Severe congenital bilateral corneal ulceration due to Wolf-Hirschhorn syndrome: a case-report and review of the ophthalmic literature

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A newborn boy with genetically confirmed Wolf-Hirschhorn syndrome presented with severe bilateral corneal ulceration that required emergency surgical tarsorrhaphies and permanent lower punctal occlusion. The patient healed completely, with no recurrence over 18 months of follow-up.

Wolf-Hirschhorn syndrome (WHS) is a rare chromosomal abnormality first described in 1965 independently by Wolf and colleauges[1] and Hirschhorn and Firschein,[2] caused by partial deletion of the short arm of chromosome 4. The main clinical features of WHS include growth retardation, seizures, craniofacial anomalies ("Greek warrior helmet" facies), microcephaly, ocular abnormalities, sensorineural hearing loss, cardiac anomalies, and renal abnormalities. Ophthalmic manifestations are present in approximately 30% of cases (see Table 1).[3] We report a severe case of WHS with bilateral corneal ulceration requiring surgical intervention.

Case Report

Following intrauterine growth retardation and suspected oesophageal atresia at the 20-week prenatal ultrasound, a prenatal amniocentesis performed at 26 weeks revealed a large chromosome 4p deletion, confirming WHS. The boy was born at 38 weeks' gestational age by induced labor and weighed 1780 g. At 5 days of age the neonatologists at the Royal Berkshire Hospital noticed bilateral large corneal ulcers, worse in the left eye. The child was initially commenced on levofloxacin drops every 2 hours in both eyes from 6 am to midnight and referred to the pediatric ophthalmology team.

On ophthalmological examination, the right eye revealed a large (3.0 × 1.5 mm) epithelial defect, with no corneal thinning outside the visual axis. The left eye demonstrated a larger (4.0 × 4.0 mm) epithelial defect, with 10% corneal thinning and involving the visual axis (Figures 1 and 2A). The underlying causes for the severe corneal ulcerations included a combination of bilateral severe lagophthalmos, poor blink, marked corneal hypoaesthesia with minimal corneal blink on corneal touch and absence of any Bell's ocular phenomenon in either eye. The remainder of the cranial nerve examination was normal, although no formal testing of auditory function was obtained. Intraocular pressures were normal, and no glaucomatous cupping was found. Additional ophthalmic abnormalities included euryblepharon, thin lid skin with absent eyelashes, and hypertelorism (Figure 1). Also noted were bilateral dysplastic optic disks. The anterior chambers were deep and quiescent, and there was no discharge. Conjunctival swabs and corneal scrapes revealed no bacterial or viral infections.

Because of the potential risk of corneal perforation, immediate closure of the eyelids was carried out for corneal protection, initially with wound closure strips and a hydrocolloid dressing while awaiting urgent surgery.[4] Surgical treatment included an urgent temporary surgical eyelid closure, performed with releasable central tarsorrhaphies, using 4-0 nonabsorbable polypropylene sutures on plastic bolsters (Figure 2B)[4] for 1 week.

The temporary central tarsorrhaphies were then replaced by bilateral permanent lateral tarsorrhaphies, and

Table 1. Previously described ophthalmic features of Wolf-Hirschhorn syndrome[3,5-10]

External	Anterior segment	Posterior segment
Absence of medial half of eyebrows	Axenfeld's anomaly	Dysplastic optic nerves
Absent eyelid creases	Cataract	Foveal hypoplasia
Downslating palpebral fissure	Glaucoma	Megalopapilla
Epicanthus	Iris colobomas	Optic nerve colobomas
Euryblepharon	Microcornea	Chorioretinal colobomas
Exposure keratopathy	Peters anomaly	
Eyelid retraction	Refractive errors	
Hypertelorism	Rieger anomaly	
Lagophthalmos		
Lid colobomata		
Microphthalmia		
Nanophthalmia		
Nasolacrimal duct obstruction		
Nystagmus		
Orbital colobomas		
Reduced Bell's phenomenon		
Shallow orbits		
Strabismus		

