INTRODUCTION

Cornelia de Lange syndrome (CdLS) is a multiple anomaly congenital syndrome with great variability in its manifestation. It is inherited in an autosomal dominant fashion, characterized by a distinctive facial appearance, pre- and postnatal growth retardation, psychomotor delay, behavioural problems, and malformations of the upper extremities.\(^1\)

Exact incidence of the condition is unknown, but it is estimated to be 1 in 10,000.\(^2\) Facial findings include characteristic shape of the eyebrows, long philtrum, thin lips, crescent-shaped mouth and a low set hair line. These are the most important diagnostic features of CdLS.\(^3\)

We are presenting a case of Cornelia de Lange syndrome with characteristic facial features and physical findings.

CASE REPORT

A 22 days old male newborn was referred to Paediatric Unit III, Civil Hospital, Karachi, with the complaints of regurgitation of feed and choking. He was the only child of a consanguineous marriage, born at 35 weeks of gestation through normal vaginal delivery.

Physical examination revealed a 35 weeks old pre-term (small for gestational age) SGA baby weighing 2 kg, with a length of 45 cm and head circumference of 31 cm (below 3rd percentile).

On presentation, the patient had arched confluent and bushy eyebrows, well-defined long curly eyelashes (Figure 1E), low set anterior and posterior hair line (Figure 1B & F), short neck, depressed nasal bridge, anteverted nares with long philtrum, down turned angles of the mouth, thin lips (Figure 1A), microcephaly, and excessive body hair (Figure 1B & C) with no limb deformity. He had a low pitched cry, and limited neck movement and evidence of initial hypertonicity. He also had hypo-plastic nipples and umbilicus, hypo-plastic external genitalia, and seizures. The cardiovascular, respiratory and endocrine systems were normal. Ophthalmologic and ear examination also revealed normal findings.

The complete blood count, biochemical parameters and urine analysis were normal. Echocardiography was normal. Upper GI contrast studies for gastroesophageal reflux, one of the cardinal diagnostic features of CdLS, showed the same (Figure 1D). Manometry studies and upper GI endoscopy for confirmation of the diagnosis of GERD were planned but unfortunately they could not be performed because the patient was taken away from the hospital against medical advice. Due to the unavailability of genetic testing in Pakistan, the same could not be performed for this case.

On the basis of positive clinical findings and investigations, a diagnosis of CdLS was made.
DISCUSSION

Cornelia de Lange syndrome is a rare, but well-known multiple congenital anomaly/mental retardation (MCA/MR) disorder. Most cases are sporadic, but familial occurrence and parental consanguinity are considered important. No age, racial or gender predilection has been reported with Cornelia de Lange syndrome. Approximately one-third of children with CdLS are delivered prematurely.

Estimation of the overall prevalence of Cornelia de Lange syndrome (CdLS) is difficult because of the unknown proportion of milder cases. Diagnosis is based on the characteristic phenotype, in particular a striking facial form, prenatal and postnatal growth retardation, various skeletal abnormalities, hirsutism and developmental delay.

Based on the clinical variability, a diagnostic scoring system has been proposed for CdLS. CdLS type-I is the classic presentation and these patients have the characteristic facial and skeletal changes, a progressive prenatal growth deficiency, mental retardation and major malformations resulting in severe debility or death. Patients with CdLS type-II (the milder variant) have facial and minor skeletal abnormalities similar to those seen in type-I; however, they have less severe psychomotor retardation and milder growth deficiency. The prognosis is more optimistic, but paradoxically, behavioural dysfunction may be more evident.

The most frequent causes of death in CdLS are pneumonia, cardiac malformations, and gastrointestinal malformations. Most recorded deaths (approximately two-thirds) occur during the first year of life or in the following 2 years.

The patient history in Cornelia de Lange syndrome (CdLS) provides relevant clues to the diagnosis, such as the course of pregnancy and delivery. Preterm delivery is noted in approximately 30% cases. The difficulties in weight and height gain persist as a result of feeding difficulties, along with psychomotor delay. Recurrent respiratory tract infections and behavioural problems are atypical manifestations of gastroesophageal reflux disease (GERD). Pubertal development and fertility are normal in BdLS individuals. Some patients with CdLS tend to survive well into adulthood.

The differential diagnosis of Cornelia de Lange syndrome includes fetal alcohol syndrome and various other genetic syndromes. Prenatal diagnosis is made after careful evaluation of CdLS abnormalities on prenatal ultrasonography. These include growth retardation, limb defects, diaphragmatic hernia, hypoplastic forearms, underdeveloped hands and typical facial defects.

Most recorded deaths occur in infancy, and they mostly happen in severely affected individuals. Aspiratory pneumonia or apnea, cardiac defects, and/or GI anomalies are reported as the most frequent direct causes of death. The prognosis for patients with mild form of Cornelia de Lange syndrome (CdLS) is much better than that for patients with the classic form. Life expectancy is generally normal.

REFERENCES