case differs from previous reports in that the hemorrhages appeared in a circumferential pattern along the neovascular ridge, similar in appearance to a beaded necklace.

The exact mechanism of the retinal hemorrhages is not fully understood; however, it may be related to changes in intraocular pressure (IOP) during scleral depression, which may damage the immature pathologic vessels seen in babies with ROP. Immature retinal vasculature is relatively fragile because of a lack of structural support from smooth muscle, collagen, pericytes, and elastin, making it more susceptible to rupture.[6] An immature autoregulatory system in preterm babies may further predispose to ischemia and hemorrhage.[7]

The baby in this report was treated with intravitreal bevacizumab 2 weeks prior to the incident, further differentiating this case from previous reports. One might have expected the vascular endothelial growth factor inhibitor to lower the risk of bleeding in this baby, because it causes regression of neovascularization. It is possible, though, that the bevacizumab increased the fragility of the vessels. We speculate that this bleeding was caused by the trauma of the examination, which also may have been exacerbated by pressure from the lid speculum and RetCam. A very high IOP during repeat scleral depression, followed by release of that tension could have caused the hemorrhages.

Physicians performing ROP examinations should be aware of the possibility of causing retinal hemorrhages with scleral depression and proceed with appropriate caution. The retinal hemorrhages resolved spontaneously in all reported cases, including the current case. To the best of our knowledge, examination-induced retinal hemorrhages in children have never been reported in the absence of active ROP.

Literature Search

PubMed was searched on November 5, 2018, without date restriction, for English-language records using the following terms: *retinal hemorrhages* AND *scleral depression*.

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Exophthalmos in Kearns-Sayre syndrome

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Kearns-Sayre syndrome (KSS) is a rare mitochondrial DNA (mtDNA) deletion syndrome that typically presents before 20 years of age and is characterized by chronic progressive external ophthalmoplegia, pigmentary retinopathy, and a combination of cardiac conduction defects, cerebellar ataxia, and elevated cerebrospinal fluid protein levels. The mtDNA defects interfere with oxidative phosphorylation and can affect a number of cellular energy processes in various organs. We report the case of a 15-year-old girl with KSS that was uniquely associated with bilateral, symmetrical exophthalmos.

Case Report

A 15-year-old girl presented emergently at Montefiore Medical Center with bilateral eye pain. She was in the United States from the Caribbean visiting relatives, who noted more pronounced proptosis and ptosis than they recalled seeing several years before. The patient reported that these features had progressed gradually over 4 years' time, but pain began only 1 month prior to presentation. She had no known relevant medical or developmental history, and there was no relevant family history.

On examination, visual acuity was 20/30 in the right eye and 20/25 in the left eye. The examination was significant for bilateral ophthalmoplegia (Figure 1), exophthalmos (27 mm in each eye by Hertel exophthalmometer), ptosis (right eye, MRD1 −3; left eye, MRD1 −2), and a lack of diplopia. Alternate cover testing did not reveal any movement because of the ophthalmoplegia; however, exotropia of approximately 30^{Δ} in primary gaze was measured by Hirschberg testing. On slit-lamp examination, there was no conjunctival injection or chemosis. No corneal microcysts were present; however, there were 1+ punctate epithelial erosions over the inferior cornea bilaterally. Dilated fundus examination disclosed bilateral pigmentary retinopathy. Magnetic resonance imaging of the brain and orbits revealed global cerebral and cerebellar volume loss,

