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## Upgrade Your Dysphagia Expertise: How to Diagnose Oculopharyngeal Muscular Dystrophy



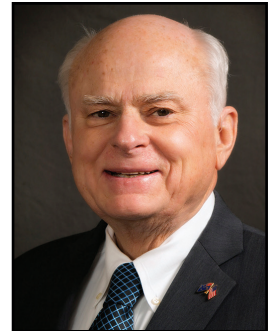
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**Oculopharyngeal muscular dystrophy (OPMD) is rare, adult-onset, familial muscular dystrophy, which has been mainly characterized clinically by progressive dysphagia and ptosis. Dysphagia determines prognosis due to an increase in the risk of aspiration pneumonia and also poor nutrition. OPMD is suspected clinically in older adults with the combination of ptosis and dysphagia. A positive family history may be obtained. Impairments in cricopharyngeal relaxation and hypertonicity of the upper esophageal sphincter (UES) can be best documented through a modified barium swallow. Molecular genetic testing confirms the diagnosis. Treatment options include cricopharyngeal myotomy, cricopharyngeal dilatation and cricopharyngeal botulinum toxin injection. Dilatation of the upper esophageal sphincter by the gastroenterologist is a safe and effective procedure. It has the advantage that can be repeated over the years and complications are rare. Cricopharyngeal (UES) myotomy is the most common surgical intervention. Improvement is seen immediately after surgery, but high recurrence rates and the procedure itself leave the patient at risk for aspiration pneumonia. Botulinum toxin injection has limited literature support and unclear outcomes. We present our experience with three patients with OPMD and the challenges in the diagnosis and treatment.**

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### CASE 1

**A** 71-year old female with past medical history of asthma, diabetes, hypertension, hypothyroidism, rheumatoid arthritis, obstructive sleep apnea, gastroesophageal reflux disease (GERD) and a surgical history significant for cardiac pacemaker was referred for progressive dysphagia over the past ten years. The dysphagia was initially to solids, worsening in the last three years and now is to both solids and liquids. The patient also noticed hoarseness. She developed

bilateral ptosis four years ago, and at that time underwent blepharoplasty. The patient also reported difficulty climbing stairs.

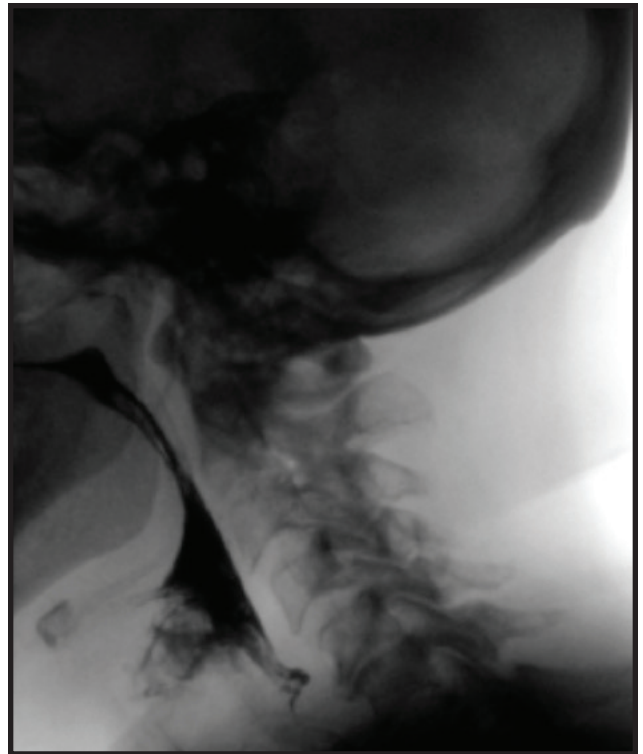
On physical exam, the patient had bilateral ptosis with normal extraocular muscles movement, mild hoarseness and weakness of deltoid, supraspinatus and iliopsoas muscles bilaterally. The patient demonstrated a steady gait.

Initial evaluation for dysphagia utilizing a modified barium swallow study showed irregular filling in the piriform sinus esophageal stenosis at the C5-C6 level, cricopharyngeus hypertrophy and silent aspiration. Upper endoscopy revealed a normal esophagus, thrush in the oropharynx, non-bleeding gastric erythema and normal duodenum. High-resolution esophageal manometry documented decreased lower esophageal sphincter pressure with adequate relaxation. Findings of normal peristalsis in smooth muscle portion of the esophagus as well as striated muscle weakness were noted. Also, pharyngeal contractions and esophageal mobility at cervical level appeared reduced.

