Malaria-induced ptosis

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ABSTRACT

Purpose: This study reports two cases of malaria-induced ptosis with surgical resolution.
Observations: Case 1 is a 27-year-old female with a past medical history of bilateral ptosis following childhood malaria. Case 2 is a 63-year-old male with left-side ptosis following adult-onset malaria. Both patients required revision surgery but ultimately did well after surgical correction.
Conclusions and importance: Malaria-induced ptosis is a rare entity that should be suspected in patients presenting with ptosis following infection and treatment of malaria. It is unknown if the patients' malaria results from malarial infection, antimalarial treatment, or a combination of both. Surgical correction is the mainstay of treatment.

1. Introduction

Blepharoptosis most commonly arises from myogenic, involutional, neurogenic, mechanical, traumatic, and congenital causes.[1] Less commonly, ptosis has been documented to arise from infectious sources. This study presents two cases of patients with malaria-induced ptosis.

2. Case reports

2.1. Case 1

A 27-year-old female was referred for evaluation of painless bilateral ptosis that occurred following an episode of childhood malaria. Her eyelids were in a normal position before developing an acute episode of malaria during childhood. The ptosis was visually significant and required her to adopt a chin-up head position. She denied diplopia and systemic weakness. Her family history was negative for ptosis or other ocular or systemic disease. Ocular history included refractive ambly-opia. Past medical history was negative for neurological disease, and a review of systems was negative.

An ophthalmologic exam revealed a visual acuity of 20/50 in the right eye (oculus dextrus - OD) and 20/60 in the left eye (oculus sinister - OS). Pupils were equally round, briskly reactive, and 4 mm in room lighting in both eyes (oculus uterque - OU). Extraocular movements revealed a −1 deficit in the superior temporal directions bilaterally. An external exam revealed bilateral ptosis with marginal reflex distance 1

(MRD1) of −2 mm right upper eyelid and −3 mm left upper eyelid (Fig. 1). Eyelid excursion was 7 mm in the right upper lid and 8 mm in the left upper lid with normal fornices and no lagophthalmos of either eye. Each eyelid had an upper lid crease that was present but effaced. There was no response following the administration of 10% phenyl-ephrine to the right eye. Eversion of the eyelids showed no scarring. A corneal exam revealed superior circular scars at the limbus with pitting OU. All other slit lamp exam (SLE) findings were unremarkable. The fundoscopic exam was unremarkable. The Humphrey visual field revealed obscuration of the superior visual fields that resolved when the lids were manually elevated to a normal position.

The patient elected to undergo bilateral upper eyelid external levator advancement four months later. Although this procedure improved the ptosis in both eyes, the patient had residual ptosis with a marginal reflex distance (MRD) of zero and elected to undergo bilateral silicone frontalis sling placement two years later. At her one-month surgical follow-up, she reported symptom improvement and denied any eye pain. Examination revealed a marginal reflex distance of +1, which increased to +4 with brow activation, good lid symmetry, and no lagophthalmos (Fig. 1).

2.2. Case 2

A 63-year-old male was referred for severe ptosis of the left upper eyelid. The ptosis began in 2012 after a hospitalization for malaria in Cameroon, during which he was treated with chloroquine. He described needing restraints to prevent him from rubbing his left eye during his

Fig. 1. A 27-year-old female with bilateral malaria-induced ptosis, preoperatively (top). Postoperative photo shows the eyelid position following frontalis sling surgery (bottom).

hospitalization. The patient denied diplopia, floaters, and orbital trauma.

Family history was negative for ptosis or other ocular or systemic disease. Ocular history was negative. Past medical history was positive for human immunodeficiency virus (HIV) and impaired glucose tolerance. The review of systems was negative.

An ophthalmologic exam revealed a visual acuity of 20/25 OU. Intraocular pressure was 15 mm Hg OD and 16 mm Hg OS. Pupils were equally round, prompt, and 3 mm in room lighting OU. Extraocular movements were full. Perimetry demonstrated a visual field defect inferior to the horizontal meridian with >50° improvement when the eyelid was manually raised to a normal position in the left eye.

An external examination revealed a 5 mm left upper eyelid ptosis with an MRD1 of −3 mm. Lid excursion was 10 mm right upper eyelid

Fig. 2. A 63-year-old male with unilateral malaria-induced ptosis, preoperatively (top). Postoperative photo shows the eyelid position following frontalis sling surgery (bottom).

and 3 mm left upper eyelid with normal fornices and no lagophthalmos OU (Fig. 2). Eyelid creases were present and symmetrical, but the left eyelid crease was effaced. The patient used his frontalis muscle to elevate the left eyelid. The remainder of the eye exam was unremarkable.

Evaluation for the patient's myogenic ptosis included cranial magnetic resonance imaging (MRI) scanning, myasthenia gravis antibody, and ice pack testing, all of which were negative.