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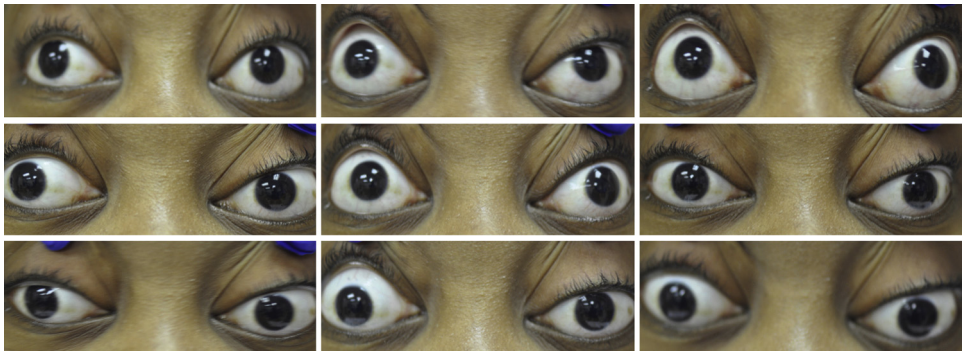

FIG 1. External photographs demonstrate bilateral proptosis, exotropia in primary gaze, and severe motility restriction with all directions of gaze.

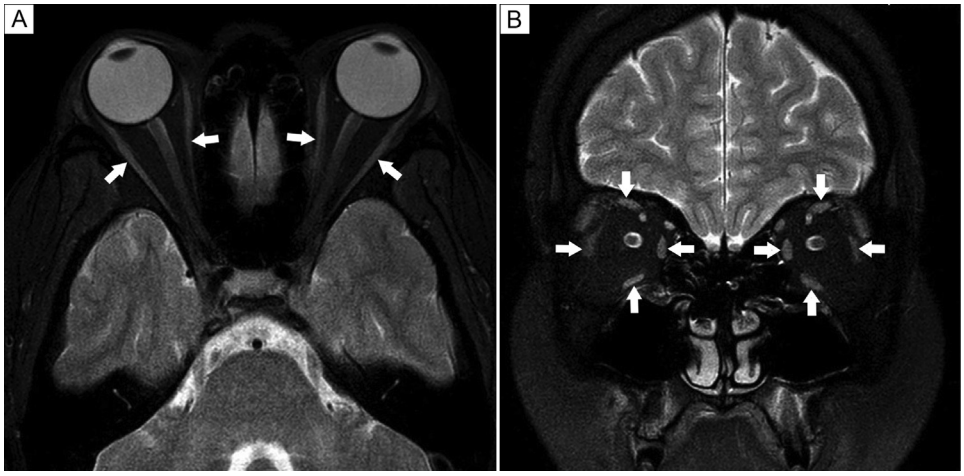

FIG 2. Magnetic resonance imaging of the brain and orbits showing significant atrophy of all extraocular muscles: axial (A) and coronal (B) views.

bilateral proptosis, and thinning of all extraocular muscles (Figure 2). In the emergency room, she was found to be bradycardic, with a heart rate of 40-50 beats per minute; the subsequent electrocardiogram revealed intermittent episodes of third-degree heart block. Laboratory workup was negative for thyroid disease (T3, free T4, TSH, TBII, anti-TPO, TSI, thyroglobulin), myasthenia gravis (acetylcholine receptor antibodies, MuSK antibody test), underlying inflammatory disorders (ESR, CRP), and diabetes mellitus (hemoglobin A1c).

Based on clinical ophthalmologic and cardiac findings, a provisional diagnosis of Kearns-Sayre syndrome (KSS) was made. The patient was referred to neurology and medical genetics, and cardiology continued to follow her. Neurologic examination revealed an abnormal Romberg test and difficulty completing a heel-to-toe walk. Within 1 week of presentation, the patient underwent urgent cardiac intervention, and a dual chamber pacemaker was implanted. Results of a combined mitochondrial genome plus mitochondrial focused nuclear gene panel (Test Code 615; *GeneDx*, Gaithersburg, MD) revealed a 4.9kb mitochondrial genome deletion encompassing genes *MTND3*, *MTTR*, *MTND4L*, *MTND4*, *MTTH*, *MTTS2*, *MTTL2*, *MTND5*, *MTND6*, *MTTE*, and *MTCYB* of the mitochondrial genome, consistent with KSS.

The patient has remained stable since undergoing pacemaker implantation. Due to ongoing tearing and discomfort caused by ptosis and proptosis, the patient and her family are considering surgical repair by oculoplastics.

