Clinical Reports

Colobomata associated with Noonan's syndrome

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Summary: A patient with Noonan's syndrome and fundal colobomata in both eyes is described. To our knowledge, this is the first report of the association of colobomata with Noonan's syndrome. Although the patient had poor sight since early childhood and dyspnoea on exertion as a teenager, the diagnosis of Noonan's syndrome was not made until early adulthood. We hope this report will encourage recognition of this syndrome and its implications at an earlier stage.

Introduction

Noonan's syndrome is a rare disorder, often considered to be a variant of Turner's syndrome with a normal complement of 46 chromosomes, which may be either 46 XY or 46 XX.^{1–4} The usual clinical features include skeletal, endocrine, cardiac and ocular abnormalities, but colobomata have not been previously reported in association with Noonan's syndrome. We describe a patient with Noonan's syndrome and fundal colobomata, with impairment of vision in both eyes.

Case report

A 21 year old Caucasian female presented with a year's history of shortness of breath on moderate exertion and primary amenorrhoea. A heart murmur had been noticed in infancy. She had a full term normal delivery and early developmental milestones were normal. At the age of 10 years partial bilateral deafness was noticed, and at the age of 11 years she became aware of poor vision, most marked in the right eye. She was born of non-consanguineous parents and her brother and sister were both of normal height and appearance, with none of the phenotypic features of Noonan's syndrome.

General examination revealed a female of short stature (height 1.53 m) with poorly developed secondary sex characteristics. She had a webbed neck and cubitus valgus, pectus excavatum and widely spaced nipples. Her face showed hypertelorism, a flat nasal

bridge, broad forehead, low set ears and a low neck hair-line. She had normal palmar and plantar dermatoglyphics. Examination of the cardiovascular system demonstrated a regular heart rate of 60/minute and normal blood pressure (120/80 mm Hg). Auscultation revealed normal heart sounds, apart from a pulmonary ejection click and accompanying ejection systolic murmur. She was of normal intelligence, but had mild bilateral sensorineural deafness. Examination of the remaining central and peripheral nervous system was normal.

Ocular examination

Uncorrected visual acuity was reduced to counting fingers in the right eye and 6/60 in the left eye. Vision could not be improved beyond 6/60, N48 with a – 8.00 dioptre sphere in the right eye but corrected to 6/12, N5 in the left eye with a – 7.50 dioptre sphere. She made three errors on the Ishihara plates with the right eye, but had normal colour vision in the left eye. The visual fields to a 3 mm white target revealed a central scotoma in the right eye and an upper arcuate defect contiguous with the blind spot in the left eye. She had a right convergent squint and a right relative afferent pupillary defect. She did not have any ptosis, ptosis or epicanthic folds, and the anterior segments and intraocular pressures were normal. Examination of the fundi revealed a coloboma of the optic disc in the right eye with abnormal exit of retinal vessels from the optic disc and a chorioretinal coloboma inferior to the optic disc in the left eye (Figure 1).

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Figure 1 (a) Fundus photograph of the right eye. The entire disc is colobomatous with abnormal exit of the retinal vessels. (b) Fundus photograph of the left eye. A chorioretinal coloboma is present inferior to the myopic optic disc along the line of closure of the embryonic fissure. A bridge of normal retina is present between the optic disc and the coloboma.

Investigations

Routine haematology and biochemistry, a chest radiograph and electrocardiogram proved normal. A buccal smear showed the chromatin positive pattern of a normal female, and chromosomal analysis demonstrated the normal female karyotype of 46 XX.

Cardiac catheterization revealed a normal pulmonary artery pressure with a small gradient across the pulmonary valve, consistent with mild valvular pulmonary stenosis. M-mode and two-dimensional echocardiography were normal with no evidence of aortic coarctation. Pure tone audiometry confirmed the presence of mild bilateral sensorineural deafness.

Discussion

Noonan originally described a series of nineteen patients^{1,2} and Summitt subsequently reviewed 260 published and personally observed cases,³ which delineated a syndrome with the following characteristic clinical features: a distinctive facial appearance with a broad forehead, hypertelorism, a flat nasal bridge, low set ears with widely spaced nipples, pectus excavatum, short stature, infantilism and cryptorchidism. Congenital heart defects are frequently found, the most common being pulmonary valvular and infundibular stenosis. The condition is thought to be inherited as an autosomal dominant trait and near relatives may show partial expression of the typical features.

The ocular abnormalities previously described in Noonan's syndrome include hypertelorism, epicanthic folds, ptosis, proptosis, slanting palpebral fissures, keratoconus, posterior embryotoxin, myopia and strabismus.^{2,5,6} However, the ocular abnormalities associated with Turner's syndrome are many and diverse^{7,8} and since the phenotypic features of the two diseases are identical and Noonan's syndrome was first described 23 years after Turner's syndrome, it is clearly possible that many of the ocular features described in the earlier papers on Turner's syndrome, might actually apply to Noonan's syndrome which had not been verified genotypically. However, despite this proviso colobomata have not been described in either Noonan's or Turner's syndrome. Our patient presented with many of the characteristic phenotypic features of Turner's syndrome. However, the presence of a normal female chromosomal karyotype and pulmonary valve stenosis strongly favour the diagnosis of Noonan's syndrome.¹⁻⁵

Colobomata of the retina were first described by von Ammon,⁹ and are characteristically inherited as an autosomal dominant trait with incomplete penetrance.¹⁰ Colobomata usually occur alone as isolated defects but may rarely be one facet of a variety of syndromes of multiple congenital abnormalities; fundal colobomata are sometimes associated with chromosomal abnormalities, particularly trisomies 13 and 18.¹¹ Recently colobomata have been described in association with microphthalmia, dysplastic external ears, mental retardation and congenital heart disease.¹² However, to our knowledge this is the first report of the association of colobomata with Noonan's syndrome. We hope this report will encourage both ophthalmologists and cardiologists to recognize this syndrome and its implications at an earlier stage and so provide optimum management for their patients.

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