Case Report

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Familial Neuromyelitis Optica: A Case Report and Literature Review

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ABSTRACT

Neuromyelitis Optica Spectrum Disorder (NMOSD) is an autoimmune rare disorder that involves the endfeet of *astrocytes*. The role of genetics in the disease is not well known. Rare cases of familial NMOSD were reported worldwide. In this report, first, we presented a young man with myelitis and his cousin who suffered from this disease. Then we reviewed some reports around the world about familial NMO. The prevalence of familial NMO is nearly 3%. First cases are reported from East Asia. Its characteristics are similar to the sporadic type. Recent data suggest genetics play role in NMO.

Case presentation

Case 1

A 21-year-old woman was previously entirely presented [1].

In brief, she was referred to the emergency room with precarious conditions. she complained of progressive memory decline, quadriparesis, generalized tonic-clonic seizure 2 years ago. On admission, she was febrile with pancytopenia and renal failure. The brain's magnetic resonance imaging (MRI) showed diffuse bilateral white matter lesions with significant cortical atrophy. In the cervicothoracic MRI, the longitudinal involvement was evident. Complete investigation was done. The anti-aquaporin-4 antibody was found to be positive. She underwent treatment with methylprednisolone, plasma exchange, and rituximab, and her state improved considerably.

Case 2

Four years later, in October 2021, a 23-year-old previously healthy man, the cousin of patient 1, presented left optic neuritis, which was described as a central scotoma one month ago. He denied eye movement pain or color desaturation. After 14 days, her visual acuity began to improve, but he felt weakness in his lower extremities. Seven days later, upper extremities were involved.

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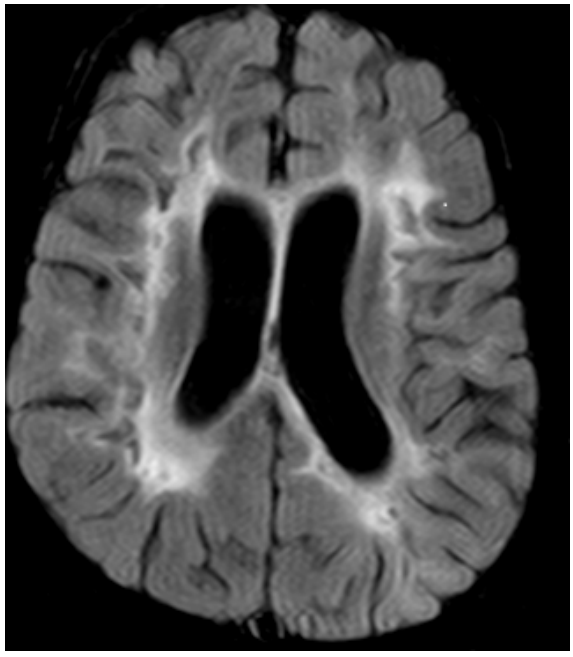

Fig. 1. The fluid-attenuated inversion recovery magnetic resonance (FLAIR) sequence of the brain MRI in patient 1 revealed extensive bilateral lesions with cortical atrophy.

