

Ocular manifestations of Noonan syndrome in twin siblings: A case report of keratoconus with acute corneal hydrops

Anna Lee, Monali V Sakhalkar

Ocular manifestations of Noonan syndrome (NS) in a set of healthy 20-year-old African-American fraternal twins are reported with emphasis on a rare finding of keratoconus with acute corneal hydrops in one twin. Both the twins had learning disabilities and attended a special needs school. Evaluation included visual acuity assessment, tonometry and external eye, slit lamp and dilated fundus examinations, topography with Pentacam and external photographs. The first case was more remarkable as keratoconus with acute corneal hydrops was observed. The patient presented with severe cloudy vision that had worsened over a span of 1 month. It improved significantly on follow-up. The second case included a unique constellation of ocular pathology that highlights the diversity of NS manifestations even amongst twins. Conservative treatment of keratoconus with acute corneal hydrops in a NS patient helped largely resolve the patient's condition. We report the diverse spectrum of ocular manifestations associated with this rare congenital disorder.

Key words: Acute corneal hydrops, keratoconus, noonan syndrome

Noonan syndrome (NS) is a rare, multi-systemic condition usually inherited in an autosomal dominant manner. Physical manifestations include but are not limited to cardiac defects, short stature, chest deformity, sensorineural deafness, muscle hypotonia, typical facies (ptosis, neck webbing, triangular facial features, prominent nasolabial folds, high anterior hairline and transparent wrinkled skin) and mental retardation.^[1] Ocular abnormalities remain the most common findings.

In the literature, only three cases of NS with keratoconus have been reported.^[2-4] This is the second account of NS with keratoconus associated with acute corneal hydrops^[2]

among a constellation of other ocular manifestations that are typically seen in these patients. In order to further elucidate the variability of this condition, we present two cases of fraternal twins with NS.

Case Report

The first case is a 20-year-old African-American female with NS and systemic manifestations of short stature (58 inches), webbed neck and prior surgery for atrial septal defect (ASD) presented with cloudy vision in the right eye that had acutely worsened over 1 month. She also had complained of intense eye rubbing as an associated symptom. The patient was prescribed glasses at 4 years of age by an optometrist with whom she followed-up annually. Her best corrected visual acuity was hand motions in the right eye and 20/50 in the left eye. The intraocular pressures were 10 and 12 in the right and left eye respectively. Her extra ocular motility was full in all fields of gaze. Upper eyelid examination revealed mild bilateral ptosis [Fig. 1a]. There was a positive Munson's sign in the right eye. Slit lamp exam of the right eye showed central corneal edema and a very prominent cone. Slit lamp exam in the left eye showed early keratoconus. Dilated fundus exam on follow-up visit showed a cup-to-disk ratio of 0.6 in both eyes.

To address her acute corneal hydrops in the right eye, the patient was immediately started on the topical hypertonic agent Muro 128 5% ophthalmic solution 4 times a day in the right eye. At the 3-month follow-up visit, the acute corneal hydrops had largely resolved with paracentral scarring, prominent cone and stromal thinning [Fig 2a]. Further improvement was seen at the 7-month follow-up with limited regain of visual acuity of 20/100. The patient had very high myopia with a refraction of - 18.75D sphere - 2.00D cylinder × 15 in the right eye and - 13.50D sphere - 7.00D cylinder × 165 in the left eye. Topography with Pentacam in both eyes showed high keratometric readings with thin paracentral pachymetry, consistent with keratoconus [Fig. 3].

