A newborn with trisomy 13 presenting with cloacal exstrophy

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Received: 20 June 2014, Revised: 28 August 2014, Accepted: 26 September 2014

SUMMARY : Kader Ş, Mutlu M, Sarıaydın M, Aslan Y, Erduran E, Çebi A. A newborn with trisomy 13 presenting with cloacal exstrophy. Turk J Pediatr 2015; 57: 198-201.

Trisomy 13 syndrome is a rare disorder that carries a high mortality rate due to abnormal prenatal development resulting in serious birth defects. Although genitourinary malformations are commonly seen in trisomy 13 syndrome, to our knowledge, the association of cloacal exstrophy with trisomy 13 has been extremely rarely reported. Herein, a newborn with trisomy 13 syndrome having multiple congenital anomalies, including cloacal exstrophy, is presented, and the importance of structural anomalies of the neutrophilic leukocytes on a blood smear in supporting diagnosis of trisomy 13 is discussed.

Key words: trisomy 13 syndrome, cloacal exstrophy, neutrophilic leukocytes, nuclear projections, blood smear, newborn.

Trisomy 13, also called Patau syndrome, is a rare genetic disorder that is characterized by severe to profound intellectual disability and multiple congenital anomalies, including orofacial clefts, microphthalmia or anophthalmia, and postaxial polydactyly[1]. Its prevalence ranges from 1 in 5,000 to 1 in 12,000 total births[2]. Examination of structural anomalies of neutrophilic leukocytes on the blood smear is important in supporting the diagnosis in patients with characteristic features of trisomy 13[3, 4]. Although genitourinary abnormalities are also common, cloacal exstrophy is extremely rare in patients with trisomy 13[5]. Herein, we describe a newborn baby with trisomy 13 having multiple congenital anomalies, including cloacal exstrophy, and discuss the importance of structural anomalies of the neutrophilic leukocytes on the blood smear in diagnosing trisomy 13.

Case Report

A two-day-old newborn was admitted to our neonatal intensive care unit with complaints of multiple congenital anomalies. She was born to a 31-year-old G4P3 mother at 38 weeks gestation via normal vaginal delivery. Her mother did not have routine prenatal care during her pregnancy. The mother's third pregnancy had been terminated due to molar pregnancy. There was no consanguinity. The family history revealed no birth defects or congenital anomalies.

The patient's body weight was 3390 g (50th-75th percentile), length 46 cm (10th percentile) and head circumference 34.5 cm (25th-50th percentile). On physical examination, low-set and hypoplastic ears, aplasia cutis congenita areata on the vertex (Fig. 1A.), cleft lip and palate, a broad nasal bridge (Fig. 1B.), postaxial polydactyly of the hands, omphalocele, cloacal exstrophy (Fig. 1C.) and heart murmurs were noted.

Echocardiography showed double outlet right ventricle, pulmonary atresia, large vertical aortopulmonary collateral arteries, secundum atrial septal defect (ASD) and hypoplastic left ventricle. Transfontanelle ultrasound (USG) was normal. Spina bifida was not observed on radiologic examination.

Review of a peripheral blood smear revealed two or more small threadlike pedunculated projections attached to the surface of the nuclei in more than 80% of the neutrophils (Fig. 2A).

Karyotyping of the cultured lymphocytes was

done; the final karyotype report confirmed the existence of trisomy 13 (47,XX,+13) (Fig 2B). The infant died at three days of life because of complex cardiac malformations.

Discussion

Trisomy 13 is one among the severe chromosomal anomalies clinically characterized by the presence of serious malformations, with a limited survival rate. There are three cytogenetic abnormalities that may be involved in trisomy 13: trisomy 13 (47, +13); Robertsonian translocation involving the long arm of chromosome 13; and trisomy 13 mosaicism (47, +13/46)[6, 7]. The majority of trisomy 13 cases are trisomy 13 (47, +13)[8]. The etiology is usually attributed to advanced maternal age[9], but our patient's mother was only 31 years old.

