

Extensive reversible periependymal ventricular enhancement on magnetic resonance imaging scan in a patient with neuromyelitis optica

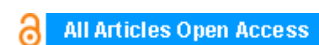
Anza B. Memon, Kumar Rajamani, Robert P. Lisak

ABSTRACT

Introduction: Neuromyelitis optica (NMO) is an inflammatory central nervous system (CNS) disorder which predominately affects the optic nerves, chiasm, tract and spinal cord. Both symptomatic and asymptomatic brain lesions have been reported. We describe a patient with neuromyelitis optica spectrum disorder (NMOSD) with suspected prior thoracic cord ependymoma and unusual radiological picture.

Case Report: A 69-year-old woman with history of thoracic cord ependymoma ten years earlier was diagnosed with NMOSD with elevated aquaporin (AQP4) antibodies. In addition to contrast enhancement along optic chiasm and optic tract, brain MRI scan showed increased signal on FLAIR and post-contrast enhancement in the subependymal region around the aqueduct and lateral ventricles. Spinal MRI showed thoracic cord atrophy. After corticosteroids and plasma exchange (PLEX), vision improved and imaging 2 weeks later showed resolution of lesions except periaqueductal enhancement, which resolved completely after three months.

Conclusion: This case report is striking for two reasons. The patient had virtually all of the previously described MRI lesions described in literature at different stages of the NMOSD. Enhancing lesions outside the brain and optic pathways, seen in this patient are rare in NMOSD. Complete resolution of enhancing lesions after IVMP and PLEX on several occasions was striking. Occurrence of NMOSD in patients with ependymoma has not been reported but can be reasonably speculated in this patient as some cases of NMOSD represent a paraneoplastic disorder. Moreover, ependymal cells are having abundant AQP4 channels raising a possibility of molecular mimicry.



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Keywords: Devic's disease, Neuromyelitis optica, Neuromyelitis optica spectrum disorder (NMOSD)

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INTRODUCTION

Neuromyelitis optica (NMO) is an autoimmune autoantibody-mediated inflammatory disorder of the

central nervous system (CNS). The classic description of NMO involving optic pathway and spinal cord has evolved into a broad spectrum of disease with involvement of cerebral hemisphere, brain stem and hypothalamus. Extensive CNS involvement with multiple recurrences and atypical neuroimaging findings are now characterized as a neuromyelitis optica spectrum disorder (NMOSD) [1]. The autoantigen targeted by the antibody is aquaporin4 (AQP4) a bidirectional osmosis driven protein, abundant at the astrocytic foot processes at the blood brain barrier (BBB) and the brain cerebrospinal fluid (CSF) barrier [2]. Recent evidence supports the involvement of Th 17 effector cells as well as antibody determined complement activation pathogenic mechanisms within the CNS [2].

Although NMOSD predominately affects the optic nerves, chiasm, tract and spinal cord, symptomatic and asymptomatic lesions have been reported within the brain [3]. Most of the lesions are found in areas where AQP4 is found abundantly. This case report of a patient with classic NMOSD illustrates the added affection of these regions based on imaging and the response to immunological therapy. Moreover, this patient illustrated virtually all the known radiological features at various stages of her illness, many of which were reversible with immunosuppressive treatment.

CASE REPORT

A 69-year-old woman was diagnosed with NMOSD on the basis of bilateral optic neuritis with rapidly progressive loss of vision and presence of AQP4 antibodies.

Eleven years earlier she had developed weakness of her lower extremities progressing over one year and was found to have a longitudinally extensive spinal cord lesion from T2-T7. Cerebrospinal fluid (CSF) was negative for inflammatory or demyelinating disease. Biopsy of the lesion was performed and was diagnosed at another tertiary medical center as an ependymoma. She underwent radiation therapy and was able to walk with assistance of a walker for approximately two years but then developed progressive worsening of lower extremity strength, sensory loss and loss of sphincter control. The patient had been paraplegic with loss of bladder and normal bowel function for five years at the time of her first episode of optic neuritis. Review of histopathology slides from her biopsy was felt by the neuropathologist to be compatible with, but not diagnostic of an ependymoma. Unfortunately, no additional tissue is available for further study.

