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Neonatal syndrome present in adulthood: A new perspective of cornelia de lang syndrome - A case report

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ABSTRACT

Cornelia de Lange is a genetic syndrome which affects between 1/10.000 and 1/60.000 neonates, but its genetic bases is still not clearly established. Delay in growth and development, hirsute, structural anomalies in the limbs and distinctive facial characteristics are the classical presentation. Dental problems are frequent and include: ogival palate, micrognathia, dental malalignment, delayed teething, microdontic teeth, periodontal disease and dental erosion produced by gastric reflux. The authors discuss here the case of a family affected with this syndrome i.e. 40 year old female patient, her sibling of 47 years old and also father. The oldest reported case till date is of 29 years where as in present case the patent aged 40 years and 47 years of the sibling. The patient also presents with uncommon radiographic findings which are not mentioned in the literature.

INTRODUCTION

Cornelia de Lange Syndrome (CDLS) is relatively rare disorder which affects neonates. However, the actual incidence may be higher as the clinical presentations are quite variable and milder cases are likely to be underestimated [1]. There is no racial predilection, and it is more frequent in women than men. In 1933 Cornelia de Lange, a Dutch pediatrician, described two unrelated infant girls with a syndrome characterized by mental retardation and physical anomalies involving face and limbs [2]. Brachmann had reported a similar condition from Amsterdam in 1916. Opitz et al suggested the syndrome to be designated as Brachmann-de Lange syndrome [3]. It is now reckoned that a Dutch anatomist named Vrolik described the first case in the 18th century. Other less frequently used synonyms are Brachman-De Lange Syndrom, Typus degenerativus Amstelodamensis and Amsterdam dwarfism [4].Cornelia de Lange Syndrome as is a congenital syndrome most of the signs and symptoms may be recognized at birth or shortly thereafter. First two cases in India were reported in 1970s [5,6]. About 250 cases were recorded from various parts of the world in the same year [7]. May 12, 2007, is known as Cornelia de Lange Syndrome Awareness Day in the United States.

The diagnosis of the syndrome is based solely on the clinical grounds; there are no biochemical or chromosomal markers for CDLS till date. This lack of biological markers makes determination of its incidence difficult [3] The authors report a case of De Lang Syndrome in a 40year old female patient which was diagnosed clinically as Type I and the patients sibling and father as type II form of de lang syndrome.

CASE REPORT

A 40 years female patient visited to the OPD of Oral medicine and Radiology, Jaipur dental college, with the chief complaint of pain and mobility in upper front tooth since 2- 3 months (Fig.1). Pain was mild, intermittent, throbbing in nature, non-radiating. Due to the mobility of the tooth the patient had difficulty in mastication. On further history patient's mother revealed that she was underweight at birth. Also had GI problems like, mal-absorption, diarrhea, indigestion & loss of appetite since birth. Patient felt weakness on mild exertion. She was physically and mentally challenged, afraid of strangers and did not socialize. On general examination patient's height was 112cm; weight was 17 kg, with an abnormal gait. Vital signs were in normal range. She had a lean body and was poorly nourished. Patient was responding to her mother only.

Family history revealed that she had four siblings of which one of her brother and also father presented with similar clinical features (Fig. 2). Patients elder brother's age was 47year but weighed only 22kgs height was 151cms with an abnormal gait. Patient's father also presented with BMI below normal percentile. This family had not consulted any physician for the same till date. Extra oral examination of patient revealed microbrachycephaly,

low & outward placed ears, long eyelashes, bilateral ptosis, depressed nasal bridge, thin and slanting lips and mental spur (Fig. 1). Intraoral examination showed poor oral hygiene, generalized inflamed gingiva, gingival recession depicting periodontitis. Hard tissue showed high arched palate, spacing in all the teeth, mal-alligned anteriors, with some grossly decayed teeth (Fig. 3,4).

