ISSN 0378-6323 May - June 2003

Indian Journal of Dermatology, Venereology & Leprology

EDITORIAL OFFICE
Dr. Uday Khopkar
Editor, IJDVL
2/7, Govt. Colony, Haji Ali,
Mumbai-400034.
E-mail: editor@ijdvl.com

PUBLISHED BY
Medknow Publications
12, Manisha Plaza,
M. N. Road, Kurla (W),
Mumbai-400070, India.
Phone: 91-22-25032970
Fax: 91-22-25032398
E-mail: publishing@medknow.com
Website: www.medknow.com

Manuscript submission
www.journalonweb.com/ijdvl

Cover design courtesy
Sudler & Hennessey

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CONTENTS (CONTD.)

The Indian Journal of Dermatology, Venereology and Leprology is a bimonthly publication of the Indian Association of Dermatologists, Venereologists and Leprologists and published by Medknow Publications.

The Journal is **indexed/listed** with Health and Wellness Research Center, Health Reference Center Academic, InfoTrac One File, Expanded Academic ASAP, NIWI, INIST, Uncover, JADE (Journal Article Database), IndMed, Indian Science Abstract's and PubList.

Cornelia de Lange syndrome

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ABSTRACT

Two cases of Cornelia de Lange syndrome with similar phenotypic features are reported.

KEY WORDS: Cornelia de Lange syndrome, Dwarfism

INTRODUCTION

Cornelia de Lange syndrome (CDLS), also known as Brachman de Lange syndrome or Amsterdam dwarf, is characterized by a typical facies along with hypertrichosis, cutis marmorata and a bluish discoloration of the facial skin. Skeletal abnormalitites, mental retardation and abnormal cry are also present. Credit for the description of the syndrome is generally given to Cornelia de Lange, a Dutch pediatrician who reported it in 1933, almost two decades after Brachman's original description. The incidence is 1 in 10,000 live births. Early death usually occurs in these patients.

Although several significant cutaneous manifestations are seen in CDLS, the dermatological literature has little information about them. The characteristic facies includes a bluish cast about the eyes, nose and mouth, overgrowth and confluence of eyebrows (synophrys), long curly eyelashes, a small red nose with low bridge, anteverted nostrils, increased inter-alar distance and a broad upper lip, which is thin and down-turned, producing a grim mask-like appearance. The ears may be low set. Hyperplastic epidermal ridges of the palms, soles, fingers and toes may occur. There is a possible correlation between epidermal ridge pattern and survival,[1] in that the syndrome appears to be less severe in patients with a relatively normal ridge pattern.

An important feature of the syndrome is the striking delay in the maturation of structure and function of most organ systems. A dominant mutation has been postulated as the most likely etiologic possibility.

CASE REPORT

Case 1

An 8-year-old boy, born of a non-consanguinious marriage, presented with generalized hypertrichosis since early childhood (Figure 1). There was a history of delayed milestones, and poor performance at school. His birth weight had been 2.8 kg. The present height, weight and head circumference were 125 cm, 21 kg and 53.3 cm respectively. The patient had a low-pitched, growling and gutteral deep voice. His eyebrows were bushy, eyelashes long and synophrys was present. The scalp hairline was low set. The upper lip was thin and long, angle of mouth turned down and facial hypertrichosis was present (Figure 2). The patient had long vellus and intermediate hair on the trunk and limbs. His nipples were hypoplastic and the joints of hands were hyperextensible.

The baseline blood and urine investigations and thyroid function tests were within normal limits. Serum FSH and testosterone levels were lower than normal. An X-ray of both hands showed decreased bone age. Ultrasonography of the abdomen did not reveal any