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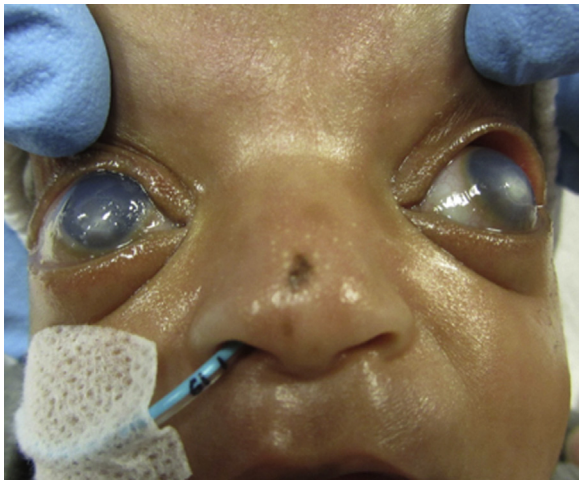

FIG 1. Typical facial features of Wolf-Hirschhorn syndrome, including severe bilateral corneal ulceration.

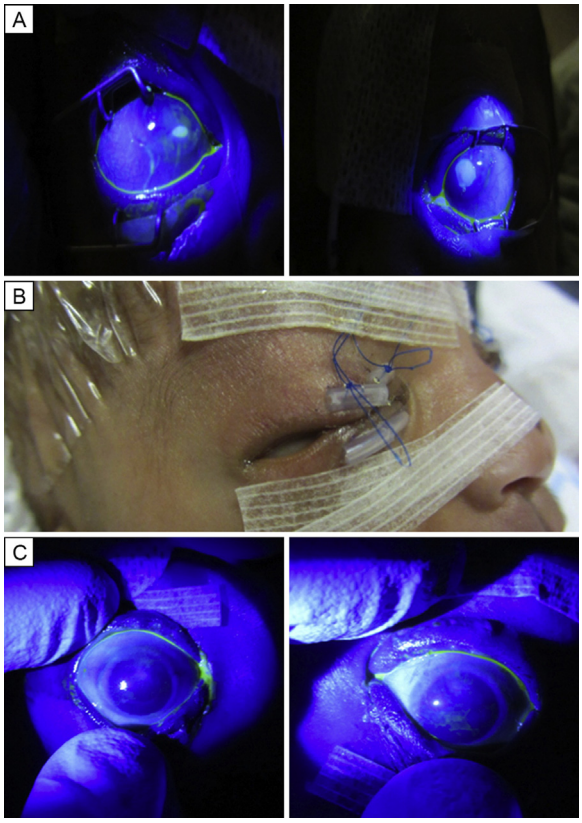

FIG 2. A, Bilateral epithelial defects on fluorescein staining. B, Temporary central tarsorrhaphy. C, Healed epithelium at 5 weeks after surgery.

the inferior puncta in both eyes were cauterized. Both corneal ulcers healed completely by 5 weeks after surgery, with minimal subepithelial scarring in the inferior third of both corneas below the visual axes (Figure 2C). No recurrent ulcers or epithelial defects occurred over the 18 months following discharge, and no further surgery was required. Topical antibiotics were continued until the epithelium healed; thereafter, the infant was prescribed 1- to 2-hourly preservative-free lubricating drops and lubricating ointment.

Discussion

Severe corneal ulceration in neonates poses significant challenges, especially when it involves the visual axis and increases the risk for amblyopia. The management of severe congenital corneal ulceration is even more challenging when combined with factors such as corneal hypoesthesia, disturbed tear film, poor Bell's phenomenon, and dysmorphic facies, as in our patient. This case highlights the need for urgent and vigorous intervention in neonates with exposure keratopathy secondary to WHS, including nonsurgical options, such as immediate use of temporary eyelid closure techniques, followed by definitive surgical tarsorrhaphies combined with punctal occlusion and intensive ocular lubrication with excellent outcomes. Because WHS is associated with seizures, cardiac anomalies, and renal abnormalities, a multidisciplinary therapeutic approach is required, including neonatologists and anesthetists when planning surgery in patients with WHS. To our knowledge, the absence of eyelashes, as in our case, has not previously been described in the existing ophthalmic literature of WHS.

Literature Search

PubMed was searched on May 2, 2018, without date or language restriction, using the following search terms: *Wolf-Hirschhorn syndrome*, *eye*.