Cerebrospinal fluid (CSF) studies revealed an acellular fluid with a total protein of 61 mg/dL, no oligoclonal bands, non-reactive VDRL and cytology negative for tumor cells. Brain MRI revealed gadolinium enhancement of the optic chiasm, around the aqueduct and subependymal increase signal on FLAIR sequence.

There was no enhancement or swelling of the cord in the area above her previous spinal cord atrophy. Her symptoms started to improve after treatment with intravenous methylprednisolone 1 gm daily for five days and mycophenolate 500 mg twice daily.

Three months later she presented again with another episode of bilateral painful visual loss and bitemporal hemianopia evolving over four days. Brain MRI scan revealed increased signal on FLAIR sequences along the subependymal lining of the lateral ventricles and cerebral aqueduct (Figure 1A–B) associated with gadolinium enhancement (Figure 1C–D). Gadolinium enhancing lesions were present involving the optic chiasm, right optic tract and prechiasmatic optic nerves on orbital views (Figure 1F, G, H) which can be seen on MRI scan of the head (Figure 1E). Magnetic resonance imaging scan of spine showed the prior atrophy (Figure 1I). Cerebrospinal fluid (CSF) studies revealed 3 nucleated cells/mm³, cytology negative for malignancy, glucose of 51 mg/dL (serum 96 mg/dL), total protein of 86 mg/d, IgG index 0.59 (normal), no oligoclonal bands detected and cytology negative for tumor cells. Blood ANA, dsDNA, and ENA antibodies were not detectable, C3 and C4 complement levels were normal and syphilis serology was nonreactive.

The patient was treated with 1 g of IV methylprednisolone daily for five days. Visual acuity (VA) improved from 20/400 to 20/200 in the left eye (OS) but there was no change in acuity in the right eye (OD) or in her hemianopsia. She received six cycles of plasma exchange (PLEX) over 10 days and her VA improved to 20/40 OD and 20/70 OS with complete resolution of her hemianopsia. Repeat imaging two weeks after her onset of symptoms of this attack (Figure 2) revealed complete resolution of the periventricular ependymal and subependymal gadolinium enhancement as well as enhancement of optic nerves, chiasm and optic tract and aqueductal region seen earlier (Figure 1, H, E, G, D) as well as resolution of increased signal on FLAIR with the exception of the periaqueductal region (Figure 2B, arrow). Mycophenolate 500 mg twice/day was increased to 1 g twice/day and she was placed on a schedule of one PLEX per month. Repeat MRI scan of brain three months after treatment with IVMP and PLEX showed complete resolution of high signal intensity in the periaqueductal region (Figure 3B, arrow). Four months later she presented with spasms of the right hand and MRI of brain and the cervical spine with and without contrast showed multiple new foci of T2 hyperintensity, including bilateral lateral thalami (Figure 4A), medullary lesion (Figure 4D), a rounded focus within the right aspect of the mid brain (Figure 4B). The latter lesion exhibits faint enhancement (Figure 4C). At that time patient was started on rituximab. Magnetic resonance imaging scan of cervical spine showed abnormal intramedullary signal and enhancement involve the thoracic spinal cord at the T1-2 level on the left (Figure 4G).