The sibling presented with microbrachycephaly, low & outward placed ears, long eyelashes, depressed nasal bridge, thin and slanting lips and mental spur (Fig. 5). Edentulous upper and lower arches with history of early loss of teeth due to periodontitis. Intra oral presentation of the father was that of partially edentulous arches with periodontitis. Analyzing the history and clinical features, the diagnosis of de lang syndrome was made. With the patients father's consent they were subjected for radiographic evaluation. OPG of the patient revealed missing 11,21,27,38,48 with generalized bone loss and root stumps 17, 37, 45,46,47 (Fig. 6). OPG of sibling showed complete edentulous maxillary ridge and mandibular arches except for a root stump of 43(Fig 7). Father's OPG showed generalized bone loss and partially edentulous ridges (Fig. 8). Lateral skull radiograh of the patient and sibling showed small pituitary fossa with enlarged and prominent post clinoid process, sutures of the skull not appreciated well, inner and outer diploic table were not demarcated and increased overall density of the skull which are some of the unusual findings that are as such not associated with this syndrome in the literature (Fig. 9). Patient was advised for oral prophylaxis, extraction of root stumps and replacement of missing teeth. Patient's parents were counseled for regular checkup and informed about the genetic nature of the disease. To confirm the diagnosis CGH microarray could be performed but as the family is completely reluctant towards the disorder so it was not possible.

DISCUSSION

The features of Cornelia de Large syndrome are so characteristic that it can be diagnosed clinically. Classically it is defined by hypo growth of body, mental retardation, micromelia and distinctive facial features. Hypo-growth is at first evident in intrauterine life, with delays in osseous maturation and mental deficiencies (100% of the cases). At birth and during the length of their life, these patients present a weight and size inferior to that corresponding to their age. The intellectual coefficient is not above 50%. The facial features are distinctive, with microcephaly, the eyebrows very close together, generalized hirsute (the frontal implantation of the hair is low), the ears are implanted low, small nose, nostrils antiverities and other features which were observed in this case.

These patients have feeding problems related to swallowing in-coordination, poor esophageal motility, and gastro-esophageal reflux, also reported in our case. Genitalia are in general hypoplastic with cryptorchidism, micropenis and hypospadias being commonly seen in males and small labia majora in females. Normal puberty occurs with slight delay in some cases [8], these features are consistent with the reported case. Behavioral phenotype The average IQ ranges from mild to moderate mental retardation; however, both borderline normal and severe mental retardation are commonly reported. Learning continues throughout life without evidence of regression [9]. Low pitched crying, non social, inexpressive face and certain type of kinesthetic stimulation was pleasurable to patient [10], which was also evident in this case.

Figure 1 : 40 year old patient revealed microbrachycephaly, low & outward placed ears, depressed nasal bridge, thin and slanting lips and mental spur.

Figure 2 : Family affected with De lang

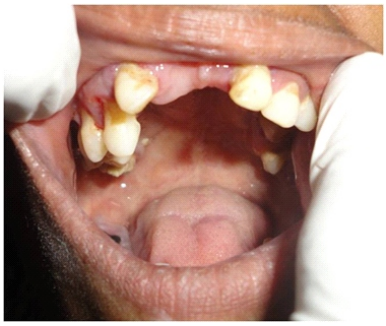

Figure 3 : High arched palate, spacing in all the upper teeth

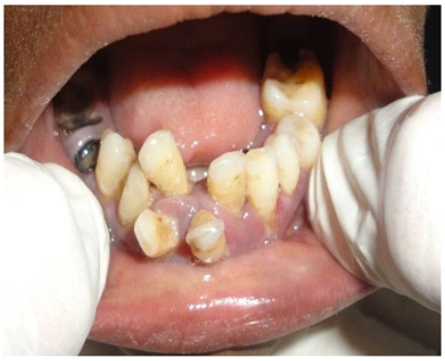

Figure 4 : Mal-aligned anteriors

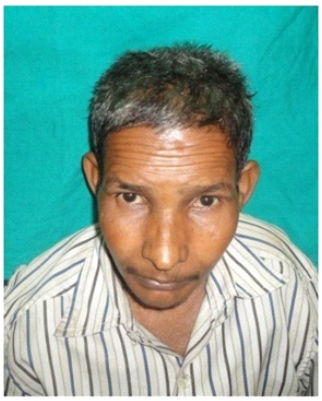

Figure 5 : Sibling of the patient with microbrachycephaly, low & outward placed ears, long eyelashes, depressed nasal bridge.

