsing disease that predominantly targets the optic nerves and spinal cord. The core clinical characteristics for diagnosis include clinical syndromes related to the optic nerve, spinal cord, area postrema, other brainstem, diencephalic or cerebral presentations.² Diagnostic criteria for NMOSD with AQP4-IgG requires at least one core clinical characteristic with a positive test for AQP4-IgG using the best available detection method (cell-based assay strongly recommended). Diagnostic criteria for NMOSD without AQP4-IgG or NMOSD with unknown AQP4-IgG status requires at least two core clinical characteristics occurring as a result of one or more clinical attacks and meeting all of the following requirements: a) At least one core clinical characteristic must be ON, acute myelitis with LETM, or an area postrema syndrome; b) Dissemination in space (two or more different core clinical characteristics); c) Fulfilment of additional magnetic resonance imaging (MRI) requirements, as applicable.³ Our patient fulfilled the above criteria with three episodes of optic neuritis and positive AQP4-IgG.

The most frequent symptom at onset in NMOSD is ON in 37–54% of the patients, followed by LETM in 30–47%. Approximately one-half of these patients present only with ON, which is bilateral in 20% of cases.¹ Profound and persistent visual loss is a hallmark of ON in NMOSD with 80% of patients experiencing severe loss of visual acuity (<20/200) during an acute attack.¹ Optic neuritis in NMOSD generally causes severe visual field defects, and, given its potential to involve the optic chiasm and tracts, may manifest with bitemporal or homonymous visual field defects. ON can be the first or the presenting symptom in patients of NMOSD. Five to eighteen percent of cases present only with recurrent episodes of ON, as was noted in our patient.

For a long time ON has been considered as a harbinger of multiple sclerosis. Atypical features for ON including rapid progression, recurrent episodes, severe visual loss, bilateral involvement, retinal changes, non-responsiveness to corticosteroids or corticosteroid dependency should alert the treating

physician to consider alternative causes. Apart from NMOSD, granulomatous inflammatory conditions like sarcoidosis, vasculitis, infections, space-occupying intracranial lesions, malignancies and many autoimmune conditions can present with atypical features of ON and should be adequately ruled out. In our patient, although a history of TSM and radiation treatment was present, the onset, recurrences, sequential involvement of the optic nerves, duration, time to peak of vision loss and good response to corticosteroids gave clues to the diagnosis. The first episode was considered as a compressive optic neuropathy and patient received corticosteroids following the surgical procedure as mentioned above. The second episode was considered to be radiation-induced optic neuropathy by the treating clinician. The patient again received steroids and anti-VEGF injections, to salvage vision before being referred to our Neuro-ophthalmology clinic. Isolated case reports and case series are available wherein anti-VEGF agents have been used as vision salvaging therapy in patients with radiation-induced optic neuropathy.⁴ Transient visual improvement in earlier episodes could be due to the effect of corticosteroids and as a hindsight, the meningioma was an incidental finding. The rapid improvement in vision in our patient after the first episode is also unusual for a compressive lesion. Compressive optic neuropathy due to an intracranial space-occupying lesion (TSM in the current case)⁵ and radiation-induced optic neuropathy may also present with visual loss and visual field defects, hence it becomes very important for the clinicians to distinguish these from inflammatory optic neuropathies. TSM can cause a compressive optic neuropathy; the onset is subacute to chronic and visual fields have a typical pattern depending upon the direction of compression. Similarly, the presence of a temporal correlation, subacute to chronic onset after radiation therapy with latency ranging from 8 to 48 months (average 18 months), typical imaging findings delineating necrosis in the exposed areas and poor visual prognosis help the clinician to diagnose radiation-induced optic neuropathy.^{6,7} The improvement in vision in our patient over six to seven months roused the clinical suspicion of a demyelinating disorder although the response to corticosteroids was not marked in this episode. [Table 1](#) depicts important clinical pointers which may help differentiate these conditions from ON related to NMOSD.

Table 1. The differentiating features of optic neuropathy secondary to compression, radiation-induced optic neuropathy, and neuromyelitis optica spectrum disorder.

	Compressive optic neuropathy ⁵	Radiation-induced optic neuropathy ^{6,7}	Neuromyelitis optica spectrum disorder
Onset	Insidious	Sudden (Ranging from 3 months to 8 years)	Acute – Subacute
Course	Progressive	Progressive	Progresses over a few days
Recurrences	Uncommon	Rare	Common
Neuroimaging	Depending upon the aetiology	Site of involvement depends upon the radiation site. Optic nerve and chiasmal enhancement on T1-weighted magnetic resonance imaging	Involves more than half of the entire length of the optic nerve with prominent retrobulbar/posterior/optic chiasm involvement. Optic nerve enhancement on T1-weighted magnetic resonance imaging
Antibodies	Negative	Negative	Anti-aquaporin 4 antibodies present
Prognosis	Good (with early intervention)	Modest	Good (with early intervention)
Response to corticosteroids	Minimal	Minimal	Good

As the clinical features of ON related to NMOSD may overlap with other inflammatory CNS disorders, ancillary investigations, specifically neuroimaging forms an important early step in its diagnosis. Optic neuritis related to NMOSD is characterised by bilateral, and longitudinally extensive involvement, affecting more than half the length of the optic nerves. Preferential compromise of the posterior optic pathway including the intracranial segment of the optic nerve, extending to the optic chiasm is usually noted. The brain lesions are seen in areas where AQP 4 is expressed including the subpial regions, perpendymal regions, circumventricular organs, brainstem, chiasm/hypothalamus, and corpus callosum. Forty per cent of patients with NMOSD may also present with a normal orbital MRI.⁸

Current treatment regimens for acute attacks of ON include corticosteroids and plasma exchange.⁹ The status of intravenous immunoglobulin, which is frequently used in other antibody-mediated neurological diseases, in NMOSD is controversial. Immunomodulation therapies including azathioprine, mycophenolate mofetil, and rituximab are used as long-term preventive therapies for NMOSD.¹⁰

Conclusion

This case underscores the importance of a detailed clinical history and high index of suspicion for NMOSD in patients presenting with recurrent visual loss. This case also illustrates the complexity of diagnostic challenges in patients with NMOSD. It is important to recognise inflammatory ON clinically. The onset and progression of symptoms, severity of visual loss,

pattern of visual field loss and radiological findings may provide clues to diagnosis. Severe or recurrent bilateral visual loss with posterior predominant extensive optic nerve involvement are important clinical pointers towards NMOSD. Given the prognosis and the potential of the disease to recur, early diagnosis and prompt management with aggressive immunomodulation is indicated.

Author contribution

Nandita Prabhat: Acquisition of data, analysis and interpretation of data; manuscript preparation.

Karthik Vinay Mahesh: Involved in diagnosing the patient and manuscript revision.

Aastha Takkar: Drafting the article and revising it critically for important intellectual content.

Manjul Tripathi: Revising the article for important intellectual content.

Chirag Ahuja: Manuscript revision and correction.

Ramandeep Singh: Manuscript revision and correction.

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