The patient elected to undergo frontalis sling surgery of his left eyelid five months later. At the one month follow-up, the MRD1 was +4.5 mm right upper eyelid, and +3 mm left upper eyelid with maximum frontalis use and no lagophthalmos. The patient elected to undergo frontalis sling revision surgery three months later. At the one-month follow-up, the MRD1 was +3 mm right upper eyelid and +4 mm left upper eyelid with good frontalis activation and trace lagophthalmos (Fig. 2).

3. Discussion

There are numerous causes for acquired ptosis, including myogenic ptosis, chronic progressive external ophthalmoplegia, myasthenia gravis, and third nerve palsy. We are aware of a single case of malaria-induced ptosis in the medical literature.[3] This report expands our knowledge about the clinical features and surgical management of malaria-induced ptosis.

Numerous malaria cases associated with skeletal muscle weakness, pain, and in severe cases, myoglobinuria, have been documented.[4] The characteristic histopathological finding of *Plasmodium falciparum* infection is cytoadherence of parasitized erythrocytes to the microvasculature and has been documented to occur in the central nervous system and retina.[5–7] The primary pathogenic mechanism in malaria-induced myopathy is reduced skeletal muscle perfusion due to microvascular obstruction of parasitized red blood cells.[8,9] This leads to decreased oxygen delivery and decreased waste product removal.[8,9]

Mauro and Brotto postulate that the combination of ischemia, inflammation, and oxidative stress contributes to this myopathy.[8] Damaged fibers release higher amounts of creatine kinase, myoglobin, and other contractile proteins into the bloodstream, which support the muscle weakness and fatigue observed in malaria patients.[8] The infectious state leads to increased cytokine levels and free radicals, which could further contribute to skeletal muscle damage.[8]

A single case of malaria-induced ptosis exists in the literature.[3] Dass et al. describe ptosis in one of 162 cases of pediatric malaria in northeast India.[3] The authors hypothesize the ptosis resulted from pathogenically similar microvascular cytoadherence of parasitized erythrocytes in the vasa nervosa of the third cranial nerve.[3] In another study, Beare et al. describe pediatric cerebral malaria cases presenting with papilledema.[5] Using laser Doppler flowmetry, they found higher microvascular blood volumes at the optic nerve head in patients with papilledema, which suggests blood flow stasis.[5] Therefore, malaria-induced ptosis could arise from erythrocyte sequestration in the vasa vasorum, occluding venous drainage, thereby promoting stasis and causing hypoxic damage to specific nerve fibers associated with eyelid elevation.

It is unknown if treatment was a component of our patients' ptosis. Hydroxychloroquine (HCQ) and chloroquine (CQ) are mainstays of antimalarial treatment, and chloroquine treatment remains one of the most common monotherapy interventions in sub-Saharan Africa.[10] HCQ and CQ are nearly identical in structure, and as a result, both drugs have comparable pharmacokinetics, pharmacodynamics, and metabolism.[11] The side effect profile of chloroquine at high doses includes neuromyopathy, a myasthenia-like syndrome, retinopathy, QT_C prolongation, and extrapyramidal disorders.[10]

Chloroquine-induced neuromyopathy is characterized by progressive weakness and proximal muscle atrophy.[12] Chloroquine affects the pre-synaptic and post-synaptic neuromuscular transmission, which promotes the muscular weakness seen in malaria patients.[10] Typical microscopic features of antimalarial-induced myopathy include rimmed

vacuoles in skeletal muscle fibers.[13–15] Neuromyopathy typically appears in patients after long term use (≥1 year) and reverses within several months after cessation.[10] However, it is possible that our patients may have had experienced a rare side effect of prolonged neuromyopathy as a result of antimalarial therapy, despite a shorter duration of treatment.

Bedu-Addo describes the case of a four-year-old boy who was diagnosed and treated for malaria with chloroquine with an initial dose of 10 mg/kg followed by 5 mg/kg every 6 h for two days. The day after starting chloroquine, the boy developed bilateral partial-pupillary sparring ptosis. Upon chloroquine cessation, the boy's ptosis improved within 24 hours and completely resolved within 48 hours.[10]

4. Conclusion

The cases presented herein highlight a rare entity of malaria-induced ptosis, which should be suspected in patients presenting with ptosis following infection and treatment of malaria. Malaria-induced ptosis appears to be a severe myopathic ptosis requiring frontalis sling correction in both cases described here.

Research ethics

This study was exempt from Institutional Review Board (IRB) approval.

Written consent to publish the case report was obtained from the patients. This report does not contain any personal information that could lead to patient identification.

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Conflict of interest disclosure

The authors have no relevant conflicts of interest to declare.

Authorship

All authors attest that they meet the current *International Committee of Medical Journal Editors* (ICMJE) criteria for Authorship.

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