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Neuromyelitis Optica in Marfan Syndrome

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Neuromyelitis optica (NMO) is one of the differential diagnoses that should be considered in a patient with unilateral or bilateral loss of vision. It should be evaluated by history, examination, serological testing and neuroimaging studies.

We report a case of a 39-year-old gentleman who was known to have Marfan's syndrome and presented with progressive loss of vision in one eye followed by the other one within one month. Neurological examination showed bilateral optic neuritis (ON) with optic atrophy and unilateral upper motor neuron signs. CSF analysis was positive for NMO-IgG; MRI of the brain and spine showed enhancement in both optic nerves pathways and the optic chiasm with normal spine appearance.

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Neuromyelitis optica (NMO) is an uncommon severe autoimmune inflammatory demyelinating central nervous system disorder in which clinical spectrum ranges from severe attacks of recurrent isolated optic neuritis to extensive myelitis with bilateral neuritis. Visual impairment is common, blindness affecting at least one eye in 60-70% at a mean time of 5 years[1].

On the other hand, Marfan syndrome is an autosomal dominant systemic disorder of connective tissues. Individuals affected by the Marfan syndrome carry a mutation in one of their two copies of the gene that encodes the connective tissue protein fibrillin-1 (FBN1)[3]. Clinical diagnosis depends on a combination of major and minor signs defined in the revised 1996 Ghent criteria[4]. The hallmark features are noted in the cardiovascular, skeletal and ocular systems[4,5].

The rarity of NMO with coexistence of genetic diseases is a challenge in diagnosis and therapy.

The prime objective is to identify any association or linkages between NMO and genetically inherited disorders, such as Marfan's syndrome and identify possible relationships that may influence diagnosis and treatment of both coexisting conditions in the future.

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THE CASE

A thirty-nine-year-old man was referred to the outpatient department of KFHU in December 2012 with chief complaints of painful, subacute onset of blurry vision in both eyes three months before referral. Report shows that blurred vision has initially occurred on his left eye followed by the right eye in two weeks. Patient's vision progressively deteriorated. The patient denied any other visual or neurological symptoms in the past. The patient was known to have Marfan syndrome and two of his children were affected.

Physical examination of the patient showed tall and thin built presenting with Marfanoid features. Cranial nerve examinations showed bilateral loss of vision with no light perception. Left pupil was 4 mm in size with sluggish reactivity to light; on the right the pupil was 5 mm and non-reactive. Fundoscopic examination showed bilateral pale discs (optic atrophy) with displaced right lens, other cranial nerves showed no abnormalities, see figure 1. Motor system examination showed normal tone, power of 5/5, asymmetrical deep tendon reflexes (DTR) with hyperreflexia and upgoing plantar on right side.

Laboratory investigations including ANA, rheumatoid factor, VDRL, viral serologies, ESR, lactate level and folate are unremarkable. Cardiac evaluation including color Doppler echocardiography did not reveal any abnormal findings. However, there was a positive titer for CSF AQP-4 antibody, which prompted further neuroimaging studies. Brain MRI was performed revealing bilateral enhancements of optic nerves and optic chiasm, see figure 2. Spinal cord MRI was normal. The patient was given five-day course of intravenous methylprednisolone with no visual improvement.

