Umblical hernia, hypertelorism, sensorineural deafness: Is it Donnai–Barrow syndrome?

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ABSTRACT

Introduction: Donnai–Barrow syndrome is a rare autosomal recessive disorder first described in 1993 and characterized by diaphragmatic hernia, hypertelorism, agenesis of the corpus callosum and deafness. Case Report: A 23-year-old female with clinical features similar to Turner patients were sent to our department by cardiology department. The main features were umblical hernia, hypertelorism (interpupillary distance 45 mm), and sensorineural deafness. Other findings included mid-face hypoplasia, a broad forehead, exotropia, frontal bossing and wide anterior fontanel, down slanting palpebral fissures, short nose with a broad tip, cubitis valgus and posterior rotated ears, webbed neck and short stature (height - 144 cm, weight - 47.5 kg). Magnetic resonance imaging (MRI) scan of the brain confirmed arachnoid cyst, cervical spinal stenosis (thought to be secondary to hydrocephalus) and absent corpus colosum. Autosomal recessive inheritance was suspected because patient’s parents were also first cousins. Cytogenetic analysis demonstrated normal karyotype (46, XX). Conclusion: We describe a female patient who shares identical characters to the patients described by Donnai and Barrow. Although our patient has got a large number of malformations, her karyotype was normal, which makes this case extremely interesting. Such patient’s have moderate levels of mental life which is consonant with the disease, and the patients can adapt to social life.

Keywords: Donnai–Barrow syndrome, Autosomal recessive inheritance, Normal karyotype, Umblical hernia, Hearing loss

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INTRODUCTION

Donnai and Barrow reported two sets of siblings and an unrelated individual with a new syndrome. [1] Although karyotype is normal, some typical clinical features of the Donnai–Barrow syndrome overlap the phenotype of the 9q microdeletion syndrome [2]. The phenotype associated are diaphragmatic hernia, exomphalos, absent corpus callosum, intestinal malrotation, myopia, sensorineural deafness, and particular face. Donnai–Barrow syndrome
Faciooculoacousticorenal syndrome (DB/FOAR) is a rare autosomal recessive disorder resulting from mutations in the LRP2 gene located on chromosome 2q31.1 [3]. Small deletions or insertions causing frameshifts, as well as conserved splice site, nonsense and missense mutations of low-density lipoprotein receptor related protein 2 (LRP2) gene in seven DBS/FOAR families were recently reported [4]. The 79 exon LRP2 gene mapping to human chromosome 2q31.1 encodes megalin, an endocytic transmembrane glycoprotein [5].

CASE REPORT

A 23-year-old female, with clinical features similar to Turner patients was referred to our department by the cardiology department. The echocardiographic examination was normal. The main features were umbilical hernia (Figure 1), hypertelorism (interpupillary distance 45 mm) and sensorineural deafness. Autosomal recessive inheritance was suspected because her parents were first cousins. She had mild to moderate intellectual disability. Craniofacial examination showed the presence of marked ocular hypertelorism, telecanthus, large anterior fontanelle, wide metopic suture, widow’s peak in anterior hairline, depressed nasal bridge, short nose, and posterior rotation of the ears (low set ears). The facial appearance, although not coarse, was characteristic. Other findings were mid-face hypoplasia a broad forehead, exotropia, frontal bossing and wide anterior fontanel, downslanting palpebral fissures, short nose with a broad tip, cubitis valgus and posterior rotated ears and webbed neck (Figure 2). Ocular findings included enlarged globes (leading to the appearance of prominent eyes) and downslanting palpebral fissures. Ocular measurements were 45 for inner canthal and 65 mm for interpupillary distances. Intraocular pressure in right eye was 12 mmHg and left eye was 19 mmHg. Left exotrophia of approximately 45° was seen. She had strabismus. She did not have keratokonus, myopia, retinal dystrophy, coloboma or cataracts. Omphalocele (or umbilical hernia) was present. Sensorineural hearing loss was positive as measured by audiometric testing. Neuroradiologic examination showed mucosal thickening in the right maxillary sinus and ethmoid cells. Odontoid process and clivus were posteriorly dislocated towards foramen magnum and compression and edema was observed at the level of C1 spinal cord level. At the level of C2, expansion of the central channel was seen. At this level, the spinal canal was narrowed, in accordance with cervical spinal cord atrophy (antero-posterior diameter of six mm). MRI scan of the brain confirmed agenesis of corpus callosum and presence of arachnoid cyst (2 cm). The cervical spinal stenosis (6 mm) was thought to be secondary to hydrocephalus. Developmental delay was present with short stature (height - 144 cm, weight - 47.5 kg) Karyotype determined on white blood cells was normal (46, XX), (Figure 3). Full abdominal ultrasound (USG) scan showed normal liver contours, size and parenchymal echogenicity. Intrahepatic and extrahepatic biliary tract, portal vein, hepatic veins and porta hepatis was normal. USG scan showed large number of stones in the gallbladder measuring few mm size and right ovarian cyst measuring 26x17 mm in size. Spleen size was 125 mm and contours and parenchymal echogenicity were normal. Pancreatic size, parenchymal thickness and echogenicity were normal. Both kidneys were normal in