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Medial transposition of a split lateral rectus muscle in synergistic divergence

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Synergistic divergence is a rare congenital ocular motility disorder characterized by paradoxical abduction during attempted horizontal gaze to the contralateral side. It is generally unilateral and associated with limited adduction of the affected eye and large-angle exotropia in primary position. Various surgical techniques have been used to manage this condition, with limited success. We describe our experience using splitting and medial transposition of the lateral rectus muscle on the affected side to treat an 18-month-old girl with synergistic divergence. Postoperative improved motor alignment remained stable through 6 months' follow-up.

Case Report

An 18-month-old girl presented at the Strabismus Service of Cairo University Hospital with an outward deviation of the left eye since birth. Her perinatal and developmental history were unremarkable. On examination, she had a central, steady, and maintained fixation in her right eye and poor fixation in her left eye. Cycloplegic refraction was +2.00 DS in both her eyes. Anterior segment and fundus examination were unremarkable for both eyes.

Motor evaluation revealed a left exotropia of 100$^{\Delta}$ (Krimsky test). Ductions and versions were full in the right eye. The left eye was fixed in the exotropic position, with complete limitation of adduction and inability to reach the midline in both versions and ductions. On attempted right gaze, the left eye showed paradoxical abduction together with downward movement and an increase in the exotropia suggestive of synergistic divergence (Figure 1). In addition, the vertical movements of the left eye were limited. There was no significant narrowing of the palpebral fissures of either eye on horizontal gaze.

Magnetic resonance imaging of the brain and orbits revealed mild subvolemia of the brain tissue, thinning out of the corpus callosum, and areas of incomplete myelination of white matter consistent with age. No abnormalities were seen in the extraocular muscles or in the orbits.

Intraoperatively, forced duction showed moderate tightness of the left lateral rectus, which was explored through a limbal incision. The muscle insertion was 7 mm from the limbus, and the width of the insertion was 7 mm. The muscle was originally hooked and secured with 6-0 polyester sutures, as a preliminary step for lateral rectus orbital wall fixation. After hooking the muscle, the length and tightness of the muscle were assessed for the possibility of splitting and transposition to the medial rectus insertion. This was tested by sliding the muscle above and below the globe and confirming that the distal end of the muscle could reach both the upper and lower borders of medial rectus insertion. The muscle was split along its horizontal axis for approximately 15 mm. The 5-0 polyester sutures were removed, and each half was secured with 6-0 polyglactin 910. The sutures were passed under the superior and inferior rectus muscles and then secured to the sclera 1 mm posterior to the upper and lower poles of the medial rectus insertion.[1] Forced duction testing was performed again at the close of surgery and showed minimal restriction to abduction.

The patient was examined 1 day, 1 week, 3 months, and 6 months after surgery. There was marked improved of the ocular alignment postoperatively, with a residual left exotropia of about 8$^{\Delta}$ (Figure 1). The synergistic divergence disappeared completely, with complete limitation of abduction of the left eye. There was minimal improvement of left eye adduction, but the eye was able to reach the midline. Fundus examination showed no changes in the color of the optic disk. Pupillary reactions remained intact. The motor alignment remained stable through the last follow-up, at 6 months. The patient was advised to continue to do part-time occlusion.

Discussion

Synergistic divergence is a rare ocular motility disorder, with simultaneous abduction of both eyes on attempted gaze to the normal side.[2] Several surgical techniques have been suggested for the management of synergistic divergence, including unilateral or bilateral lateral rectus muscle recession, total tenotomy of the lateral rectus muscle, lateral rectus muscle extirpation and denervation, lateral rectus muscle orbital wall fixation, large resection of the medial rectus muscle, oblique muscles weakening, and transposition of the vertical rectus muscles.[2-6] In general, there is a high rate of undercorrection.[4,5] In addition, synergistic divergence usually persists after surgery, and it is difficult to achieve any adduction with these surgical procedures.[4] Although most lateral-rectus-weakening procedures have been shown to reduce the exotropia, only lateral rectus extirpation and orbital wall fixation have been shown to eliminate the synergistic divergence postoperatively. No

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