A new case of Balcı's syndrome (corneal opacity, microphthalmia, microcephaly, mental retardation, and generalized muscular spasticity associated with congenital heart disease)

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SUMMARY: Balcı S, Demirçeken FG, Öcal B, Zorlu P, Teziç T. A new case of Balcı's syndrome (corneal opacity, microphthalmia, microcephaly, mental retardation and generalized muscular spasticity associated with congenital heart disease). Turk J Pediatr 2001; 43: 366-368.

The association of corneal opacity, microphthalmia, microcephaly, mental retardation, and generalized muscular spasticity with hyperglycinemia was presented for the first time by Balcı and colleagues in 1974. After this report, some similar cases in the literature were referred to as Balcı's syndrome. In this paper we describe a new case of Balcı's syndrome, a 2.5-month-old female patient with corneal opacity, microphthalmia, microcephaly, mental retardation, and generalized muscular spacticity. All of these findings are acceptable as Balcı's syndrome, and in addition she had congenital heart disease (ventricular septal defect) and renal anomalies. In this paper other syndromes associated with corneal opacity and mental retardation are discussed.

Key words: Balcı's syndrome, congenital heart disease, corneal opacity, mental retardation, microcephaly, microphthalmia.

Balcı et al.[1] first described a new autosomal recessive syndrome characterized by corneal opacity, microphthalmia, microcephaly, mental retardation and generalized muscular spasticity associated with hyperglycinemia in 1974. Similarly, an oculocerebral syndrome involving corneal opacity, microphthalmia, mental retardation and spastic cerebral palsy without any metabolic disorders was reported by Pinsky et al.[2] in 1965. After Balcı's report, similar cases were reported by Young et al.[3] in 1982, Siber[4] in 1984, Kaloustian et al.[5] in 1985, and Chenevix-Trench et al.[6] in 1986. We herein present a new case of Balcı's syndrome with additional findings of congenital heart disease.

Case Report

A 2.5-month-old female patient suffering from ocular abnormalities, cyanosis, mental and motor retardation and mild spasticity was admitted to our clinic. The patient was the sixth child of nonconsanguineous parents. The mother and the father were 40 and 38 years old, respectively. The family history revealed that the second male child died at seven days without any specific diagnosis, but he had problems of umbilical bleeding, generalized spasticity, and jaundice. The fifth male child died at seven years old with spasticity, and mental and motor retardation.

On admission the patient's weight was 3600 g (<5th percentile) and her length was 55 cm (10-25th percentile). The had circumference was 35 cm (<3rd percentile). The patient had an unusual and dysmorphic facial appearance. Cloudy corneas, and microphthalmia, and short philtrum, low-set ears and short neck were observed. She usually kept her eyes closed (Fig. 1). There was a III/VI° pansystolic murmur on the third left side intercostal space. She had Simian line bilaterally. There were coarse rales on the lung auscultation indicating an acute respiratory infection disease. All extremities showed mild stiffness.

On laboratory studies serum biochemical values and complete urine analysis were normal. Complete blood count revealed decreased

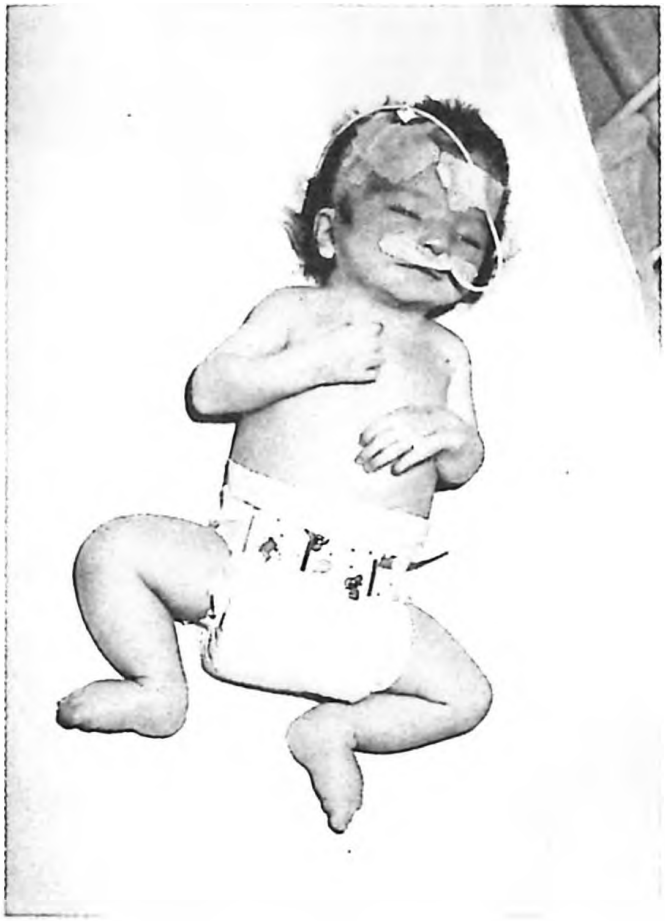

Fig. 1. Facial appearance of the patient showing bilateral diffuse corneal opacity, microphthalmia and generalized spasticity.