The second case is the fraternal twin sibling who also exhibited systemic manifestations of NS, including short stature (56 inches), webbed neck and prior surgery for ASD. Like her sister, she was also prescribed eyeglasses at 4 years of age. Her best corrected visual acuity was 20/20 in the right eye and 20/25 in the left eye with a manifest refraction of Plano - 1.00 diopter cylinder × 170° in the right eye and - 1.50 diopter sphere - 2.25 diopter cylinder × 160° in the left eye. Intraocular pressures were 16 and 18 in the right and left eye respectively. Her extra ocular motility was full in all fields of gaze other than restricted elevation in the left eye. She demonstrated bilateral proptosis with Hertel measurements of 25 mm in the right eye and 26 mm in the left eye. External examination revealed bilateral epicanthal folds, anti-mongoloid slant, upper eyelid ptosis (left greater than right) and bilateral lower lid retraction [Fig. 1b]. Slit lamp exam revealed prominent corneal nerves and bilateral fine punctate cortical cataracts [Fig. 2b]. Dilated fundus exam showed a cup-to-disk ratio of 0.6 in the right eye and 0.3 in the left eye respectively [Fig. 2c]. Topography with Pentacam was normal.

Discussion

NS was first described in 1883^[5] and later recognized as a distinct syndrome in 1963^[6] after systemic manifestations

Access this article online	
Quick Response Code:	Website: www.ijjo.in
	DOI: 10.4103/0301-4738.126992

Department of Surgery, Mercer University School of Medicine, Middle Georgia Ophthalmology, Medical Center of Central Georgia, Macon, GA, USA

Correspondence to: Dr. Monali V Sakhalkar, Middle Georgia Ophthalmology, Medical Center of Central Georgia, 770 Pine Street, Suite 500, Macon, GA 31201, USA. E-mail: sakhalkar.monali@mccg.org

Manuscript received: 11.06.13; **Revision accepted:** 02.12.13

were observed to co-occur. The incidence of NS is between 1 in 1000 and 2500 live births, affecting both sexes equally with no predominance in any one race. An observational study^[7] examining ocular manifestations of NS found, in decreasing

prevalence, external features of hypertelorism, ptosis, epicanthic folds and downward sloping palpebral apertures. Orthoptic exam showed refractive errors, strabismus, amblyopia and nystagmus. The majority of cases also exhibited prominent corneal nerves, fundal changes and cataracts. Both our patients had increased cup-to-disk ratio, a risk factor for glaucoma.^[8] No literature has stated glaucoma as part of the ocular picture for NS, it may be worth understanding whether this finding is fortuitous or a new association with NS.

Our first patient had complained of intense eye rubbing associated with worsening cloudy vision over the right eye in the past month. A review of studies found that one may first have a genetic predisposition to keratoconus^[9] and a second "hit," such as eye rubbing, provides the impetus for disease progression.^[10] Given that NS is not known to have collagen defect associated with the syndrome, it is unlikely to be of the spontaneous acute corneal hydrops form, unless the keratoconus itself was at a very advanced stage. Our patient was at an advanced stage of keratoconus and the intense eye rubbing might have triggered the corneal hydrops.^[10] There is one report regarding spontaneous corneal rupture in a patient with NS in the absence of keratoconus.^[11] Given that only three cases of NS with keratoconus have been previously reported, it is not clear whether the association is serendipitous. While keratoconus is most often seen sporadically, the condition has been associated with Down's syndrome, atopic disease and connective tissue disorder

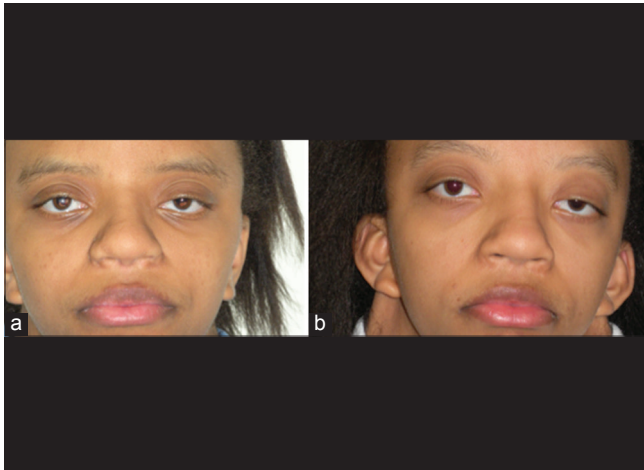


Figure 1: Facial characteristics resembling those of Noonan syndrome including, (a) mild bilateral ptosis and short, webbed neck of the first case. (b) Bilateral epicanthic folds, low-set ears, anti-mongoloid slant, upper eyelid ptosis, bilateral lower lid retraction and short, webbed neck of the second case

