Case report

Lobster Claw hand deformity - Cornelia de Lange syndrome

Consent

Informed consent has been taken from the parents of the patients' involved in the study. Informed consent form is attached along with submitted files.

Abstract

Background: Cornelia de Lange syndrome is a genetic syndrome characterized by intellectual disability, facial features with synorphrys or fused eyebrows, upper limb anomalies and atypical growth. It is caused by spontaneous mutations in genes responsible for structural or regulatory function of cohesin complex.

Report: We present two newborns cases admitted to our NICU with characteristic dysmorphic features of microcephaly, ectrodactyly and thick eyebrows. One baby also had associated congenital heart defect and sensorineural hearing loss. Both babies are under followup with developmental early intervention programs. Parents were offered genetic counselling for future pregnancies.

Conclusion: Cornelia de Lange is predominantly a clinical diagnosis by identifying typical dysmorphic features. Labelling a syndromic diagnosis helps to provide genetic counselling to the parents, identify associated co-morbidities at earlier stages and improve the quality of living of such children.

Keywords - Cornelia de Lange Syndrome, synorphrys, dysmorphism, ectrodactyly

Introduction

Cornelia de-Lange syndrome (CdLS) is a multisystem syndrome encompassing congenital malformations, growth retardation and neurodevelopment delay, with incidence estimated to be 1in 10,000.[1] Characteristic facial dysmorphic features with microcephaly, arched eyebrows, synophrys, depressed nasal bridge, long philtrum, down-turned angles of the mouth; upper-extremity malformations, hirsutism, cardiac defects, and gastrointestinal alterations define this syndrome[2] and is usually fatal by 2 years of life in severe cases. We report two such newborns with this syndrome in this report.

Case Presentation

Case 1

A term, low birth weight, female neonate, was admitted to our Level III NICU at a South Indian tertiary care hospital, in view of congenital anomaly detected at birth. She was third born child of non consanguineous marriage, with no significant antenatal or family history. Baby had microce-

phaly (Head circumference = 31.5 cm), low set posteriorly placed ears, prominent occiput, short neck, thick bushy eyebrows, short nose, high arched palate, long philtrum, retrognathia, thin upper lip, proximally implanted thumb over left forearm, claw hand, short fingers, hirsutism and tuft of hair over the lower back. (Fig. 1)

Case 2

A late preterm, low birth weight, female neonate was admitted to our NICU with Lobster claw hand deformity. She was the second born to a non-consanguineously married couple with normal antenatal history. Baby also had microcephaly (Head circumference = 29 cm), short neck, thick bushy eyebrows, short nose, high arched palate, excessive body hair and long philtrum similar to the neonate described prior. Micromelic shortening of upper extremities and polythelia were also noted in her. (Fig. 2)

MANAGEMENT AND OUTCOME

The first neonate's imaging studies of heart, cranial vault, abdomen and pelvis were normal. Karyotyping turned out as 46XX, female. Screening ophthalmological and hearing evaluation were also normal. While the second neonate's 2D Echocardiography revealed multiple defects including osmium primum atrial septal defect, patent ductus arteriosus and apical ventricular septal defect, all with left to right shunts and moderate pulmonary hypertension with tricuspid regurgitation. Baby also had bilateral sensorineural hearing loss. Other laboratory parameters were normal in both neonates.

The diagnosis of Classical Cornelia de Lange syndrome was made solely on clinical grounds with the presence of typical phenotypic features. Genetic counselling was offered to the parents and long term prognosis of their children were explained. Both neonates are enrolled to developmental early intervention centres and offered supportive care with multidisciplinary interventions to improve quality of life and are under followup.

DISCUSSION

Cornelia de lange (CdLS) is a multi-system disorder with physical, cognitive and behavioral characteristics that is named after the Dutch paediatrician Cornelia de Lange, who first described the developmental disorder in two infants in 1933.[3] Brachmann described similar features at autopsy in 1916, hence also known as Branchmann-de Lange syndrome.[4]

The facial characteristics are the most diagnostic , microcephaly, well defined and arched eyebrows growing across the base of nose (synophrys or confluent eyebrows), long curly eyelashes, short neck with low anterior hair line , long philtrum, generalised hirsutism, thin downturning upper lips, microganthia, a small nose with low bridge, low set ears and crescent shaped mouth. These patients show marked growth retardation of prenatal onset, and fail to thrive. Micromelia with oligodactyly, clinodactyly, proximal implantation of thumb, syndactyly of toes are common. Feeding difficulties with gastroesophageal reflux, with higher predisposition to Barrett oesophagus and adenocarcinoma later in life. There is evidence of premature aging in these individuals. Hearing loss secondary to canal stenosis, cochlear anomaly or ossicular malformation and visual disturbances secondary to high myopia, strabismus, nystagmus are common. Cardiac defects like pulmonary stenosis, VSD, ASD and coarctation of aorta show higher incidence. Intellectual disability, severe language and speech delay, hyperactivity, autism spectrum disorder are developmental and behaviours issues noted. Even as adults they are short statured and obese.[5,6]

