CASE REPORT

A Mild Form of Bushy Syndrome in a Neonate: A Rare Case Report

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Abstract

The paper reports a rare case of mild form of Bushy syndrome with facial abnormalities. Other names for this syndrome are Cornelia de Lange syndrome/Brachmann- de Lange syndrome/Amsterdam dwarfism/Bushy syndrome. Few case reports were reported in the literature and this case report was presented with the motto of fabricating feeding palate in this syndromic patient and the procedure is similar to that of any other cleft palate.

Keywords: Bushy syndrome, Cornelia de Lange syndrome, Feeding plate.

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Introduction

Bushy syndrome, also called Brachmann-de Lange syndrome/Amsterdam dwarfism/Cornelia de Lange syndrome (CdLS), is a multiple congenital anomaly syndrome characterized by a distinctive facial appearance, prenatal and postnatal growth deficiency, psychomotor delay, behavioral problems, and malformations of the upper extremities. It was first reported by Dr. Cornelia de Lange, a Dutch pediatrician in 1933. Brachmann in 1916 had observed similar features with an additional feature of deficiencies of the upper limb in a child with autopsy. For the reason of their contributions, both names have been attached to the name of the syndrome.[1] Cardiac defects and gastrointestinal anomalies are common, and many additional physical features occur, including myopia, palatal abnormalities, genitourinary abnormalities, congenital diaphragmatic hernias, and hearing loss. Facial dysmorphism includes arched eyebrows, synophrys, short nose with anteverted nares, long philtrum, thin upper lip, and micrognathia.[2,3] The majority of the cases are sporadic, but a few cases showing an autosomal-dominant inheritance have been reported.[4] Although the exact incidence is unknown, CdLS likely affects 1 in 10,000 newborns.[5] This syndrome should be considered in the differential diagnosis of congenital anomalies and mental retardation.

This case report represents the neonates reported with the atypical form of the above-mentioned syndrome, had difficulty in feeding because of cleft palate and feeding plate was fabricated and provided.

Case Description

A 10-day-old male presented to the Department of Pedodontics and Preventive Dentistry, SCB Dental College and Hospital, Cuttack with the chief complaint of difficulty in feeding because of nasal regurgitation. He was born at term via a spontaneous normal vaginal delivery to two consanguineous parents, from a 28-year-old female (gravida 5, para 5), without prenatal care or ultrasounds. The family history was not relevant. There was no any associated systemic disorders.

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The craniofacial examination revealed excess facial hair, synophrys, long and arched eyebrows, long eyelashes, hypertelorism, bilateral low-set ears (malformed ears), long philtrum, thin upper lip, microsomia, excess soft tissue mass of 2 cm × 1 cm pedunculated on the left side of the lower cheek region, depressed corners of the mouth, and short neck (Fig. 1 to 3). Also, the patient was found to have a cleft palate (Fig. 4). Physical examination of the extremities was normal (Figs 5 and 6). A complete blood count and a basic metabolic panel were within normal limits.

The elastomeric impression of the maxillary arch was taken with the prior fabricated custom-made tray (Fig. 7). The feeding plate was fabricated with the thermoplastic sheet of 1.5 mm and placed into the oral cavity (Figs 8 and 9).

The patient was referred to the pediatric surgeon, ENT, a plastic surgeon for further management. We were unable to identify issues related to hearing loss, and learning ability at the present age, so the patient was advised to be in regular follow-up.

Discussion

The features of this disorder vary widely among affected individuals and range from relatively mild to severe. Based

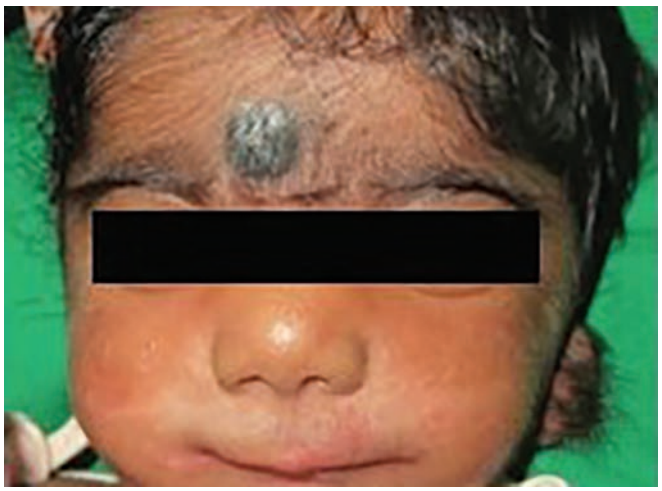


Fig. 1: Frontal view (synophrys)

