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CASE REPORT

## Juvenile Myasthenia Gravis: Frequent Presentation with Bulbar Symptoms

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**Abstract:**

*Juvenile myasthenia gravis usually presents with ocular findings. Rarely, children may present with generalized weakness, sometimes with accompanying bulbar symptoms (dysphagia, facial weakness). However, presentation with isolated bulbar symptoms is extremely unusual. We present four consecutive cases of JMG presenting with predominant bulbar symptoms including voice nasality, dysarthria, and swallowing difficulty (even leading to significant weight loss). Our cases emphasize that primary care physicians should suspect neuromuscular disease such as JMG in children with bulbar symptoms and signs.*

**Keywords:** myasthenia gravis, children, bulbar, swallowing

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### Introduction

Autoimmune juvenile myasthenia gravis (JMG) is an uncommon disorder in the pediatric population, characterized by fatigable weakness due to antibody-mediated destruction of the acetylcholine receptor (AChR) at the neuromuscular junction [1-3]. Children typically present with ocular symptoms (ptosis, diplopia, ophthalmoplegia) but can also present with generalized weakness or bulbar symptoms (facial weakness, voice change, difficulty chewing/swallowing). Presentation with isolated bulbar symptoms is distinctly unusual in the literature, yet we encountered a series of 4 consecutive patients at our institution who presented with either isolated or predominantly bulbar symptoms. In all these patients, the diagnosis was delayed because of this relatively uncommon presentation.

### Case Reports

Patient 1 is a 10-year-old prepubertal girl with a 4-month history of progressive worsening of speech, swallowing and facial movements but no impairment of vision, extraocular movements, limb strength, or respiratory function. Her swallowing difficulty was so severe that she lost several pounds of weight. On examination by her primary care physician, there was bilateral facial weakness and impaired elevation of the soft palate. The patient was referred for evaluation by an otolaryngologist and a speech/swallowing pathologist who corroborated the examination findings on endoscopic exam and recommended further diagnostic evaluation with an MRI scan of the brain, suspecting a central origin for the deficits. The brain MRI scan was normal. On examination by a pediatric neurologist, she was found to have

symmetric tongue weakness and atrophy without fasciculations and weakness of the neck extensors and sternocleidomastoid muscles. AChR antibodies (blocking, binding, modulating) were found to be positive. Her bulbar symptoms improved initially with pyridostigmine but symptoms recurred. CT chest was negative for thymoma. She underwent thymectomy (no pathology) followed by clinical stabilization.

Patient 2 is a 12-year-old prepubertal boy who presented with difficulty swallowing for 8 months. He described choking on food, pooling of saliva in his mouth, and frequent nocturnal awakenings because of choking on saliva. For about one year he also had difficulty with articulation, resulting in a nasal quality to his voice. He lost 7 pounds in the month preceding presentation, reportedly due to excessive time eating a meal. He had no diplopia or limb weakness. There was no variation in his symptoms over the course of the day. On examination, his speech was hypophonic and dysarthric, extraocular movements were full, and he was able to maintain up gaze for more than 90 seconds. He had bilateral lower facial weakness with difficulty puffing the cheeks. There was no discernible weakness of the arms or legs. The possibility of myasthenia gravis was initially discounted given the lack of fatigability on examination. However, AChR antibodies (binding, blocking, modulating) were positive. The patient did not respond to a trial of pyridostigmine. A chest CT showed an enlarged thymus. He underwent a thymectomy (no pathology) following which his symptoms improved significantly. Other than some swallowing difficulty which worsens over the course of the day, his symptoms are well controlled on pyridostigmine.

Patient 3 is an 8-year-old girl who presented with difficulty speaking, smiling and drinking through a straw for one year. She had a 4 pound weight loss over the 3 months prior to presentation. Other symptoms included intermittent ptosis, nasal voice and neck weakness. On examination she was dysarthric with a diminished smile and prominent Bell phenomenon with bilateral weakness of eyelids but normal extraocular movements. She had fatigable hand grip strength and 4/5 strength in biceps and deltoids. AChR binding antibodies were positive. One month after diagnosis she had an episode of myasthenic crisis requiring intubation. She underwent plasmapheresis and immunosuppression with steroids, followed by a thymectomy, with histopathology showing normal tissue. Subsequently, her symptoms are well controlled with pyridostigmine. Two years following diagnosis she is doing well off pyridostigmine with no residual fatigability or bulbar symptoms.

