Both siblings affected by tetrasomy 18p in a dichorionic twin pregnancy

Inan C, Sayın NC, Gurkan H, Erzincan SG, Ulusal S, Ateş EI, Varol FG
Trakya University, Faculty of Medicine, Departments of Obstetrics & Gynecology, Trakya University, Faculty of Medicine, Departments of Medical Genetics, Edirne, Turkey

Objective
Tetrasomy 18p is a very rare condition which is characterized by the presence of four copies of the short arm of chromosome 18 and is accompanied by various abnormalities including congenital heart defects, lower extremity abnormalities, micrognathia, high arched palate, kyphoscoliosis, microcephaly, and myelomeningocele. Here we present a case of dichorionic diamniotic pregnancy, which both fetuses were diagnosed with tetrasomy 18p. This is the first reported case in literature where tetrasomy 18p is diagnosed in both fetuses in a twin pregnancy.

Methods
The first prenatal evaluation carried out at the 12th week of pregnancy, revealed omphalocele, single leg and foot deformity in one sibling (Fetus I). Major congenital anomaly were not detected in the other twin (Fetus II). On the 18th week, large omphalocele, extremity anomaly, anhydramnios and early growth restriction were observed in fetus I, but no anomaly was found in fetus II. Amniocentesis was performed to non-anomalous fetus II, and no invasive procedure was performed to fetus I due to anhydramnios. Amniocentesis result of fetus II revealed trisomy 18 by FISH analysis. Culture of amniotic fluid cells for karotyping failed. Then on the 24th week of pregnancy, cordocentesis was performed to rule out a possible amnion contamination from the fetus with ultrasound abnormalities (Fetus I) to the healthy-looking fetus II. Level II ultrasonography (USG) of fetus II indicated growth restriction (-2 SD), increased prenasal translucency (3.98 mm); anomalous crux of the heart with an ASD and a small muscular VSD; short and cleft right toe. The result of the chromosome analysis indicated tetrasomy 18p in fetus II. Fluorescent in situ hybridization reactions were performed with both 18p subtelomere and 18q FISH probes which revealed 4 and 2 signals respectively. Thus, we verified that the pieces of the 18th chromosome were tetrasomy 18p. The pregnancy was terminated, and skin biopsies and placenta samples were taken from both fetuses, and chromosome analysis was performed once again. All samples verified the result of tetrasomy 18p for both fetuses. At the same time, the chromosome analysis was performed by using the maternal and paternal blood samples, those of which revealed normal results.

Results
We think that, in this case, in which the maternal and paternal karyotypes were normal, the formation of tetrasomy 18p was de novo. The previous ultrasound examinations did not indicate an anomaly, but in the 23rd week, growth restriction, increased prenasal translucency, congenital heart disease, and foot anomalies were detected in one of the twins. The result of amniocentesis (FISH) indicated trisomy 18, and the result of cordocentesis revealed tetrasomy 18p. Since only centromeric probe was used in the FISH analysis after the amniocentesis procedure, 3 signals of the 18th chromosome were seen, and since there was no reproduction in the culture, trisomy 18 was suspected. Cordocentesis indicated that the karyotype was tetrasomy 18p, and the genetic examinations of the samples taken after the termination established the final diagnosis as tetrasomy 18p for both fetuses. While various congenital anomalies were detected in our case, the presence of an omphalocele covering the whole abdomen in one fetus (Fetus I) have not been reported in literature before in fetuses with tetrasomy 18p.

Conclusion
Although tetrasomy 18p were detected in both fetuses in a diamniotic dichorionic twin pregnancy, the phenotypic appearance was different that seems to be due to variability in expressivity. It is interesting that tetrasomy 18p was detected in the fetus; in which no major structural anomaly had been detected on ultrasound examinations performed before 24th week of pregnancy, which have shown growth restriction and various subtle congenital anomalies in this case. Therefore, serial sonographic examinations in the healthy looking co-twin will contribute to the detection of congenital anomalies that might be distinguished in further weeks.