MILLER FISHER SYNDROME PRESENTS AS AN ACUTE VOICE CHANGE TO HYPERNASAL SPEECH

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Educational Objective: At the conclusion of this presentation, the participants should be able to describe various clinical presentations of Miller Fisher Syndrome and to expand their differential diagnosis of an acute voice change with hypernasal speech. Additionally, current concepts in the management of Miller Fisher syndrome will be elucidated.

Objectives: To report an alternative presentation of an already rare variant of Guillain-Barré syndrome in the otolaryngology literature. To discuss the differential diagnosis and early management of Miller Fisher syndrome in an acute setting in order to make clinicians more aware of this previously recorded neurologic disease.

Study Design: Case report and review of the literature.

Methods: Medline was queried for Miller Fisher syndrome, Guillain-Barré variants, acute vocal changes, hypernasal speech. The results were reviewed and articles were correlated with the topic under discussion.

Results: The authors describe a 38-year-old man who presented with hypernasality, perioral and acroparesthesias, tongue numbness, dyspnea, and dysphagia. Further evaluation revealed a diagnosis of Miller Fisher syndrome.

Conclusions: Miller Fisher syndrome is a variant of Guillain-Barré syndrome previously described in neurology and critical care journals. While there are significant clinical findings in the head and neck, there is a paucity of literature concerning this disease in the Otolaryngology literature. An acute change in voice is usually second to simple inflammatory processes such as post-infection and post-infection, or as complex as a neuropathy such as Guillain-Barré syndrome or Miller Fisher syndrome. As such, clinicians should consider this in their evaluation of neuropathic voice change, as in this condition; early diagnosis and subsequent treatment with intravenous immunoglobulin are necessary.

Introduction: Miller Fisher syndrome (MFS) characterized clinically as a triad of ophthalmoplegia, ataxia, and areflexia was first described by Charles Miller Fisher in 1956.1 MFS, is an acute onset and a self-limiting disease; it is the most common variant of Guillain-Barré syndrome (GBS). It is a rare demyelinating disease affecting the cranial nerves and closely associated with autoimmune antibodies to the nerve ganglioside GQ1b. Classically, GBS is defined as a lower extremity weakness as opposed to MFS, which is typically a cranial neuropathy compared to the central nervous system involvement typically diagnosed as Bickerstaff’s brainstem encephalitis (BBE).2 A variety of additional neurological symptoms including optic neuritis, divergence paralysis, lid retraction, internuclear ophthalmoplegia, convergence spasm, defective vestibulo-ocular reflex, areflexia mydriasis, convergence failure, acute angle closure, abducens’ nerve palsy, and other facial nerve palsies have been included in the clinical presentation of Miller Fisher syndrome.2,3 When this neurological syndrome presents with features such as progressive nasal regurgitation or hypernasal speech an otolaryngology consult should be obtained. At present, there are no reports describing acute voice changes with hypernasal speech as the presenting symptom.

Case Report: A 38-year-old man returning from Japan presented to the emergency room with a 2-day history of progressive dysphonia, dysphagia, perioral/paresthesia, acroparesthesia, tongue numbness, and dyspnea. Two weeks prior, he had experienced diarrhea, fever, and right thumb pain that resolved after 3 days. He was seen at a hospital in Japan where he underwent a brain MRI that was unremarkable. One day prior to the onset of his symptoms he admitted to consuming raw fish and chicken. His prior medical history was only significant for a herniated lumbar disc.

On examination at our hospital, his speech was slow, muffled, and hypernasal. The neurological exam revealed decreased sensation to light touch on palms and soles with no loss of strength. The remainder of the exam was normal and the patient was admitted to the ICU for airway precautions and consults were obtained by otolaryngology and neurology. On hospital day #2, neurological exam revealed decreased oculococular abduction and upward gaze palsy bilaterally, 5/5 palate paralysis, trace deep tendon reflexes throughout, mild dysmetria of the upper extremities, and moderate dysmetria of the lower extremities. The patient was diagnosed clinically with Miller Fisher syndrome: ophthalmoplegia, ataxia, and areflexia. A Dobhoff tube was placed on day #3 second to dysphagia and aspiration risk. Nerve conduction studies and CSF cytology were within normal limits. Serum anti-GQ1b antibody titer was found to be positive at 1:1600 (>1:800 is the upper level of normal). Based on his clinical and laboratory findings, he was subsequently started on intravenous immunoglobulin 2 g/m2 for three days. Cranial neuropathy quickly improved following treatment and the patient was transferred from the ICU. On day #6 he was discharged to an acute rehabilitation unit for physical, occupational, and speech therapy. The Dobhoff was removed on day #8 after passing a swallow evaluation and he began tolerating a mechanical soft diet. On day #13, the patient was discharged home with no complaints and an overall resolution of symptoms.