Fetal growth restriction is usually seen in Patau syndrome[10], but our patient's weight was appropriate for gestational age, and her mother had no history of diabetes.

Patau syndrome has a high mortality rate because of abnormal prenatal development, which results in serious birth defects. Anomalies including those of the central nervous system (holoprosencephaly, posterior fossa anomalies, agenesis of the corpus callosum, ventriculomegaly, neural tube defects, absence of the olfactory nerve or bulb, sloping forehead, microphthalmia, coloboma, cyclopia, anophthalmia, deafness), genitourinary system, cardiovascular system, skeletal system (polydactyly, ectrodactyly, rocker bottom feet, narrow convex fingernails, scalp defects) and gastrointestinal system (omphalocele, umbilical hernia, diaphragmatic hernia), as well as aplasia cutis congenita areata on the vertex, superficial hemangiomas, cleft lip and/or palate and hypoplastic nose have been reported in trisomy 13[11-14]. In our case, aplasia cutis congenita areata on the vertex, cleft lip and palate, a broad nasal bridge, low-set and hypoplastic ears, postaxial polydactyly of the hands, omphalocele, ambiguous genitalia and cloacal exstrophy were noted. Because of the patient's compromised condition, we could not obtain central nervous system imaging other than transfontanelle US.

Genitourinary abnormalities, including polycystic kidneys, enlarged echogenic kidneys, horseshoe kidney, renal cysts, hydronephrosis, vesicouretral reflux, hypoplastic pelvis, cryptorchidism, cystic ovaries, uterine anomalies, genital anomalies, micropenis, scrotal hypoplasia and inguinal hernia, are also common in cases of trisomy 13.

Cloacal exstrophy is one of the rarest and most complex abdominal wall defects, thought to result from a mesodermal abnormality[5]. It is extremely rare in trisomy 13, as far as is known; only two infants (one without karyotype confirmation) with cloacal exstrophy and trisomy 13 have been reported[5]. Cloacal exstrophy cases can be classified into four groups: OEIS complex (omphalocele, bladder exstrophy, imperforate anus and spinal defects), OEI complex, EIS complex and cloacal exstrophy alone[5]. In our patient, omphalocele and bladder exstrophy were present, but imperforate anus and spinal defects were not.

Studies on cardiac findings of patients with trisomy 13 have described the frequency of heart defects as ranging from 56% to 86%[15]. Commonly reported heart malformations in Patau syndrome are septal defects, tetralogy of Fallot, hypoplastic left ventricle, patent ductus arteriosus, aortic stenosis, dextrocardia, pulmonary artery hypoplasia and echogenic intracardiac foci[7,15]. Double outlet right ventricle, pulmonary atresia, large vertical aortopulmonary collateral arteries, secundum ASD and hypoplastic left ventricle were noted in the echocardiographic evaluation of our patient. The frequencies of the cardiac malformations seen in our patient have been reported in the literature as 7-15% for double outlet right ventricle, 11-18% for pulmonary atresia, 19-53% for atrial septal defect and 4% for hypoplastic left ventricle[15].

Trisomy 13 can be diagnosed with sonography during the prenatal period in more than 90 percent of cases. Our patient's mother did not have routine prenatal care during her pregnancy, and so the disorder was not diagnosed prenatally.

A definitive diagnosis of trisomy 13 is made by chromosome analysis, and if early diagnosis is required, one of several techniques such as polymerase chain reaction, quantitative fluorescence polymerase chain reaction or array comparative genomic hybridization can be used until such time as the diagnosis is confirmed

