Oculopharyngeal Muscular Dystrophy: Diagnosis and Management of this Unique Disorder
Vanessa Ceglia, O.D.
Jennifer Gustafson, O.D., FAAC
VA Boston Healthcare System

Abstract: An 83 year old white male presents with recurrent bilateral ptosis and diplopia. Genetic testing reveals Oculopharyngeal Muscular Dystrophy. We discuss the condition including genetics, symptoms, and role of optometrists in managing these rare cases.

I. Case History

a) Patient Demographics: 83 year old white male of French Canadian descent

b) Chief Complaint: Decreased vision at distance and near and intermittent diplopia distance>near.

c) Ocular history:
   * Recurrent Ptosis OU s/p ptosis repair OU x3
   * Dry Macular Degeneration
   * Glaucoma suspect
   * Dry Eye Syndrome
   * Pseudophakia

d) Medical history:
   * Muscular Dystrophy
   * Dysphagia
   * Coronary Artery Disease s/p CABG and valve replacement
   * Chronic Obstructive Pulmonary Disease
   * Vitamin D Deficiency
   * Herpes Zoster

e) Medications:
   Albuterol, Amlodipine, Aspirin, Clopidogrel, Cyclosporin, Fluticasone propionate, Guaifenesin, Loratadine, metoprolol succinate, Ensure nutrition supplement, Oladaterol/titro, Ranitidine, Rosuvastatin

f) Additional Information:
   Family History:
   Mother: ptosis, no dysphagia
   Sister: ptosis, no dysphagia
   Daughter: dysphagia, weight loss
   Son: ptosis, no dysphagia
   Niece: dysphagia
II. Pertinent Findings

a) Clinical

BCVA: OD: 20/100
OS: 20/40-

Pupils: PERRL, no APD
EOMS: full upgaze, limitation in abduction and adduction (~20% limited), most significant limitation in downgaze (~60-70% limited)
Cover Test: Distance: 2 exotropia
Near: 14 exotropia
Palpebral Fissure: OD: 7.5cm OS: 8.5cm
MRD: OD: 1mm OS: 1 mm
Levator Function: OD: 2mm OS: 4mm

Anterior Segment:

Lids: Ptosis with floppy lids OU, peaked RUL, mild lag OS>OD, meibomian gland dysfunction
Conjunctiva: White and quiet
Cornea: Diffuse SPEE with significant tear debris OU
AC: Deep and quiet
Iris: Flat OU
Lens: PCIOL OU, PCO mainly peripheral OU
IOP: WNL

Posterior Segment:

ONH: OD: .55 OS: .45
Macula: pigmented defects, geographic atrophy, drusen OU, no heme or fluid OU.
Vessels: normal caliber OU
Periphery: retinae intact 360 degrees without holes or tears, or RD OU

b) Physical:

*Dysphagia
Initially unable to swallow steak progressed to difficulty swallowing fluids
*Mild dysarthria
*Proximal>distal muscle weakness
*Bilateral lower extremity weakness

c) Other Testing:

Imaging:

Macula OCT:
OD: Extensive drusen and outer segment irregularity,
geographic atrophy centrally, no SRF/CNVM
OS: Extensive drusen and outer segment irregularity, patchy geographic atrophy, no SRF/CNVM

RNFL OCT:
OD: Borderline: SN, WNL all other sectors
   Progression analysis stable to 2011
OS: ONL: ST borderline: SN, G WNL all other sectors
   Progression analysis stable to 2012

*Genetic Testing:* PAPB2/PABPN1 allele 1: 11 GCG repeats
                     PAPB2/PABPN1 allele 2: 6 GCG repeats

**III. Differential Diagnosis**

* Oculopharyngeal muscular dystrophy (leading)
* Myotonic dystrophy
* Chronic progressive external ophthalmoplegia
* Myasthenia Gravis