One month later she presented with progressive right sided upper extremity weakness and dysarthria. Repeat

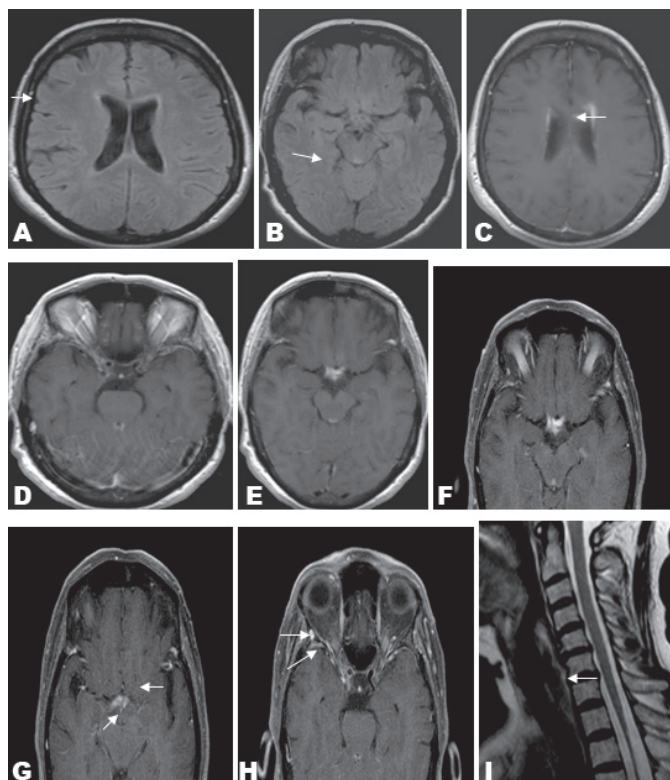


Figure 1: Magnetic resonance imaging of brain and orbit with second episode of optic neuritis prior to treatment with IVMP and plasma exchange. (A) Lateral ventricle subependymal high signal intensity, (B) High signal at the cerebral aqueduct. (C) Subependymal ventricular enhancement, (E) Cerebral aqueduct enhancement, (F) Optic chiasm enhancement, (G) Right optic tract enhancement, (H) Bilateral optic nerve enhancement, and (I) Thoracic cord atrophy (radiation induced) but no abnormal cord signal.

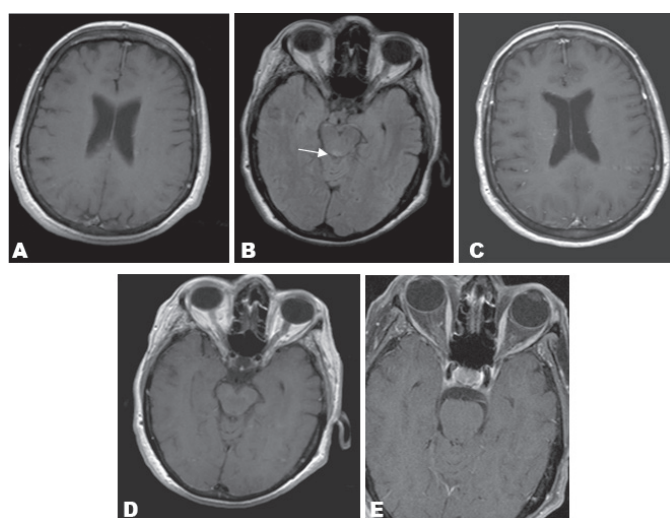


Figure 2: Two weeks after treatment with IVMP and PLEX. (A) Complete resolution of lateral ventricle subependymal high signal intensity, (B) High signal intensity at the cerebral aqueduct. (C) Resolution of lateral ventricle subependymal ventricular enhancement. (D, E) Resolution of optic chiasm (thick arrow) and cerebral aqueduct (thin arrow) enhancement.