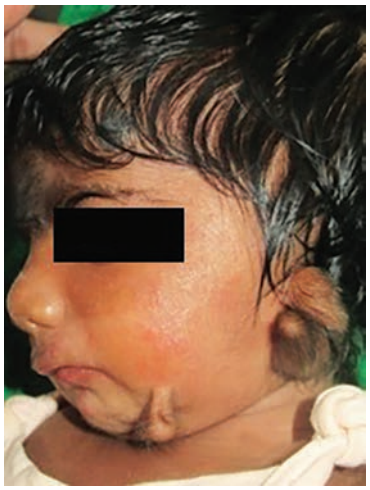


Fig. 2: Left lateral view (malformed low-set ear, pedunculated soft mass)

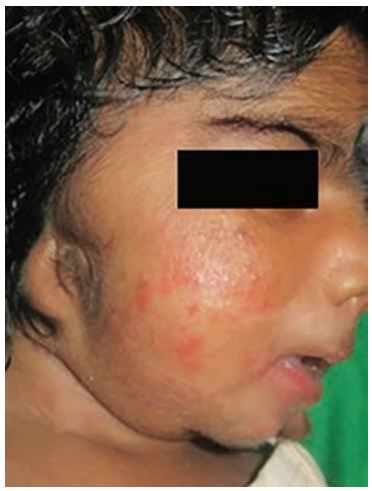


Fig. 3: Right lateral view (malformed low-set ear)

on the clinical variability in CdLS, Van Allen et al.[6] proposed a classification system. Type I, or classic, CdLS patients have the characteristic facial and skeletal changes of the diagnostic criteria established by Preus and Rex.[7] They have prenatal growth deficiency, moderate to profound psychomotor retardation, and

