Cornelia de Lange syndrome – a rarely seen disorder

Y Çekmez,1 MD; N Pişkinpaşa,2 MD; T Tos,3 MD

1 Department of Obstetrics and Gynaecology, Umranıye Medical and Research Hospital, İstanbul, Turkey
2 Department of Obstetrics and Gynaecology, Manisa Government Hospital, Manisa, Turkey
3 Department of Obstetrics and Gynaecology, Dr Sami Ulus Medical and Research Hospital, Ankara, Turkey

Corresponding author: Y Çekmez (yaseminkandicekmez@hotmail.com)

Cornelia de Lange syndrome (CdLS) is a rare genetic disorder of unknown causation, associated with multiple congenital anomalies. Prenatal genetic diagnosis is possible, and the syndrome can occur in subsequent pregnancies of families with affected children as a result of mosaicism. The syndrome has been diagnosed antenatally by careful ultrasound examination, but is usually only diagnosed after birth. We report the case of a patient admitted to our clinic with intrauterine death of the fetus. CdLS was diagnosed on the basis of multiple structural abnormalities seen after delivery.

Discussion

Some signal pathways with important modulation roles in development of the embryo, starting from the early stages of morphogenesis, also have a basic role in creating the anatomical structure of the musculoskeletal system. Although malformations related to the basic differentiation processes are very rare in humans, most congenital anomalies are related to these processes in the early phases of morphogenesis. This applies especially to disorders that have syndromic characteristics as a result of their anomaly pattern and are therefore easily recognised. CdLS is one of these.[9]

CdLS is a rare and clinically well-defined syndrome. Growth retardation, microcephaly, synophrys, long curved eyelashes, thin lips with facing-down convexity and a
long filtrum are seen in all cases.\textsuperscript{1,4} Verma et al.\textsuperscript{2} reported in their series of 180 cases that all patients had microcephaly and pubertal delay, 97% had hirsutism, and 68% were of low birth weight.\textsuperscript{20} In case of synophrys, a wide frenulum and a hirsute forehead were noted.

The cause of CdLS is unknown. A defect on chromosome 3q26.3 has been shown in cases with a family history or intermarriage.\textsuperscript{5} In sporadic and familial cases, mutations of the NIPBL (nipped-B-like) gene, which is a cohesin regulator at the 5th chromosome, have been described.\textsuperscript{6} Bhuiyan et al.\textsuperscript{7} reported NIPBL mutation in 56% of 39 cases of CdLS. Our patient reported no intermarriage or family history.

Findings suggesting a diagnosis of CdLS in the prenatal period are increased nuchal translucency in the first trimester, symmetrical intrauterine developmental restriction (SIDR), significant defects in the upper extremities, and a dysmorphic facial appearance.\textsuperscript{8-10} Sekimoto et al.\textsuperscript{9} reported SIDR in 95% of patients diagnosed with CdLS, skeletal anomalies in 81%, facial dysmorphism in 50% and fetal diaphragmatic hernia in 50%. Polyhydramnios was reported in 2 cases and nuchal translucency in 4. A prenatal diagnosis could be made in 6 cases only.\textsuperscript{11-12} Our patient also had a dysmorphic facial appearance and phocomelia on the right.

As in our case, because the findings on prenatal ultrasonography are nonspecific, CdLS can usually only be diagnosed after birth. As prenatal genetic diagnosis is possible and there is a risk that the syndrome will recur in subsequent pregnancies because of mosaicism, genetic counselling should be provided to the families of affected children.\textsuperscript{13}