Classic (or typical) CdLS is easily recognized from birth by experienced pediatricians and clinical geneticists owing to a distinctive craniofacial appearance and growth pattern, as well as limb malformations. However, not all individuals have the classic phenotype, and presentation is a spectrum with the disorder can varying widely, from mild to severe phenotypes, caused by pathogenic variants in genes involved in cohesin functioning. 500 genetic mutations have been associated with the condition; occurring on 7 different genes. Inheritance maybe autosomal dominant or sporadic when there are mutations in NIPBL gene (50%) or X linked when SMC1L1 gene (5%) is affected. [7,8]

An interdisciplinary approach is recommended to treat the issues associated with CdLS. A team for promoting the child's well-being includes speech, occupational and physical therapists along with paediatricians and parents.

LEARNING POINTS

1. Cornelia de Lange syndrome has distinctive craniofacial appearance and can be easily diagnosed based on clinical phenotypic presentation
2. Arched, confluent eyebrows or synophrys and limb anomalies are the most characteristic features
3. These children need early developmental interventions with multidisciplinary team approach as they have a delayed neurodevelopment.

REFERENCES

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LEGENDS FOR ILLUSTRATIONS

Fig. 1 - Images of first neonate showing short neck, thick bushy eyebrows, depressed nasal bridge, long philtrum, retrognathia, thin upper lip, proximally implanted thumb over left forearm, claw hand with oligodactyly, clinodactyly in right hand, hirsutism and tuft of hair over the lower back.

Fig. 2 - Images of second neonate showing bilateral lobster claw hand deformity, short neck, thick bushy eyebrows, depressed nasal bridge, excessive body hair, long philtrum, micromelic shortening of upper extremities and left sided polythelia.