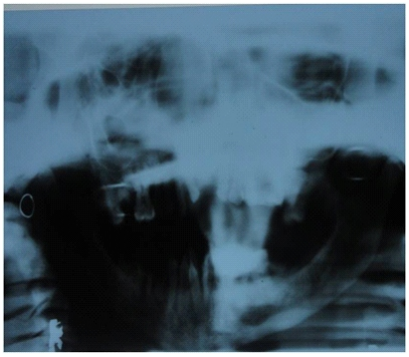

Figure 6 : OPG of patient revealed missing 11,21,27,38,48 with generalized bone loss

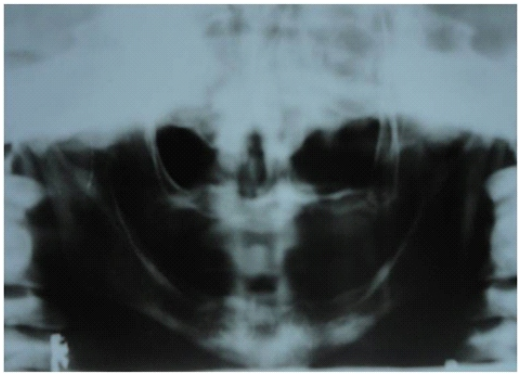

Figure 7 : OPG of sibling illustrates complete edentulous maxillary ridge and mandibular arches except for a root stump of 43

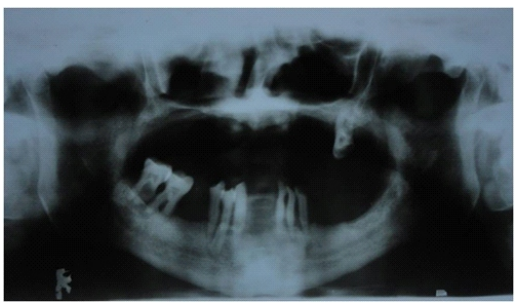

Figure 8 : OPG of father showed generalized bone loss and partially edentulous ridges

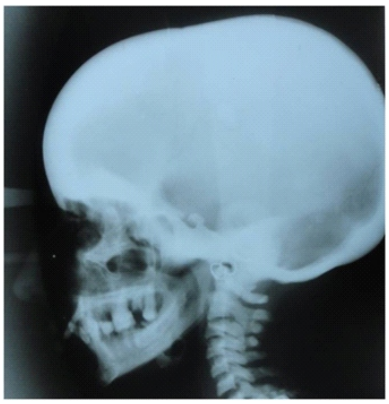

Figure 9 : Skull view of patient presented small pituitary fossa with enlarged and prominent post clinoid process with not well appreciated sutures.

Oral manifestations of CDLS included fish-like mouth, thin upper lip & perioral cyanosis, high arched palate, long philtrum & cleft palate, micrognathia, macroglossia, mandibular spurs & prominent symphysis, microdontia and delayed tooth eruption [11].

The Cornelia de Lange syndrome is a rare polimalformation genetic disease. Based on the clinical variability in CdLS, Van Allen et al. [12] proposed a classification system which includes - Type I "classic" patients with the characteristic facial and skeletal changes of CDLS. Type II "mild" CDLS patients having similar facial and minor skeletal abnormalities as that of type I; however, these changes may develop later or may be partially expressed. Type III phenocopies CDLS includes the patients who have phenotypic manifestations of CDLS, which are causally related to chromosomal aneuploidies or teratogenic exposures.

Etiopathognesis is related to mutations in some specific genes. *NIPBL* on chromosome 5 discovered in 2004, *SMC1A* on X chromosome discovered in 2006 and *SMC3* on chromosome 10 discovered in 2007 [13]. This syndrome is caused by mutations in the NIPBL gene, the human homologue of the Drosophila Nipped-B gene [14].

The cases reported till date were of patients with very young age and the maximum reported age was 29 yrs of a female patient [15]. This article documents a case of de lang syndrome in fourth decade of life which is not reported so far. Also the unusual (skull) radiographic findings like missing sutures, increased density of the skull, small pituitary fossa with prominent posterior cliniod process, inner and outer diploic table were not differentiated well. The reasons and effect of these findings were not ascertain by the authors as also the patient had not consulted for this before.

Proper care and counseling is advised for such patients and family, as it is a genetic disorder which has no treatment and we can only provide psychological support for their well being.

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