BRIEF COMMUNICATION

Cricopharyngeal Myotomy in the Treatment of Oculopharyngeal Muscular Dystrophy

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Abstract Oculopharyngeal muscular dystrophy (OPMD) is an autosomal dominant myopathic disease which provokes oropharyngeal dysphagia, palpebral ptosis and proximal limb weakness. It is the abnormal expression of the GCG triplet in the PABPN1 gene on chromosome 14 that causes this disease. The study of the oropharyngeal dysphagia that these patients suffer from should include upper gastrointestinal endoscopy, barium video-radiology and oesophageal manometry. Genetic study confirms the diagnosis. We report 6 patients (3 of whom were siblings) referred to our department with a confirmed diagnosis of OPMD, who underwent cricopharyngeal myotomy to achieve normal swallowing.

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PALABRAS CLAVE
Distrofia muscular oculofaringea; Disfagia; Tratamiento; Miotomía del cricofaringeo

Miotomía del cricofaringeo en el tratamiento de la distrofia muscular oculofaringea

Resumen La distrofia muscular oculofaringea (DMOF) es una enfermedad hereditaria autosómica dominante que causa disfagia orofaringea, ptosis palpebral y debilidad muscular proximal. Es causada por una expresión anormal del triplete GCG del gen PABPN1, situado en el cromosoma 14. El estudio de la disfagia orofaringea que sufren estos pacientes se basa en la historia clínica, la endoscopia digestiva alta, la radiología con contraste baritado y la manometría esofágica. El diagnóstico definitivo se confirma con el estudio genético. Presentamos 6 casos, 3 de ellos de una misma familia, remitidos a nuestro departamento con el diagnóstico confirmado de DMOF, los cuales se sometieron a una miotomía del cricofaringeo para conseguir una deglución normal.

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Introduction

Oculopharyngeal muscular dystrophy (OPMD) is a late-onset autosomal dominant muscular illness. Progressive weakness of the ocular musculature was described by von Greafe in 1868 as "external progressive ophthalmoplegia".1
OPMD causes palpebral ptosis, oropharyngeal dysphagia and proximal weakness in the limbs. OPMD was finally described by Taylor in 1915.\(^2\) The incidence and prevalence of this illness are very low, but cases have been reported all over the world. The population most affected by OPMD is to be found in the Quebec region of Canada, with a prevalence estimated at 1:1000\(^3\) and in Israeli immigrants, with an estimated prevalence of 1:600.\(^4\) OPMD is caused by the short expansion of the repeated triplet (GCG) 8–13 in the \textit{PABPN1} gene located in chromosome 14.\(^5\) In this paper, we report on 6 patients, 3 of them from the same family, referred to our department with a confirmed diagnosis of OPMD for the performance of cricopharyngeal myotomy (CM) in order to improve swallowing.

### Materials and Methods

We conducted a prospective observational study of 6 patients diagnosed as having OPMD and referred to our department for assessment of surgery as treatment for their symptoms. The diagnosis had been genetically confirmed in all patients. Following surgery, they were monitored via the Otorhinolaryngology Out-Patients Clinic. Patients’ clinical and epidemiological characteristics are listed in Table 1.

During the surgical procedure, a sample of the cricopharyngeal and sternocleidomastoid muscles was taken from each patient for study by pathologists. These samples were subjected to the normal tests for muscles (haematoxylin-eosin, Gomori’s trichromic test, Oil Red O and PAS), as well as special histoenzymatic techniques (COX, SDH, NADH and ATPases 9.4, 4.6 and 4.3) (Figs. 1–3).

### Results

CM was performed on all 6 patients. The approach consisted in a right cervicotomy, after placement of an inflated Foley catheter at the level of the Upper Oesophageal Sphincter (UOS), followed by exposure and identification of the cricopharyngeal muscle, and the performance of myotomy on the latter. Patients were discharged without complications the day after the procedure and were monitored through the ENT Out-Patient Clinic, with a minimum follow-up of 18 months and a maximum of 37 months. The improvement in dysphagia was moderate in 2 patients (33.3%) and considerable in the other four (66.6%). The results obtained and the review fibroendoscopic examinations are shown in Table 2.