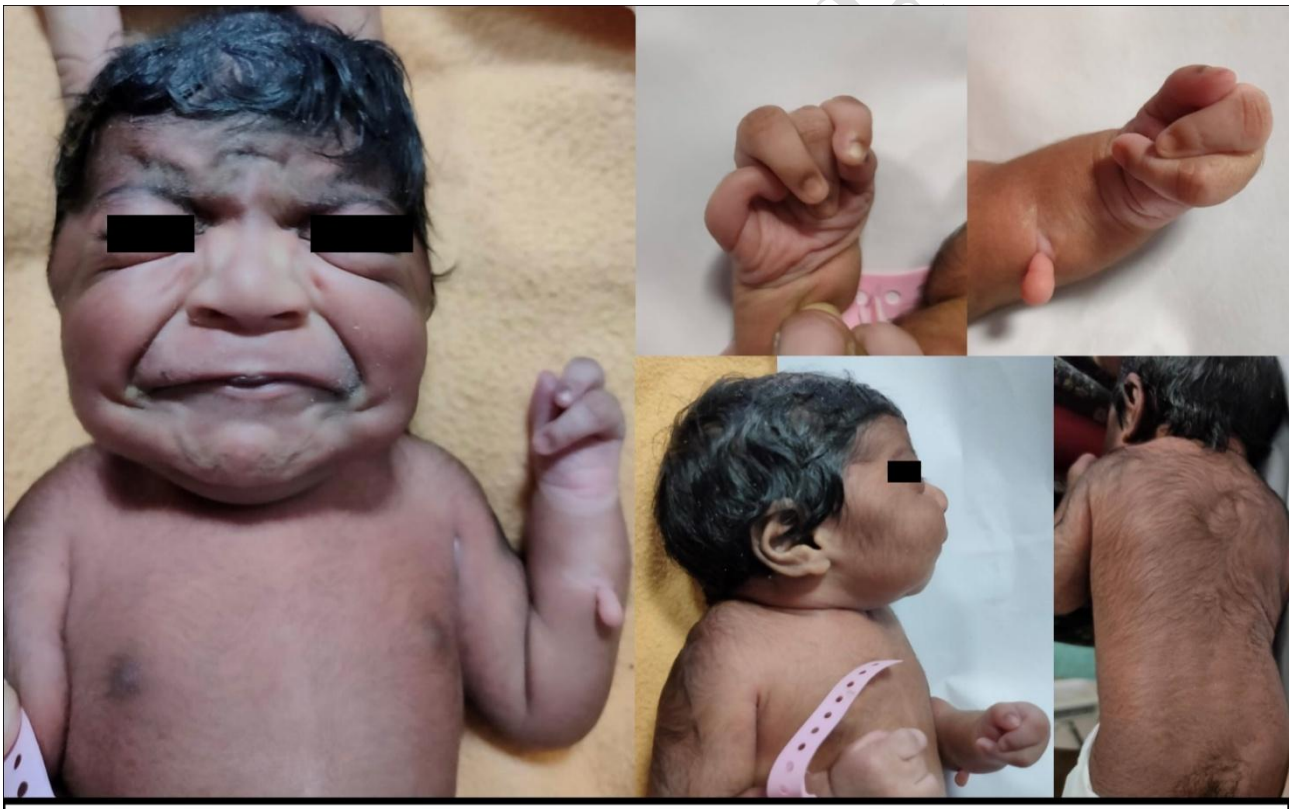

Figure 1 - Images of first neonate showing short neck, thick bushy eyebrows, depressed nasal bridge, long philtrum, retrognathia, thin upper lip, proximally implanted thumb over left forearm, claw hand with oligodactyly, clinodactyly in right hand, hirsutism and tuft of hair over the lower back.

FIGURES

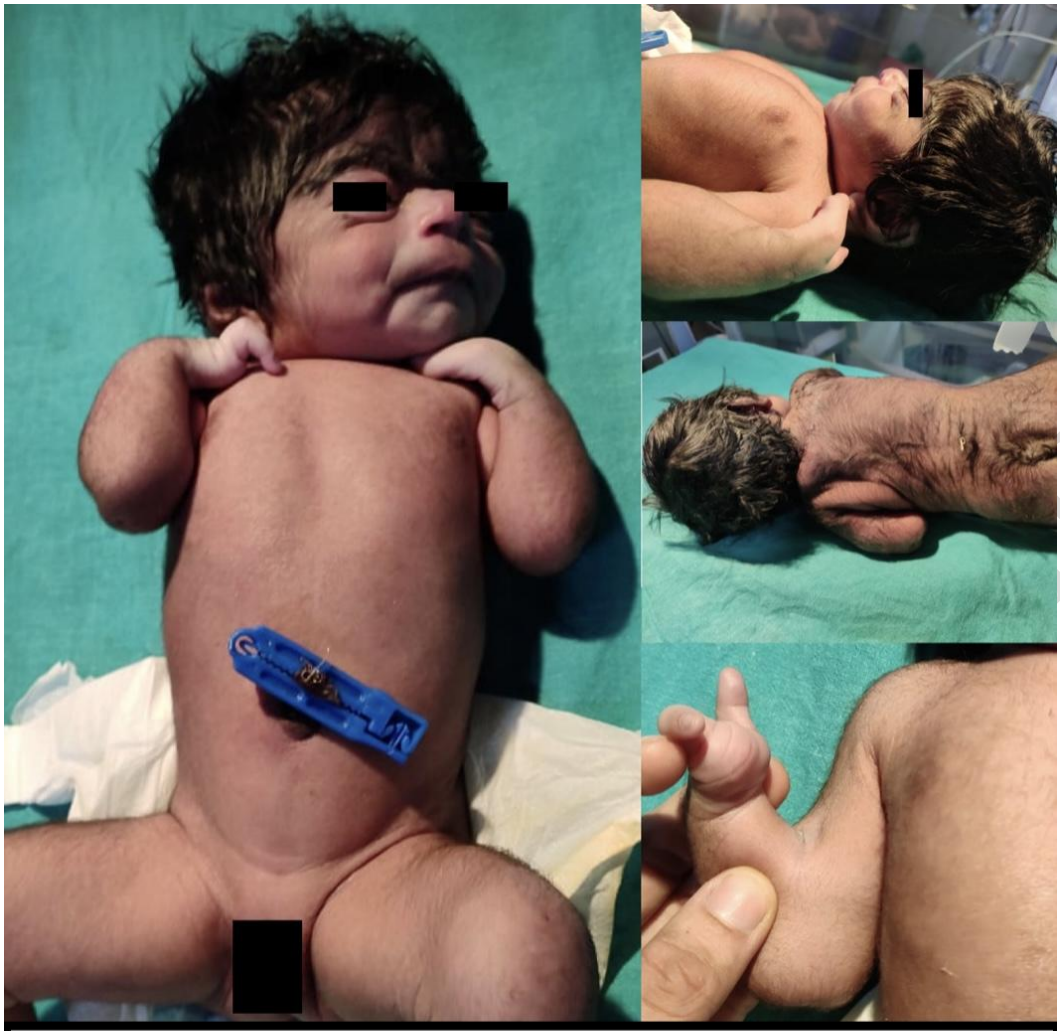

Figure 2 - Images of second neonate showing bilateral lobster claw hand deformity, short neck, thick bushy eyebrows, depressed nasal bridge, excessive body hair, long philtrum, micromelic shortening of upper extremities and left sided polythelia.