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Long survival in a 69,XXX triploid infant in Greece

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ABSTRACT. The live birth of a triploidy infant is a very rare event and death usually occurs within the first hours of life. Triploid cases with a survival of more than two months are infrequent. We report on an infant with a 69,XXX chromosome constitution who survived 164 days. Chromosomal analysis demonstrated a 69,XXX karyotype with no evidence of mosaicism. This is the longest survival reported for this condition to date in Greece and the fourth longest worldwide. The infant was admitted to our clinic several times due to respiratory problems, and supplementary oxygen was required. The improved survival of our case was possibly due to better management of respiratory illness and prematurity, and these are essential factors that physicians should consider carefully with such rare cases.

Key words: Triploidy, 69,XXX, Long survival

INTRODUCTION

Triploidy is a chromosomal abnormality characterized by an extra-haploid set of chromosomes (Fryns et al., 1977). This extra-haploid set of chromosomes may be maternal (digynic) or paternal (diandric). Triploidy is estimated to occur in 3% of recognized human conceptuses. Most triploids are aborted spontaneously between 7 and 17 weeks of gestation, while those who proceed to live birth die at an early postnatal stage (Hasegawa et al., 1999). Twenty different clinical features have been described in 69,XXX triploid infants (Doshi et al., 1983). According to the literature, triploid cases with a survival of more than 60 days are very rare (Sherard et al., 1986). In this report we present a case of a 69,XXX triploid infant who survived for 164 days. This is the longest survival reported for this condition to date in Greece. A review of the literature uncovered six cases of a 69,XXX triploid infant who survived more than 45 days.

CASE REPORT

Two hours after delivery, an infant girl was admitted to the 2nd Department of Pediatrics at AHEPA University Hospital due to multiple anomalies. It was the first child of healthy parents. The father was 28 years old and unrelated to the mother, who was 26 years old. The duration of gestation was 39 weeks. The development of the fetus was normal until the 26th week; however, during the 30th week the size of the head was large compared to the rest of the body. In the 34th week, amniotic fluid was reduced. The baby was delivered at 39 weeks of gestation by cesarean section.

Birth weight was 1850 g, length 42 cm and head circumference 30.2 cm (below the 3rd percentile). The baby had an asymmetric head, small palpebral fissures, anterior fontanel 3 x 2 cm and posterior fontanel 2 x 2 cm. Also, she had low-set ears, a flat nasal bridge and small tongue. In addition, she had hexadactyly of the right hand, a clinical feature never described previously in 69,XXX triploid infants. In addition, she had bilateral overlapping of the 3rd and 4th fingers, single palmar creases and bilateral overlapping of the 2nd and 3rd toes. Heart rate was 112 bpm. The findings from chest auscultation and abdominal examination were normal. The liver and the spleen were both not palpable, while the femoral pulses were within normal. During the 2nd day of her life, we encountered generalized tonic clonic convulsions and on the 4th day, respiratory distress. The brain CT revealed dilation at the cortical subarachnoid space at the occipital lobe, with aplasia of the inner part of the occipital lobe on the same side. Moreover, there was a great possibility of aplasia of the corpus callosum.

Chromosomal analysis was performed from peripheral blood samples using standard procedures on the third day of its life. Fifty GTG-banded metaphases from PHA-stimulated peripheral blood lymphocytes demonstrated a karyotype of 69,XXX. The karyotypes of both parents were normal (mother - 46,XX and father - 46,XY, 9 h+).

On the 15th day of life, the infant was discharged after improvement and no respiratory problems. At age 53 days, she was admitted to the clinic. Body weight was 3160 g, length 51 cm and head circumference 35 cm. The newborn presented hypotonia. At 4.5 months, the infant was admitted again due to respiratory problems and required supplemental oxygen. One month later, she died due to cardiorespiratory problems. The child lived for a total of 164 days (5.5 months), a very long survival for a triploid individual.

DISCUSSION

Triploidy is the third most frequent chromosomal anomaly and is responsible for 15-18% of spontaneous abortions (Dyban and Baranov, 1990). Only 1 in 1,200 triploid fetuses live after birth. The frequency of triploidy in live births is 1/10,000 (Jacobs et al., 1974), and males represent 51-69% of the cases (McFadden and Langlois, 2000).