The pathology study of the cricopharyngeal muscle revealed severe atrophy of the muscle fibres, with fibrosis and adipose substitution, with identification of vacuoles rimmed with basophilic material, characteristic of OPMD; there was neither necrosis nor inflammatory infiltrates. There were much more discreet in the sternocleidomastoid muscle, with no fibrosis but some atrophic fibres with rimmed vacuoles.

### Discussion

OPMD is an autosomal dominant myopathic disorder causing palpebral ptosis, oculopharyngeal dysphagia and proximal muscle weakness. This disease is included within those caused by triplet repetition. OPMD is caused by the expansion of a GCG triplet located on the first exon of gene 1 in the polyadenylate binding protein \textit{(PABPN1)}, in chromosome 14 (14q11.2–q13).\(^3\) Nonetheless, cases have been described with other mutations and other phenotypes, albeit rarely.\(^6\) Cases of OPMD have been reported all over the world. The 2 largest populations of these individuals can be found in Canada, due to a family of French origin that emigrated to Canada in 1634,\(^7\) and among Bukhara Jews who emigrated to Israel from Uzbekistan.\(^4\) Smaller populations have been described in Europe and in the United States of America. Clinical signs include palpebral ptosis, dysphagia and proximal muscle weakness. Palpebral ptosis may precede or appear together with dysphagia in most patients; muscle weakness may appear after ptosis and dysphagia.

Swallowing is a neurophysiologically complex action. The correct operation of the UOS is an essential part of correct swallowing; its alteration may lead to potentially life-threatening dysphagia. Barium meals and video-endoscopy are 2 major tools for determining the severity of dysphagia.

### Table 1 Clinical and Epidemiological Characteristics of the Patients.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Age</th>
<th>Symptoms</th>
<th>Personal History</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Female</td>
<td>67</td>
<td>Dysphagia +++&lt;br&gt;Operated palpebral ptosis&lt;br&gt;Proximal muscle weakness +</td>
<td>Of no interest</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>71</td>
<td>Dysphagia +++&lt;br&gt;Operated palpebral ptosis&lt;br&gt;Proximal muscle weakness +</td>
<td>Of no interest</td>
</tr>
<tr>
<td>3</td>
<td>Female</td>
<td>72</td>
<td>Dysphagia ++&lt;br&gt;Palpebral ptosis</td>
<td>Of no interest</td>
</tr>
<tr>
<td>4</td>
<td>Male</td>
<td>78</td>
<td>Dysphagia ++&lt;br&gt;Palpebral ptosis</td>
<td>Raised blood pressure</td>
</tr>
<tr>
<td>5</td>
<td>Male</td>
<td>58</td>
<td>Dysphagia ++&lt;br&gt;Palpebral ptosis</td>
<td>Of no interest</td>
</tr>
<tr>
<td>6</td>
<td>Male</td>
<td>57</td>
<td>Dysphagia ++&lt;br&gt;Palpebral ptosis</td>
<td>Of no interest</td>
</tr>
</tbody>
</table>

+: mild symptom; ++: moderate symptom; +++: severe symptom.
Cricopharyngeal myotomy in the treatment of oculopharyngeal muscular dystrophy

Table 2  Results Obtained and Follow-up.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Date of Operation</th>
<th>Follow-up, months</th>
<th>Improvement in Dysphagia</th>
<th>Fibroendoscopic Examination</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>October, 2008</td>
<td>37 months</td>
<td>++</td>
<td>Discreet salivary stasis in right pyriform sinus</td>
</tr>
<tr>
<td>2</td>
<td>September, 2009</td>
<td>28 months</td>
<td>+++</td>
<td>Paralysis of left vocal cord with good glottal closure</td>
</tr>
<tr>
<td>3</td>
<td>March, 2010</td>
<td>18 months</td>
<td>+++</td>
<td>Normal</td>
</tr>
<tr>
<td>4</td>
<td>March, 2010</td>
<td>18 months</td>
<td>++</td>
<td>Minimal salivary stasis in pyriform sinuses</td>
</tr>
<tr>
<td>5</td>
<td>March, 2010</td>
<td>18 months</td>
<td>+++</td>
<td>Normal</td>
</tr>
<tr>
<td>6</td>
<td>March, 2010</td>
<td>18 months</td>
<td>+++</td>
<td>Normal</td>
</tr>
</tbody>
</table>

*: mild improvement; ++: moderate improvement; +++: considerable improvement.