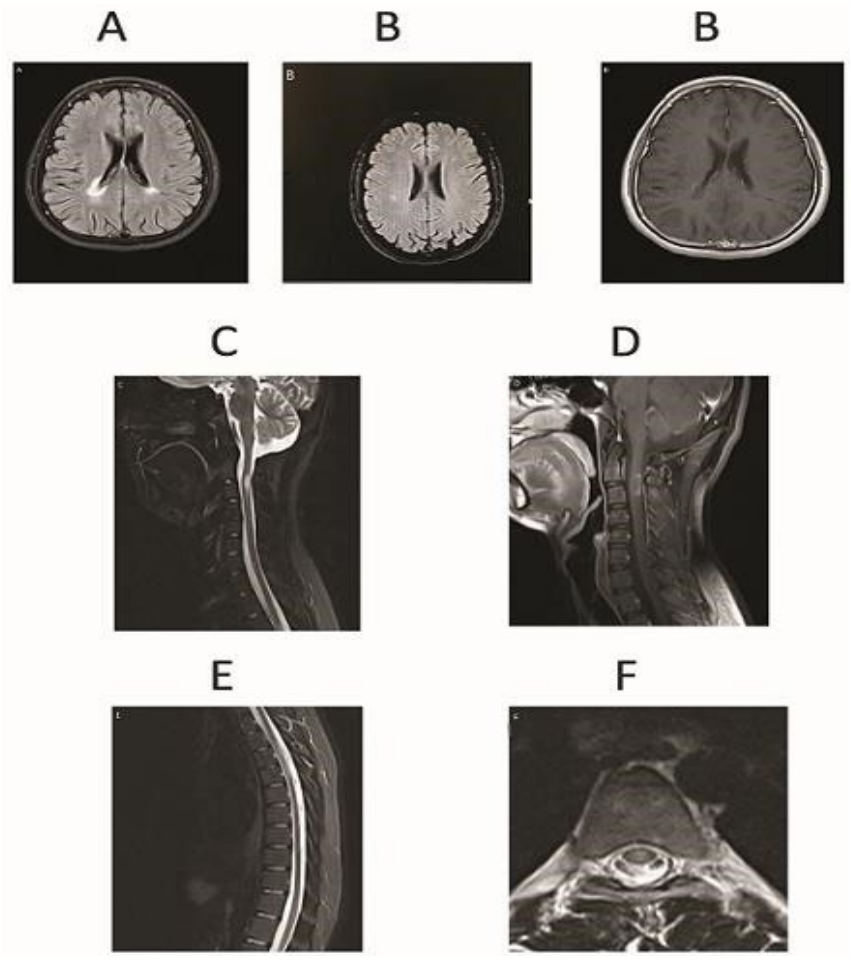

Fig. 2. A, B, Axial fluid-attenuated inversion recovery magnetic resonance (FLAIR) and T1-weighted images with contrast agent in case 2. Images show ependymal lesions with peripheral enhancement. C, D, E, F, Sagittal spinal MRI revealed a short segment hyperintense lesion with ring enhancement.

Table 1. Demographic, MRI, and laboratory information about two patients, IVMP: Intravenous methylprednisolone, LETM: Longitudinally extensive transverse myelitis

	Case 1	Case 2
Sex	Female	Male
Age	21	23
Location	Hormozghan	Hormozghan
Symtoms	Cognitive deline Quadriparesia Seizure	Optic neuritis Quadriparesia
NMO	Positive	Positive
Lab data	Pancytopenia Renal failure	Neg
Brain MRI	Bilateral extensive Lesions with cortical atrophy	Periependymal lesion Subcortical
Brain Contrast enhancement	-	Periependymal Enhancement
Cervical MRI	LETM	Short segment/central position
Thoracic MRI	-	Short segment
Spine Contrast Enhancement	-	Ring enhancement
Acute treatment	IVMP Plasma exchange	IVMP
Maintenace Treatment	Rituximab	Rituximab

He didn't use any drugs. He didn't complain of skin lesions, oral-genital aphthous. The family history of autoimmune disorder was negative in both patients. Our patient and his cousin lived in the same city.

On admission, his mental state was normal. Visual acuity was 20/20. The strength of the upper limb was 4/5 in proximal and 3/5 in distal muscles. This item in lower extremities measured 4/5. Deep tendon reflex increased, and Babinski reflex was negative. Numerous investigations were performed on the patient. Brain MRI showed multiple subcortical, periventricular, and periependymal lesions with peripheral enhancement (Figure 2). Cervical MRI was remarkable for short segment lesion with ring enhancement (Figure 2). Thoracic MRI showed 2.5 segment lesion without enhancement (Figure 2). The vasculitis panel was negative. The aquaporin-4 antibody was tested by enzyme-linked immunosorbent assay (Elisa), which was positive with high titers.

First intravenous methylprednisolone was begun (1 gr for five days). Significant improvement was achieved. The patient was discharged. After two weeks, he was visited to evaluate the residual disability. He improved remarkably. By diagnosis of NMO, he underwent treatment with rituximab. Unfortunately, it was not possible to make a more accurate genetic assessment.

Discussion

Our hospital is a referral center in Iran for demyelinating disorders, including NMO. To our knowledge, no case has been reported in the Middle East and Iran, and this is the first case of NMO with a positive family history in Iran. Both patients fulfill NMOSD revised criteria [2].

Table 1 contains demographic, MRI, and laboratory information about two patients.

Cases of familial NMO have been reported in East Asia, including Korea and Japan [3- 6]. The first familial case was reported in China in 2019, which presented a mother and her daughter with NMOSD.

Reports from around the world suggest that the prevalence of the familial type of NMOSD is higher than previously thought and occurs in approximately 3.0%. It indicates the existence of genetic background in the occurrence of this disease. This relationship is more pronounced in MS and reflects the prominent

role of genetics [7, 8], neurological presentation, onset age, female predominance, and frequency of NMO-IgG positive ratio in Familial NMO are similar to sporadic NMO [7]

Up to 70% of patients with NMOSD are positive for AQP4 Ab, and this antibody showed

pathogenic features in vitro, [9], so this antibody plays an essential role in its pathogenesis. But the leading cause of NMO is unknown. Variations in AQP4 genes have been described to be related to NMOSD, but the results are conflicting [10].

Reports on the genetic basis of the disease are limited. In 38 Japanese seropositive NMO cases, the HLA-DPB1*0501 allele was more abundant than 52 MS patients [11].

In some reports, the disease has been seen to co-occur by infections [12] and cancer [13], but no environmental factor has been definitively confirmed in NMO pathogenesis. In the familial form of the disease, no apparent trigger or exposure of infection was found.

No ethnic or geographical limitations have been reported on the familial occurrence of the disease. Based on the evidence, including the small number of documented pedigrees, the disease appears to have a complex genetic basis [7].

Conclusion

To our knowledge, this is the first report of familial NMO in Iran. Due to the prevalence of various family cases globally, especially in Asia, proving the relationship between genetics and the incidence of NMOSD needs further investigation.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this article.

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Conflict of Interests

The authors declare that they have no conflict of interests, and no funding has been used for the manuscript.

Ethical Statement

Informed consent was obtained from the patients for publication of this report

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