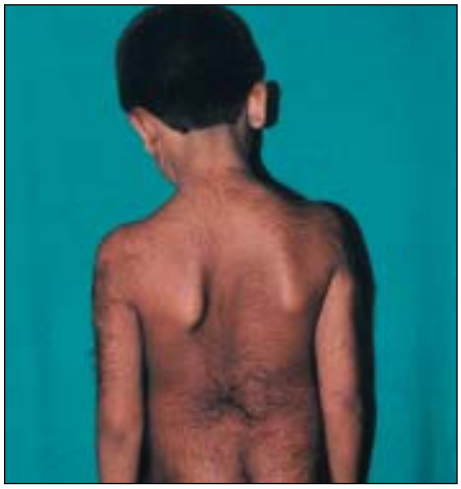

Figure 1: Generalized hypertrichosis in an 8-year-old boy

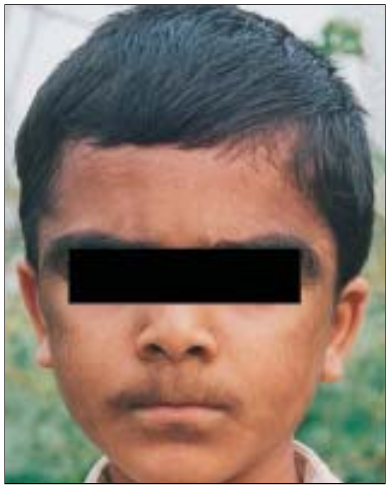

Figure 2: Characteristic facies with hypertrichosis in an 8-year-old boy

organomegaly. The child had multiple retained deciduous teeth and showed missing permanent teeth on X-ray. Shaving of the facial hair was the only treatment being followed. Laser hair removal and extraction of deciduous teeth with construction of prosthesis were suggested.

Case 2

A 3-year-old boy was brought to our outpatient department with generalized hypertrichosis since birth, and mental retardation. He was the only child of a non-consanguinious marriage, born of a full term normal delivery with a birth weight of 2.9 kg. There was a history of posterior urethral valve correction at the age of one year.

Delayed developmental milestones were present. His height, weight and head circumference were 88 cm, 10 kg and 44.5 cm respectively, with the expected normal values being 100 cm, 14 kg and 48 cm respectively at this age. He had hypognathism, clinodactyly and a characteristic mask-like facies. Coarse brownish-black silky hairs measuring 8-10 cm were present on the lower back associated with generalized hypertrichosis (Figure 3). A subsiding capillary hemangioma of 3 x 3 cm size was present just above the umbilicus. His eyebrows were bushy and synophrys was present. The eyelashes were slender and elongated. The upper lip was thin and angles of mouth were turned downward. The oral cavity showed dental caries and tongue-tie. There were simian creases on both palms. Examination of the genitalia showed undescended testes on the right side. The cry was peculiar as in the first case.

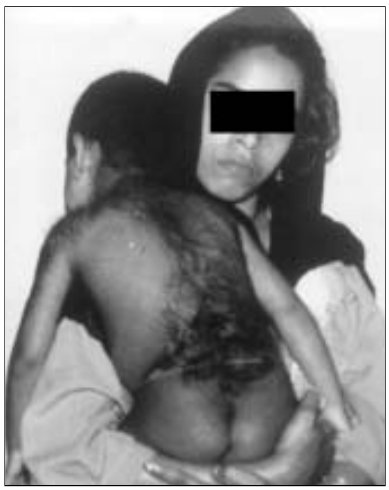

Figure 3: Generalized hypertrichosis in a 3-year-old boy

DISCUSSION

Cornelia de Large syndrome is so characteristic that once a case has been seen, another may be identified immediately because of the strikingly similar phenotype. The cry alone suffices to suggest the diagnosis without having seen the patient. Our patients had all the characteristic facial features, generalized hypertrichosis and decreased skeletal and mental growth. Undescended testes are reported in 73% of male patients. Patients may have decreased gamma globulin and increased serum alpha ketoglutarate and serum glutamate levels, which may help in the diagnosis. Postmortem examination may show

developmental retardation of all major organs of the body, with the exception of the liver.[2]

The etiology and recurrence risk of CDLS are unknown. The syndrome may be the result of an inherited metabolic error.[3] No environmental cause has been discovered. Most cases are sporadic, although an autosomal dominant inheritance has been suggested. CDLS without severe mental retardation has been reported by Pashayan and co-workers.[4] Duplication corresponding to bands q^{25}–q^{29} of chromosome 3 has been reported.[5]

Temporary or permanent removal of the hair is the only treatment that can be offered, for cosmetic improvement.

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