CASE REPORT

Bilateral Sixth Nerve Palsy and Nasal Voice in Two Sisters as a Variant of Guillan–Barré Syndrome

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ABSTRACT

A 6-year-old girl with acute pharyngitis presented with complaints of hypernasal speech and double vision. Examination revealed a bilateral abduction deficit associated with soft palate palsy causing rhinolalia aperta. Cerebrospinal fluid analysis showed albuminocytologic dissociation. Her sister also suffered from the same disorder, albeit milder, 1 month before. After treatment with intravenous immunoglobulin and steroids, the patient made a full recovery. After the case report, a brief discussion of Miller Fisher syndrome, Guillan–Barré syndrome, and their variants is made. This case highlights that bilateral sixth nerve palsy and rhinolalia aperta in the absence of ataxia should still raise suspicion for these autoimmune conditions that may rarely and atypically present in siblings.

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Case report

A 6-year-old girl presented with acute, horizontal, binocular double vision associated with hypernasal speech. She was febrile and had a 2-day history of a sore throat, but systemic examination was otherwise unremarkable. She was seen by her paediatrician, diagnosed with “pharyngitis,” and given amoxicillin 12.25 mg per kg two times per day. One week later, ophthalmological examination revealed uncorrected visual acuity of 20/20 and normal anterior and posterior segment in both eyes (OU). There was no ptosis and pupils were equal. Extraocular motility revealed a bilateral abduction deficit and a moderate incomitant esotropia (ET) measuring 25 prism diopters (PDs) in primary position at a far distance and 6 PD ET at a near distance (Figure 1). The neurological examination was remarkable for a hypernasal voice (rhinolalia) caused by bilateral soft palate paralysis. Brain and orbit magnetic resonance imaging (MRI) with contrast was normal. Pharyngeal swab resulted positive for *Streptococcus pyogenes*

and cerebrospinal fluid (CSF) analysis showed cytoalbuminologic dissociation (elevated CSF protein but no white blood cells) with CSF protein levels of 78 mg/dL (normal < 45 mg/dL). Acetylcholine receptor (AChR) antibody testing was negative. On further questioning, the relatives admitted that the 10-year-old older sister suffered from double vision and nasal voice after an episode of acute pharyngitis just 1 month before. She had been evaluated in another hospital where the neurologist noted rhinolalia aperta caused by palate palsy and bilateral weakness of lateral rectus muscles. AChR antibody testing resulted negative and symptoms regressed spontaneously in a few days. Testing for anti-GQ1b antibodies in both the patient and her sister was negative. Our patient was diagnosed with polyneuritis cranialis and given a course of daily intravenous immune globulin (40 mg for 5 days) and intravenous methylprednisolone (40 mg for 3 days) followed by oral taper. She gradually recovered and at 1 month follow-up, both voice and extraocular motility

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Figure 1. Extraocular motility on the first day when admitted into the hospital. There is 25 PD esotropia of the right eye in primary position associated to bilateral abduction deficit. Vertical movements (not shown) revealed no limitation.

Figure 2. At 1 month follow-up, the patient is orthophoric in primary position and motility is full. Voice and stereopsis returned to normal.

(Figure 2) were back to normal. Stereopsis (Lang test) was also normal.

Discussion

Guillain-Barré syndrome (GBS) constitutes a spectrum of post-infectious neuropathies, which are characterized by their anatomical patterns of weakness and neurological involvement.¹ The syndrome of ophthalmoplegia, ataxia, and areflexia was first reported as a distinct clinical entity in 1956² and thereafter was known as Miller Fisher syndrome (MFS). It is generally considered to be one of the variants of GBS, occurring in approximately 5% of patients presenting with GBS findings.³ In the weeks preceding MFS symptoms, 80% of patients had an upper respiratory tract infection and 4% had a gastrointestinal infection.⁴ The diagnosis is based on the clinical triad of ataxia, areflexia, and ophthalmoplegia, supported by CSF cytoalbuminological dissociation and presence of anti-GQ1b antibody. MFS frequently presents initially with ophthalmoplegia (78%), ataxia (46%), or both (34%).⁵ The diagnosis of MFS is a clinical one, and there are no widely accepted diagnostic criteria. The presence of anti-GQ1b antibody is a supportive feature since they may be positive in patients with isolated bilateral ptosis or isolated bilateral mydriasis, but may result negative in patients with the classical triad of ataxia, ophthalmoplegia, and areflexia.⁶ They may also result positive in other GBS variant as Bickerstaff brainstem encephalitis and pharyngeal-cervical-brachial weakness. One of the

subtypes of GBS which shares clinical findings with MFS is the oculopharyngeal subtype of GBS (also known as “polyneuritis cranialis”). In a review of 15 cases,¹ most of the patients exhibited ocular and bulbar signs (93% and 87%, respectively) in the absence of ataxia or limb weakness. Anti-GQ1b antibody resulted negative in five out of the eight patients tested for, while CSF cytoalbuminological dissociation was present in 67% of cases. In a 10-year (2000–2010) retrospective study⁷ of 43 paediatric patients affected by GBS, only 4.7% presented clinically with polyneuritis cranialis, while the most frequent variant was demyelinating polyneuropathy (67.4%), followed by acute axonal neuropathy (7.0%), MFS (7.0%), Bickerstaff brainstem encephalitis (7.0%), and pharyngo-cervical-brachial variant (4.7%).

The “classic” ophthalmoplegic pattern in MFS is a symmetric paresis of upgaze and progressive impairment of horizontal gaze,⁴ although ocular motor patterns can be variable.⁸ There can be an asymmetric ophthalmoplegia, abduction or adduction palsies, third nerve palsies, and even an “inverse” MFS with bilateral ptosis and preserved eye movements. Patients can also have central ocular motor signs such as impaired smooth pursuit and vestibulo-ocular reflex cancellation, and sometimes even present with impaired vestibulo-ocular responses with otherwise normal eye movements.⁹ Patients can have gaze-evoked, dissociated abducting, convergence retraction, or rebound nystagmus. Other cranial nerves may be affected, particularly the seventh nerve with subsequent facial palsy. An “ophthalmoplegia without

ataxia” variant of this condition has also been described⁴ and should be considered in patients presenting with bilateral sixth nerve palsies. Other associated signs and symptoms may include dysesthesia in the limbs, dysphagia, ptosis, and bilateral dilated pupils with photophobia.¹⁰ Rhinolalia aperta (or hypernasal speech) is usually indicative of either a structural or neurological disorder affecting the larynx¹¹ and it has been described in MFS.^{11,12}

The occurrence of MFS in siblings is rare. To our knowledge, there is only one similar report in the English language literature.¹⁰ In that paper, two brothers presented sequentially with ataxia and ophthalmoplegia. Anti-GQ1b antibody test was negative in both. The similarities with GBS suggest that certain families could also have a predisposition to developing MSF which may have a genetic component similar in mechanism to that of familial GBS. We believe that anti-GQ1b antibody test was negative in these two sisters because we tested too late in the course of the disorder.

Our case highlights the importance of having a high suspicion for GBS variants when patients present with horizontal ophthalmoplegia associated with hypernasal voice in the absence of ataxia.

Conflict of interest

Authors report no conflict of interest.

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