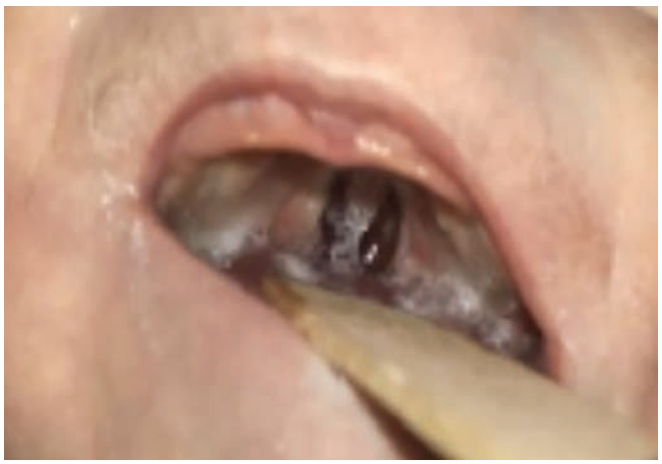


Fig. 4: Cleft palate

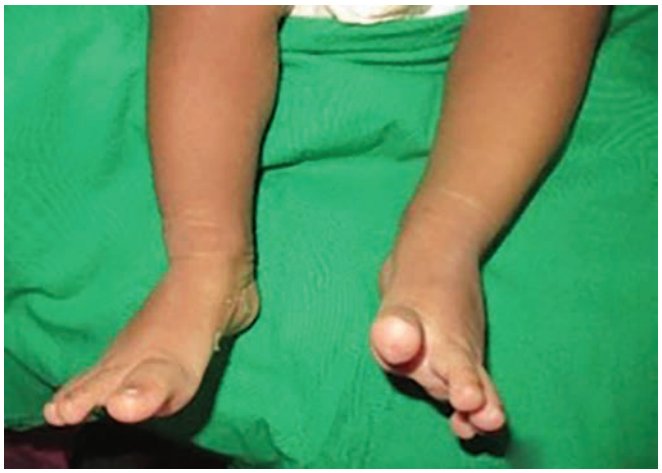
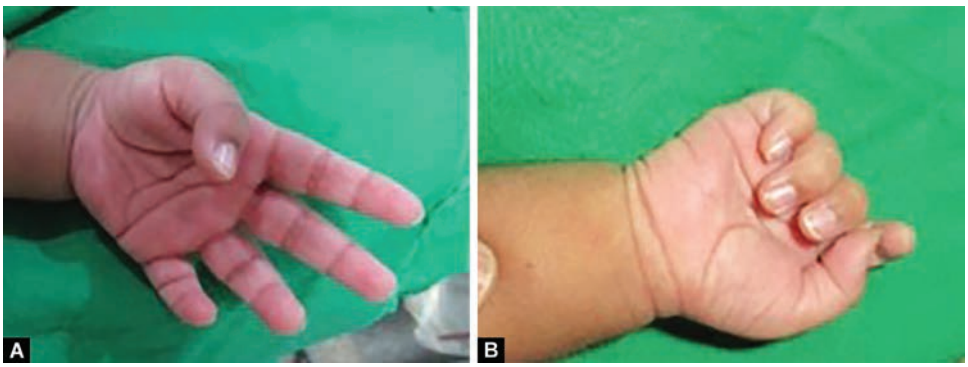
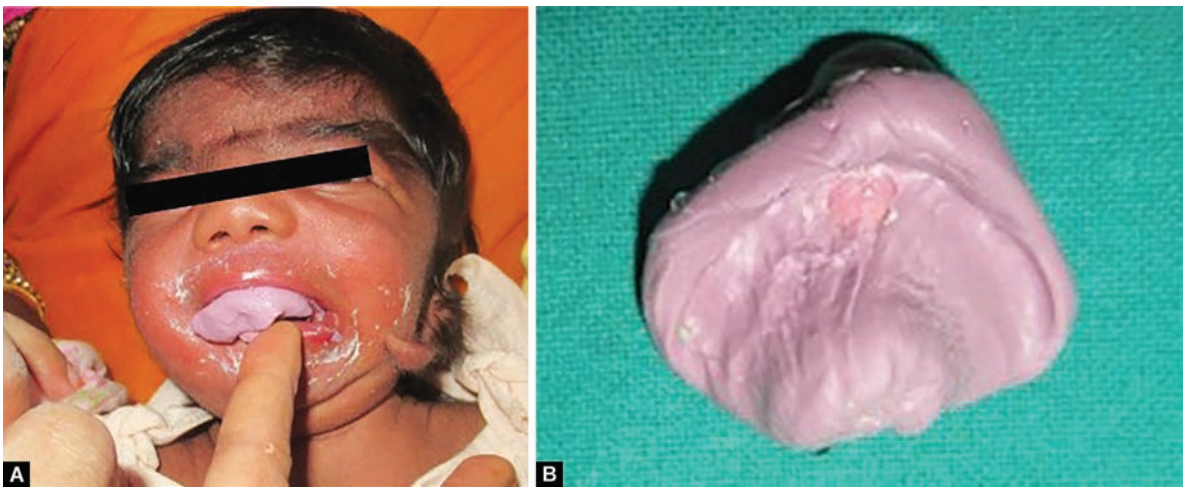


Fig. 5: Lower limb normal

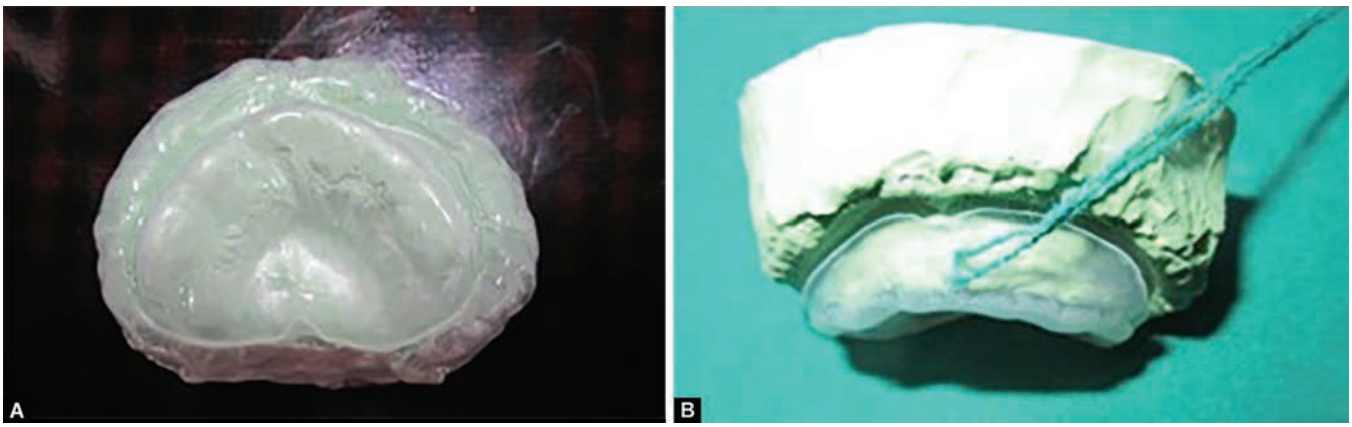
major malformations, which result in severe disability or death. Type II, or mild, CdLS patients have similar facial and minor skeletal abnormalities to those seen in type I; however, these changes may develop with time or maybe partially expressed. They have mild-to-borderline psychomotor retardation, less severe pre- and postnatal growth deficiency, and the absence of (or less severe) major malformations. Type III, or phenocopy, CdLS includes patients who have phenotypic manifestations of CdLS that are causally related to chromosomal aneuploidies or teratogenic exposures. Allanson et al.[8] in 1997 showed that, in the mild phenotype, the characteristic facial appearance may not appear until 2–3 years of age, while it is always present at birth in the classic phenotype. They also noted that the characteristic facial appearance decreased with time in the mild phenotype. In the same study, the authors concluded that objective assessments supported the clinical impression of two distinct phenotypes, and those alternative discriminators, such as birth weight greater than 2500 gm and absence of major limb anomalies, should be used to distinguish the mild from the severe phenotype early in life because of the similarity of facial features.[8] This patient can be classified as Type II/mild because only facial abnormalities were appreciated, weight >2500 gm, absence of major limb anomalies. Mutations in the NIPBL, SMC1L1 and SMC3 genes cause CdLS. In 2004, two independent groups[9,10] found that 26–56% of patients with CdLS carry a heterozygous mutation of the NIPBL