Laboratory workup results were negative for acetylcholine receptor antibodies, muscle-specific kinase (MuSK) antibodies, myeloperoxidase antibodies, and antineutrophil cytoplasmic antibodies (ANCA) profiles also came back negative.

Modified barium swallow showed a weak oropharyngeal phase of swallowing with significant pooling of contrast in the piriform sinuses and vallecula. Silent aspiration was also noted (Figure 1). The patient was referred to speech therapy, and, after a few sessions of exercise to improve swallowing, she continued to have aspirations that resulted in pneumonia.

The decision was made to dilate the upper esophageal sphincter to facilitate emptying and decrease aspiration risk. The dilation was performed utilizing a balloon through the scope to a maximum balloon size of 20 mm. Dilation was tolerated with no complications. However, her dysphagia did not improve so the decision was made to undergo a second esophagogastroduodenoscopy (EGD). This time a mild, benign-appearing, intrinsic stenosis was found in the upper third of the esophagus and was dilated utilizing a Savary dilator method over a guidewire with fluoroscopy monitoring with no



**Case 1. Figure 1.** A still frame of MBS demonstrates vallecular and piriform sinus residue with penetration and aspiration.

resistance at 18, 19 and 20 mm. The dilation site was re-examined and showed mild improvement in luminal narrowing (Figures 2 and 3).

The patient reported improvement of the dysphagia after the second dilation and started a diet of pureed food. Genetic confirmatory testing for oculopharyngeal muscular dystrophy (OPMD) was ordered.

## CASE 2

A 71-year-old woman with a past medical history of hypothyroidism and dyslipidemia experienced difficulty with swallowing starting at 40 years of age. Also, around same time noticed bilateral ptosis requiring blepharoplasty twice. She reported a family history of similar symptoms in her mother, maternal grandmother and three siblings. On physical exam, there was weakness in orbicularis oculi muscles bilaterally with limitation in extraocular muscles movements. Muscular strength of upper and lower extremities was adequate. The DNA test came back positive for 9 GCG repeat expansion in PABP2 gene confirming OPMD.

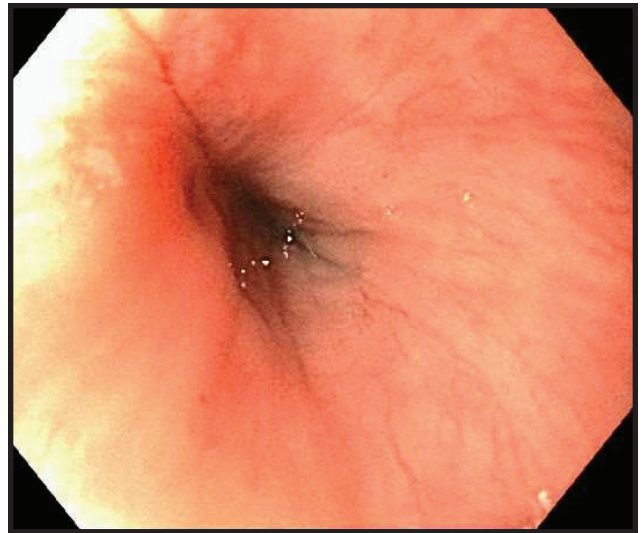
A modified barium swallow showed increased pooling in the vallecula, accumulation of contrast in the piriform sinus with penetration and aspiration of liquids. The patient started working with speech therapy weekly. Esophageal upper sphincter dilation was performed twice using a through the endoscope balloon technique with a minor improvement of the dysphagia.

### CASE 3

A 70-year-old man with a past medical history of hypertension and hyperlipidemia presented to the clinic for evaluation of muscle weakness. He reported difficulties using the stairs for the last 10 years. Also, in the previous five years, he noticed a change in his voice and swallowing problems when eating solids. Multiple family members from his mother side have similar symptoms including his mother, three aunts, one uncle and a grandmother. On physical exam, weakness of the orbicularis oculi muscles was remarkable. Extraocular movements were intact. Proximal lower extremity muscle weakness was noted. A modified barium swallow showed a marked deficiency of the swallow mechanism with increased pooling in the vallecula and piriform sinus. Penetration and aspiration were present. DNA test was ordered and came back positive for 9 GCG repeat expansion in PABP2 gene confirming OPMD. The patient refused treatment for dysphagia and also percutaneous endoscopic gastrostomy (PEG) tube placement.

