Full title: Recurrent ptosis in an adult due to isolated paresis of the levator palpebrae superioris and Müller's muscle of unknown aetiology

Short title: Recurrent ptosis

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Abstract:

We report on the case of a middle aged woman who suffers from recurrent right sided ptosis. The ptosis is always complete with preserved ocular motility. Full recovery is the rule. The involvement of both the Müller's muscle and levator palpebrae superioris is demonstrated clinically, pharmacologically and by high resolution magnetic resonance imaging. The results presented point towards a local pathology of the lid surface anatomy, the etiology however remains unknown.

Key words: ptosis, levator palpebrae superioris, Müller, Mueller.

Case report

We report on a 41 old Greek Cypriot woman who suffers from recurrent right sided ptosis. The onset of the ptosis is gradual over several hours and there is some soreness below the right brow at the same time. These attacks occur approximately every three to six months and last for about ten days. The ptosis is always complete (figure 1, right). Complete recovery is the rule (figure 1, left). She has never experienced any diplopia, speech or swallowing disturbance or limb weakness. She does not wear contact lenses. Her past medical history includes asthma but no autoimmune diseases. She is an occasional smoker and drinks a little alcohol.

The first attack occurred in 1996. At this time the diagnosis of myasthenia gravis was made. A treatment trial with mestinon had no effect. She was also treated with prednisolone for a year. During that time the attacks were less frequent but continued.

During an attack on examination levator function is absent, but eye movements and pupils are equal with normal reactions to light and accommodation. Some lid opening can be achieved by activation of the frontalis muscle (figure 1 top right). Inactivation of the frontalis disables all lid elevation. On downgaze the lid surface is entirely smooth suggestive of the absence of any muscular activity by either Müller's muscle or levator palpebrae superioris (figure 1 bottom right). The right lid margin is lower than the left in extreme downgaze, which also points towards the involvement of Müller's muscle. After adrenergic stimulation with phenylephrine 10% no muscular activity could be observed. All other cranial nerves are entirely normal. There is no

sensory deficit and the motor examination is normal without fatigue.

Nerve conduction studies, repetitive stimulation and electromyography including single fibre studies of the facial muscles are all within normal limits. The edrophonium test was negative. Serology, acetylcholine-, voltage-gated calcium-, MG striated-, thyroid- and gangliosides- (GM1, GD1a, GT1b, GQ1b, sulfatides) antibodies are all negative. There is a slight microcytic, hypochromic anemia with a Hb of 9.2 g/dL, MCV 67.2 fl, MCH 20.4 pg. The ESR during an attack was raised to 36 mm/h and the CRP to 12 g/L.

[Figure 1 about here]

High resolution magnetic resonance imaging of the brain and orbits with surface coils and gadolinium-DPTA enhancement did not reveal any abnormality. In the orbit there was increased signal from the right levator palpebrae superioris on several coronal and axial T2-weighted images which also appeared enlarged (figure 2 showing levator palpebrae/superior rectus complex larger).

[Figure 2 about here]

Discussion

This interesting presentation with involvement of Müller's muscle and the levator palpebrae superioris but normal ocular motility is suggestive of local pathology restricted to the surface anatomy of the upper lid.

Eyelid retraction is primarily achieved by contraction of the slow twitch fibres of the levator palpebrae superioris muscle (LPS) [1]. Two transverse ligaments are related to the LPS. The Whitnall's ligament crosses over the LPS at a distance of about 12 mm from the superior posterior tarsal border. The intermuscular transverse ligament underlies the LPS about 3 mm posterior to Whitnall's ligament. Both ligaments form together a sleeve of fibroelastic and fibromuscular tissues superior and inferior to the LPS near its musculotendinous junction [2]. They synergistically assist the LPS in its activity. Beyond Whitnall's ligament the LPS becomes tendinous and is intertwined with smooth muscle fibres from the superior tarsal or Müller's muscle. Contraction of Müller's muscle alone raises the upper eyelid by about 1.5 mm [3]. The levator palpebrae superioris is innervated by the superior branch of the oculomotor nerve. Müller's muscle is innervated by sympathetic fibres originating from the ganglion cervicale superius.

