Cleidocranial dysplasia with hearing loss

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Abstract

Cleidocranial dysplasia is an inherited skeletal anomaly that affects primarily the skull, clavicle, and dentition, which can occur spontaneously, but most are inherited in autosomal dominant mode. The skull findings are brachycephaly, delayed or failed closure of the fontanelles, presence of open skull sutures and multiple wormian bones with pronounced frontal bossing. The syndrome is notable for aplasia or hypoplasia of the clavicles. The neck appears long and narrow and the shoulders markedly droop. Oral manifestations exhibit a hypoplastic maxilla with high-arched palate. Crowding of teeth is produced by retention of deciduous teeth, delayed eruption of permanent teeth, and the presence of a large number of unerupted supernumerary teeth. We report a case of CCD in a 12-year-old girl who presented with an unaesthetic facial appearance, unerupted permanent dentition with hearing loss.

Key words: *Cleidocranial dysostosis, delayed tooth eruption, hearing loss, hypoplastic clavicle, supernumerary teeth*

INTRODUCTION

Cleidocranial dysplasia (CCD), also known as cleidocranial dysostosis or mutational dysostosis, is a genetic condition affecting bone growth, exhibiting defective endochondral and intramembranous bone formation. It is characterized by a larger than expected head with delayed closure of the soft spots (fontanelles), underdevelopment or absence of one or both collar bones (clavicles), and short stature. The patients may have unusual positioning of the hip joints, abnormalities of the bones of the spine, and unusual formation of bones of the fingers and hand. This condition was first reported by Meckel in 1760 and later by Martin in 1765. The syndrome was named by Pierre Marie and Paul Sainton in 1898, and hence the name Marie–Sainton disease.[1,2] Human osteoblast-specific, core binding factor α1 (CBFA-1), i.e. runt-related transcription factor 2 (*RUNX2*) gene located on chromosome 6p21, is identified as the gene responsible for CCD.[3]

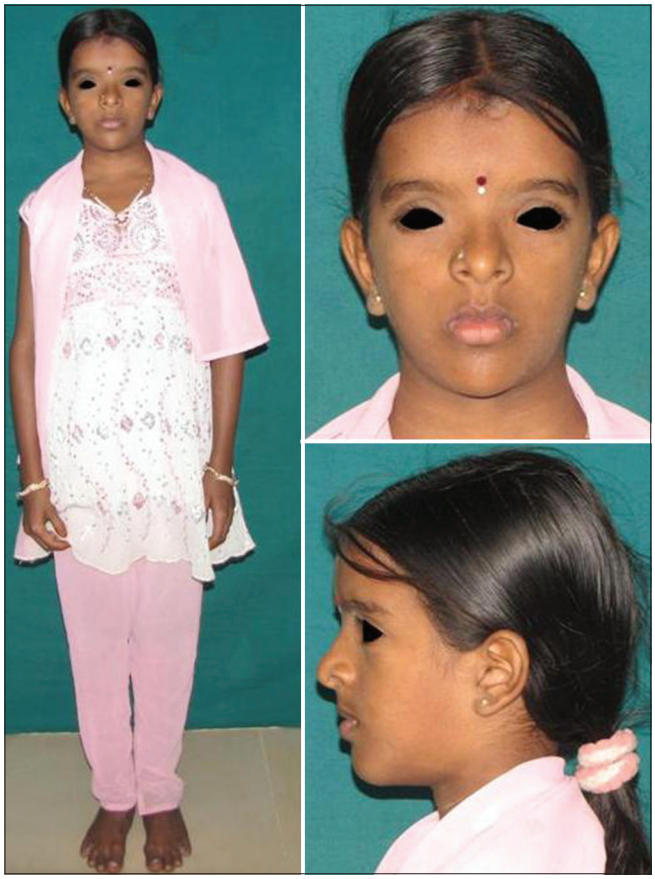

Figure 1: Profile pictures showing short stature, hypertelorism, depressed nasal bridge, underdeveloped maxilla, and frontal bossing