### Discussion

Oculopharyngeal muscular dystrophy (OPMD) is rare, adult-onset, familial muscular dystrophy which has been mainly characterized clinically by progressive dysphagia and ptosis due to an involvement of the pharyngeal and palpebral musculature, respectively. E. W. Taylor first described it in 1915 emphasizing the unusual combination of ptosis and pharyngeal palsy in a family of French-Canadian descent. However, Taylor believed that the cause of this rare entity was a degeneration of vagus and glossopharyngeal nuclei. He called it progressive vagus-glossopharyngeal paralysis with ptosis. It was not until 1951 after the observations of Kiloh and Nevin of cases with similar symptoms but also had involvement of



**Case 1. Figure 2.** Endoscopy visualization of the UES.

limb and trunk muscles suggesting the myopathic nature of the disease. In 1962, Victor et al. reported three cases in Jewish family from eastern Europe with a dominant mode of inheritance with clinical features of progressive dysphagia and ptosis in the late life and named the disease oculopharyngeal muscular dystrophy.<sup>1</sup>

Cases of patients with OPMD have been reported in numerous countries in all five continents. The most significant clusters of patients are in Quebec of French-Canadian origin,<sup>2</sup> in Israel from Bukhara Jewish immigrants<sup>3</sup> and in Hispanics living in New Mexico.<sup>4</sup>

The mean age of onset for ptosis is 48 years and for dysphagia is 50 years. Dysphagia determines prognosis due to an increase in the risk aspiration pneumonia and also poor nutrition. As the disease progresses, there are other signs like hoarseness, weakness of the tongue, facial muscles and proximal upper and lower extremities. Involvement of the central nervous system (CNS) also has been reported.<sup>5</sup> Severe OPMD represents five to 10% of all cases and is characterized by symptoms before age 45 years and incapacitating proximal leg weakness before age 60 years.<sup>6</sup>

The mechanisms contributing to dysphagia in OPMD patients include reduced lingual pressure generation, impairments in cricopharyngeal relaxation and hypertonicity of the UES and incomplete laryngeal vestibule closure and

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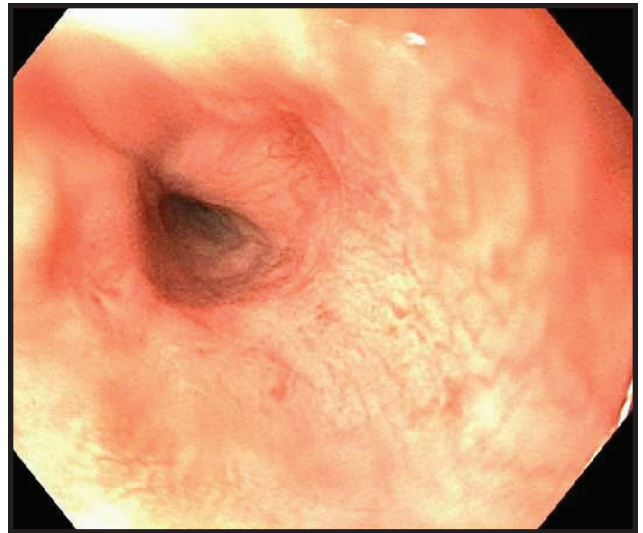
subsequent airway compromise. Swallowing efficiency and safety are affected and is a significant determinant of prognosis due to an increase in the risk aspiration pneumonia and also poor nutrition. In the end stages of disease is recommended the use of PEG tubes to address both malnutrition and aspiration risks.<sup>7</sup> Swallowing-related quality of life is moderately impacted characterized by prolonged mealtime durations and increased burden that contribute to social withdrawal and decrease enjoyment of meals in these patients.<sup>8</sup>

OPMD is suspected clinically with a combination of ptosis, defined as either vertical separation of at least one palpebral fissure measuring less than eight mm at rest or previous corrective surgery and dysphagia, characterized by a swallowing time greater than seven seconds when drinking 80 ml of ice-cold water. Modified barium swallow (MBS) using applesauce, cereal, liquids and videofluoroscopic swallowing study (VFSS) are essential to document aspiration and dysfunction of the pharyngeal muscles and upper esophageal sphincter (UES).<sup>6</sup> Standard esophageal motility studies to analyzed upper esophageal sphincter function have not been rewarding or diagnostic.