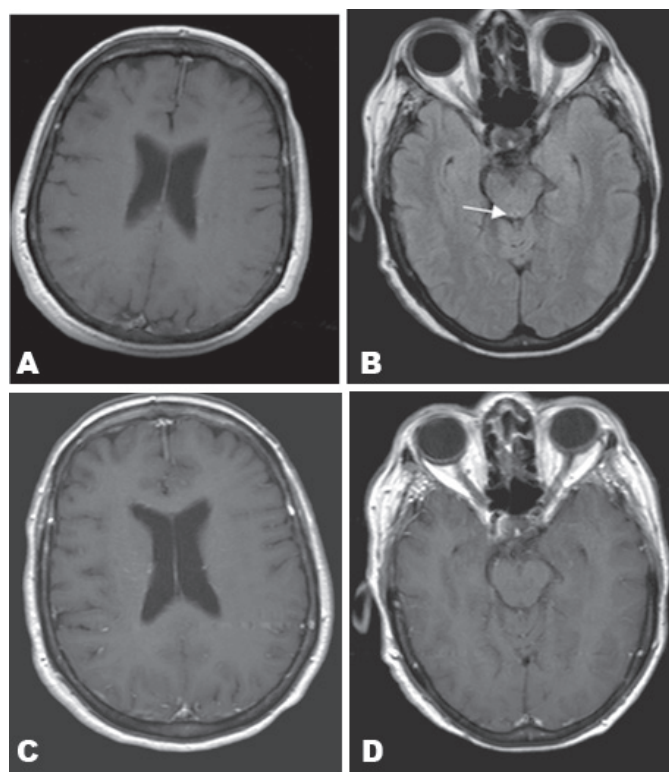


Figure 3: Three months after treatment with IVMP and PLEX (A) Resolution of subependymal high signal intensity, (B) Resolution of high signal intensity at the cerebral aqueduct. (C) Resolution of subependymal ventricular enhancement. (D) Resolution of optic chiasm and cerebral aqueduct enhancement.

MRI scan of brain and cervical spine was performed. Interval development of at least two new white matter lesions in the subcortical medial left parietal lobe and corpus callosum (Figure 4E–F) with no enhancement on the T1 post gad images. MRI scan of cervical spine showed interval resolution of the abnormal enhancement at T1-T2 (Figure 4H).

DISCUSSION

Although NMO predominately affects optic nerves and spinal cord but the NMOSD, at least when defined by the presence of anti-AQP4 antibodies, clearly includes lesions in other parts of the CNS [3]. In some instances, the lesions are symptomatic and uncommonly the extra opticospinal clinical syndrome and imaging lesion is the predominant if not exclusive manifestatin of the disease [3].

Our patient presented with optic neuritis and manifested both symptomatic and asymptomatic lesions of the brain and a spinal cord lesion at level where she had no symptoms presumably because it was just above her region of radiation associated spinal cord atrophy. During her course to date she has manifested virtually all of the MRI findings of the brain on FLAIR

