A well-documented trisomy 13 case presenting with a number of common and uncommon features of the syndrome

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Trisomy 13 is a very rare and lethal autosomal chromosomal malformation syndrome. Its incidence is 1/12,000 births. In this paper, we present a new trisomy 13 case associated with unusual and undescribed findings. This patient was the first child of unrelated parents with advanced maternal and paternal age, at 36 and 38 years, respectively. Unfortunately, the parents did not accept the prenatal diagnosis. The baby was born after 34 weeks of gestation by cesarian section. His birth weight was 1,865 g and he demonstrated typical craniofacial abnormalities for trisomy 13 such as severe microphthalmia, microcephaly and scalp defects, and peripheral chromosome analysis revealed trisomy 13. He died of congenital heart disease and sepsis on the 12th hospital day. A complete autopsy revealed a scalp and a skull defect at the vertex, aplasia of the 5th finger nails, a complex heart disease including pulmonary trunk atresia, patent foramen ovale, membranous ventricular septal defect (VSD), main aorticopulmonary collateral artery (MAPCA) and aortic dextroposition, arrhinencephaly, partial agenesis of the corpus callosum, and neuronal heterotopias in the cerebellum. He also had bilateral cystic renal dysplasia, Meckel's diverticulum, right inguinal hernia, ectopic splenic tissue in the pancreas, and ectopic thymus tissue adjacent to the thyroid.

To our knowledge, this is a unique trisomy 13 case with numerous common and uncommon features including a bone defect in the skull, partial agenesis of the corpus callosum, aplasia of the 5th finger nails, and a complex heart disease including pulmonary atresia, patent foramen ovale, membranous VSD, MAPCA and aortic dextroposition, which have not been published previously in the relevant literature all together.

Key words: trisomy 13, Patau syndrome, MAPCA (main aorticopulmonary collateral artery), aplasia of 5th finger nails, scalp and calvarial defect, autopsy, arhinencephaly, Meckel's diverticulum, cystic renal dysplasia.

Trisomy 13 (Patau syndrome) is a rare but lethal autosomal chromosomal abnormality with an incidence of 1/12,000 births[1-4]. This syndrome usually presents with microcephaly, microphthalmia, scalp defects, congenital heart defects, holoprosencephaly, orofacial clefting, polydactyly, and severe growth and mental retardation[2]. Scalp defects are commonly seen in the vertex and usually without an underlying bone defect. The most commonly associated cardiac anomalies are atrial septal defect (ASD), patent ductus arteriosus (PDA) and ventricular septal defects (VSDs) followed by other rare cardiac anomalies including dextrocardia, aortic and pulmonary valve abnormalities and hypoplasia of the aorta or pulmonary trunk[5]. As for the limb anomalies in trisomy 13 syndrome, postaxial polydactyly, flexion of fingers and hyper-convex nails are the most frequently observed anomalies[2,6]. We herein report a well-documented trisomy 13 case presenting with common and uncommon findings including a scalp and a skull bone defect at the vertex, aplasia of the 5th finger nails and a complex

heart disease that consisted of pulmonary trunk atresia, patent foramen ovale, membranous VSD, main aorticopulmonary collateral artery (MAPCA) and aortic dextroposition.

Case Report

This male newborn was the first child of unrelated parents with advanced age and was born by cesarian section following 34 weeks of gestation. His birth weight and length were 1865 g and 42 cm, respectively. The parents had not accepted the prenatal diagnosis. Since the baby had typical craniofacial abnormalities for trisomy 13 such as coarse facial appearance, severe microphthalmia (Figs. 1, 2), microcephaly, scalp defects on the vertex, and flexion contractures of the fingers (Fig. 3), trisomy 13 was suspected and was confirmed by peripheral chromosome analysis (47,XY+13) (Fig. 4). There was no cleft lip or palate. On physical examination, he was cyanotic and in a poor general condition. However, sucking, rooting, grasping and Moro reflexes were all positive. He had scalp defects, severe microphthalmia, microcephaly and a coarse face. Peripheral blood smear demonstrated nuclear projections in neutrophils. He died of congenital heart disease and sepsis on the 12th hospital day. A complete autopsy revealed a scalp and a skull defect at the vertex (Fig. 5), aplasia of the 5th finger nails (Fig. 3), a complex heart disease including pulmonary trunk atresia, patent foramen ovale, membranous VSD, MAPCA, and aortic dextroposition (Fig. 6). The examination of the central nervous system showed arrhinencephaly, partial agenesis of the corpus callosum (Fig. 7) and neuronal heterotopias in the cerebellum (Fig. 8). He also had bilateral cystic renal dysplasia (Fig. 9), Meckel's diverticulum, right inguinal hernia, ectopic splenic tissue in the pancreas, and ectopic thymus tissue adjacent to the thyroid.

