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Clinical and electrophysiologic features of oculopharyngeal muscular dystrophy: Lack of evidence for an associated peripheral neuropathy

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ABSTRACT

Objective: To describe the clinical and electrophysiologic features of an unselected population of patients diagnosed clinically or genetically with oculopharyngeal muscular dystrophy (OPMD), and to discern any association with a peripheral neuropathy.
Methods: Patients with a clinical or genetic diagnosis of OPMD were retrospectively identified and characterized in terms of clinical and electrophysiologic features.
Results: Fourteen patients who met the design criteria were identified and included. All had progressive ptosis and dysphagia, and most had ophthalmoparesis and proximal limb weakness. The electromyographic findings were similar to findings in other dystrophic diseases. Nine out of 10 patients had normal sural sensory nerve action potentials (mean amplitude 14.2 μV, range 0–22 μV).
Conclusions: The electrophysiologic findings associated with OPMD are similar to changes noted in other dystrophic diseases. These findings argue against an association between OPMD and peripheral neuropathy.
Significance: OPMD may not be associated with a peripheral neuropathy, as has been previously suggested.

1. Introduction

Oculopharyngeal muscular dystrophy (OPMD) is an inherited myopathy characterized by onset in adulthood of ptosis, dysphagia, ophthalmoparesis and limb weakness (Bouchard et al., 1997). Most cases are transmitted in an autosomal dominant fashion, although some occur in a recessive or sporadic pattern (Brais and Tome, 2004). Given the typical dominant inheritance pattern, most of the descriptive series of this disease have emphasized the clinical findings in large kindreds of affected adults.

The histopathologic, molecular, and genetic features of OPMD have become increasingly well-characterized (Bouchard et al., 1997 and Brais et al., 1998). Although initial descriptions of the disease suggested a neuropathic mechanism (Taylor, 1915), subsequent work by Victor and colleagues clearly identified the myopathic and specifically dystrophic nature of OPMD (Victor et al., 1962). A review of muscle biopsies by Dubowitz and Brooke (1973) recognized the presence of rimmed vacuoles in affected patients (Dubowitz and Brooke, 1973). Subsequent ultrastructural studies revealed characteristic intranuclear tubular filaments in patients with OPMD (Tome and Fardeau, 1980). With the identification of the responsible gene and gene product (*PABPN1* and PABPN1, respectively), several hypotheses have been advanced regarding the molecular pathogenesis of the disease (Brais et al., 1998).

Despite the clear predominance of muscular pathology in patients with OPMD, several authors have described patients with clinical and pathological evidence of concomitant neuropathy. In one series, 6 of 7 clinically defined OPMD patients were said to have peripheral nerve involvement based on electromyographic findings as well as muscle and sural nerve biopsy (Hardiman et al., 1993). There are other reported similar cases in isolation (Boukriche et al., 2002).

The purpose of this series is to describe the clinical and electrophysiologic findings of an unselected population with clinical or genetic diagnoses of OPMD, and to determine any association with a large-fiber peripheral neuropathy.

2. Methods

Prior to review of clinical records, approval was obtained from the Mayo Institutional Review Board. The Mayo Clinic patient database was searched for patients with a clinical diagnosis of ocu-

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Table 1
Patient characteristics.

Women	10/14 (71.4%)
Age of symptom onset	49.3 years (range 34–60 years)
Symptoms at presentation	
Ptosis	12 (85.7%)
Dysphagia	8 (57.1%)
Proximal limb weakness	4 (28.6%)
Age at EMG	60.6 years (range 39–78 years)
Symptoms and findings at time of NCS/EMG	
Ptosis	14 (100%)
Dysphagia	14 (100%)
Ophthalmoparesis	10 (71.4%)
Symmetric proximal limb weakness	12 (85.7%)
Distal paresthesias	1 (7.1%)
Sensory loss	1 (7.1%)*
Creatine kinase	262 U/L (range 75–877 U/L, $n = 11$)
Family history of ptosis and dysphagia	11 (78.6%) (all occurring in an autosomal dominant pattern)†
Number of *PABPN1* GCG repeats	6/9.9 (mean, $n = 7$, range 9–13)

* This patient had length-dependent sensory loss preceded several years prior by a diagnosis of diabetes mellitus.
† One of the genetically confirmed cases had no suggestive family history. The remaining two were clinically diagnosed patients, and their family history was either unremarkable or not available.

lopharyngeal muscular dystrophy from 1976 to 2004. Clinical, laboratory and pathological data were recorded on all patients who underwent nerve conduction studies and needle electromyography at Mayo Clinic with genetically confirmed or clinical diagnoses of OPMD. Clinically confirmed cases all had progressive, adult onset bilateral ptosis, ophthalmoparesis, and dysphagia with pathologic demonstration of a dystrophic process consistent with OPMD.