Molecular genetic testing confirms the diagnosis with a detection of an expansion of a GCN trinucleotide repeat in the first exon of PABPN1 (previously named PABP2). Normal alleles contain 10 GCN 6 GCG trinucleotide repeats. Autosomal dominant alleles range in size from 12 to 17 GCN repeats. Patients with longer PABPN1 expansion and homozygotes are, on average, diagnosed at an earlier age, the disease is more severe and shows a faster progression.<sup>9</sup>

Autosomal recessive alleles comprise 11 GCN repeats and present later in life usually after the six decades.<sup>6,10,11</sup>

Muscle biopsy is only necessary if suspicion of the disease exists and there is a presence of two normal PABPN1 alleles. The biopsy of muscle shows in some patients with OPMD, intranuclear inclusions of tubular filaments that are 250 nm in length, dystrophic changes such as atrophic muscle fibers of different width, ragged red fibers, and rimmed vacuoles. Electromyography (EMG) is not specific or necessary for OPMD diagnosis and



**Case 1. Figure 3.** Endoscopy visualization of the UES showing stenosis.

often shows signs of myopathic changes that could also be related to age. Serum creatine kinase (CK) concentrations are usually in range or twice the upper limit. CK level is not sensitive or specific for the diagnosis of OPMD.<sup>6</sup>

### Differential Diagnosis

- Facioscapulohumeral dystrophy (FSHD) symptoms usually begin in the 2nd decade, in contrast to OPMD that presents later in life. The muscular weakness has a different distribution than OPMD with facial, scapular, abdominal upper and lower extremities affected. Facial muscles weakness is milder compared to OPMD. Dysphagia is rare in this entity.<sup>12</sup>
- Myotonic dystrophy presents with different genotypes and onset of presentation. There is a combination of proximal and distal weakness. Myotonia and muscle pain are cardinal symptoms, and both are absent in OPMD.<sup>13</sup>
- Mitochondrial myopathies have variable clinical expression. Myopathy could be a major or a minor clinical feature depending on presentation. Muscles symptoms range from fatigue, myalgia and exercise intolerance. Other associated features are retinitis pigmentosa, ataxia. These are not present in OPMD patients. The inclusion body myositis found in mitochondrial

myopathies are 15-18 nm filaments compared to 250 nm filaments in OPMD.<sup>14</sup>

- Myasthenia Gravis usually presents with ptosis, diplopia and bulbar involvement as dysarthria, dysphagia, generalized weakness and positive test results for anti-AChR or anti-MuSK antibodies. These serologic markers are negative in patients with OPMD.<sup>15</sup>

### Treatment

The treatment in OPMD patients is supportive in most cases. Avoiding secondary complications such as aspiration pneumonia, malnutrition and social withdrawal is the primary focus. Blepharoplasty is the treatment of choice for ptosis. Surgery is usually done for cosmetic reasons and is recommended when it affects vision in the central position of gaze and neck pain due to retroflexion of the neck.<sup>16,17</sup> It has been hypothesized that this compensatory position also affects dysphagia in OPMD patients.<sup>18</sup> Exposure keratitis is a known complication of this surgery.<sup>16</sup>

Cricopharyngeal (UES) myotomy is the most common surgical treatment for dysphagia. Clinical improvement is seen immediately after surgery, but long-term follow-up shows a decrease in success due to the progression of the myopathic process in the pharyngeal muscles, making early diagnosis and treatment necessary. This procedure also carries the increased risk of aspiration when gastroesophageal reflux occurs in the setting of weakened pharyngeal protection.<sup>19-21</sup>

Botulinum toxin injections for dysphagia are another alternative to treatment. Safety and efficacy of this intervention is dose-dependent, requires frequent retreatment and is expensive. Higher doses have led to worsening of the dysphagia and also dysphonia due to diffusion of neurotoxins in nearby muscles.<sup>24,25</sup>

Dilatation of the UES through an upper GI endoscope is a relatively safe, well-tolerated procedure that is usually performed as an outpatient and only requires moderate sedation. The Savary dilatation method is recommended where a guidewire is passed and dilatation with increasing sizes is performed under fluoroscopic monitoring. This procedure can be repeated throughout the

years and complications are rare and include perforation or hemorrhage. This technique has a reasonable success rate in improving dysphagia, weight maintenance, prolongation of oral feedings and avoidance of necessity for PEG which is an option.<sup>22,23</sup> ■

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## POSITION AVAILABLE

Johns Hopkins University School of Medicine, Division of Gastroenterology is looking for a gastroenterology hospitalist with experience in ERCP, EUS, and enteroscopy. Applicants should have at least five years of post fellowship experience in gastroenterology and have completed a two year advanced interventional endoscopy fellowship. Experience in motility and fluency in Spanish helpful.

For further information please contact:

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