Neuromyelitis optica in the setting of Human Immunodeficiency Virus Infection

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INTRODUCTION

Neuromyelitis optica (NMO) is a severely disabling inflammatory demyelinating disease distinct from multiple sclerosis (MS). It preferentially targets optic nerves and the spinal cord, and in many cases is associated with autoantibodies to aquaporin-4 (AQP4-IgG) water channels. Unlike typical MS, NMO frequently relapses resulting in irreversible damage and permanent disability. In the United States, there are approximately 4,000 to 8,000 patients with NMO, and compared to MS patients; non-Caucasians are over-represented among NMO patients. Acute viral and bacterial infections have been reported to precede the onset of NMO; however, little is known about the disease in the context of HIV infection. Here, we describe two patients with known HIV infection, who developed NMO. The two patients were followed up prospectively for three years with regular neurology clinic visits.

Table 1. Summary of the two cases.

	Case 1	Case 2
Age (years)	32	49
Gender	Male	Female
Ethnicity	African American	African American
Time to diagnosis of HIV	At least 5 years	At least 15 years
CD4 count (cells/mL), viral load (copies /ul)	>350, <3000	>500, <75
Patient on HAART?	Yes	Yes
Presenting symptom	Unilateral blindness	Unilateral blindness
Time to the first relapse	5 months	9 months
Extensive CSF infectious work up	Negative	Negative
RPR and serologic autoimmune workup	Negative	Negative
Oligoclonal bands detection	Detected	Not detected
AQP4-IgG detection	Negative X 2	Positive at 301U/mL (N<4)
Immunotherapy: relapse prevention	1gram rituximab infusion monthly X2	MMF 500mg oral once daily
Outcome	Paraplegic with unilateral blindness	Paraparetic and functionally blind

AQP4-IgG: autoantibodies to aquaporin-4 water channels; CD4: cluster of designation; HAART: Highly active antiretroviral treatment; HIV: Human immunodeficiency virus infection; MMF: mycophenolate mofetil; RPR: Rapid Plasma Reagin test.

CASE 1

A 32-year-old African American male with HIV-1 infection of 5 years, receiving highly active antiretroviral treatment (HAART), presented with left eye vision loss of one day. Neurological examination was unremarkable except for absent light perception and positive relative afferent pupillary defect (RAPD) in the left eye. Brain MRI showed diffuse enhancement of the left optic nerve (Figure 1A). No recovery of left eye vision occurred following administration of intravenous methylprednisolone (1g for 5 days).Five months later, he was readmitted with sudden onset of painless bilateral lower extremity weakness. Neurologic examination revealed flaccid paraplegia and a sensory level at T4. Spine MRI revealed T2-signal hyperintensity spanning the entire cervical cord to the mid-thoracic cord (Figure 1C). Methylprednisolone (1g for 5days) followed by five sessions of plasma exchange (PLEX) was given without any significant improvement. He subsequently received 1 gram of rituximab infusion monthly for 2 consecutive months as maintenance therapy. Clinical and biological parameters (i.e. CD19. count) were assessed before and after rituximab. To date, there has been no further disease relapse; however he remains severely paraparetic with complete left eye blindness. A summary is provided in table 1.

CASE 2

A 49-year-old African American female with known HIV-1 history of 15 years, receiving HAART, presented with right eye vision loss for two days. Neurological examination was unremarkable except for absent light perception and positive RAPD in the right eye. Brain MRI showed uniform enhancement of the right optic nerve (Figure 1D).Despite treatment with intravenous methylprednisolone (1g for 5days), no recovery of the right eye vision occurred. The patient returned in nine months with painless bilateral lower extremity weakness of one week. Neurological examination was significant for spastic paraparesis. Spine MRI revealed T2 signal hyperintensity spanning C4 through T6 cord segments (Figure 1F). She was treated with IV methylprednisolone (1g for 5days) followed by five sessions of PLEX without significant recovery of lower extremity strength. She received mycophenolate mofetil 500mg orally daily as maintenance therapy. Twelve months later, she presented with worsening lower extremity weakness and again received IV methylprednisolone (1g for 5days) followed by seven sessions of PLEX. At subsequent follow-up, she reported mild improvement of the lower extremity weakness and remains severely paraparetic and functionally blind without relapse. A summary of case 2 along with pertinent laboratory findings is provided in table 1.