![Figure 1: Facial dysmorphism is including a severe hypertelorism with downslanting palpebral fissures, a short bulbous nose, and posteriorly rotated ears were present.](image1.png)

![Figure 2: Umbilical hernia in the patient.](image2.png)

![Figure 3: Cytogenetic analysis demonstrated normal karyotype (46, XX).](image3.png)
location and dimensions (right kidney - 91x36 mm, parenchymal thickness of 10 mm; left kidney - 97x34 mm, parenchymal thickness 11 mm). Renal contours, parenchymal echogenicity and thickness were normal. The bladder contours, the wall thickness and the lumen were normal. Left ovary was normal. In the lobe of the

clinic with a presumed diagnosis of Turner syndrome. Cytogenetic analysis to assess the metaphase chromosomes of peripheral blood lymphocytes showed 46, XX karyotype in our patient. This findings in our patients were very similar to those described in this syndrome. [8]

For Donnai–Barrow syndrome, Pober et al. gave a classification in 2009. According to this classification; Donnai–Barrow syndrome and FOAR syndrome, referred to as DB/FOAR syndrome, is a unique malformation complex. Based on this review of published cases the core features of this syndrome consist of:

1. Congenital anomalies found in approximately 90% patients: hypertelorism; partial or complete agenesis of the corpus callosum; enlarged anterior fontanelle; characteristic facial features.
2. Functional anomalies found in approximately 90% patients: proteinuria; high myopia, sensorineural hearing loss; developmental delay.
3. Anomalies found in approximately 50% patients: congenital diaphragmatic hernia and omphalocele/umbilical hernia; additional features such as coloboma and macrocephaly also appear to occur in approximately 50% of cases, but the numbers are too small to state this with certainty [9].

Some of the major malformations were also seen in our patient such as; hypertelorism, telecanthus, hydrocephalus, enlarged anterior fontanelle, characteristic facial features, proteinuria, starbismus, sensorineural hearing loss and developmental delay. Diaphragmatic hernia, as in umbilical hernia, has been observed in our patient's.

CONCLUSION

Donnai–Barrow syndrome is an autosomal recessive disease. Short stature, characteristic facial appearance, hearing loss and umbilical hernia point towards a diagnosis of Donnai–Barrow syndrome. Although a large number of malformations are present, a normal karyotype makes Donnai–Barrow syndrome an extremely interesting entity. Moderate levels of mental life is consistant with the disease and patients easily adapt to social life.

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Yaşar Svaci – Substantial contributions to conception and design, acquisition of data, Drafting the article, revising it critically for important intellectual content, Final approval of the version to be published
Ersel Onrat – Drafting the article, revising it critically for important intellectual content, Final approval of the version to be published
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Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

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REFERENCES