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Chronic progressive external ophthalmoplegia is an inherited or sporadic form of dystrophy that preferentially affects the extraocular muscles of the eye. While this dystrophy can manifest systemically, the extraocular muscles are commonly involved due to their constant metabolic demands and vulnerability to oxidative stress.[1] This preferential involvement of the eyelid levator muscle and extraocular muscles makes CPEO an important condition to consider in a differential diagnosis for eyelid asymmetry and double vision among other conditions such as myasthenia gravis, thyroid-associated ophthalmoplegia, and other mitochondrial myopathies.[2] This dystrophy tends to occur in the third or fourth decade of life. Nearly 60% of cases are de novo and occur due to mitochondrial DNA deletions; less commonly, this dystrophy can be inherited in an autosomal dominant or recessive fashion.[2–4]

Symptoms of CPEO develop over the course of several years, differentiating it from other acute or subacute forms of ophthalmoplegia.[2,3,5] The most common ocular manifestation of CPEO is ptosis, however non-ocular manifestations such as dysphagia or sensorineural hearing loss may also be present. CPEO can lead to diplopia, however, given typical bilateral involvement of the extraocular muscles, patients may also not notice their due to gradual symmetric progression of disease until their function is more severely impaired.[3,6]

When CPEO is associated with characteristic systemic findings, it is referred to as CPEO-plus syndrome. In addition to ophthalmoplegia, CPEO plus syndrome may include systemic changes such as retinal pigmentary changes, cardiac conduction disorders, endocrine disorders. ataxia, tremor, polyneuropathy, and dementia.[7] The differential diagnosis for CPEO-plus syndrome primarily includes oculopharyngeal muscular dystrophy (OPMD), which is an autosomal dominant inherited myopathy.[8] In addition to the symptoms of ptosis and ophthalmoplegia seen in CPEO, OPMD manifests with weakness of the pharyngeal muscles, leading to dysphagia, weakness of the orbicularis oculi muscles, contributing to difficulty with forceful eye closure and weakness of the proximal limbs.[2,3] The pathophysiology is not well understood, but it is hypothesized that pathologic GCG trinucleotide repeat expansions in a gene encoding polyalanine-alanine binding protein leads to failure of muscle regeneration.[7] This disorder is most commonly seen in patients of French-

Canadian descent and typically presents in the fifth decade of life.[2,3]

Kearns-Sayre syndrome (KSS) is another disease on the differential diagnosis for CPEO-plus syndrome with a younger age of onset more commonly seen before the age of 20.8 Patients with Kearns-Sayre syndrome present with pigment retinopathy and progressive loss of peripheral and night vision.[3] Other manifestations of the disease include cardiac issues and cerebellar ataxia.[2,8] Therefore a thorough cardiac and neurologic work-up is crucial if this condition is suspected.[8]

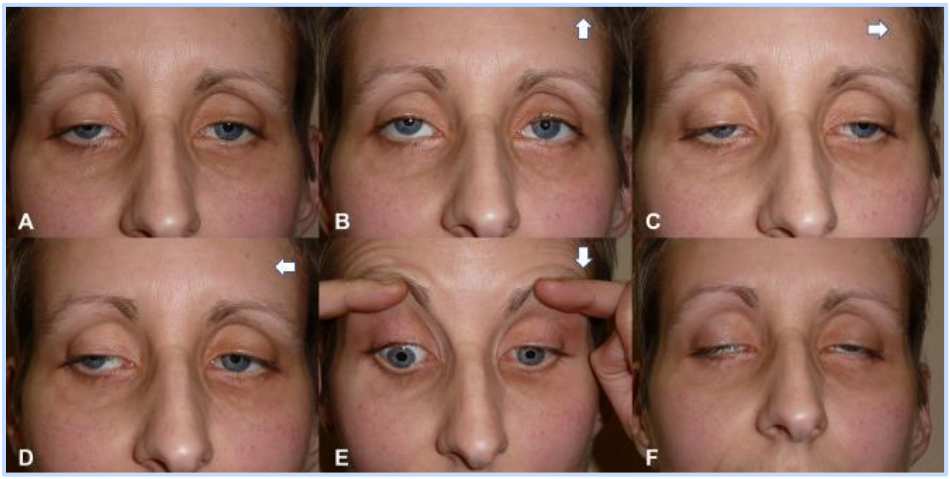

Figure 1: Patient with Chronic Progressive External Ophthalmoplegia (A) Bilateral Ptosis (B-E) Ophthalmoplegia in all directions (F) Orbicularis Oculi weakness[12]

The management of CPEO is largely dependent on patient symptoms. Surgical repair of ptosis may be indicated based on severity. In situations where the levator palpebrae superioris still maintains moderate to good function, procedures such as external levator advancement or resection may be performed.[3,2,10] However, it is common for levator function to deteriorate progressively, leading to the need for further surgery and reoperation. In cases where levator function is poor, an eyelid suspension maneuver may be necessary, connecting the eyelid to the frontalis muscle using either autogenous or synthetic sling material.[2,3,10]

Overcorrection of ptosis can lead to complications with corneal exposure and lagophthalmos.[2,10] In order to prevent this overcorrection and decrease the chance of corneal exposure, a proposed surgical technique includes a palpebral fissure transfer with lower eyelid elevation and no spacer.[11] For symptomatic diplopia, prism lenses may be used as a nonsurgical option. These can be incorporated into the patient's glasses prescription to improve diplopia by refracting light to align where the image projects onto the macula, compensating for the ocular deviation.[3] If deemed appropriate strabismus surgery can be considered, but progressive deterioration in extraocular muscle function can lead to recurrence of diplopia.[3]

Overall, CPEO describes an assortment of myopathies affecting the extraocular muscles with varied presentations. CPEO may be difficult to diagnosis, so it is important to consider it in

the differential diagnosis for ptosis and ophthalmoplegia.

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