A girl with Cornelia de Lange syndrome with good response on GH therapy- Case Report

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Introduction

➢ Cornelia de Lange Syndrome (CDLS) is a genetic disorder which causes a wide range of physical and cognitive anomalies. It affects both genders equally and has typical facial features.(1,2)
➢Characteristics of CDLS include: growth retardation, developmental delay, distinctive facial features, hirsutism, mental retardation and structural abnormalities (2,3).
➢Causative mutations in at least three genes involved in chromosomal cohesion (a group of proteins with an important role in directing development before birth): NIPBL on chromosome 5 (more than 50% of patients), SMC1A on X chromosome, and SMC3 on chromosome 10 (1,4,6).
➢Diagnosis of CDLS is primarily a clinical one, no clinical diagnostic criteria have been established yet. Clinical status of patients with CDLS implies a individual interdisciplinary therapy (4,5,7).
➢GH deficiency and resistance causes the short stature in CDLS, a key feature for diagnosis.(5,8)
➢Growth hormone deficiency treatment does not seem to be common in CDLS. Nevertheless, the patients show good response to GH therapy (5,9).

Case report

9 years old girl, B.A. with Cornelia de Lange syndrome (CDLS)

- only child of non-consanguineous marriage
- naturally delivered on term
- Apgar score of 8
- **Small for gestational age (SGA)** weighing 1850 g
- delays in milestones during development.

Clinically diagnosed with Cornelia de Lange syndrome at the age of 3 (Figure 1):

- low anterior hair line
- bushy eyebrows meeting in mid-line
- low set ears
- maxillary hypoplasia
- small hands
- clinodactyly
- hypertrichosis
- severe short stature (86 cm, -3 SD) and underweight (11,5 kg, -3 SD)
- delayed bone age (2 years)
- **normal GH profile.**

One year later, because of the stationary height, she was reevaluated for GH deficiency:

- GH was not stimulated (4.93 ng/mL)
- low IGF1 (85,1 ng/ml, N:49-283)
- GH therapy was started.

Fig 2: **After 5 years of treatment with GH :**

- gained 38 cm (7.5 cm/year of treatment)
- actual height 124 cm, -2.9 SD
- with ameliorated bone age (7 years).

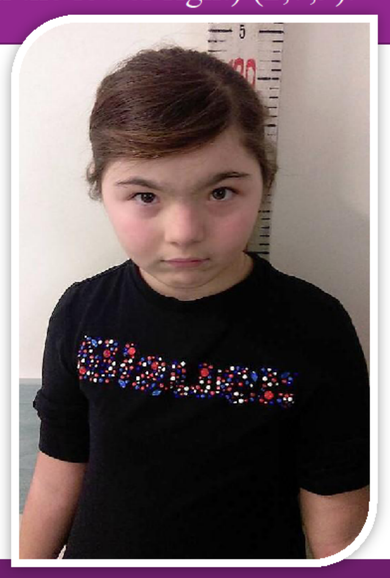
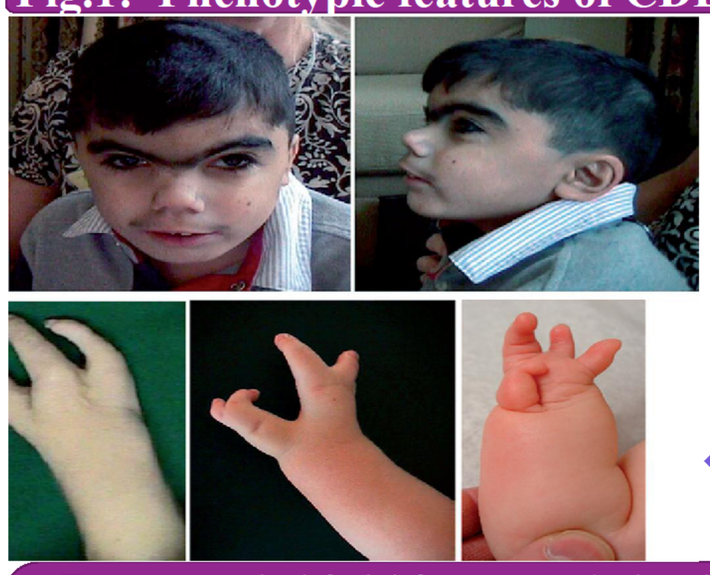


Fig.1: Phenotypic features of CDLS.



a.)Top row: typical facial features (arched eyebrows connected in midline - synophrys, ptosis, long eyelashes, short upturned nose, long philtrum, thin upper lip, and small chin –micrognathia, with low set and posterior rotated ears. **b.)Bottom row:** particular abnormalities of the lower arms and hands (ranging from severe olygodactyly on the left, through variable types of reduction defects to small hands as seen on the lower right) (2,7,9). *
* All pictures are reproduced with informed consent.

Discussions and Conclusion

➢ CDLS has been characterized by congenital abnormalities inducing distinctive appearance, small gestational age, growth deficiency, psychomotor delay, moderate intellectual disability, behavioral problems (4,6).
➢ Diagnosis of CDLS is based on a clinical picture (recognizing the distinctive craniofacial features, limb abnormalities, growth failure – pre- and post natal) and/or detecting heterozygous pathogenic variant NIPBL, RAD21, or SMC3 or hemizygous pathogenic variant in HDAC8 or SMC1A (3,8). Clinical progression leads to psychomotor retardation with speech delay, behavioral disorders in the autism specter. No cure is yet available for CDLS patients, efforts are made to relieve symptoms and minimize disabilities(1,2,7).
➢ Symmetric slow growth ends in a proportionate short stature, hypothalamic-pituitary function affected or compromised in at least some CDLS patients. CDLS patients have a mean height and weight below fifth percentile, a normal puberty without growth spurt (final stature ~155 cm in men and ~133 cm in women). Despite bKIGS data which did not find an appropriate short term response at GH treatment, our patient showed a satisfactory growth velocity, probably due to the associated GH deficiency (5,9).

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