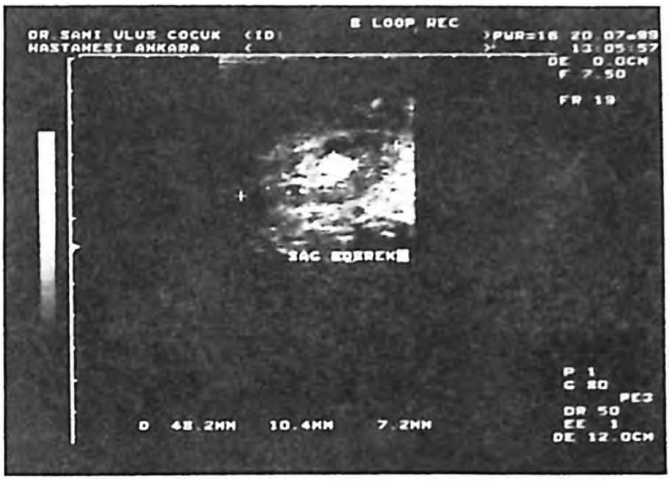

Fig. 2. Renal ultrasonography showing increased echogenicity on the right kidney.

hemoglobin concentration. Peripheral blood chromosome analysis was normal (46 XX pattern). Urine and blood amino acid chromatographic studies were normal at each analysis (three times). TORCH examination was negative. The chest X-ray showed lobar pneumonia on the right side and enlargement of the heart. Renal ultrasonography showed increased echogenicity fetal lobulation, and mild rotational anomalies in the pelvis of the right kidney (Fig. 2). Echocardiogram revealed ventricular septal defect pulmonary hypertension.

The patient died at three and a half months with pulmonary infection and heart failure.

Discussion

Balcı et al.[1] described a new autosomal recessive syndrome characterized by corneal opacity, microphthalmia, microcephaly, mental retardation, and generalized muscular spasticity associated with hyperglycinemia. Later, other entities with corneal opacities, microphthalmia, microcephaly, spastic quadriplegia, hypospadias, and cryptorchidism were reported in three males in two generations by Siber et al.[4], possibly suggesting X-linked recessive inheritance.

Table I shows that corneal opacities or cloudy corneas are associated with many congenital anomalies and syndromes. Diagnosis of this new syndrome is very important for genetic counseling for further pregnancies. Generally, cloudy corneas or corneal opacities occur together with central nervous system (CNS) abnormalities such as microcephaly, spastic quadriplegia, or spastic cerebral palsy, because the CNS and eye come from the same ectodermal origin. Corneal opacity is a very rare congenital eye malformation which can be included in many syndromes such as an oculocerebral syndrome (X-linked recessive) and spastic paresis, glaucoma, and mental retardation – a probable autosomal recessive syndrome (Table I). The chromosome analysis and urine-blood amino acids of our patient were normal, and intrauterine infections were ruled out. Unfortunately, the patient died and the family refused a postmortem examination. For the mother of our patient, there was a 25% risk of recurrence, and microcephaly could be detected in future by early and careful sonography. Our patient did not have any glycinuria or other aminoacidopathy, but she had the additional VSD and renal anomalies compared to previously reported Balcı's syndrome. The importance of this case was the

Table I. Summary of the Syndromes Associated with Corneal Opacity, Mental Retardation and Other Findings

Syndromes	Other findings	Mode of inheritance	References
Microphthalmia, corneal clouding, mental retardation and spasticity	Ventricular septal defect glycinuria	Autosomal recessive	Balcı et al.[1]
Microphthalmia, corneal opacity, mental retardation and spastic cerebral palsy-an oculocerebral syndrome	Mother had microphthalmia and three female offspring had corneal opacity	X-linked recessive	Pinsky et al.[2]
Keratoconus posticus circumscriptus, cleft lip and palate, genitourinary abnormalities, short statuse and mental retardation in sibs	Corneal opacities, retinal coloboma, ptosis, short stature, vertebral anomalies	Autosomal recessive	Young et al[3].
Microencephaly, microphthalmia with corneal opacities, spastic quadriplegia, hypospadias and cryptorchidism	Corneal opacities	X-linked recessive	Siber[4]
Familial spinocerebellar degeneration with corneal dystrophy	—	—	Kaloustian et al.[5]
Spastic paresis, glaucoma and mental retardation - a probable autosomal-recessive syndrome	Secondary cataracts, glaucoma	Autosomal recessive	Chenevix-Trench et al.[6]
Corneal opacity, microphthalmia, microcephaly, mental retardation, and generalized muscular spasticity - a new case of Balcı's syndrome	Ventricular septal defect, renal anomalies	Autosomal recessive	Balcı et al. (present case)

association with cloudy cornea, microphthalmia, microcephaly, spasticity, and VSD, all of which were compatible with Balcı's syndrome (corneal opacities, microphthalmia, microcephaly, and spasticity)[1]. Although there was no consanguinity between the parents, there were two sibling deaths in infancy. There were no known etiological factors in these siblings; however, they may have had the same entity. Furthermore, the presented patient was female, but non-living siblings were male. These points also suggested autosomal-recessive inheritance in spite of absence of consanguinity between the parents. Further studies of similar cases are needed to shed light on the problem. Determination of the mutant gene of this syndrome may be possible through molecular studies.

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