Cortical Blindness: An Unusual Manifestation of Neuromyelitis Optica Spectrum Disorder

Dear Editor,

The clinical armamentarium of neuromyelitis optica spectrum disorders (NMOSD) has gradually evolved over the years, encompassing variable involvement of the brain and spinal cord. Episodes of optic neuritis and transverse myelitis are the most common presentations that often pose a diagnostic challenge in differentiating it from multiple sclerosis (MS).[1] The usual cause of vision loss in a patient with NMOSD is optic neuritis, which is more severe and often bilateral as compared to multiple sclerosis.[2] Cortical blindness in NMOSD without optic neuritis is very rare.[3,4]

A 21-year-old right-handed lady presented with a two-week history of bilateral decreased visual acuity and sensory motor quadriparesis with bladder bowel involvement. She had a past history of an attack of quadriparesis one year back without any visual symptoms. For the past episode, she was treated by a physician with a course of intravenous methyl prednisolone followed by oral steroids (prednisolone) for one month, after which her symptoms resolved. Her current neurological examination revealed that she was oriented to place and person and not to time. Her visual testing revealed perception of light positive (PL + ve) PR projection of Rays (PR) − ve, hand motion close to face (HMCF), and ger counting close to face (FCCF) also − ve. Visual fields could not be tested because of markedly reduced visual activity. Motor power revealed normal bulk in both upper and lower limbs; tone was normal in both upper limbs with a slight increase in muscle tone in both lower limbs (modified Ashworth scale of 1); power was medical research council scale (MRC) grade 4/5 at the shoulder and elbow joints, 3/5 at the wrist joint with hand grip of 40% in both upper limbs. Both the lower limbs revealed a power 3/5, at hip joints, knee joints, and ankle joints. Her Expanded Disability Status Scale (EDSS) was 8. There was a sensory level at C5, below which all the sensations (pain, touch, temperature, and vibration) were absent. The deep tendon reflexes were brisk and deep in both upper and lower limbs; abdominal reflexes were absent in all quadrants, with bilateral extensor plantars. Ophthalmological examination revealed normally sized pupils with normal reaction, no relative afferent pupillary defect (RAPD) with normal fundus. Nystagmus and other extraocular movements could not be commented upon because of markedly diminished visual acuity.

Routine biochemical parameters like complete blood count, liver and renal function tests, random blood sugar, and thyroid function tests were normal. Connective tissue panel testing including ANA, dsDNA, SS-A, SS-B, RO, LA, RA factor, CRP, ANCA antibodies, HIV, and HBsAg were all negative. Anti-aquaporin-4 IgG (AQP4-IgG) was positive and myelin oligodendrocyte glycoprotein antibodies were negative. The cerebrospinal fluid examination revealed a total cell count of 40 cells/mm^3 with 100% lymphocytes, normal sugar (54 mg/dl, corresponding blood sugar 70 mg/dl) with mildly elevated protein (60 mg). Visual evoked potential (VEP) could not be done because of marked reduced visual acuity. The cryptococcal antigen test, TB-PCR test, panel sent for viral markers (HSV/EBV/CMV PCR), and oligoclonal bands in the cerebrospinal fluid were all negative.

Magnetic resonance imaging (MRI) of the brain revealed T2 and fluid-attenuated inversion recovery (FLAIR) hyperintensities in periventricular, pericallosal regions, and bilateral occipital cortex [Figure 1a]. No involvement of the medulla, area postrema or diencephalon could be appreciated. MRI of the spine [Figure 1b] revealed T2 hyperintense signal from (C2 to C5), suggestive of long segment myelitis of the cervical spine. Rest of the spine was normal.

The severely decreased visual acuity with normal optic nerve examination, normal pupillary response, and bilateral occipital MRI lesions can be attributed to cortical blindness. In addition to this, the patient had long segment myelitis and positive aquaporin-4 antibody titer. The patient was treated with a course of pulse intravenous methylprednisolone for five days with which there was no symptomatic relief. Later, she was treated with five cycles of plasma exchange (50 ml/kg), with which her motor power and visual acuity started improving. She was discharged on oral steroids of 50 mg (1 mg/kg) and azathioprine (50 mg/day; with a plan to further increase the dose). The patient showed significant clinical improvement in the form of ability to count fingers at a distance of three feet, with improvement in motor power to an MRC grade 4/5 in both lower limbs.