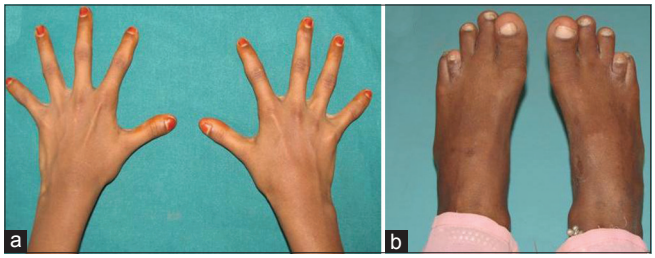

Figure 2: (a) Fingers showing broad thumb and hypoplastic distal phalanges; (b) Brachydactyly of fourth toe

CASE REPORT

A 12-year-old girl reported to our department with a complaint of missing lower teeth and an unaesthetic facial

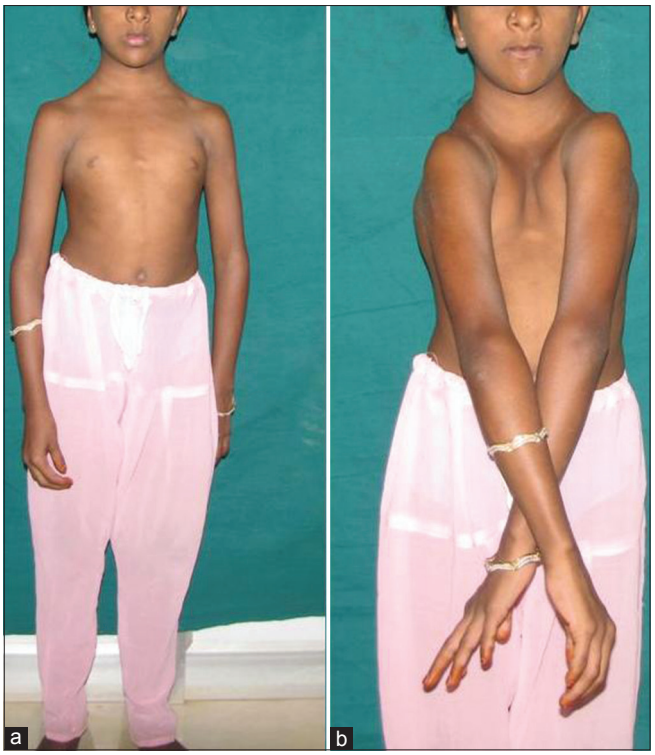

Figure 3: (a) Cone-shaped narrow thorax; (b) Approximation of shoulders to midline

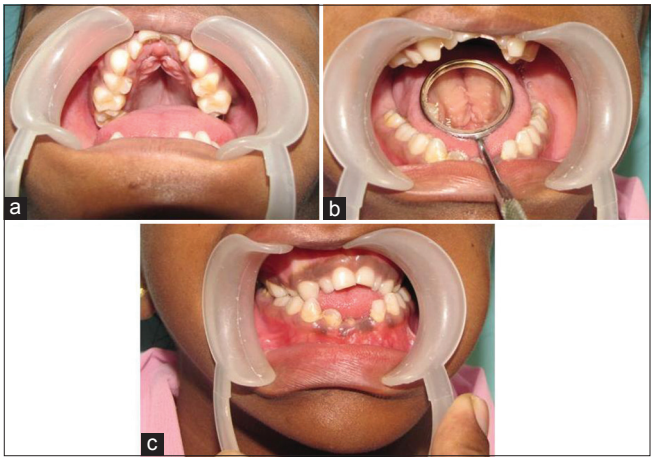

Figure 4: Intraoral pictures showing delayed eruption of permanent teeth, retained deciduous teeth, and high-arched narrow palate

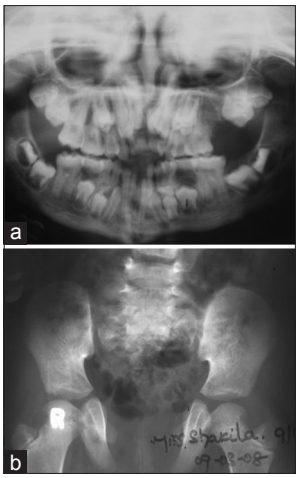

Figure 5: (a) Panoramic radiograph showing few impacted teeth, multiple retained deciduous teeth, delayed eruption of permanent teeth, and underdeveloped maxillary sinuses; (b) AP pelvis showing widened pubic symphysis and triradiate cartilage