A manometric study will show repetitive weak contractions of the hypopharyngeal and oesophageal muscles; relaxation of the UOS may be delayed and incomplete due to the weakness of the hypopharyngeal muscles. The role of muscle biopsy has been relegated to a secondary level; no biopsy is necessary with a complete case history for the individual and the immediate family, and a positive genetic study. However, when faced with a strong diagnostic suspicion and a negative genetic study, the biopsy may clarify the diagnosis. Differential diagnosis must include mitochondrialopathies and illnesses affecting neuromuscular transmission, such as myasthenia gravis.

Figure 1  Patient four. Severe fibrosis can be seen in the cricopharyngeal muscle, with adipose substitution and severe atrophy; there are rimmed vacuoles; in the sternocleidomastoid muscle, the fibrosis is mild, with scant rimmed vacuoles.
There is so far no curative treatment. Treatment consists of measures to reduce the impact of palpebral ptosis and dysphagia, with its subsequent malnutrition. The optimization of the swallowing process begins with rehabilitation therapy, including advice on food consistency or the positioning of the head during swallowing.\textsuperscript{2-5} A protein-rich diet is recommended for an optimal nutritional balance.\textsuperscript{11} Pneumonia due to aspiration is a frequent complication that must be forestalled.\textsuperscript{12}

If the manometric study shows hypertonia of the UOS, treatment with nifedipine (20–40 mg) or isosorbide dinitrate (5 mg) may be started.\textsuperscript{13}

Around 80\% of patients may benefit from CM, according to the series published. However, these studies do not refer to the duration of the follow-up of patients.\textsuperscript{14-17} The presence of dysarthria is a prognostic factor for poor response to CM.\textsuperscript{14} In our paper, we have performed clinical follow-up of at least 18 months, with a mean of 22.8 months of follow-up; none of the patients presented dysarthria at the time of the procedure.

The injection of botulinum toxin into the cricopharyngeal muscle, under endoscopy, with 50–100 U per session, achieves paralysis (relaxation) of the muscle and swallowing in a few days. The disadvantage is that the effect gradually wears off, but the sessions can be repeated.\textsuperscript{13} It is indicated in patients at high risk for surgery.\textsuperscript{18}

Percutaneous gastrostomy constitutes the definitive treatment for dysphagia but definitively alters the patient’s feeding through the natural route.\textsuperscript{5} Nonetheless, percutaneous gastrostomy does not completely prevent aspiration; the use of a jejunostomy catheter during gastrostomy diminishes the risk of aspiration with respect to a standard gastrostomy catheter. Baseline aspiration (i.e. non-food-related aspiration) is still present in patients with gastrostomy. Gastrostomy in patients with altered sensitivity may increase the risk of aspiration.\textsuperscript{19}

Gastrostomy improves quality of life and longevity in patients with muscular dystrophy. Its use should be considered in the following situations: (1) initial stages of dysphagia, prior to gradual weight loss, and pulmonary alteration; and (2) during peri-operative periods in which patients must be checked exhaustively due to their unstable pulmonary status.\textsuperscript{20}

In our case, CM was performed on all 6 patients. After being discharged the day after the surgical procedure, they were monitored via the Ear, Nose and Throat Out-Patients Clinic. The improvement in dysphagia was moderate in 2 patients (33.3\%) and considerable in the other 4 patients

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**Figure 2** Patient five. The changes are less marked with respect to Fig. 1.
(66.6%). In terms of complications, one patient presented paramedian paralysis of the left vocal cord, but with good compensation in the contralateral cord and good glottal closure. Patients improved in terms of choking and aspiration episodes. None of the patients have required any other kind of endoscopic treatment or open surgery, they merely continue with swallowing therapy.

In summary, CM must be considered as a good method for treating dysphagia in patients with OPMD and a moderately or severely compromised swallowing function as it eliminates the barrier effect present at the level of this muscle (Figs. 1–3).

Conflict of Interest

The authors have no conflict of interests to declare.

References