Discussion

KSS is a rare mtDNA deletion syndrome affecting 1-3 per 100,000 individuals.[1] Because oxidative phosphorylation is impaired, reduced energy production affects individuals systemically and heterogeneously. The condition can result in myopathy, sensorineural hearing loss, endocrinopathy, and renal dysfunction, among other manifestations (OMIM #530000).

KSS was suspected in this patient with ophthalmoplegia, ptosis, retinopathy, sensory ataxia, and heart block; however, the presence of bilateral exophthalmos was initially confounding. Although blood work alone does not rule out a diagnosis of juvenile myasthenia gravis, gold standard

testing with single muscle nerve fiber electromyography was not required in this particular case because of subsequent testing. Additionally, thyroid eye disease would not provide a unifying diagnosis for the patient's other ocular or systemic findings. When the thyroid workup was negative and results from genetic testing were obtained, the patient's exophthalmos was determined to be an atypical manifestation of KSS.

Ophthalmic involvement in mitochondrial disease is well described,[2] yet chronic progressive external ophthalmoplegia (CPEO) with exophthalmos has only been described in one other report.[3] Differential diagnosis for proptosis includes inflammatory, vascular, infectious, cystic, neoplastic, and traumatic factors, all of which were excluded in our patient. CPEO usually presents with ptosis, progressing to weakness and eventual complete paralysis of extraocular muscles. Maeda and Idehara[3] presented an unusual case of exophthalmos in CPEO, although this patient did not have a pigmentary retinopathy. As in our patient, thyroid disease was ruled out, and imaging showed atrophic extraocular muscles. The authors suggested that exophthalmos might be secondary to advanced loss of support by extraocular muscles. Per our patient's history, ophthalmoplegia began at least 4 years before she sought care, and thus, such an explanation is plausible in her case.[3]

Although muscle biopsy typically confirms the diagnosis of KSS, noninvasive genetic testing was pursued in our patient because of the increased risk of adverse reaction to anesthesia associated with mitochondrial disorders.[4] 96% of mitochondrial DNA deletions in KSS are sporadic. Maternal transmission, however, has been reported, and it is therefore important to examine an affected individual's mother for clinical or genetic manifestations of disease.[5]

To our knowledge, this is the first patient with KSS to present with bilateral exophthalmos with the classic findings of CPEO, pigmentary retinopathy, sensory ataxia, and heart block. We hypothesize that exophthalmos may be a finding in late presentations of KSS because of decreased globe support by atrophic extraocular muscles. Our findings contradict the commonly accepted notion that significant pain, proptosis, or pupil involvement are not associated with CPEO, although such findings should still prompt evaluation for alternative etiologies. Because of the systemic nature of this genetic condition, it is imperative to involve a multidisciplinary team of providers in KSS patients' care. If an ophthalmologist suspects such a diagnosis, an EKG and thorough cardiac examination must be prioritized, because cardiac involvement may be life threatening. Although there is currently no cure, early diagnosis can facilitate optimal management of systemic disease manifestations and may reduce patient morbidity and mortality.

Literature Search

PubMed was searched on December 13, 2018, without date or language restriction, using the following terms singly or in combination: *Kearns-Sayre syndrome*, *exophthalmos*, *proptosis*, *chronic progressive external ophthalmoplegia*.

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Congenital glycosylation disorder: a novel presentation of coexisting anterior and posterior segment pathology and its implications in pediatric cataract management

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We report a case exhibiting the coexistence of anterior and posterior segment pathology in the same eye secondary to a congenital disorder of glycosylation resulting from a *DPAGT1* gene mutation. This case details a novel gene mutation in a male infant found to have bilateral congenital cataracts, removed at 6 and 7 weeks of life, only to uncover bilateral retinal and optic atrophy. Our report highlights issues of surgical timing for syndrome-related pediatric cataracts, given the risks related to secondary glaucoma versus deprivation amblyopia, in an infant born with both cataracts and vision-limiting posterior segment pathology.

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