Discussion

Trisomy 13 is the third most commonly observed autosomal trisomic syndrome. Patau et al.[1] first described trisomy 13 in 1960. This trisomic syndrome has a characteristic triad including microphthalmia, cleft lip and palate and polydactyly. The clinical course is very poor and about 45% of the cases die during the first month and 86% during the first year due to cardiac and renal malformations.

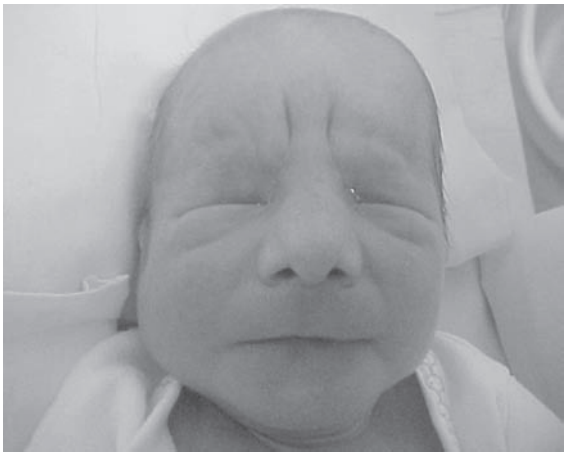

Fig. 1. Coarse facial appearance with microphthalmia is seen.

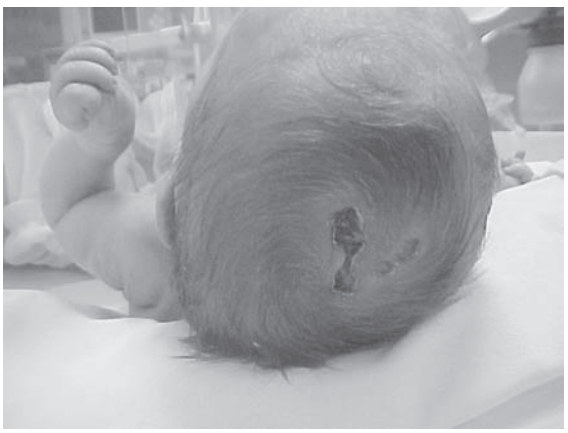

Fig. 2. A group of scalp defects are seen at the vertex.

Fig. 3. Flexion contractures of the fingers and absence of the nail on the fifth finger are noted.

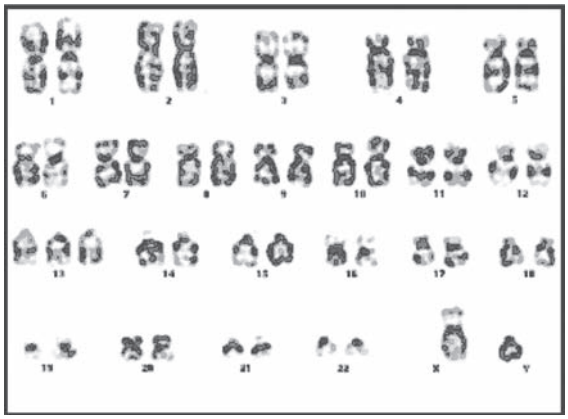

Fig. 4. Karyotype of the patient showing 47,XY+13 with Giemsa banding.

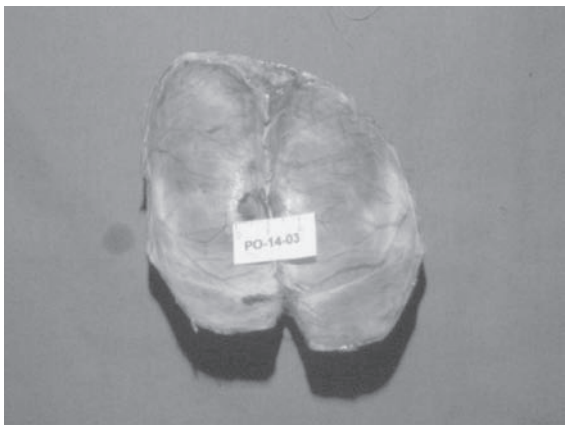

Fig. 5. The defect in the occipital bone is seen (1.5 cm in diameter).

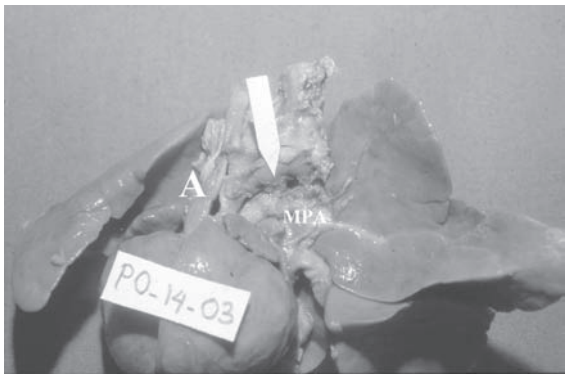

Fig. 6. Severely hypoplastic pulmonary trunk and main aorticopulmonary collateral artery (MAPCA) (white arrow) are shown (A: Aorta. MPA: Main pulmonary artery).

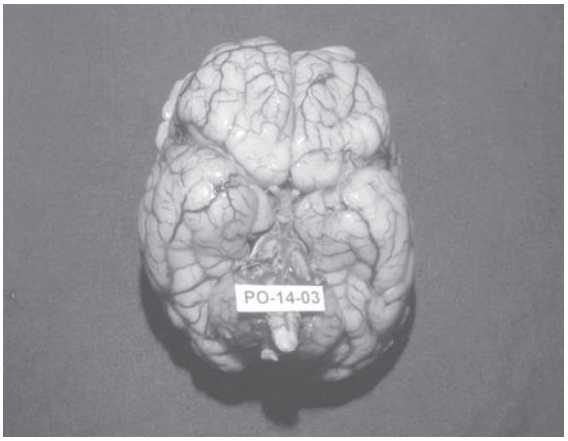

Fig. 7. Bilateral absence of olfactory tractus (arrhinencephaly) is noted.

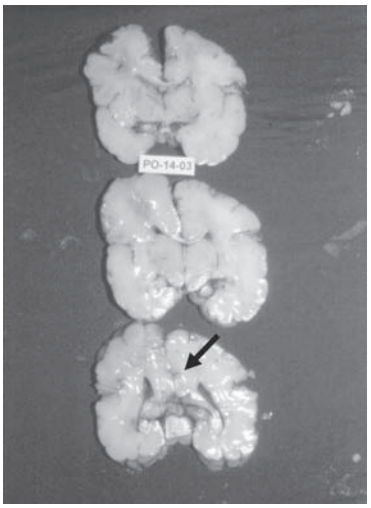

Fig. 8. Agenesis of caudal portion of the corpus callosum is seen in coronal sections of the brain (arrow).

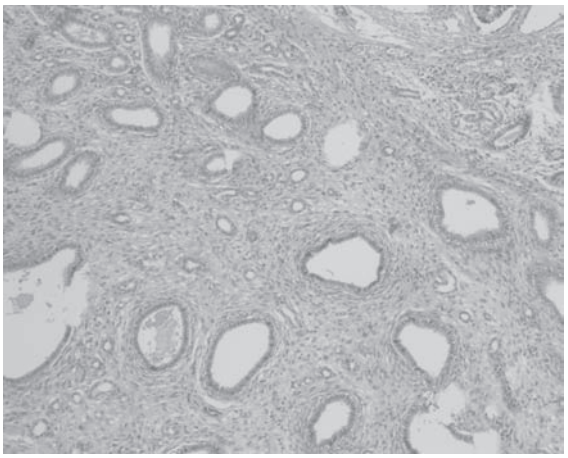

Fig. 9. Renal parenchyma shows cystic primitive tubules and mesenchyme (hematoxylin and eosin X200).

Postmortem examination is thus very important in this syndrome for demonstrating the many unrecognized malformations[5]. Furthermore, unrecognizable lethal syndromes should also be evaluated with postmortem chromosomal analysis and autopsy. Otherwise, severe anomalies such as arrhinencephaly, Meckel's diverticulum, cardiac malformations and kidney abnormalities likely go undetected.

Though the prognosis of cases with Patau syndrome is poor, a small number of patients have recently been reported to have had a long survival by Tunca et al.[7], Iliopoulos et al.[8] and Duarte et al[9]. The absence of holoprosencephaly is an important factor for determination of long survival since lobar or semilobar holoprosencephaly may lead to early fetal death[10,11].

Tennstedt et al.[5] reported congenital heart defects and extracardiac malformations associated with chromosomal abnormalities in a study performed on 815 fetuses, and chromosomal anomalies were detected in 33% of the cases in whom karyotyping was possible. Of 19 cases with chromosomal abnormalities, six were demonstrated to be trisomy 13 with various cardiac malformations. Common cardiovascular anomalies observed in trisomy 13 are summarized in Table I. The present case had a complex cardiac anomaly consisting of pulmonary trunk atresia, patent foramen ovale, membranous VSD, MAPCA, and aortic dextroposition, which has not been described previously as seen in Table I.

Table I. Common Cardiovascular Anomalies in Trisomy 13 (Gorlin et al.[2])

Defect	Percent
Atrial septal defect	91%
Patent ductus arteriosus (PDA)	82%
Ventricular septal defect (VSD)	73%
Dextrocardia	24%
Aorta from right ventricle	11%
Coarctation of aorta	9%
Bicuspid aortic valve	8%

Table II describes the comparison of the clinical findings of our patient with the frequency of various defects reported in the literature. Our case had all of the characteristic findings plus bilateral absence of olfactory tractus, nail dysplasia in the 5th fingers and a scalp and occipital bone defect. The scalp defects are known to constitute 85% of all solitary lesions of aplasia cutis congenita, and several factors such as intrauterine trauma, vascular compromise or teratogens have been implicated in the pathogenesis of these lesions[12]. However, the etiology of scalp and skull defect in trisomy 13 is still unclear.

Prenatal ultrasonography (USG) may be very helpful for the diagnosis of trisomy 13 (Patau) syndrome. Unfortunately, the parents of the present case did not accept the prenatal diagnosis. Prenatal USG, particularly three-dimensional (3D) sonography, permits a more detailed evaluation than routine 2D sonography[13,14]. Visualization of the facial dysmorphisms in the fetus will help them accept

Table II. Comparison of the Present Case with the Frequency of Various Defects Reported in Trisomy 13 (Gorlin et al.[2])

Trisomy 13		Present Case
Cardiac defects	94%	(+)
Microcephaly	86%	(+)
Holoprosencephaly	70%	(+)
Cleft palate	69%	(–)
Cleft lip	58%	(–)
Polydactyly	76%	(–)
Nail	Dysplasia	Absence in the 5th fingers
Capillary hemangioma	88%	(+)
Short neck	100%	(+)
Hypotelorism	83%	(+)
Scalp defect	75%	(+)
Skull defect	(–)	(+)

prenatal genetic counseling approaches such as amniocentesis and therapeutic abortion, and it may also facilitate their granting permission for a postmortem study.

In conclusion, the presented case is a complete autopsy that demonstrated very well several common and uncommon findings in trisomy 13 syndrome, such as a complex heart disease, malformations of the central nervous system, pancreas, kidney, and 5th finger nails, and defects of the scalp and calvaria.

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