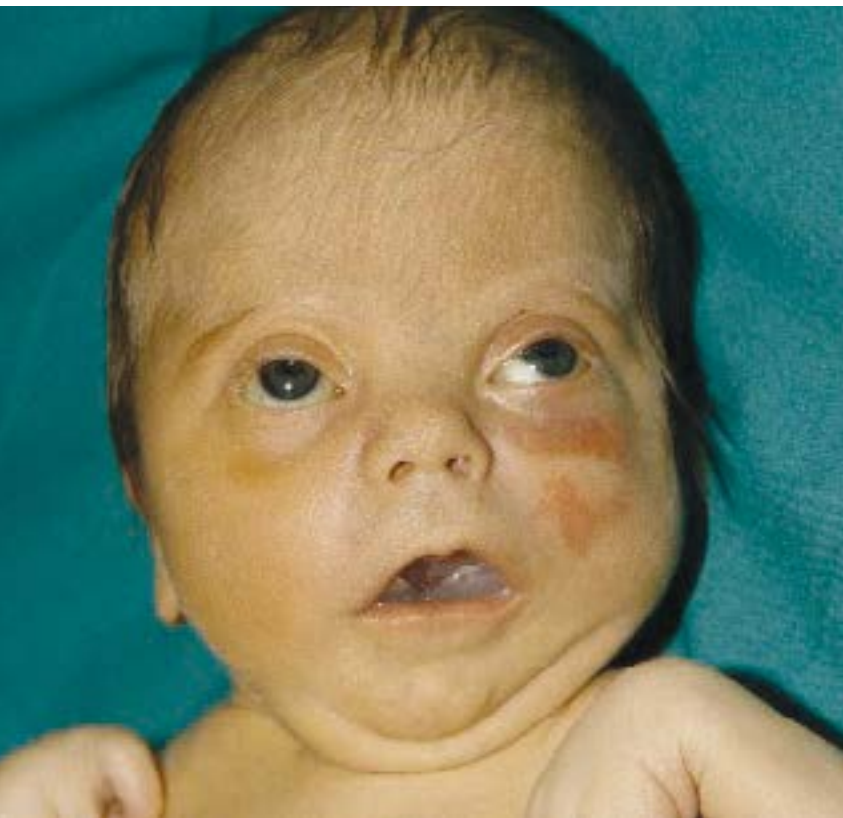


SWISS SOCIETY OF NEONATOLOGY

Partial trisomy 6

April 2005



A female infant was born to a 27-year-old G3/P3 with a history of two previous normal pregnancies. In the 16th week of gestation, dilatation of the cerebral ventricles and a ventricular septal defect were seen on routine ultrasound. Amniocentesis revealed a karyotype of 46 XX, 6q+ (elongated long arm of chromosome 6). Intrauterine growth parameters were within the normal range. In spite of the poor prognosis, the parents opted to continue the pregnancy.

The baby was delivered by Cesarean section at the 38 5/7 weeks of gestation. The Apgar scores were 7, 8, and 9 at 1, 5, and 10 minutes, respectively. Birth weight was 2780 g (P10-25), length 48 cm (P3-10), head circumference 33 cm (P10-25). Physical examination revealed prominent eyes, upslanting palpebral fissures (Fig. 1), a depressed nasal bridge, cleft of the hard and soft palate, a "carp" mouth, a small mandible (Fig. 2), multiple folds in the ear helices, as well as pterygia and loose skin in the neck region. The extremities showed ulnar deviation of the hands as well as a fixed camptodactyly of digits II-V, clinodactyly of digit V (Fig. 1), narrow fingernails, bilateral single transverse palmar creases, an extension deficit of the elbows and hips, a calcaneo-valgus position of the left foot, and adduction and supination of the right foot (Fig. 3). In addition, hyperreflexia and poor spontaneous movements were observed.

On chest X-ray, 11 narrow, paired ribs and clavicae bipartitae (pseudoarthrosis) were seen (Fig. 4). An ophthalmologic examination revealed hypoplastic irides and shallow orbits bilaterally. Cerebral ultrasound and later magnetic resonance imaging (Fig. 5) showed partial agenesis of the corpus callosum and bilateral colpocephaly. Echocardiography confirmed the ventricular septal defect with predominant left-to-right shunt as well as a patent ductus arteriosus showing mainly a left-to-right shunt. The foramen ovale was open.

Examination of the chromosomes from cultured lymphocytes revealed that the additional segment on 6q was part of the long arm of chromosome 6, specifically the segments 6q21-q24 (painting with a whole chromosome 6 library and with specific segments on chromosome 6). The karyotype therefore was: 46 XX, dup(6)(q21q24) de novo. Chromosome examinations of the parents revealed normal results and thus excluded a balanced rearrangement in either of them.

Following delivery, the infant developed signs of respiratory distress and required 30% oxygen. The initial respiratory situation improved and oxygen could be stopped within the first day of life. However, at the age of ten days, the pulmonary situation began to deteriorate with rising oxygen requirements and increased secretions possibly secondary to aspiration.

In the second week of life, the baby developed diabetes mellitus which had to be treated with subcutane-

ous insulin injections starting on day fifteen. It was extremely difficult to maintain blood glucose levels within acceptable limits leading to polyuria, vomiting and subsequently dehydration.

In view of the worsening metabolic and pulmonary problems as well as the poor overall prognosis of distal duplication of chromosome 6q, it was decided - in agreement with the parents - to discontinue further intensive care. The child was taken home by the parents on the 22nd day of life. She died the very same day.

Prominent eyes, „carp” mouth.