Patient information, including relevant clinical, paraclinical, and pathologic data, were recorded.

3. Results

The clinical and genetic features of the 14 patients who met the inclusion criteria are summarized in Table 1. All had progressive ptosis and dysphagia with onset in adulthood, and most had ophthalmoparesis and proximal limb weakness. Seven had genetic testing confirming GCG expansions in the OPMD locus. The limb weakness was uniformly described as symmetric and primarily proximal; no patients had distal-onset weakness or involvement of selected muscle groups such as the deep finger flexors, quadriceps, or foot dorsiflexors. One patient had distal paresthesias, and one other had mild length-dependent multimodal sensory loss in the setting of longstanding diabetes mellitus. Eight patients underwent muscle biopsy (representative findings are demonstrated in Fig. 1).

3.1. Electrodiagnostic findings

All identified patients had nerve conduction studies and needle electromyography performed using standard techniques. Nerve conduction studies were performed using surface electrodes. Skin temperature was recorded on all limb studies, and was higher than 32.0 °C for upper limb studies and 30.0 °C for lower limb studies. Repetitive nerve stimulation studies included three baseline measurements utilizing four supramaximal stimuli at a rate of 2 Hz. Repeat recordings were obtained after one minute of exercise in all cases, up to 3 min after exercise. Needle electromyography was performed with a standard concentric needle. Results of the nerve conduction studies and needle electromyography are summarized in Tables 2 and 3, respectively. Those patients who did not have nerve conduction studies performed in a lower limb had needle electromyography of at least two leg muscles ($n = 2$).

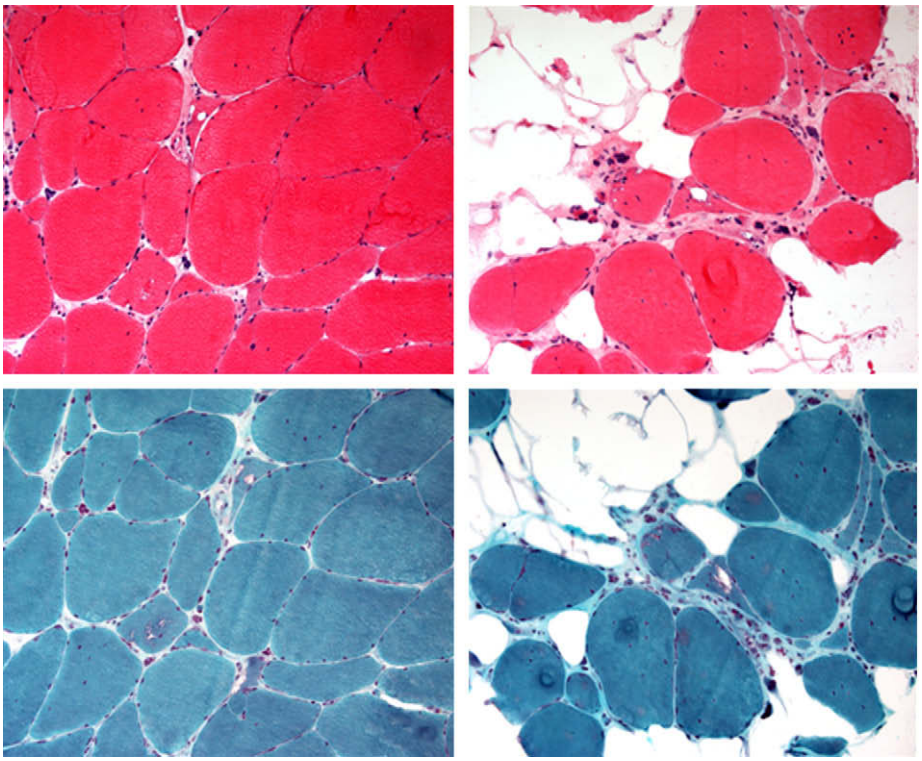

Fig. 1. Hematoxylin and eosin (top) and trichrome stains (bottom), contiguous sections, in a patient with genetically confirmed OPMD (vastus lateralis, clinically mildly weak). Typical features of chronic myopathy are demonstrated, including abnormal fiber size variation, increased numbers of internal nuclei, some angulated fibers, increased amounts of connective tissue elements, and fiber splitting. Rimmed vacuoles are apparent in some fibers.