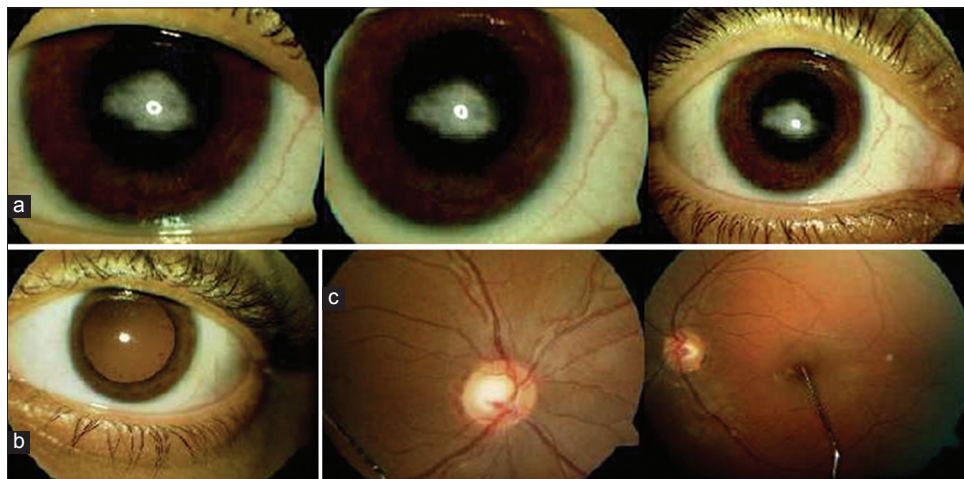


Figure 2: (a) Paracentral scarring of right eye at 3-month follow-up following treatment for acute corneal hydrops of the first case. (b) Cortical cataracts (arrows) in left eye of the second case. (c) Fundus photographs revealing increased cup-to-disk ratio in the right eye and cup-to-disk ratio asymmetry between the two eyes of the second case

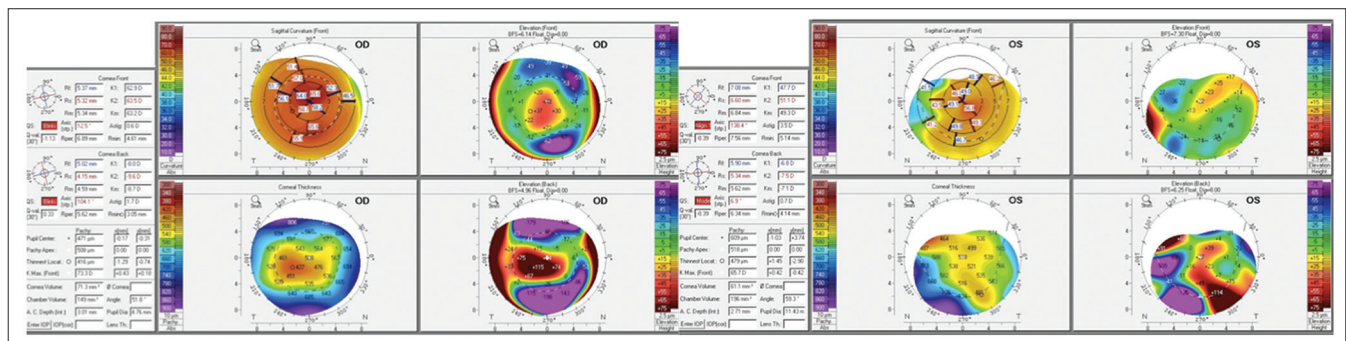


Figure 3: Pentacam anterior and posterior corneal curvature map for the right and left eyes at 3-month follow-up, revealing paracentral cone with thinning and increased keratometric indices suggestive of keratoconus in the first case