Two different mechanisms have been described that are responsible for triploidy (O'Neill and Kaufman, 1987). The extra-haploid set of chromosomes may be maternal (digynic triploids) or paternal (diandric triploids). Digynic triploidy may result from the fertilization of a normal oocyte produced through an error at either the first or second meiotic division. Diandric triploidy may occur through fertilization of a normal oocyte by a diploid sperm as a result of an error at either the first or second meiotic division or through fertilization of an oocyte by two sperms (dispermy). According to previous reports, 66.4% of triploid infants are due to dispermy, 23.6% due to a diploid sperm and 10% due to a diploid oocyte. Usually, the extra-haploid set of chromosomes has a paternal origin. Digynic embryos have a better chance to reach the second trimester of gestation or even to be born.

The sex chromosomes in triploid individuals of maternal origin should be in 50% of the cases XXX and 50% XXY, and in those of paternal origin, 25% XXX, 50% XXY and 25% XYY. According to previous studies, the frequency of triploids is the following: 31-49% 69,XXX, 49-68% 69,XXY and 0-3% 69,XYY. The low frequency of the 69,XYY chromosomal aberration suggests that this karyotype leads to low viability and early abortion of the zygote, otherwise the mechanism through which it occurs is very rare.

Two distinct phenotypes are known in triploids that survive up to the second trimester. Type I phenotype is characterized by a relatively well-grown fetus with either proportionate head size or relative microcephaly, an abnormally large placenta associated with partial hydatidiform mole, which is also diandric in parental origin. Type II phenotype includes severe intrauterine growth retardation, relative macrocephaly, a small noncystic placenta and digynic origin. Our case according to the clinical features is the type II phenotype.

As our patient lived longer than usual, we became concerned about the possibility of mosaicism with a diploid cell line. Repeated analyses yielded a 69,XXX constitution; however, the absence of a normal cell line does not eliminate the possibility of cryptic mosaicism.

The infant showed the common clinical features of 69,XXX liveborns such as relative microcephaly, hypotonia, respiratory distress, blepharoptosis, microphthalmia, low-set and malformed ears, micrognathia, asymmetric chest, cutaneous syndactyly and overlapping of fingers and/or toes.

The most frequent cause of death is pneumonia and generally respiratory problems. The improved survival of our case was due to better management of respiratory illness and prematurity, factors worth noting in counseling on such rare conditions. However, a significant statement cannot be made regarding what actually contributed to the longevity of our infant. Different risk factors determine the frequency of triploidy, such as the age of the parents, diabetes and ultraviolet exposure. However, previous studies and our study showed that the age of the parents do not have an influence on the frequency of the syndrome. Neuber et al., 1993, suggest that the age of mother is an important factor.

Since 1977, six cases of triploid infants with long survival have been described (more than 45 days). In this report, we present the 4th longest surviving triploid case and the 1st in

Greece. The infant lived for 164 days. In Table 1, we describe and compare the clinical features and the survival of these six cases (Fryns et al., 1977; Schrocksnadel et al., 1982; Arvidsson et al., 1986; Sherard et al., 1986; Niemann-Seyde et al., 1993; Hasegawa et al., 1999) and our case. According to this table, 5/7 infants with long survival were girls. In addition, it is interesting that the phenotype in 5/7 cases was type II, and in all known cases the babies were delivered by cesarean section. Data from more live-birth triploid cases are needed to make a meaningful analysis.

Table 1. Clinical features of triploid infants with long survival.

Parameters	Fryns et al. (1977)	Schrocksnadel et al. (1982)	Arvidsson et al. (1986)	Sherard et al. (1986)	Niemann-Seyde et al. (1993)	Hasegawa et. al. (1999)	Present case
Sex	Female	Female	Male	Male	Female	Female	Female
Gestational age (weeks)	Term	?	31	37	34	31	39
Delivery	Cesarean section	?	Cesarean section	Cesarean section	?	Cesarean section	Cesarean section
Weight (g)	1810	?	700	1417	800	650	1850
Length (cm)	43.5	?	?	?	37	31	42
OFC (cm)	32.7	?	?	30.5	26.5	26	30.2
Placenta size (g)	Small	?	115	Small	?	152	Small
Cystic villi	No	?	?	?	?	No	No
Survival days	60	210	189	308	74	45	164
Karyotype	69,XXX	69,XXX	69,XXY	69,XXY	69,XXX	69,XXX	69,XXX
Phenotype	Type II	?	Type II	Type II	Type I	Type II	Type II
Origin of triploidy	Mat II	?	Mat II	Mat	Pat	Mat II	?

OFC = occipitofrontalis circumference; Mat = maternal; Pat = paternal.

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