Anterior Uveitis and Congenital Fibrosis of the Extraocular Muscles in a Patient with Noonan Syndrome

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ABSTRACT
We describe a patient with Noonan syndrome who presented with Human Leukocyte Antigen B27-associated recurrent acute anterior uveitis and manifestations of congenital fibrosis of the extraocular muscles, which has not been reported before.

Noonan syndrome is a congenital condition characterised by short stature, facial dysmorphism, skeletal anomalies, congenital heart defects, bleeding diatheses and reproductive anomalies in males. It occurs in 1/1000 to 1/2500 and the inheritance is either autosomal dominant or sporadic. Ocular anomalies occur in about 95% of these patients; with hypertelorism, refractive errors and strabismus being the most commonly encountered features and nystagmus, prominent corneal nerves, cataracts and pan-uveitis occurring less frequently. Congenital fibrosis of the extraocular muscles (CFEOM) syndrome is a complex neuro-developmental abnormality that encompasses a spectrum of related disorders that have in common non-progressive external ophthalmoplegia and marked restriction to passive movements of the extraocular muscles on forced-duction test with often a compensatory head posture. Three phenotypes of the syndrome have been described. CFEOM1, which is an autosomal dominant variant, is characterised by bilateral restrictive ophthalmoplegia and ptosis. Ocular motility disorders include infraduction and limitation of elevation above the midline. CFEOM2 is also characterised by bilateral ptosis and exotropia with limited horizontal and vertical movements. CFEOM3 gives rise to a more variable expression of ptosis and motility disorders. Other ocular manifestations such as astigmatism, ambyopia and nystagmus; and systemic manifestations such as cranio-facial dysmorphism, dental anomalies, syringomyelia, spina bifida and congenital heart disease, were also described in association with CFEOM.

We describe a patient with Noonan syndrome who presented with recurrent acute anterior uveitis and manifestations of CFEOM, which has not been reported before.

Case History
A 32-year-old female presented to the eye casualty with blurred vision and photophobia of the left eye. She had been diagnosed clinically to have Noonan syndrome several years before and showed features consistent with that syndrome including short stature and short neck (Figure 1). Clinical cardiological assessment and echocardiography had established the presence of pulmonary artery stenosis.

There was no past ocular history of relevance except for recurrent uveitis during the previous two years. On examination, corrected visual acuity was 6/12 in both eyes. Anterior chamber of the left eye showed a mild flare and cellular reaction (2+) but posterior segment examination was unremarkable. She assumed a head posture of left face-turn and chin-elevation. There was bilateral ptosis, epicanthal folds, hypertelorism and down-slanting palpebral fissures (Figures 2). There also was right exotropia and an intermittent mixed horizontal and rotary nystagmus. Ocular motility examination revealed limitation of adduction, elevation and depression in the right eye, and slight limitation of abduction in the left eye (Figure 2).

She was treated with topical steroids and cycloplegic drops and after 4 weeks, all the signs of inflammation had subsided and her visual acuity was 6/12 in right and 6/9 in the left eye.
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Features of Noonan syndrome: short stature with normal arm span, short neck and head tilt towards the left

Ocular manifestations: bilateral ptosis, right hypotropia and exotropia. Ocular motility shows limitation of adduction, elevation and depression in the right eye but only slight limitation of abduction in the left eye.

Hess chart showing mechanical-type limitation in all directions of gaze in the right eye and only mild limitation of abduction in the left eye.

Further orthoptic assessment revealed that there was no diplopia in any of the gaze positions and that her binocular function was reduced, demonstrating only simultaneous perception on near fixation and right-sided suppression at distance. Hess’ chart showed a severe mechanical-type limitation of adduction, elevation and depression of the right eye and only mild limitation of abduction of the left eye (Figure 3). The limitation in both eyes was confirmed to be restrictive by the forced-duction test.

Examining the patient’s old photographs confirmed that the facial features, including the ptosis and the head posture had existed since early childhood. The patient’s father possibly had Noonan syndrome as he had a short-neck, sensorineural deafness and cardiomegaly. She also had a sister that had similar facial features and pulmonary stenosis, and died at the age of 19. Her 3-year-old daughter did not seem to have significant ocular motility abnormality and was generally healthy for her age.

HLA-B27 was positive but none of the autoimmune markers was positive. Other routine blood and biochemical investigations were normal. Magnetic resonance imaging of the orbit and brain did not reveal any abnormality.

Discussion

Our patient had HLA-B27-associated acute anterior uveitis and ocular motility abnormalities consistent with CFEOM in association with other clinical features of Noonan syndrome. Although both uveitis and strabismus are among the ocular manifestations reported before in Noonan syndrome, this is the first case report of CFEOM in a patient with that syndrome.

The patient’s sister and father had clinical features suggestive of Noonan syndrome and indicate a likely autosomal dominant inheritance. The fact that the syndrome appears to have skipped her daughter and the lack of detailed information about her family do not rule out a dominant inheritance because of the known variable expressivity of the Noonan gene.[8]

The occurrence of anterior uveitis could either be a mere coincidence or rather perhaps a reflection of a possible predisposition of Noonan patients to develop autoimmune disorders. Thyroiditis, vasculitis, pericarditis, vitiligo and systemic lupus erythematosus are among the other autoimmune disorders that have been reported with Noonan syndrome.[9-11]

Restrictive ocular motility disorders have not been described before in Noonan syndrome. The presence of features of CFEOM-most probably of type 3 in view of its asymmetry—could yet be another coincidence. We, however, believe that it is more likely to be a true association given the preponderance of strabismus in Noonan syndrome[3] and the similarity of ocular and cranio-facial anomalies reported in the two syndromes.

In summary, this is the first report to describe CFEOM and Noonan syndrome in the same patient. It seems likely that CFEOM might have been rather an underreported feature of Noonan syndrome. The possibility of this association is important to keep in mind since early diagnosis and correction of CFEOM during childhood in these patients could prevent later complications such as abnormal head posture and amblyopia.

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References