Patient 4 is a 15-year-old girl who presented with progressive swallowing difficulty for 1 month and two choking episodes necessitating emergency room visits. She also had voice nasality for 3 months which worsened over the day or with prolonged speaking. She had ptosis for 3 weeks prior to presentation but no visual symptoms. The patient was tried on multiple allergy medications by her primary care physician for seasonal allergies. Her food intake decreased because of dysphagia. Examination by a neurologist demonstrated difficulty swallowing water as well as bilateral ptosis, normal extraocular movements without diplopia, fatigable upgaze and mild weakness at elbow flexors and extensors. Ice pack test showed very mild transient improvement in the ptosis. She was clinically diagnosed with myasthenia gravis and started on pyridostigmine empirically. There was improvement in her voice, ptosis and facial expression within 24 hours. Serum acetylcholine receptor antibodies were elevated, including the binding, blocking and modulating types; MuSK antibodies were negative. Chest MRI scan revealed a normal appearing thymus gland. Over the subsequent 3 months, she did not tolerate a pyridostigmine wean. She exhibited persistent fatigue and generalized weakness in all muscle groups, though her swallowing difficulty subsided. She underwent thymectomy with negative pathology, followed by slow taper off pyridostigmine; she is now off all medication and is symptom free.

### Discussion

The differential diagnosis of bilateral bulbar symptoms in children is broad and includes JMG, congenital myopathies, congenital myasthenic syndromes, toxins, hypothyroidism, mitochondrial myopathies, multiple sclerosis, demyelinating polyradiculopathy such as Guillain-Barre syndrome and brainstem tumors [4]. The diagnosis is based upon clinical signs and symptoms, with laboratory and electrophysiological studies used for confirmation.

JMG is an uncommon clinical condition with two major forms: ocular, and ocular plus generalized (types 1 and 2 by Osserman's grading system [5]). (This grading system does not classify patients with bulbar symptoms only.) The ocular form is by far the most common in children, accounting for more than 85% of cases in a recent study of 135 children [6]. About 50-69% of JMG patients are seropositive, compared to 80% of adult MG patients (in both age groups, generalized MG has a higher seropositivity rate than pure ocular MG) [2, 7]. Of seronegative cases, approximately 40% of patients have antibodies to muscle specific tyrosine kinase (MuSK)

rather than antibodies to AChR; these patients tend to have more severe bulbar and respiratory symptoms [3].

Our cases are noteworthy for several reasons. First, patients 1 and 2 presented with isolated bulbar symptoms and signs, delaying the eventual diagnosis because other conditions were sought (e.g., tumor, allergy); even in patients 3 and 4, bulbar symptoms predominated although these children also exhibited some ocular and limb weakness. Therefore, clinicians need to consider the diagnosis of JMG in patients who present with facial weakness or dysphagia. Perhaps the most striking manifestation in our series, seen in cases 1, 2, and 3, was significant weight loss due to the severe dysphagia with reduced swallowing ability. Second, the time to diagnosis was likely delayed in these cases due to the unusual symptom constellation without generalized or ocular weakness, usually regarded as the primary symptoms in MG. Even in patients 3 and 4, the bulbar symptoms preceded ocular and generalized ones by up to several months. Third, our cases all had positive AChR antibodies, defying the clinical generalization that facial weakness including tongue wasting is more common in anti-MuSK MG [1, 8]. Fourth, three of our four patients were prepubertal, again countering the literature reports that ocular symptoms predominate in this age range [2]. Finally, we were able to diagnose these children based on clinical symptoms and signs and antibody tests; none of the children needed to undergo electromyography, edrophonium testing, or other extensive laboratory investigation, though patient 1 had a brain MRI scan to rule out neoplasm and patient 2 had a brain MRI scan ordered by the pediatrician prior to neurological consultation.

Ethnicity may affect the incidence of JMG; Asian patients have a higher incidence than Caucasians and individuals with African heritage have a poorer prognosis [7, 9]. All of our patients are Caucasian and none had a family history of MG or other autoimmune disease. Thymus neoplasia is extremely rare in JMG [2, 10], and none of our patients displayed this. Treatment of JMG involves an initial trial of cholinesterase inhibitors, sometimes followed by immunosuppression [4]. Each of our patients was given an initial trial of pyridostigmine; when no longer beneficial, each child underwent thymectomy, with no histopathological changes found in any case. Subsequently, all of our patients are doing well. Based on the usual natural history of bulbar MG, our patients will probably eventually be classified as generalized MG.

These cases emphasize the importance that primary care physicians are aware of the possibility of JMG in children presenting with bulbar symptoms, especially swallowing difficulty and weight loss. Early diagnosis will likely improve the long-term prognosis of these patients and avoid unnecessary or redundant testing.

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