Transverse myelitis, optic neuritis, and area postrema syndrome are the main presentations in NMOSD. Longitudinally extensive transverse myelitis (LETM)—which is usually more incapacitating to the patient compared to MS—is the hallmark feature. (1) A majority of patients (approximately 80%) have positivity for aquaporin-4 antibody, with the remaining patients being positive for myelin oligodendrocyte glycoprotein antibody. The discovery of AQP4-IgG in 2004 as a specific biomarker for NMOSD was an important landmark, enabling the clinicians to differentiate the disorder from multiple sclerosis.[5]

Bilateral optic nerve lesions with predilection for the optic chiasma and posterior visual pathways and with frequent enhancement extending more than half the length of the nerve is the most common MRI finding.[6] The regions adjoining the third and fourth ventricles (dorsal medulla/area postrema) have the highest expression of AQP4. This explains the preponderance of MRI lesions like the pencil-thin linear ependymal enhancement, leptomeningeal enhancement, and

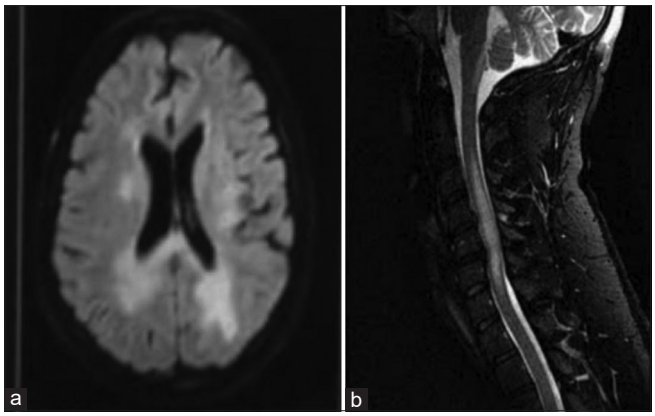

Figure 1: (a) MRI Brain showing hyperintense signals on T2 FLAIR over bilateral occipital region. (b) MRI Cervicodorsal spine showing long segment myelitis from C3 to C5

also cloud-like poorly marginated enhancement in these areas.[7] The hallmark spinal cord lesion is the LETM, which is found in approximately 85% of patients.[8] The International Panel for Neuromyelitis Optica Diagnosis (IPND) of 2015 published the updated diagnostic criteria for NMOSD.[2] With the presence of long segment myelitis and aquaporin antibody positivity and exclusion of other possible differentials, our patient fit into the criteria for NMOSD. For attack treatment, high-dose corticosteroids (1000 mg IV methylprednisolone daily for 5 days) are used initially. For severe, corticosteroid-refractory central nervous system inflammatory demyelinating attacks plasma exchange is shown to be beneficial.[9,10] For maintenance therapy, the three most commonly used medications are azathioprine, mycophenolate mofetil, and rituximab.[11]

A case of NMOSD with cortical blindness was described in 2017 by Lalji *et al.*[3] Their patient, a 73-year-old lady, had presented with complaints of reduced visual acuity, encephalopathy, and hallucinations with past history of long segment myelitis, with good response to immunotherapy. Another case of AQP4-positive NMOSD has been described with sparing of the optic nerves and cortical blindness.[4] The patient had extensive cerebral cortical involvement which is unusual in NMOSD.[4] Ours is perhaps the third case in literature with presentation of cortical blindness in NMOSD. Interestingly, our patient has no evidence of optic neuritis but a history of recurrent quadriparesis with positive titer of aquaporin antibodies, which are known to be ~ 100% specific for NMOSD. In the presence of normal pupillary reaction to light and normal fundus, reduced visual activity can be attributed to cortical lesions over bilateral occipital regions on MRI.

Although brain lesions in NMOSD are increasingly being recognized, enhancing cerebral cortical lesions are extremely unusual, described in only 3% of cases.[12] The proposed mechanism appears to be the damage to the blood–brain barrier with the parafalcine frontal cortex emerging as the most vulnerable area.[13] This could promptly be reversed by treatment with steroids and other immunosuppressant agents.

But the real diagnostic challenge lies in early identification of these lesions, especially in the absence of optic nerve involvement both clinically and radiologically.

Though cortical blindness is rare in NMOSD, it should be considered as a possibility in a patient with reduced visual acuity without optic nerve involvement. Presence of associated myelitis and area postrema syndrome further strengthens the possibility of NMOSD. Early diagnosis and prompt immunotherapy can help to prevent devastating sequalae.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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