

Case Report

Classical Cornelia de Lange syndrome in a neonate

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ABSTRACT

Cornelia de Lange syndrome is a rare developmental disorder syndrome involving multiple systems characterized by facial dysmorphism limb deformities, hirsutism, cardiac defects, growth and cognitive retardation, and gastrointestinal abnormalities. The features of this disorder range from mild to severe. We present here a case of preterm newborn with Classical Cornelia de Lange syndrome with heterozygous mutation in NIBPL gene.

Keywords: Cornelia de Lange syndrome, Congenital anomalies, Neonate

INTRODUCTION

Cornelia de Lange syndrome, also called Brachmann-de Lange syndrome involves multiple congenital anomalies characterized by a distinctive facial appearance, growth deficiency, psychomotor delay, behavioral problems malformations of the upper extremities, cardiac and gastrointestinal anomalies. It is also associated with genitourinary abnormalities, congenital diaphragmatic hernias myopia, palatal abnormalities and hearing loss. Facial dysmorphism includes low hairline anteriorly and posteriorly, arched eyebrows, fusion of eye brows above the bridge of nose, short nose with anteverted nares, long philtrum, thin upper lip, and micrognathia.¹ The majority of the cases are sporadic, but a few cases showing an autosomal-dominant inheritance have been reported.² The incidence varies from 1:10,000 to 1:40,000. It is slightly more common in females as compared to males.²

The diagnosis in neonates is made based on clinical observations as suggested by the Cornelia de Lange syndrome foundation and scientific advisory committee of the world CdLS federation.³

We report a case of Cornelia de Lange syndrome with characteristic facial features and physical findings in a neonate that can help practitioners to easily recognize

classical cases and to provide the family with information on this syndrome and its course of illness.

CASE REPORT

A preterm, 33 weeks baby boy was born to nonconsanguineous parents by emergency caesarean section due to severe IUGR and abnormal dopplers. He had a birth weight of 863 grams which was less than 3rd centile for his gestational age. The occipitofrontal circumference (OFC) and length at birth was 24 cm and 32 cm respectively which was also less than third centile for his gestational age. He was born to a 23-year-old second gravida mother who had one prior miscarriage. There were no risk factors for sepsis or antenatal TORCH infections. She required conventional ventilation and CPAP due to prematurity and respiratory distress present since birth.

On physical examination he had abnormal facial characteristics including hirsutism, bushy arched like confluent eyebrows, low anterior and posterior hairline, long eyelashes, fusion of eye brows above the bridge of nose, depressed nasal bridge, downturned angle of the mouth and micrognathia as shown in Figure 1. He also had long philtrum, thin upper and lower lip, down-turned angles of the mouth and microcephaly as shown in Figure

1. Broad hands, clinodactyly of right fifth fingers, short leg, and distal penile hypospadias with bilateral undescended testis was also noted. Ophthalmologic examinations revealed normal findings. His TORCH Ig M assay was negative for evidence of active infection. His echocardiogram showed presence of a patent ductus arteriosus. Cranial ultrasound was normal. Chromosomal analysis revealed a normal male karyotype (46, XY). He had features of Cornelia De Lange syndrome and genetic testing was done which showed heterozygous mutation in NIBPL gene. The genetic study of parents could not be done and they were missed on follow-up.

He was managed in consultation with our pediatric neurologist, geneticists, plastic surgeon, developmental specialist, speech therapist, audiologist, ophthalmologist and occupational therapist. This baby was discharge on day 53 on full feeds with a weight of 1630 gm. Parents were given proper counselling about the diagnosis and prognosis. He is under close follow-up with pediatric neurologist, speech therapist and developmental specialist.



Figure 1 (A and B): Hirsutism, bushy arched like confluent eyebrows, low hairline, long eyelashes, downturned angle of the mouth, long philtrum, thin upper and lower lip, and micrognathia.

DISCUSSION

Cornelia de Lange syndrome is characterized by a distinguishing facial appearance, prenatal and post-natal growth retardation, psychomotor delay, cognitive delay, behavioral problems and abnormal upper extremities.

Cardiac defects, genitourinary abnormalities, hearing loss and gastrointestinal disorders are common. The exact genetic background is not clear. It is thought that the main reason is the consequence of a dominant mutation in the NIPBL, SMC1L1 and SMC3 genes.⁴

According to the Cornelia de Lange syndrome classification by Van allen et al type I or classic Cornelia de Lange syndromes babies display facial and skeletal alterations.^{3,5} They have prenatal growth deficiency, moderate to severe psychomotor developmental delay and major malformations, leading to severe disability or death. Type II or mild Cornelia de Lange syndromes babies has similar facial and minor skeletal abnormalities. However, these changes may develop over time or be partially manifested. They have mild to borderline psychomotor retardation, less severe pre/ postnatal growth retardation and the absence of major abnormalities. Type III or phenocopy Cornelia de Lange syndromes includes patients with Cornelia de Lange syndrome phenotypic manifestations with causal relation to chromosomal aneuploidies or teratogenic exposures.⁶

Our neonate is non-consanguineous and has no family history of such problems. He has history of prematurity, low birth weight, hirsutism and characteristic facial dysmorphism Cornelia de Lange syndrome. His karyotype was 46, XY and DNA analysis reveals heterozygous mutation in NIBPL gene. He was managed with proper counselling about the diagnosis and prognosis. He is under close follow up with pediatric neurologist, speech therapist and developmental specialist.

Most children with Cornelia de Lange syndrome are diagnosed clinically after birth or in early childhood based upon a thorough clinical evaluation and identification of characteristic physical findings. A diagnosis of Cornelia de Lange syndrome should be considered in children who exhibit characteristic facial features in association with limb anomalies, prenatal and postnatal growth retardation and intellectual disability. Molecular genetic testing for mutations in the five genes associated with Cornelia de Lange syndrome is available to confirm the diagnosis and may be particularly helpful when the physical features are mild or unusual. Prenatal diagnosis is available if a specific NIPBL, SMC1A, SMC3, Rad21, HDAC8, ANKRD11 or BRD4 gene mutation has been identified.

The treatment of this syndrome is directed toward the specific symptoms that are apparent in each individual. Treatment may require the efforts of a team working together to systematically and comprehensively plan an affected child's treatment. Such specialists may include paediatricians, geneticist, neurologist, surgeon, plastic surgeon, orthopaedic surgeon, gastroenterologist, urologist and otolaryngologist. The team also require paediatric cardiologist, dental specialist, speech therapist, audiologist, ophthalmologist and occupational therapist.

Affected children may be closely monitored for certain abnormalities potentially associated with Cornelia de Lange syndrome to ensure early detection and prompt treatment.⁷ Genetic counselling is recommended for affected individuals and their families.

CONCLUSION

We present one case of Cornelia de Lange syndrome of neonatal diagnosis that we consider of interest due to the importance of an early recognition of the clinical condition for the family advice and the medical aid and for an appropriate development. Cornelia de Lange syndrome is a rare but well characterized syndrome. The key diagnostic features are the distinctive facial features, limb anomalies and growth retardation.

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