Letters to the Editor

Cornelia de Lange syndrome

Sir,

A 9-year-old girl was brought by parents for evaluation of short stature. The girl is a product of non-consanguineous marriage and was delivered pre-term by cesarean section with birth weight of 1.5 kg. The parents noticed delays in milestones during development. Her scholastic performance was below average and parents denied any features to suggest neurological disease. Parents denied birth trauma or similar illness in other family members. Examination revealed severe short stature (112 cm, <3rd centile), height SDS, (Standard Deviation Score) 3.5; upper/lower segment ratio, 0.9; head circumference, 46 cm; and underweight (19 kg, <3rd centile). She had low anterior hair line, synophrys (bushy eyebrows meeting in mid-line), arched eye brows, low set ears, and maxillary hypoplasia [Figure 1a]. Other examination revealed small hands, clinodactyly [Figure 1b], single palmar crease, and hypertrichosis [Figure 1c]. She was pre-pubertal with B1P1 on Tanner staging and rest of the systemic examination was normal. She was clinically diagnosed as a case of Cornelia de Lange syndrome (CDLS). Her investigations revealed normal hematological and biochemical parameters with bone age of 8 years. Thyroid panel was diagnostic of subclinical hypothyroidism (Thyroid Stimulating Hormone TSH: 8.4 mIU/mL with normal T3 and T4). She was evaluated for growth hormone deficiency after adequate thyroxine replacement. Peak Growth hormone GH < after stimulation was 2.4 ng/mL and she was started on GH replacement therapy. Her echocardiography was normal and karyotyping revealed 46XX. Intelligence Quotient testing revealed score of 70 equivalent to a 5-year-old child. She continued to receive GH and Thyroxine therapy along with psychosocial rehabilitation program. During last review, she gained 10 cm in 1st year of GH therapy.

CDLS is a relatively uncommon genetic disorder characterized by growth retardation, developmental delay, hirsutism, mental retardation, and structural abnormalities.[1] The vast majority of cases are due to spontaneous mutations involving genes like NIPBL on chromosome 5, SMC1A on X chromosome, and SMC3 on chromosome 10.[2] The diagnosis of CDLS is clinical based on signs and symptoms. Two phenotypes are described with type 1 is the classical variety and type 2 being the mild variant. Short stature in CDLS is due to GH deficiency and resistance.[3] The patients show good response to GH therapy in former. The life expectancy is limited to few years only and the common cause of death is pneumonia along with cardio-respiratory structural abnormalities.

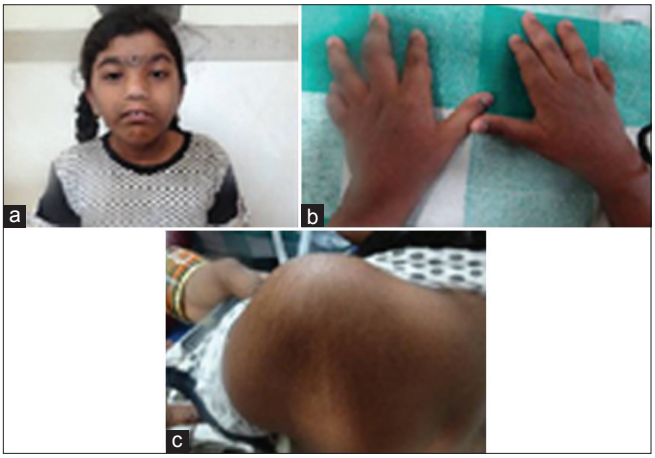

Figure 1: Clinical photograph

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