CASE REPORT

Late-Onset Development of Eyelid Ptosis in Chronic Progressive External Ophthalmoplegia: A 30-Year Follow-up

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ABSTRACT

Chronic progressive external ophthalmoplegia (CPEO) is a mitochondrial myopathy with slowly progressive, often symmetric blepharoptosis and limitation of ocular motility in all directions of gaze. The authors present an unusual case of CPEO that initially presented with the unique features of markedly asymmetric facial weakness and the lack of blepharoptosis. However, over the subsequent three decades, the patient developed progressive facial and eyelid dysfunction more consistent with a classical description of CPEO. The authors present the 30-year progression of this patient to emphasise the chronic and progressive nature of the condition.

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Chronic progressive external ophthalmoplegia (CPEO) is a mitochondrial myopathy with slowly progressive, often symmetric blepharoptosis and limitation of ocular motility in all directions of gaze.¹ CPEO without ptosis is extremely unusual, with only two reports in the English medical literature.^{2,3} One of these cases was originally presented in 1985 with the unique features of markedly asymmetric facial weakness and the lack of blepharoptosis.² Despite this unusual presentation, the diagnosis of CPEO was confirmed with peripheral muscle biopsy. Over the next three decades, however, this patient has developed progressive facial and eyelid dysfunction that is more consistent with a classical description of CPEO. We present the 30-year follow-up of this patient to emphasise the chronic and progressive nature of the condition.

Case presentation

In 1985, a then 33-year-old male presented with a 15-year history of slowly progressive right-sided weakness of the upper and lower face, ophthalmoplegia

with diplopia, and omnidirectional slowing of saccadic eye movements.² The diagnosis of CPEO was eventually made and supported with a peripheral muscle biopsy that showed ragged red fibres. This case was described as an unusual presentation of CPEO due to the lack of eyelid ptosis and the asymmetric facial weakness. Over the subsequent 25 years of consistent routine follow-up examinations, the patient was noted to have slow progression of his right-sided hemifacial weakness with the development of right midface decent, paralytic ectropion of the lower eyelid, and brow ptosis. His ophthalmoplegia and diplopia remained stable, with motility severely limited in all directions of gaze and no Bell's phenomenon in both eyes. At the age of 58 years, the patient was first noted to have developed right-sided blepharoptosis with poor levator function (Figure 1). The ptosis progressed over the next 5 years after onset, with most recent examination in 2015 showing a margin reflex distance of 0.5 mm and levator excursion of <5 mm. Due to the facial weakness, the patient has also developed significant lagophthalmos and exposure keratopathy that required surgical correction with horizontal eyelid tightening and midface elevation with a facial sling (Figure 2). The left side

Figure 1. Patient at 58 years of age with asymmetric right hemifacial weakness and ptosis of the right upper eyelid.

Figure 2. Despite the presence of upper eyelid ptosis, lagophthalmos and exposure keratopathy are present due to weakness of the orbicularis oculi muscle on the right side.

of the face has remained unaffected throughout the clinical course. He has not developed any systemic manifestations of mitochondrial DNA mutations, including cardiac, respiratory, gastrointestinal, or endocrine disease, peripheral myopathy, or neurologic deficits other than those described.

Discussion

Originally described by von Graefe in the mid-19th century, CPEO is a mitochondrial myopathy

with slowly progressive, often symmetric blepharoptosis and limitation of ocular motility in all directions of gaze.¹ Eyelid ptosis is the most common presenting finding in CPEO, and the levator palpebrae is usually severely affected with minimal functionality, whereas the frontalis muscle function of the forehead is often preserved.⁴ Although asymmetry of facial weakness and ophthalmoplegia are common, unilateral ptosis is a rare finding.^{5,6} CPEO without ptosis is extremely unusual, with only two reports in the English medical literature, one of which was the original publication of this current case.^{2,3}

Although our patient initially presented with an external ophthalmoplegia that spared the levator palpebrae muscle, he eventually developed all of the classic findings of CPEO 25 years after his initial presentation. His ptosis is most likely the result of his mitochondrial myopathy given the associated poor levator function, whereas age-related eyelid ptosis is usually associated with good levator function. Prior to this current follow-up report, only one additional case of CPEO with asymmetric ophthalmoplegia and facial weakness without ptosis has been published.³ However, that patient was followed for only 6 years to the age of 43 years, and she may have subsequently developed ptosis given that our patient did not develop eyelid ptosis until 58 years of age. Other reports have documented progression of symptoms for up to 50 years.⁷ This emphasises the importance of long-term follow-up and care of patients with CPEO. The previously reported case also underwent mitochondrial DNA testing that showed a deletion spanning the ATPase 6 gene and ND5 gene.³ Our patient did not undergo genetic testing; however, DNA testing may be a useful adjunct to such cases to determine if the severity of the clinical course can be correlated to genotype.

Even though eyelid ptosis is the most common presenting finding in CPEO, some patients may present for evaluation prior to the development of ptosis. This case demonstrates a unique temporal presentation of CPEO with asymmetric facial palsy and late-onset ptosis that developed decades later. Practitioners should consider CPEO when any progressive symptoms of facial palsy, eyelid ptosis, and ophthalmoplegia occur, whether alone or in combination, and continue close observation for delayed manifestations of the disorder.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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