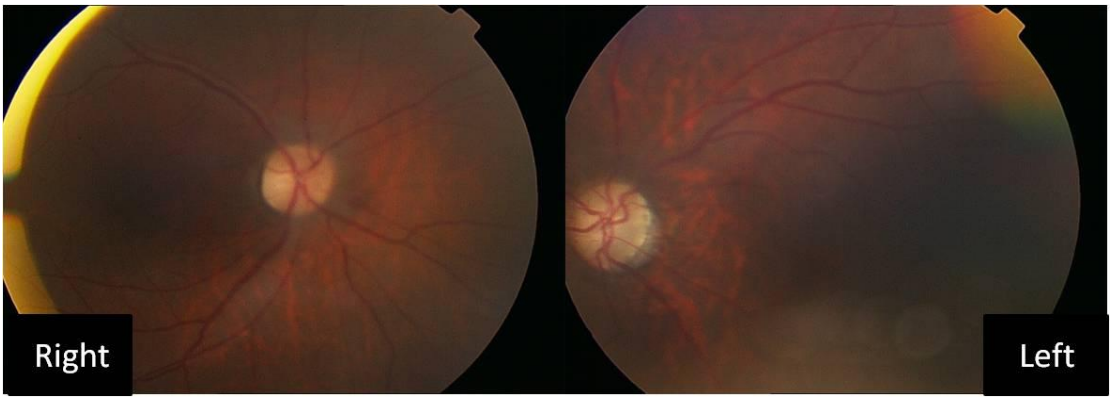

Figure 1: Funduscopy Showed Bilateral Pale Optic Disc

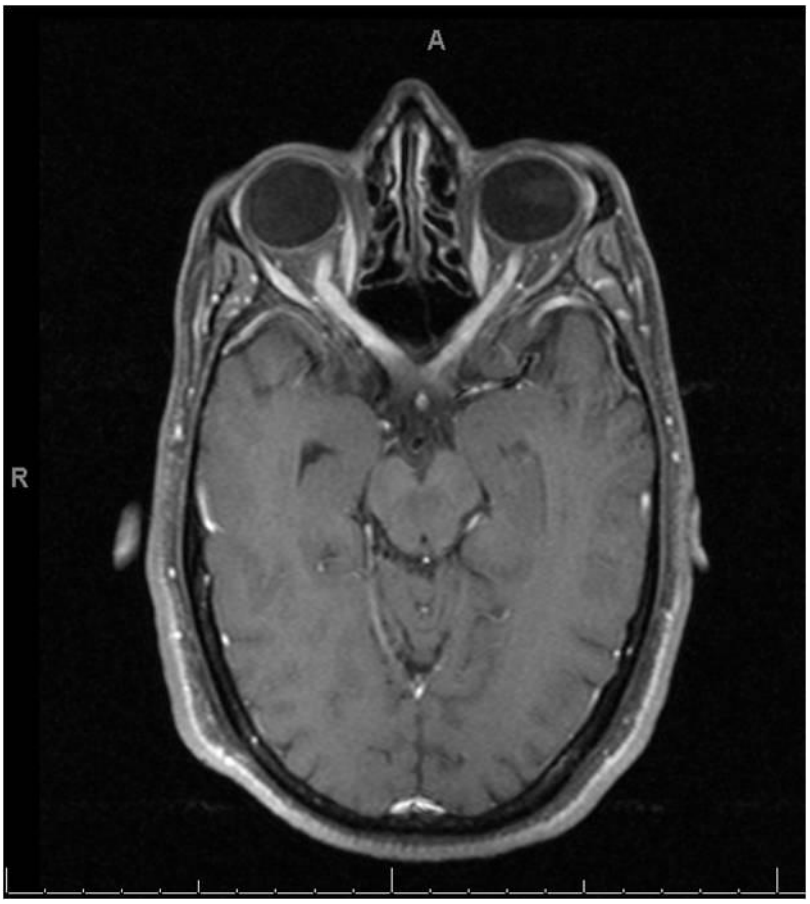

Figure 2: MRI Brain Selected Axial Cut T1 Revealed Extensive Enhancement of Optic Nerve and Optic Chiasm Bilaterally

The patient was discharged on daily oral Azathioprine 50 mg, tapering dose of oral Prednisolone and was advised and prepared for occupational aids and social supports for his blindness.

DISCUSSION

Neuromyelitis optica is recognized as a discrete, relapsing and a demyelinating disease with clinical and laboratory findings. NMO in different races and ethnic groups suggest that genetic factors are relevant.

NMO associated with Marfan's Syndrome is rare. To my knowledge, this could be the first reported case in the literature, though there were other NMO cases associated with other genetic disorders. Clinical similarities between NMO and Leber Hereditary Optic Neuropathy (LHON) have been reported by Simao[6]. However, the paucity of LHON mtDNA mutation encountered in NMO patients failed to show genetic correlations[7]. Smidt et al has reported a case of NMO and paroxysmal dystonia with familial and sporadic etiology that expressed pathophysiological relationships as channelopathies[8,9].

NMO has been suggested to have genetic influence in 3% of cases. Several of the NMO families had members with other autoimmune diseases, suggesting that these

individuals may share common genetic risk factors for autoimmunity in addition to factors that lead to AQP4-specific autoimmunity[10].

No previous reports of coexistence of NMO and Marfan syndrome were documented, but several cases of coexistent genetic connective tissue disease and autoimmunity were reported.

CONCLUSION

There could or could not be a linkage between the NMO and Marfan syndrome. However, any patient with NMO should be evaluated carefully for other genetic diseases. The therapeutic managements and preventions of genetic disorders are challenging. Future studies may show a coexistence of genetic background of NMO. While Marfan's syndrome is a multisystem disorder, there is still a need to confirm significant relationships of NMO and other genetically related disorders.

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Competing interest: No. **Sponsorship**: No.

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