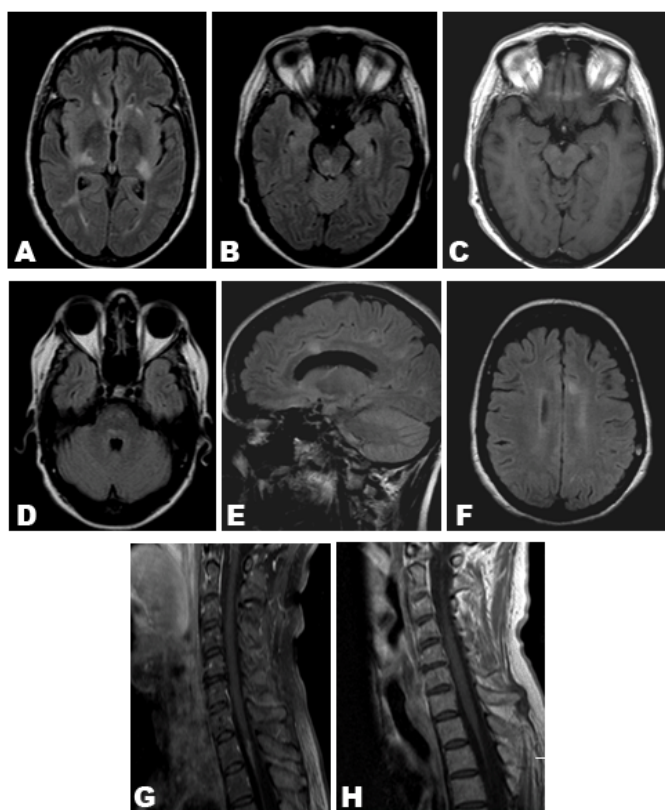


Figure 4: Magnetic resonance imaging of brain showing high T2 signal in bilateral lateral thalami. (A) Right aspect of the mid brain, (B) Faint gadolinium enhancement in the right mid brain, (C) Medullary lesion, (D) High T2 signal in the corpus callosum, (E and F) Spinal cord enhancement at T1-T2 level, (G) and interval resolution of enhancement on repeat cervical spine after 1 month (H).

sequences, as well as gadolinium enhancement of brain, optic nerve, chiasm, optic tract and spinal cord lesions. Commonly seen brain lesions seen on MRI of the brain are linear lesions involving corticospinal tracts (44%), sometimes unilateral (17%) or bilateral (27%) in the posterior limb of internal capsule and cerebral peduncles. Periependymal lesions surrounding the lateral ventricles are also common (40%). They differ from the classical periventricular lesions of multiple sclerosis with predominately oval shaped lesions perpendicular to the lateral ventricles, because of post-capillary perivenular location. In NMO, the periventricular lesions appear to follow the ependymal lining of the ventricles. Brain stem lesions, often medullary and contiguous cervical spine are commonly described (31%) Extensive confluent hemispheric lesions are seen (29%) and are associated with high titer anti-AQP4 antibodies. One might question the association in the absence of such antibodies. The same is true of non-specific patchy or round lesions with no particular relationship to the ventricles, which are frequently seen (58%), particularly in the patients with comorbidities such as hypertension in an older patient and/or no enhancements of these lesions, as is the case with our patient. Periaqueductal lesions

and lesions adjacent to the IIIrd and IVth ventricles are also reported (22%). Gadolinium enhancement, common in optic nerves and spinal cord during relapse, enhancement of brain lesions is less common (13%) [3, 4]. The response of the lesions to corticosteroids and PLEX, disappearance of gadolinium enhancement and marked reduction of intensity and amount of increase in signal intensity on FLAIR sequences is striking. These findings are compatible with reversibility of vasogenic edema as a result of the immunologic therapy and the autoimmune pathogenic processes directed against astrocytes and other cells of the CNS enriched with AQP4. However, the continued clinical and imaging evidence of disease activity as evident by recurring and new disease activity, symptomatic and asymptomatic, despite both short-term (corticosteroids and PLEX) and chronic (mycophenolate and rituximab) immunotherapy illustrates the severity of NMOSD and that irreversible damage to CNS can occur despite immunotherapy. Although admittedly uncertain, the relationship between the ependymoma ten years earlier and the development of NMOSD in our patient cannot be ignored. Review of limited histopathology slides from her biopsy done 10 years earlier, was felt by the neuropathologist to be compatible with the diagnosis of ependymoma. It is of course possible that the longitudinally extensive thoracic cord lesion was a myelitis which was irradiated. Our patient did show an upper thoracic cord lesion with enhancement on subsequent relapses which resolved on repeat imaging over a month, suggestive of myelitis. Unfortunately, no additional tissue is available for further study and characterization of the spinal cord lesion not only for diagnosis but more importantly for presence of AQP4 expression in the tumor. Based on laboratory based anti-AQP4 determinations [5] and case reports it has been suggested that some cases of NMO spectrum disorder might represent a paraneoplastic disorder. In support of that possibility is the demonstration of AQP4 in tumor cells in three recent cases including breast cancer, teratoma and metastatic carcinoid [6–12].

CONCLUSION

Enhancing lesions of the brain, as opposed to optic nerve, optic chiasm and spinal cord, are not commonly seen in NMOSD. Therapeutic approach to treat these brain lesions and their variable response to the treatment is a novel finding.

Author Contributions

Anza B. Memon – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Kumar Rajamani – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published
Robert P. Lisak – Analysis and interpretation of data, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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