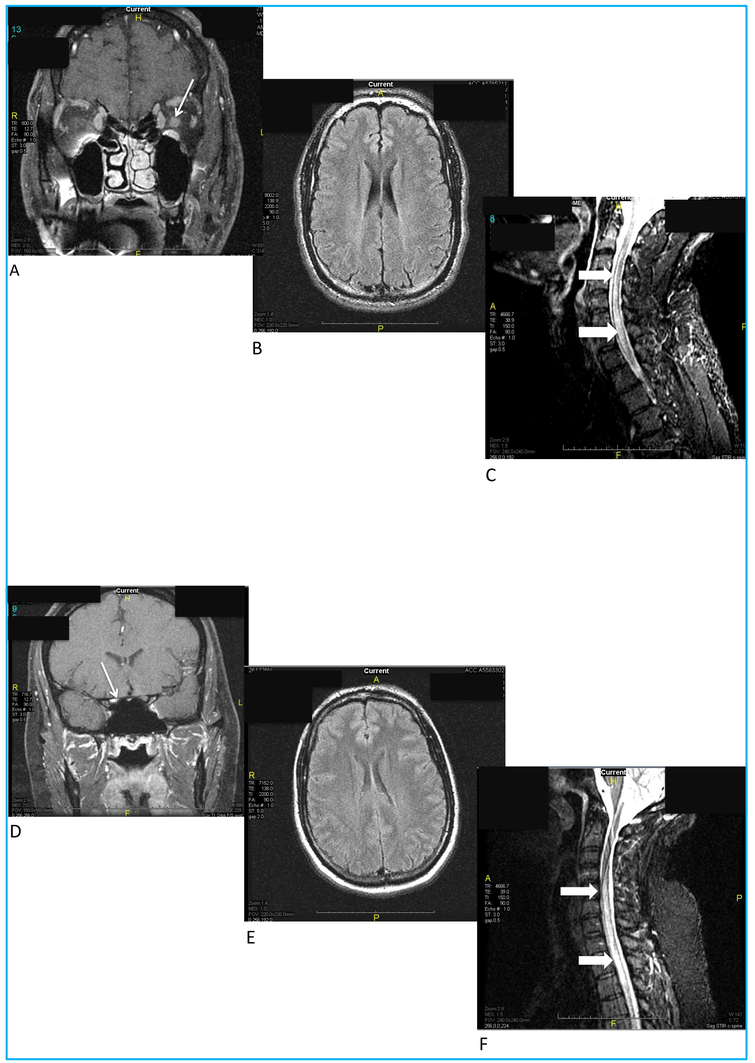

Figure 1. (A) Coronal T1 post contrast MRI of case 1 showing diffuse enhancement of the left optic nerve compatible with optic neuritis (arrow). (B) Axial FLAIR of case 1 revealed no lesions that meet multiple sclerosis imaging criteria. (C) Sagittal T 2-weighted MRI of case 1 showing increased T2/STIR signal in the cervical and thoracic cord with spinal cord thickening (arrows). (D) Coronal T1 post contrast MRI of case 2 showing uniform enhancement of the right optic nerve, crossing the optic canal (arrow). (E) Axial FLAIR of case 2 revealed no lesions that meet multiple sclerosis imaging criteria. (F) Sagittal T 2-weighted MRI of case 2 showing increased T2/STIR signal that is contiguous from C4 through T6 (arrows).

DISCUSSION

Both cases described here meet the revised diagnostic criteria for NMO, although case 1 lacked AQP4-IgG antibodies. At initial presentation and during disease relapses NMO is typically treated with high-dose IV methylprednisolone . PLEX may be attempted to treat resistant cases. Our patients received high-dose IV methylprednisolone followed by PLEX without clinical improvement. Current data suggests that NMO is more disabling than typical MS. Within five years of onset most patients become wheelchair-bound and functionally blind.

Immunosuppressive drugs such as azathioprine, rituximab, cyclophosphamide, and mycophenolate are the mainstay of NMO maintenance treatment. However, limited information exists about treatment of NMO in HIV-infected patients. With the advent of HAART, immunosuppressants once strictly contra-indicated in HIV positive individuals, are now attempted, especially in those less immunocompromised. Given the selective suppression of the B cell line and relatively lower incidence of serious infections associated with its use, we speculate that rituximab will be an attractive candidate for the maintenance treatment of NMO in the setting of HIV infection.

Given the rarity of NMO and inadequate information regarding the prevalence of NMO in less developed countries where HIV/AIDS is known to be prevalent, it is too early to comment on whether NMO is seen with greater than expected frequency in HIV positive patients.

CONCLUSIONS

- The cases presented here illustrate the rapidly disabling nature of NMO, especially in immunocompromised hosts.
- NMO can occur in the course of HIV infection and poses a therapeutic challenge.
- Further epidemiological and clinical studies are needed to demonstrate etiologic association between HIV and NMO.

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