

EP10.68. Diagnostic challenges in Cornelia de Lange syndrome: a case series.

Tamar Borkowski Tillman, Bella Davidov, Yinon Gilboa, Naama Orenstein & Dana Brabbing Goldstein

Introduction

Cornelia de Lange syndrome (CdLS) is a rare multisystem developmental disorder characterized by significant phenotypic variability, overlapping with other congenital syndromes, making prenatal diagnosis challenging.

Objective

To describe prenatal ultrasound features of CdLS and highlight the challenges in achieving accurate prenatal diagnosis.

Methods

A retrospective analysis of eight confirmed or suspected CdLS cases was conducted between 2015 and 2025. Prenatal ultrasound findings were correlated with postnatal clinical outcomes and whole exome sequencing (WES) or targeted gene panel results.

Results

Intrauterine growth restriction (IUGR) primarily in the third trimester was the most consistent finding, observed in six out of eight cases. Microcephaly was identified prenatally in only one fetus, while major structural anomalies were detected in three. Prenatal molecular diagnosis was achieved in two instances. The remaining cases were diagnosed postnatally following the observation of characteristic dysmorphic features or developmental delay. Genetic analysis identified de novo NIPBL variants in seven cases (including two with mosaicism). In one case multi-tissue WES was non-diagnostic, with the diagnosis established based on postnatal clinical phenotype.



Figure 1. Fetus with IUGR and facial dysmorphism at 32.4 weeks



Figure 2. Fetus with congenital diaphragmatic hernia and a horseshoe kidney at 31.2 weeks

Conclusion

Prenatal diagnosis of CdLS remains challenging due to its subtle, non-specific presentation. Late-onset IUGR, may be the only indicator. Furthermore, somatic mosaicism poses a significant diagnostic challenge, as standard prenatal testing may yield false negative results. Increased awareness of these limitations may improve prenatal detection and inform counseling.