

Case Report

Cornelia de Lange Syndrome - a cause of hypertrichosis in children: case report and review of literature

Lamees Mahmood Malik, Ghazala Aziz Khan, Nadia Ali Azfar, Muhammad Jahangir

Department of Dermatology Unit 1, Allama Iqbal Medical College/Jinnah Hospital, Lahore

Abstract Cornelia de Lange syndrome is a rare developmental disorder characterized by hypertrichosis, low intelligence, delayed milestones and skeletal and dental abnormalities. Gastroesophageal dysfunction, ophthalmologic, cardiac and genitourinary anomalies, learning difficulties, and mental retardation may be present in severe cases. We report a case of this syndrome who presented for laser treatment for the problem of hypertrichosis, and on examination other features of the syndrome were noted.

Keywords

Cornelia de Lange syndrome, Brachmann de Lange syndrome

Introduction

Cornelia de Lange syndrome was first described by Cornelia de Lange, a Dutch pediatrician in 1933.¹ This syndrome is also called Brachmann de Lange syndrome as a similar case was reported earlier by him in 1916.² It is a rare developmental disorder that can lead to multiple genetic anomalies characterized by growth and developmental retardation, low birth weight, hypertrichosis, anomalies in the structure of the upper limbs, gastroesophageal dysfunction, ophthalmologic and genitourinary anomalies, congenital diaphragmatic hernia, cardiac septal defect, distinctive facial features, learning difficulties, and mental retardation.^{3,4}

Incidence of this syndrome is variable, ranging from 1:10,000 to 1:100,000 live births in different population groups.⁴ No differences

based on race have been described. It is slightly more common in females as compared to males (F:M is 1.3:1).^{3,4,5}

Gastrointestinal complications are one of the most common causes of death in this syndrome. They include diaphragmatic hernia in infancy and aspiration pneumonia and volvulus at an older age. Other causes of death include congenital heart defects and apnea.^{6,7,8}

The genetic and molecular basis of this syndrome are not clear. However, it is thought to be the result of a dominant mutation. A large number of diagnosed cases seem to be sporadic and 10% of the cases present chromosomal alterations, such as a small duplication of the long arm of chromosome 3 or unbalanced chromosomal rearrangement.^{9,10} It can be associated with mutations affecting the cohesin complex.

Multiple genes have been associated with the condition. CDL1 (NIPBL) was found responsible in 50% of cases in 2004 by US and

Address for correspondence

Dr. Lamees Mahmood Malik
Assistant Professor
Dermatology Department Unit 1
Jinnah hospital, Lahore
Email: maliklamees@yahoo.com



Figure 1 Hypertrichosis over forearms.



Figure 2 Hypertrichosis on back of trunk.



Figure 3 Bushy eyebrows, synophrys and thick eyelashes.



Figure 4 Flexion contractures of little fingers.

UK researchers whereas CDLS 2 (SMC1A) and CDLS3 (SMC3) were detected in 2006 and 2007 by Italian and American doctors respectively.^{10,11}

We report a case of Cornelia de Lange syndrome who presented to us for the treatment of hypertrichosis.

Case report

A 10-year-old girl presented at a private laser centre for laser hair removal. The parents were very concerned about her excessive hair growth especially on forehead and forearms. According to her mother she had stopped going to school because she was being ridiculed by her classmates for this problem.

The patient was born of a consanguineous marriage and was the youngest of three siblings. According to the mother she was apparently normal at the time of birth. However, her developmental milestones were achieved later as compared to her other siblings although there was no exact record. At school also she was a slow learner and is two grades behind her age fellows. During early childhood parents noted excessive hair growth which gradually increased with time.

On examination she was a thin built child of average height. There was generalized hypertrichosis, especially more marked on forehead, upper lips, forearms (**Figure 1**), lower legs and lower back (**Figure 2**). She had bushy eyebrows, synophrys and thick eyelashes (**Figures 3**). Oral cavity examination showed irregular dentition and crowding of teeth. Hand examination showed flexion deformity of both

Table 1 Scoring of severity of features of Cornelia de Lange syndrome [8].

Parameter	1 point	2 point	3 point
Birth weight	>2500g	2000-2500g	<2000g
Sitting alone	<9mo	9-20mo	>20mo
Walking alone	<18mo	18-42mo	>42mo
Saying first word	<24mo	24-48mo	>48mo
Upper limb malformation	No defect	Partial defect (<2digits)	Severe defect (>2 digits)
Number of other malformations	0-1	2-3	>3
Hearing loss	Absent	--	--

A score of less than 15 points indicates mild involvement, a score of 15-22 points indicates moderate involvement, and a score of more than 22 points indicates severe involvement.

little fingers (**Figure 4**). She had a wide-based gait although rest of neurological examination was normal. Other systems examination also revealed no abnormality. The child was shy and did not answer any questions. All investigations were normal including an echocardiography.