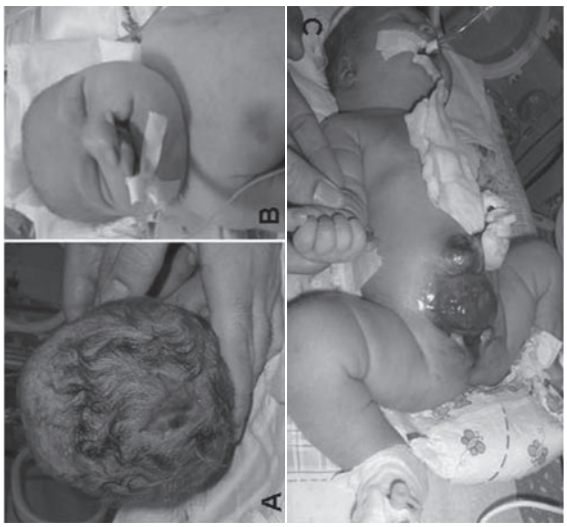

Fig. 1. Phenotypic view of the patient. A: Aplasia cutis congenita areata on the vertex. B: Cleft lip and palate and broad nasal bridge. C: Postaxial polydactyly of the hands, omphalocele and cloacal exstrophy

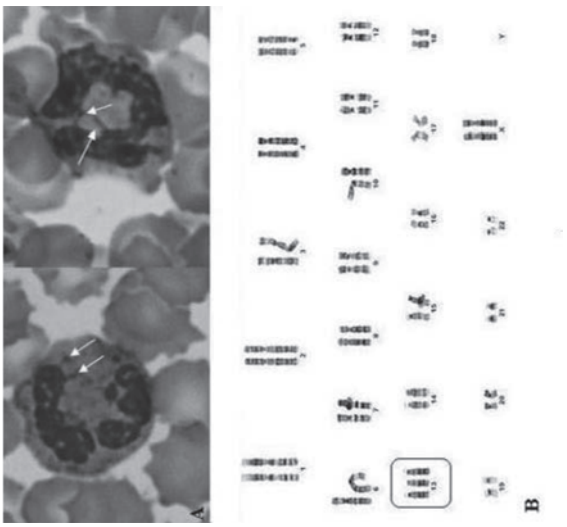

Fig. 2. Diagnosis of trisomy 13. **A:** Peripheral blood smear showing threadlike pedunculated projections attached to the surface of the nuclei of the neutrophils. **B:** Karyotyping of the cultured lymphocytes, confirming trisomy 13 (47,XX,+13).

by chromosome analysis.

Examination of a blood smear is important in the case of a patient where there is suspicion of trisomy 13. It may be used as a rapid test for supporting diagnosis of trisomy 13. Two groups of nuclear excrescences have been reported in neutrophils, one being sex-specific appendages (drumstick, sessile and club forms) and the other, nuclear projections[3]. Their morphologies were seen to be similar; however, the nuclear projections were found to be smaller in size than the sex-spesific appendages. Recent studies have shown that neutrophilic leukocytes of trisomy 13 patients possess an increased number of nuclear projections, and thus if two or more nuclear projections are detected in more than 15% of the neutrophils, it may be highly suggestive of trisomy 13[16]. Huehns et al.[3] concluded that the presence of threadlike pedunculated projections attached to the surface of the nuclei of the neutrophils is specific to trisomy 13. Electron microscopic examination revealed the presence of chromatin in these projections[3]. Review of our patient's peripheral blood smear revealed small threadlike pedunculated projections attached to the surface of the nuclei in more than 80% of the neutrophils. In our case, serious birth defects and specific blood smear morphology led to a tentative diagnosis of trisomy 13, which was confirmed by chromosomal analysis.

The survival of patients with trisomy 13 is usually short. Approximately 80% of affected infants die within the first month and 90% die within the first year of life[17]. Our patient died at three days of life.

In this case report, we aimed to point out the association of cloacal exstrophy with trisomy 13 as an extremely rare dysmorphology, alongside the more typical congenital anomalies of the disorder that have been reported in the medical literature. In addition, we wished to bring this association to the attention of pediatricians, neonatologists and medical geneticists interested in such dysmorphologies. Finally, we would like to suggest that identification of the characteristic structural anomalies of the neutrophils on a blood smear may be used as a rapid test for supporting a diagnosis of trisomy 13.

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