Figs 6A and B: Upper limb normal



Figs 7A and B: (A) Impression taken; (B) Intraoral impression



Figs 8A and B: Feeding plate fabricated

gene localized on 5p13.2. The exact function of the human NIPBL gene product, called delangin, is unknown, but its wide expression pattern, including expression in the embryonic limb bud, branchial arch, and craniofacial mesenchyme, is consistent with many of the anomalies observed in CdLS. An X-linked form of CdLS was reported in three male members from the same family and one sporadic case, demonstrating the common combination of symptoms in the spectrum of CdLS, caused by mutations in the SMC1L1 gene which encodes a subunit of the cohesion complex.[11] The SMC1L1 gene provides instructions for making a protein that helps regulate the structure and organization of chromosomes. Recently, SMC3 encoding the other SMC cohesin component was found mutated in one patient with CdLS.[12] This gene provides instructions for making a protein that interacts with the SMC1L1 protein to regulate chromosome structure. In addition, a large number of reports have been described chromosomal abnormalities associated with CdLS, involving most chromosomes except for chromosomes 6, 15, 16, 19, 20,

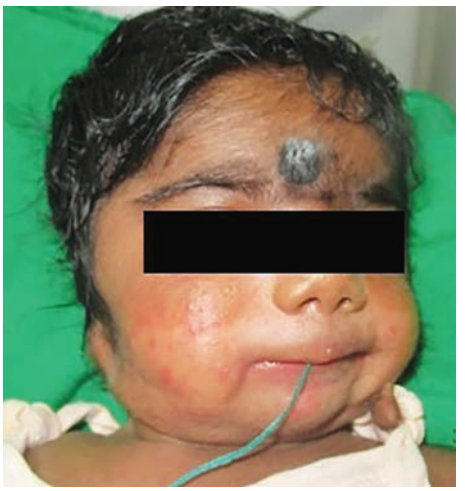


Fig. 9: Feeding plate delivered

and 22.[1] Genotype-phenotype correlations in the study of Gillis et al.[13] and Yan et al.[14] showed significant differences between patients with and without mutations in terms of the degree of growth retardation and developmental delay. In a different study on 39 sporadic cases of CdLS from the Netherlands, truncating NIPBL mutations were prevalently detected in CdLS patients of the classical type.[15] Musio et al. and Deardorff et al. noted that both SMC3 and SMC1L1 mutation-positive patients exhibit very mild facial dysmorphism, no absence or reduction of limbs or digits, and no other major structural anomalies.[11,12]

The feeding plate was fabricated from a thermoplastic sheet of 1.5 mm thickness which is biocompatible and flexible, does not cause any allergic reaction. The feeding plate can also be fabricated with acrylic but it is not flexible and might cause injury to the soft tissues. This plate improves the feeding ability of the child patient and also indirectly improves the nutritional status of the child which could be useful for further surgical repair of palate, low-set malformed ears.

The clinical phenotype of our patient is concordant with the mild type CdLS (distinctive facial appearance). Therefore, the genotype-phenotype correlation could not have been performed in our patient.

Conclusion

Bushy syndrome is a rare but well-characterized syndrome. The key diagnostic features are distinctive facial features, limb anomalies, and growth retardation. In the case of cleft palate in these patients, the feeding plate fabricated will improve the nutritional status of the child.

Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and of the clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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