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An Unusual Ocular Manifestation in Fanconi Anemia: Congenital Glaucoma

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Fanconi anemia is an autosomal recessive disorder characterized by growth retardation along with many congenital abnormalities involving the eyes. We report herein two siblings with Fanconi anemia who also have bilateral congenital glaucoma. To the best of our knowledge, this is the first report of congenital glaucoma in patients with Fanconi anemia. Am. J. Hematol. 78:64–66, 2005. © 2004 Wiley-Liss, Inc.

Key words: Fanconi anemia; congenital glaucoma

INTRODUCTION

Fanconi anemia (FA) is a rare congenital disorder classically consisting of a combination of characteristic chromosome breaks, which result in clastogenic stress, enhanced cancer risk, and many birth defects [1]. Up to 26% of patients have ocular manifestations. Review of the current medical literature revealed that specific types of eye anomalies in FA are microphthalmia, strabismus, epicanthal folds, hypertelorism, ptosis, slanting, cataracts, astigmatism, blindness, epiphora, nystagmus, proptosis, hypotelorism, and anophthalmia, in order of decreasing frequency [2]. However, congenital glaucoma (CG) in patients with this inherited condition has not yet been reported. We hereby describe these two unusual events occurring together, and we emphasize that the FA phenotype might be more variable than recognized previously.

CASE REPORT

The patient was a 6-year-old girl born from a consanguineous marriage. She was admitted with the complaint of short stature and was diagnosed to have FA on the basis of dysmorphic features with microcephaly, hyperpigmentation, café-au-lait spots, thumb anomalies, macrocytosis, stress erythropoiesis, elevated α-fetoprotein level, and strongly positive diepoxybutane (DEB) test. The most striking clinical features of the patient were severe growth failure and unusual ocular manifestation, namely, enlarged eyeballs.

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Because of severe growth retardation, endocrinological evaluation was performed and growth hormone deficiency was diagnosed based on decreased response to pharmacologic stimulation and observation of pituitary stalk interruption syndrome on magnetic imaging.

She was referred to the ophthalmology department for the differential diagnosis of megalocornea, which was evident since birth. Ophthalmologic examination revealed that visual acuity was 0.8 in the right eye (OD) and 0.9 in the left eye (OS). Intraocular pressure with Goldmann applanation tonometer was elevated bilaterally (28 mmHg in OD and 24 mmHg in OS) (normal range 10–21 mm Hg). She had bilateral buphthalmic eyes with corneal horizontal diameters of 14 mm OD and 13 mm OS (normal range 10.5–11 mm). Both corneas were clear; however, minimal Haab striae were seen in the left eye. Only minimal anterior iris insertion was noted in gonioscopy, consistent with trabeculodysgenesis. The anterior chamber was deep bilaterally. Pupillae and irises were normal with clear and normal-shaped lenses. Fundus examination

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showed normal macula, retina, and peripheral vessels with a cup–disc ratio of 0.8 in OD and 0.7 in OS.

The patient was treated with bilateral Harms trabeculotomy, which was sufficient to control the intraocular pressure postoperatively. At 1 month follow-up, slit lamp examinations were normal and intraocular pressure was 10 mmHg in both eyes without any medical treatment.

During routine postoperative follow-up, we learned that one of the patient's sisters also had CG for which she was undergoing surgery in another hospital. After further evaluation, we reached the conclusion that the sibling also was FA on the basis of a positive DEB test, short stature, café-au-lait spots, and macrocytosis. The remaining three siblings in this family had no FA or CG. Both siblings and every other family member are undergoing genetic examination regarding CG.

DISCUSSION

Fanconi anemia is a rare autosomal recessive disorder first described by Fanconi in 1927 [1]. The syndrome is characterized by pancytopenia, increased susceptibility to leukemia and other malignancies, and birth defects. Among the patients listed in International Fanconi Anemia Registry (IFAR), 60% had congenital malformations [1,2]. Data from the same registry shows that 26% of cases have various eye abnormalities (Table I); however, to the best of our knowledge, this is the first report of CG in patients with FA.

Congenital glaucoma is a very rare condition and occurs predominantly as a sporadic event. The inheritance is autosomal recessive with incomplete penetrance in 10% of cases [3]. Although we cannot entirely exclude the possibility of a coincidental occurrence, it may be reasonable to assume that severe growth hormone deficiency in the proband might be involved in development of CG. In medical literature are a remarkable number of reports stating that growth hormone is needed for normal eye development and that, in cases of growth hormone deficiency, a variety of dysgenesis in the eyes may develop [4–7]. An FA patient with growth hormone deficiency in whom various ocular developmental abnormalities are displayed has been reported as well [8]. However, as we are not aware of any report of ocular manifestations resulting from growth hormone deficiency in FA patients, and because we do not currently know the growth hormone status of the other sibling, it has not been possible for us to reach a definite conclusion about how growth hormone deficiency is related to ocular manifestations. Further data are needed to define the possible role of growth hormone in CG. In that respect, it might be important to closely evaluate the growth hormone status, especially of FA patients with developmental eye abnormalities.

TABLE I. Specific Types of Eye Abnormalities Described Thus Far With Fanconi Anemia*

Small eyes	Slanting	Hystagmus
Strabismus	Cataracts	Proptosis
Epicantal folds	Astigmatism	Small iris
Hypertelorism	Blindness	Hypotelorism
Ptosis	Epiphora	Anophthalmia

*Adapted from [1]; eye abnormalities comprise 26% of abnormalities reported with FA.

The fact that both siblings have FA and CG leads us to think that the occurrence together is not coincidental. Furthermore, the common occurrence strongly supports the probability of genetic basis. Even though the genes of FA [9] and CG [10–13] might not be the same, the mutations that cause these two diseases might be inter-related. We strongly believe that the results of genetic investigation will have an illuminating effect on the open questions.

In conclusion, we report congenital glaucoma as a part of the FA phenotype in two siblings and suggest that CG is paid extra attention during ophthalmic assessment of patients with FA in order to avoid its complications.

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