Discussion

The clinical features of hypertrichosis, low intelligence, developmental delay, skeletal and dental abnormalities led us to the diagnosis of Cornelia de Lange syndrome in our patient. A similar case has been reported earlier from Lahore, Pakistan with a co-existent finding of pustular psoriasis.¹²

Cornelia de Lange syndrome is a rare but well characterized developmental disorder that affects many parts of the body. The features of this disorder vary widely among affected individuals and range from relatively mild to severe.⁷ Severity of the disease is assessed on the basis of a scoring system with a score of more than 15 indicating moderate to severe disease (**Table 1**).⁸

Classical Cornelia de Lange syndrome is characterized by growth retardation, intellectual disability that is usually severe to profound, skeletal abnormalities involving the arms and hands, and distinctive facial features. The facial features include arched eyebrows that often

grow together in the middle (synophrys); long eyelashes; low-set ears; small, widely spaced teeth; and a small, upturned nose.⁵

Additional signs and symptoms of Cornelia de Lange syndrome can include excessive body hair, an unusually small head (microcephaly), hearing loss, short stature, and problems with the digestive tract. Children with this syndrome often suffer from gastrointestinal tract difficulties, particularly gastroesophageal reflux, vomiting, poor appetite, constipation or diarrhea.^{6,7} However, symptoms may range from mild to severe. Seizures, heart defects, eye problems, cleft palate and skeletal abnormalities also have been reported with this condition.⁸

Cornelia de Lange syndrome may also include a number of behavior problems, including self-stimulation, aggression, self-injury or strong preference to a structured routine. Many children exhibit autistic-like behavior.^{7,8} Children usually are shy and introvert with sub normal intelligence.

An interdisciplinary approach to therapy and treatment of any medical issues that arise is recommended. The problem with which the patient came to us was hypertrichosis and the parents wanted laser treatment for this. Using lasers to remove unwanted hair in adults is known to be safe and well tolerated, but what is the safety and tolerability of the procedure in

children? Although there is scarcity of well conducted randomized controlled studies in children, a few have shown that when administered appropriately, laser hair removal is safe and well tolerated in children aged <16 years.¹³ Our patient has been treated to date with three sessions of Nd:YAG laser over the face and forearms and has shown considerable improvement. Further treatment sessions will be planned according to the response. Hair removal from other exposed body sites by non permanent methods was also encouraged to improve quality of life of the patient. A dental and psychiatric consultation was also advised.

References

1. De Lange C. Sur un type nouveau de degenerescence (typus Amstelodamensis) *Arch Med Enfants* 1933; **36**: 713-9.
2. Brachmann W. Ein fall von symmetrischer monodaktylie durch Ulnadefekt, mit symmetrischer flughautbildung in den ellenbeugen, sowie anderen abnormitäten (zwerghaftogkeit, halsrippen, behaarung) *Jarb Kinder Phys Erzie* 1916; **84**: 225-35.
3. Kline AD, Grados M, Sponseller P *et al*. Natural history of aging in Cornelia de Lange syndrome. *Am J Med Genet C Semin Med Genet* 2007; **145C**: 248-60.
4. Beck B. Epidemiology of Cornelia de Lange's syndrome. *Acta Paediatr Scand* 1978; **65**: 618-31.
5. Tayebi N. Cornelia de lange syndrome *Indian J Hum Genet* 2008; **14**: 23-6.
6. Beck B, Fenger K. Mortality, pathological findings and causes of death in the De-Lange Syndrome. *Acta Paediatr Scand* 1985; **74**: 765-9.
7. Pashayan H, Whelan D, Guttman S *et al*. Variability of the De Lange syndrome: report of 3 cases and genetic analysis of 54 families. *J Pediatr* 1969; **75**: 853-8.
8. Tekin M. Cornelia De Lange Syndrome: Differential diagnoses [online cited: Nov 13, 2009] available from; <http://www.emed.med.com/article/942792-overview>.
9. Wilson GN, Hieber VC, Schmickel RD. The association of chromosome 3 duplication and the Cornelia de Lange syndrome. *J Pediatr* 1978; **93**: 783-8.
10. Krantz ID, Tonkin E, Smith M *et al*. Exclusion of linkage to the CDL1 gene region on chromosome 3q26.3 in some familial cases of Cornelia de Lange syndrome. *Am J Med Genet* 2001; **101**: 120-9.
11. Tonkin E, Wang TJ, Lisgo S *et al*. NIPBL, encoding a homolog of fungal Scc2-type sister chromatid cohesion proteins and fly Nipped-B, is mutated in Cornelia de Lange syndrome. *Nat Genet* 2004; **36**: 636-41.
12. Shahzad A, Pal SS, Khurshid K. Cornelia De Lange Syndrome with generalized pustular psoriasis: a rare co-existence. *J Pak Assoc Dermatol* 2005; **15**: 281-4.
13. Rajpar SF, Hague JS, Abdullah A, Lanigan SW. Hair removal with the long-pulse alexandrite and long-pulse Nd:YAG lasers is safe and well tolerated in children. *J Clin Exp Dermatol* 2009; **32**: 77-81.