Discussion: Dysphonia and dysarthria are common non-specific complaints for which otolaryngologists are consulted. Patients may have structural, functional, or neurological etiologies. When these changes occur acutely, they are most commonly secondary to trauma, infection, and chemical or environmental irritants.4 Less frequently, acute voice change may be the presenting symptom of malignancy, airway compromise, or an autoimmune process. The classic triad of Miller Fisher syndrome may not be part of the initial presentation. Therefore, the clinician must be aware of the spectrum of clinical features associated with MFS to include dysarthria and dysphonia, and specifically, hypernasality as described in this case.

MFS is a diagnosis not to be missed however rare. The incidence of MFS is only 0.09 per 100,000 accounting for 25% of GBS in Japan, is only 0.09 per 100,000 accounting for 25% of GBS in Japan and Taiwan, and only 5% in western countries. Clinical disease peaks in March through May and is associated with upper respiratory illness in up to 76% and gastrointestinal illness in up to 14% as described by Mori et al, 2001. MFS is specifically associated with Hemophilus influenzae and Campylobacter jejuni with molecular mimicry as the predominant pathogenetic mechanism. However, due to the self-limiting nature of the disease very few pathological specimens from autopsy have been described. Therefore, evidence of central pathology relies mostly on radiologic and electrophysiologic testing although most are unremarkable. Anti-GQ1b antibody positivity occurs with variable frequency but is most commonly correlated with ophthalmoplegia and MFS diagnosis in greater than 95% versus GBS in only 26% and BBE in 66% of cases reviewed.5

The broad constellation of clinical features is thought to be due to the autoantibody, anti-GQ1b IgG, which predomnately affects the cranial nerves and the presynaptic neuromuscular junction. The ganglioside GQ1b is a glycosphingolipid that contains a sialic acid residue of N-acetylneuraminic acid attached to the terminal galactose of an oligosaccharide core. The hydrophilic carbohydrate is exposed extracellularly as a potential autoantibody target. A similar polysaccharide with sialic acid linked to galactose was identified in C. jejuni and isolated in two patients with GQ1b positivity by Yuki et al, 2006. Abnormally elevated levels of GQ1b suggest an autoimmune etiology for neurological symptoms.6 Since this anti-antibody is associated with GBS and BBE, an overlap of the features can develop explaining the range of presentations described in the current literature.6

MFS is mostly a self-limiting condition with a median duration of infectious symptoms of 7 days, median onset from infection to neurological symptoms of 8 days, and median to nadir of neurological symptoms of 6 days.7 Since there is much overlap between the demyelinating disease, infectious causes, and other autoimmune phenomenon, with the spectrum of GBS, MFS, and BBE, it may evolve to include symptoms of bulbar palsy or respiratory failure.7 Therefore, MFS must be given serious consideration when a patient presents with acute voice change.

While most cases of dysphonia are self-limited and no medical intervention is recommended, our patient demonstrates a case in which medical therapy is beneficial.8 There are no established clinical guidelines for the treatment of MFS, however plasmapheresis or, more commonly, intravenous immunoglobulin are commonly used although the mechanism of action are not well understood.9 There are no randomized, double-blind placebo-controlled studies for treatment of MFS primarily due to the self-limiting course and low incidence. Most patients will recover their neurological deficits starting with ataxia and ophthalmoplegia followed by areflexia, within 6 months of the onset of symptoms. Although treatment is not well defined, early recognition of a broad spectrum of clinical presentations including hypernasal speech in the diagnosis of MFS is critical during the acute period, as respiratory failure can be an early and life-threatening symptom of disease.

References: