Liveborn infant with triploidy
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Triploidy is one of the most common chromosome abnormalities in humans, occurring in approximately 1 – 2 % of all conceptuses. Here, we report the case of a digynic triploid male infant that carried an additional X chromosome of paternal origin. To the best of our knowledge, this has not previously been reported.
This male infant was born to a 37-year-old G1/P1 by Cesarean section at 36 4/7 weeks of pregnancy following premature rupture of membranes (PROM), meconium-stained amniotic fluid and breech presentation. Marked intrauterine growth restriction (estimated fetal weight 1200 g) was noted for the first time when the mother was admitted. Apart from maternal smoking (2–5 cigarettes per day) pregnancy history was unremarkable.

Following delivery, the infant adapted with Apgar scores of 4, 6 and 6 at 1, 5 and 10 minutes, respectively. Umbilical arterial cord pH was 7.38. Because of poor respiratory drive, he required bag-mask ventilation. His preductal SpO₂ remained low despite use of 100% oxygen. Following placement of an umbilical venous catheter and premedication with morphine and rocuronium, he was intubated and transferred to the NICU.

On admission, he was put on high frequency oscillatory ventilation because of persisting hypoxemia. Further attempts at stabilization included administration of surfactant, iNO and cardiovascular support with dobutamine, norepinephrine and hydrocortisone. Given the patient’s critical condition and the history of PROM, broad-spectrum antibiotics were started. At one hour of age, rectal temperature was 36°C, heart rate 140 bpm, blood pressure 55/33 (mean 40)
mmHg and SpO₂ 90 % while on HFOV with an FiO₂ of 1.0. An arterial blood gas obtained at this point was normal (pH 7.32, pCO₂ 6.7 kPa, pO₂ 7.5 kPa, BE –0.9 mmol/l) and lactate concentration was 1.2 mmol/l.

On physical examination, severe symmetric growth restriction was noted (Fig. 1) with a birth weight of 1220 g (- 4 SDS, i.e., 1000 g below P3), length of 39 cm (5 cm below P3) and a head circumference of 30 cm (1.5 cm below P3). There was microstomia, micrognathia and right-sided microphthalmus and left-sided nanophthalmus (probably with no functional vision), as well as corneal opacifications. In addition, multiple contractures on hands and feet with syndactyly dig. III/IV on the right hand, clinodactyly dig. IV on the left hand, club foot deformity of the right foot with syndactyly dig. II/III, as well as cryptorchidism were noted (Fig. 2).

As outlined above, an atrial blood gas analysis and lactate levels were within normal levels. There was pancytopenia (leukocytes 2.6 G/l, hemoglobin 126 g/l, platelets 66 G/l, erythroblasts 118/100 leucocytes, i.e., 3.1 G/l). Coagulation studies were within normal limits. Urea (2.6 mmol/l) and creatinine (71 µmol/l) concentrations were normal initially, but the latter increased to 119 µmol/l on DOL 2; concomitantly, an amikacin trough level was elevated at 24.9 µmol/l (upper limit of norm: <10 µmol/l).
Growth charts illustrating the patient’s massive symmetric intrauterine growth restriction.
Growth restricted male infant with microphthalmia, microstomia, right-sided club foot deformity and proximal syndactyly II/III.
A babygram revealed a bell-shaped chest with small-appearing lungs, thin ribs (11 pairs); in addition, sacral vertebral bodies 2 and 3 were not normally aligned (Fig. 2). Echocardiography demonstrated a hypoplastic aortic arch, a 3 mm PDA with right-to-left shunt, decreased biventricular function and severe pulmonary arterial hypertension with mild tricuspid regurgitation and dilatation of right atrium and right ventricle. An abdominal ultrasound examination showed hypoplastic kidneys (Fig. 3) and a vascular malformation in the form of a porto-systemic fistula in the right lobe of the liver. Finally, a cerebral ultrasound examination showed bilateral plexus cysts (Fig. 4).

Based on the clinical findings, a genetic defect was felt to be very likely (i.e., trisomy 13 or 18); combined with the patient’s respiratory and cardiovascular instability, an interdisciplinary team consisting of neonatologists, a pediatric geneticist and a pediatric neurologist recommended redirection of care. The parents agreed and the patient was extubated on the 2nd day of life and died 15 minutes later in the arms of his parents.

The results of a chromosomal analysis became available after the infant’s death. It revealed triploidy with a karyotype of 70,XXXY. This means that apart from the additional set of chromosomes, there was an additional X chromosome. To determine the origin of this additional X chromosome, further genetic analyses in the parents were performed. The results indicated
that the additional set of chromosomes was of maternal origin (digynic triploidy) whereas the additional X chromosome was of paternal origin.
Babygram: bell-shaped chest with small-appearing lungs, thin ribs (11 pairs); in addition, sacral vertebral bodies 2 and 3 are not normally aligned.
Abdominal ultrasound examination: hypoplastic kidneys (lower norm for an AGA preterm infant with a birth weight of 1200 g would be 3 cm).
Cerebral ultrasound examination: apart from bilateral plexus cysts unremarkable.
Patient’s karyotype revealing digynic triploidy and an additional X chromosome (shown to be of paternal origin by microsatellite analysis).
In a series of 87 cases of human triploid spontaneous abortions, Zaragoza et al. have analyzed the origin of the additional haploid chromosome set. The majority of cases (69%) were diandric in origin (i.e., paternally-derived) because of dispermy. This very likely involves failure of the zona reaction, which acts normally to prevent polyspermy. In contrast, the maternally-derived or digynic cases (31%) mainly originated through errors in meiosis II (1).

In addition, their results demonstrated a complex relationship between phenotype and paternal origin: paternally-derived cases predominate among typical spontaneous abortions, whereas maternally-derived cases are associated with either early embryonic demise or with relatively late demise involving a well-formed fetus (as illustrated in our case). Finally, they observed an association between diandric – but non digynic – triploidy and the development of partial hydatiform moles (1). The main findings of the study are summarized in Fig. 7.

Many of the physical findings in our patient are quite characteristic for patients with digynic triploidy syndrome: marked intrauterine growth restriction, hypertelorism with eye defects ranging from colobomata to micro-/nanophthalmia, syndactyly, talipes equinovarus, congenital heart defects, cryptorchidism, and renal anomalies (2). Most triploid conceptions die
Fig. 7

Parental origin and phenotype of triploidy, adapted from Zaragoza et al. (2) (the respective contribution of paternal chromosomes are marked in red).
early in development, accounting for up to 10% of all spontaneous abortions. It is rare that triploid fetuses come to term, with the longest surviving non-mosaic case dying at age 10½ months (3).

See also: COTM 07/2006 – Two cases of live born infants with triploidy syndrome.