The lower or anterior tarsus is only 3.5 - 5 mm high at the center of the lower lid. Clinically muscle activity is observed above the lower tarsus by lid elevation of increased wrinkling of the skin. Smoothness of the skin is suggestive of paresis of both the LPS and the Müller's muscle. Adrenergic stimulation (e.g. Phenylephrine

10%) is required to confirm involvement of Müller's muscle. Any defect previous to the neuromuscular junction would result in muscular activity. Thus in the reported case the defect must be within the neuromuscular junction or within the muscle itself.

Additional evidence for a myopathic etiology is derived from the MRI findings. In several axial and coronal sections of the orbit an increased T2 signal is seen for the upper part of the right superior rectus muscle. Figure 2 shows the coronal MRI of the orbit. Müller's muscle and levator palpebrae superioris are located at the upper part of the superior rectus muscle (see figure 2). There is also evidence for enlargement of the right lid retractor muscles on axial and coronal sections. The interpretation of contrast enhancement in the extraocular muscles is problematic as extraocular muscles always show contrast enhancement owing to their loose capillary network. Rice and Gray (1988) however suggested enhancement of LPS on CT as one criteria of levator myositis [4].

In our patient the clinical examination, adrenergic stimulation, electromyography and high resolution magnetic resonance imaging are highly suggestive of an isolated and recurrent myogenic paresis of the right LPS and Müller's muscle. This condition has to our knowledge not been reported before.

The differential diagnosis of myopathic conditions of the eye includes myasthenia gravis, local infiltration, microvascular pathology, myositis and mitochondrial cytopathies. However, which of these conditions could give rise to the paroxysmal phenomenon observed in this case? Snead et al. (1991) reported a patient who

presented with isolated ptosis from noncaseating granulomas of the levator palpebrae due to sarcoidosis [5]. Gonnering and Sonneland (1986) described a patient with occult primary systemic amyloidosis who presented with ptosis and dermatochalasis [6]. Selective affection of the levator palpebrae has been observed in lymphoid infiltration and idiopathic inflammatory disease of the orbit. Patients with diabetes mellitus may develop ptosis in association with microangiopathic changes. Recurrent orbital myositis of acute onset with diplopia has been published [7] and there is now some evidence for genetic involvement [8]. Rice and Gray have described a patient with isolated levator myositis, which presented with incomplete ptosis and symmetrical lid crease [4]. There is evidence of restriction as well as paresis because lid descent on downgaze was also impaired. Restriction is common in myositis of extraocular muscles and not seen at all in our case. Rice's patient responded within two weeks to prednisolone treatment. There was no relapse. We know of no other case of an isolated ptosis which spontaneously relapses and remits, as ours has done, due to any of the above diseases.

We suggest a recurrent myogenic paresis of unknown aetiology with selective involvement of the levator palpebrae and Müller's muscle in this case.

Figure 1: A 41 year old patient with recurrent right sided ptosis. On the right the patient is shown during an attack and on the left during recovery. On the top row the patient is shown in upgaze, in the middle row in primary position and on the bottom row in downgaze. Note the missing crease on the upper tarsal part of the eyelid indicating loss of function of Müller's muscle as well as the levator palpebrae superioris. There is no ``upside-down ptosis'' of the lower lid. Also the fact that the right lid is lower in extreme downgaze indicates involvement of the Müller's muscle. In top right image frontalis has not been disabled and the small amount of lid movement is entirely due to frontalis activation.

Figure 2: T2 weighted MRI of the extraocular muscles. The coronal slide shows an enlarged superior palpebrae muscle which is adjacent to and immediately above the superior rectus. Comparison of serial axial slides confirms muscular enlargement on the right side.

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