**IV. Discussion and Diagnosis:**

Oculopharyngeal muscular dystrophy (OPMD) is a late onset neuromuscular dystrophy. It is considered a rare disease and affects 1/100,000 people worldwide. While it occurs worldwide, it has been found to occur in higher incidences in certain populations, particularly the French-Canadian population, Bukhara Jewish immigrants in Israel, as well as the Hispanic population in New Mexico. Our patient is French-Canadian; the incidence of OPMD in the Canadian province of Quebec is estimated to be 1/8000 individuals. It is most commonly inherited through autosomal dominant transmission, however, it has been found to be transmitted via autosomal recessive mode as well. The condition is caused by a triplet expansion mutation in the poly-adenylate RNA binding protein 1 (PABPN1). This expansion causes a misfolding, exposing the hydrophobic alanine. The longer a repeat expansion, the more exposure will occur. A correlation has been found between repeat length and disease severity. The improper folding of the protein causes the protein to be insoluble. These insoluble proteins then accumulate in the muscle nuclei eventually leading to a fibillar formation. The aggregates of proteins in cell nuclei are also known as intranuclear inclusions and are a pathological hallmark for the disease.

Patients will commonly develop a slowly progressive bilateral ptosis, difficulty swallowing (dysphagia), and proximal limb weakness usually beginning in the fifth to sixth decade of life. In additional to ptosis, ocular symptoms can also include gradual extraocular muscle weakness. As the ptosis increases, patients frequently adopt a new head posture involving retroflexion of the neck and using downward gaze. The symptoms of dysphagia are first noticed by avoidance of solid foods, later on progressing to difficulty with liquids. Life expectancy is not expected to be shortened by this disorder, however, the leading cause of death in
patients that have OPMD is usually related; either from aspiration pneumonia, malnutrition, or starvation.

V. Treatment/management

*Distance vision glasses with 1 base-in prism to relieve distance diplopia.
*Near vision glasses with high +3.50 add to improve reading ability.
*4x/16D Powermag handheld magnifier for spotting and reading.

*Referral to Speech Language Pathology for swallowing strategies while eating (Mendelsohn Maneuver)
*Dietary changes: soft food, Ensure nutritional beverages, vitamin supplements to maintain weight
*Potential PEG feeding tube in the future
*Chair lift for assistance reaching 2nd floor of home
*Family to learn Heimlich maneuver and CPR
*Genetic counseling for children

There is currently no cure for OPMD. Therapies consist of symptom management including surgical procedures of the eyelids and pharyngeal muscles. Two surgical options are currently used for ptosis management; resection of levator palpabrae aponeurosis and fixation of tarsus at the frontal muscle. The first offers a less invasive surgery but often relapses resulting in additional surgery. The second technique is more durable but also more invasive.

Research has shown potential benefit from molecular intrabodies and cell therapy. Intrabodies are small fragments of antibodies used to target intracellular proteins or intranuclear inclusions. Using Drosophila models, studies have been able to show intracellular expression of the intrabodies can stop aggregation of PABPN1 as well as reduce the aggregates that already exists.

Gene therapy has also been applied by addressing the correlation between levels of soluble PABPN1 and muscle depletion, where a decreased level in PABPN1 shows increased muscle depletion. It has been proposed that introducing functional PABPN1 to affected muscles can fix muscle depletion. This in combination with an anti-aggregate pharmaceutical can give maximal therapeutic effect and fix the dystrophy on the histological level.

Bibliography:


**VI. Conclusion**

Optometrists play an important role in diagnosis of this disease. An optometrist will very likely become the first doctor the patient sees when they begin to develop symptoms of this dystrophy. With the knowledge of the specific combination of clinical signs, optometrists play an important role in recognizing currently undiagnosed patients. In patients that have already been diagnosed it is important to educate patients on current treatments including expectation of repeat surgeries for the same condition. As the condition can be passed down to future generations, genetic testing is recommended for future generations.