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Oculopharyngeal muscular dystrophy as a rare cause of dysphagia

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Abstract

Oculopharyngeal muscular dystrophy (OPMD) is a rare cause for late-onset dysphagia. OPMD normally follows an autosomal dominant inheritance. Herein we describe a rare case of an autosomal recessive inheritance of OPMD. An 80-year-old male presented with progressive dysphagia, frequent aspiration and change of voice getting inarticulate and hoarse. Physical examination showed ptosis of the right eyelid. Endoscopic and manometric investigation revealed a nonspecific motility disorder with hypopharyngeal esophageal hypotension. The severity of dysphagia became apparent when significant aspiration occurred during a barium swallow. Magnetic resonance imaging of the head ruled out a malignant or cerebral ischemic process. Based on the neurological examination, neurogenic muscular dystrophy was suspected and DNA analysis was performed. The analysis confirmed the extremely rare diagnosis of an autosomal recessive inheritance pattern of OPMD with homozygous $(GCN)_6(GCN)_4(GCN)$ expansion of the *poly-(A) binding protein nuclear 1* gene. As OPMD normally follows an autosomal dominant inheritance, consanguinity of the patient's parents was suspected.

Keywords Dysphagia, oculopharyngeal muscular dystrophy, neurogenic muscular dystrophy, ptosis

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Introduction

Dysphagia is a very common phenomenon in the elderly population. Even though studies indicate that 15-30% of patients older than 65 years are estimated to be affected by dysphagia, the exact prevalence of dysphagia remains unclear [1]. Swallowing disorders can be divided into oropharyngeal dysphagia and esophageal dysphagia. Usually they can be distinguished by history, which often will also suggest the specific cause. The most common cause of oropharyngeal dysphagia is cerebrovascular accidents; other causes may include oropharyngeal structural lesions, systemic muscular diseases, and diverse neurological disorders. Complications of dysphagia, such as malnourishment, dehydration and aspiration can occur, rarely even death [1,2]. Oculopharyngeal muscular dystrophy (OPMD) is a rare cause for late-onset dysphagia. OPMD is one of nine types of muscular dystrophy, a group of genetic, degenerative diseases primarily affecting voluntary muscles. Progressive eyelid ptosis, followed by dysphagia and proximal limb weakness are the clinical findings. The swallowing difficulties begin with solid food but as the condition worsens liquids become difficult to swallow as well [3]. OPMD normally follows an autosomal dominant inheritance pattern. However, less commonly, OPMD can be inherited in an autosomal recessive pattern as well [4]. Hereby we report a case of OPMD as a cause of dysphagia.

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Conflict of Interest: None

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Case report

An 80-year-old male patient presented with progressive dysphagia over a period of 5 years. The dysphagia primarily concerned solid foods, but also liquids to a lesser extent. He reported difficulties with swallowing his saliva, nasal regurgitation and frequent coughing. Furthermore, he noticed a change of voice that became poorly articulate. His weight remained relatively stable over the years. The general medical history was unremarkable. Physical examination showed phlegm in the oral cavity, hoarseness and unilateral ptosis of the eyelid (Fig. 1: The authors declare that they have obtained the patient's written informed consent to publish his photo in the *Annals of Gastroenterology*). Laboratory evaluation only revealed elevated levels of the C-reactive protein, creatinine kinase and lactate dehydrogenase. Intubation of the esophagus during esophagogastroduodenoscopy was

Figure 1 Patient with unilateral ptosis of the right eyelid

difficult owing to an asymmetry of the pharyngeal recess, especially on the right side. Histology revealed only moderate esophagitis. Barium swallow showed severe hypotension of the hypopharynx with aspiration (Fig. 2) of contrast dye into the airways. Esophageal manometry showed a non-specific motility disorder with more than 10% simultaneous contractions and dropouts whereas complete relaxation of the upper esophageal sphincter was noticed. Magnetic resonance imaging of the head and the neck ruled out a malignant or central ischemic process. The combination of ptosis and dysphagia on the neurological exam suggested possible OPMD. A DNA analysis was performed and revealed a rare homozygous elongation of the GCN repeat area ($(GCN)_6(GCN)_4(GCN)$) of the *poly-(A) binding protein nuclear 1 (PABPN1)* gene and the diagnosis of an unusual autosomal recessive inheritance of OPMD was made.

Discussion

OPMD is a rare cause of late-onset dysphagia. In Europe, the prevalence of OPMD ranges from 0.5 to 1:100 000 [5]. Typical symptoms besides dysphagia include ptosis and sometimes proximal muscle weakness. Symptoms usually appear at the age between 40 and 60 years. First symptoms ordinarily are slowly progressive eyelid ptosis due to affected function of the levator palpebrae superioris muscle, followed by dysphagia caused by pharyngeal muscle dysfunction. Later on extraocular and facial muscles can also be involved [6]. OPMD normally follows an autosomal dominant inheritance showing expansion of the *PABPN1* gene leading to elongation of a poly-alanine-sequence. Patients with autosomal dominant OPMD express an expanded allele with 12 to 17 GCN-triplets whereas wild type allele only has 10 GCN-triplets [7].

The diagnosis can be made by molecular analysis which can detect the expansion of a GCN trinucleotide repeat in the first exon of *PABPN1*. Muscle biopsy is only applied to patients with strongly suspected OPMD who have normal *PABN1* alleles [8].

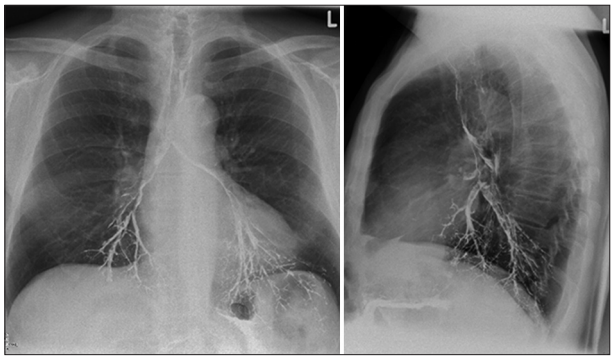

Figure 2 Chest x-ray. The film showed aspiration of swallowed barium in both the right and left main stem bronchi. The barium also spread into the smaller airways, producing a tree-in-bud appearance

To our knowledge, so far only five patients have been described with OPMD following autosomal recessive inheritance [9]. Those patients expressed only mild symptoms contrary to autosomal dominant cases. Accordingly, this case also revealed a mild course of the disease. Prevalent symptoms were dysphagia and a right-sided ptosis. Proximal muscle weakness was not found. Initial symptoms in terms of dysphagia appeared at the age of 70, much later than the usual disease onset of the autosomal dominant form of OPMD, which usually becomes symptomatic at the age between 40 and 60 years.

Neither the parents nor one of the five siblings showed signs of dysphagia but some of them died young. Analyses of family photographs surprisingly revealed unilateral ptosis of the eyelid in one sister.

Unfortunately, up to the present day causal therapy for OPMD is not possible. The patient under discussion suffered from severe aspiration, and percutaneous endoscopic gastrostomy was recommended to maintain nutritional intake. The only daughter (49 years) of the patient does not show any symptoms of dysphagia or ptosis of the eyelid and therefore is most likely not affected by OPMD. As she is childless, the role of being an asymptomatic carrier is negligible.

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