like Ehlers-Danlos syndrome and osteogenesis imperfecta.^[12] A few studies have shown keratoconus in Turner's syndrome. Although NS shares a few clinical features with Turner syndrome, NS patients have normal karyotypes. The development of keratoconus is most likely multi-factorial—studies have shown eye rubbing as a behavioral etiology that is often instigated by allergic disease.^[13] Furthermore acute hydrops has a fairly rare occurrence—incidence is 2.6-2.8% in patients with keratoconus.^[14]

Conclusion

We found keratoconus with acute corneal hydrops in one twin among a constellation of ocular findings that the patients shared as part of the NS presentation. It might be beneficial to assess if there is a particular genetic mutation associated with keratoconus in NS patients. Given the patient's unique phenotypic makeup and previous reports of corneal thinning in NS, it may be necessary to consider whether a new risk factor emerges as part of the spectrum of ocular pathologies.

References

- Noonan JA. Noonan syndrome. An update and review for the primary pediatrician. *Clin Pediatr (Phila)* 1994;33:548-55.
- Schwartz DE. Noonan's syndrome associated with ocular abnormalities. *Am J Ophthalmol* 1972;73:955-60.
- Ascaso FJ, Del Buey MA, Huerva V, Latre B, Palomar A. Noonan's syndrome with keratoconus and optic disc coloboma. *Eur J Ophthalmol* 1993;3:101-3.
- Förster W, Lenz W, Busse H. Ocular symptoms in a family with pseudo-ullrich-turner syndrome. *Klin Monbl Augenheilkd* 1991;199:362-6.
- Kobylnski O. Über eine flughautähnliche ausbreitung am halse. *Arch Anthropol* 1883;14:342.
- Noonan JA. Hypertelorism with turner phenotype. A new syndrome with associated congenital heart disease. *Am J Dis Child* 1968;116:373-80.
- Lee NB, Kelly L, Sharland M. Ocular manifestations of noonan syndrome. *Eye (Lond)* 1992;6 (Pt 3):328-34.
- Stewart WC, Kolker AE, Sharpe ED, Day DG, Holmes KT, Leech JN, *et al.* Factors associated with long-term progression or stability in primary open-angle glaucoma. *Am J Ophthalmol* 2000;130:274-9.
- Edwards M, McGhee CN, Dean S. The genetics of keratoconus. *Clin Experiment Ophthalmol* 2001;29:345-51.
- Sugar J, Macsai MS. What causes keratoconus? *Cornea* 2012;31:716-9.
- Au YK, Collins WP, Patel JS, Asamoah A. Spontaneous corneal rupture in noonan syndrome. A case report. *Ophthalmic Genet* 1997;18:39-41.
- Krachmer JH, Feder RS, Belin MW. Keratoconus and related noninflammatory corneal thinning disorders. *Surv Ophthalmol* 1984;28:293-322.
- Romero-Jiménez M, Santodomingo-Rubido J, Wolffsohn JS. Keratoconus: A review. *Cont Lens Anterior Eye* 2010;33:157-66.
- Grewal S, Laibson PR, Cohen EJ, Rapuano CJ. Acute hydrops in the corneal ectasias: Associated factors and outcomes. *Trans Am Ophthalmol Soc* 1999;97:187-98.

Cite this article as: Lee A, Sakhalkar MV. Ocular manifestations of Noonan syndrome in twin siblings: A case report of keratoconus with acute corneal hydrops. *Indian J Ophthalmol* 2014;62:1171-3.

Source of Support: Nil. **Conflict of Interest:** None declared.