Fig. 1



Fig. 2

Depressed nasal bridge, „carp“ mouth, small mandible.

Calcaneo-valgus position of the left foot, and adduction and supination of the right foot.

Fig. 3





Fig. 4

11 narrow, paired ribs and clavulae bipartitae (pseudoarthrosis).

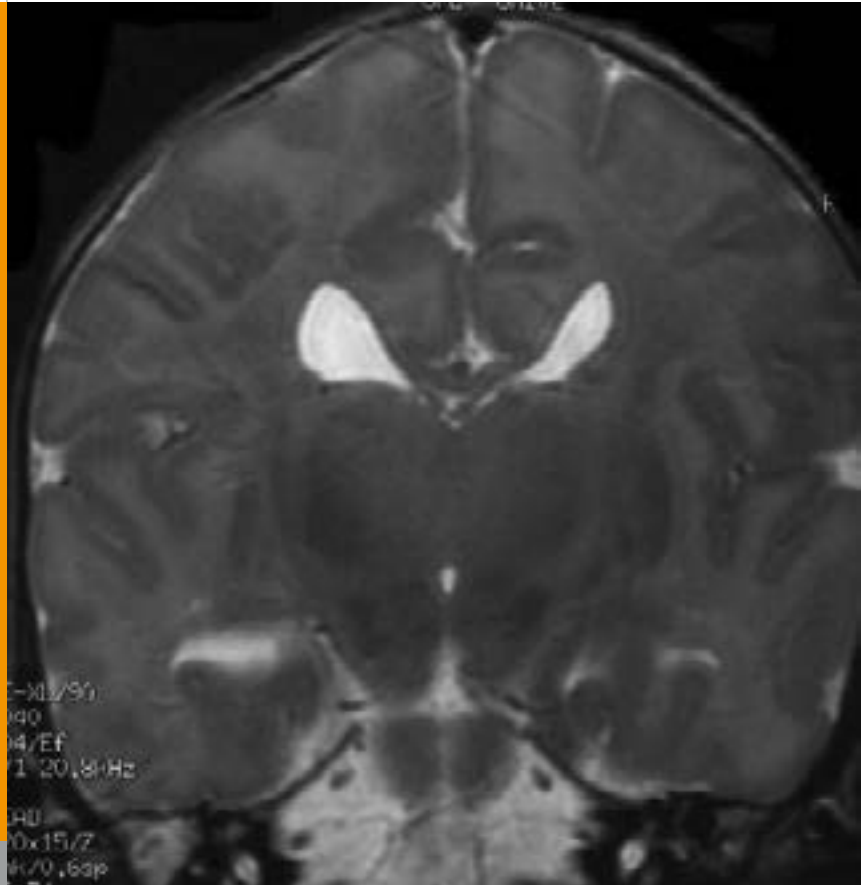


Fig. 5

Partial agenesis of the corpus callosum and bilateral colpocephaly.

Duplication of 6q is a very rare finding in live born infants. Full trisomy 6 is incompatible with fetal survival, however, it has been found in spontaneous abortions (1). The duplication 6q syndrome in live born infants has been documented in more than 30 cases since it was first presented by Breuning in 1977 (2).

Several different phenotypes have been described with variable clinical findings. The most consistent include mental retardation, pre- and postnatal growth restriction, microcephaly, prominent forehead, downward slanting palpebral fissures, hypertelorism, flat/broad nasal bridge, "carp" mouth, small mandible, low set/posteriorly rotated ears, short/webbed neck, joint contractures, clinodactyly, syndactyly, talipes equinovarus, cardiac anomalies, cerebral anomalies, abnormal palmar creases and in some cases cleft palate, eye and genital anomalies (3).

Duplications of 6q are the result of either an abnormal segregation of a balanced translocation or inversion carried by a parent or of a de novo unbalanced rearrangement. Often, the duplication is combined with a deletion of the other chromosomal segment involved in the rearrangement. Very few patients - as in our case - have a pure 6q duplication (4). Geneticists have tried to identify certain bands within the duplicated region that could be responsible for specific phenotypic features. However, it seems that the phenotype in general tends to have a variable expression.

Henegariu (3) has described a mild duplication 6q syndrome. In our case, the clinical course seemed to be more severe. The pulmonary complications that occurred in our case have not been described in the literature. They may have been related to the cleft palate and the profuse secretions eventually leading to repeated aspirations.

Diabetes mellitus especially transient neonatal diabetes mellitus (TNDM) seems to be associated with uniparental disomy of chromosome 6. The findings of Cavé et al (5) confirm that TNDM may result from the overexpression of a gene located on chromosome 6q that is expressed from the paternal allele. The imprinted gene for diabetes appears to be localized on chromosome segment 6q22-q23 (6, 7). Our patient developed insulin-dependent diabetes mellitus that was difficult to control on the 15th day of life. This finding would suggest that the duplication arose in the paternal genome and thus there were 2 paternal copies of the critical segment.

The spectrum of outcome of patients with a partial trisomy 6q is very broad. Most fetuses with this anomaly die early in pregnancy. The outcome of live born infants is dependent on the clinical manifestations. With special care and specific therapies, some children have managed to reach adulthood. Others, like our patient, died shortly after birth.

Partial trisomy 6q is a distinct syndrome which needs further evaluation. In the future it may be possible to identify more specifically, which band on the long arm of the chromosome is responsible for a particular clinical feature. Up until now it appears that genes from different regions of 6q interact and influence phenotypic traits so that over-expression of various bands may modulate gene expression and determine similar outcomes as cited by Henegariu et al (3).

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