BLURRING THE LINES BETWEEN OCULOPHARYNGEAL MUSCULAR DYSTROPHY AND OCULOPHARYNGODISTAL MYOPATHY: A CASE REPORT AND LITERATURE REVIEW

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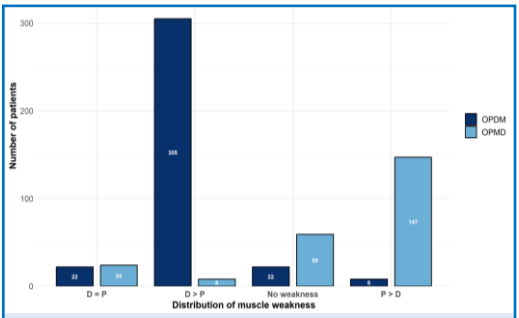
AIMS

Oculopharyngeal muscular dystrophy (OPMD) and Oculopharyngodistal myopathy (OPDM) are adult-onset myopathies characterized by progressive ptosis and dysphagia, typically associated with proximal and distal limb weakness, respectively [1]. We aimed to highlight the nuances of this dichotomy in clinical practice and its diagnostic implications.

RESULTS

A 65-year-old woman presented with a 15-year history of progressive bilateral ptosis and dysphagia. The family pedigree was consistent with an autosomal dominant inheritance pattern, given the occurrence of identical symptoms in her sister, father, paternal grandfather, and a paternal aunt. Muscle strength assessment using the Medical Research Council (MRC) grading system showed bilateral weakness of the extensor digitorum (MRC 4/5). Needle electromyography revealed myopathic signs in the left tibialis anterior and bilateral finger interossei. Direct sequencing of PABPN1 detected a heterozygous GCG triplet expansion from 6 (wild-type) to 9 repeats, leading to the diagnosis of OPMD. Among 1,341 individuals from 125 studies, 9 genetically confirmed OPMD cases with an exclusive or prevalent distal pattern of muscle weakness were identified. Conversely, among the 357 individuals with OPDM in whom PABPN1 mutations were excluded, 8 exhibited a more prominent pattern of proximal muscle weakness.



D: distal limb weakness; **P:** proximal limb weakness.

METHODS

We describe a previously unreported case of OPMD presenting with an atypical distal pattern of muscle weakness. Additionally, we conducted a PubMed literature review, identifying 697 individuals with genetically confirmed OPMD (mean age at diagnosis: 55.8 ± 11.9 years) and 357 individuals with OPDM in whom OPMD was genetically excluded (mean age at diagnosis: 34.9 ± 8.0 years).

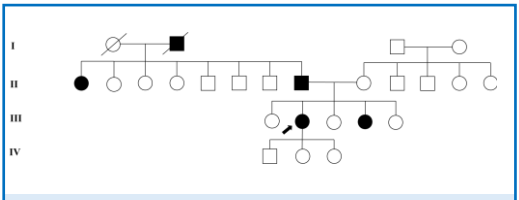


Figure 1. Family pedigree.

Table 1. Comparative summary of our two cohorts.

Clinical findings	OPMD	OPDM
Total n. of patients	697	357
EMG pattern	M 98/138 (71%) Normal 26/138 (19%) N 8/138 /6%) M e N 6/138 (4%)	M 79/94 (84%) Mn 21/94 (8%) N 8/94 (85%) M and N 6/94 (64%)
Initial symptom	P 158/458 (34%) D 147/458 (32%) Op 133/458 (29%) Lw 15/458 (3%) O 5/458 (1%)	P 108/223 (48%) O 58/223 (26%) Dw 30/223 (13%) D 19/223 (8%) Dt 7/223 (3%) Op 6/223 (3%)

D: dysphagia; **Dw:** distal weakness; **Dp:** dysphonia; **Dt:** dysarthria; **M:** myopathic pattern; **Mn:** myotonic discharges; **M and N:** both myopathic and neurogenic; **N:** neurogenic pattern; **O:** other (muscle weakness, fatigue, tired leg, facial atrophy); **Op:** oculopharyngeal; **OPDM:** Oculopharyngodistal myopathy; **OPMD:** Oculopharyngeal muscular dystrophy; **P:** ptosis.

DISCUSSION

Emerging evidence indicates that it is the repeat motifs of the expanded sequences—rather than the altered functions of the genes in which these expansions occur—that play a pivotal role in the underlying disease mechanisms [2]. Notably, the same repeat motif undergoes pathological expansion in both OPMD and OPDM, although in different gene regions: the coding region in OPMD and the 5' untranslated region in OPDM.

CONCLUSION

As highlighted by our case and literature review, the clinical phenotypes of OPMD and OPDM may significantly overlap in practice. Therefore, subjects exhibiting this clinical presentation should be screened not only for the presence of CGG or CCG repeat expansions in LRP12, GIPC1, NOTCH2NLC, RILPL1 (if from East Asia) or ABCD3 (if from Europe)[3], but also for (GCN)n repeat expansion in the PABPN1 gene.

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