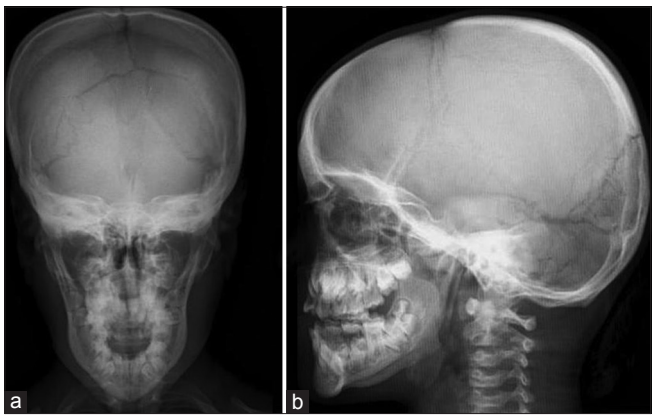

Figure 6: AP and lateral skull radiographs showing patent fontanelles and multiple wormian bones

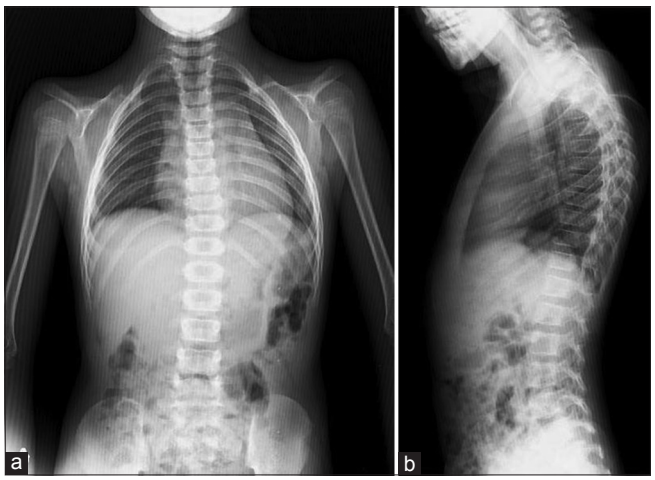

Figure 7: Chest radiograph shows bell-shaped thorax and bilateral hypoplasia of clavicles

appearance with progressive loss of hearing over a period of 3 months. Patient complained that only few permanent teeth had erupted and she had difficulty in chewing and was unable to eat. Past dental history revealed extraction of upper left permanent molar by a private dentist because of gross decay. There was no relevant medical history or family history. Her general examination revealed short stature and she was well oriented with normal intelligence. Extraoral examination revealed hypertelorism (increased intercanthal distance of eyes), frontal bossing with brachycephalic skull, depressed and flattened nasal bridge, malar hypoplasia, and an underdeveloped maxilla with a prognathic mandible and concave facial profile [Figure 1]. Hand showed hypoplastic distal phalanges [Figure 2a], and brachydactyly of the fourth toe [Figure2b] was seen. The thorax was narrow and cone shaped, and spinal abnormalities like mild scoliosis and kyphosis were appreciated [Figure 3a]. On palpation, a depression over the sagittal suture with presence of metopic suture of the frontal bone was felt and the patient could approximate her shoulders in midline [Figure 3b]. Intraoral examination revealed normal mouth opening and jaw movements. Erupted upper right permanent first molar and retained deciduous teeth were seen with high arched and narrow palate [Figure 4a, b] with erupted right permanent first molar and retained deciduous teeth [Figure 4c] were seen. Panoramic radiograph revealed few impacted teeth, multiple retained deciduous teeth, and underdeveloped maxillary sinuses [Figure 5a]. AP view of pelvis demonstrated a widened pubic symphysis and triradiate cartilage [Figure 5b]. Skull AP and lateral views showed the presence of multiple wormian bones with open fontanelles [Figure 6]. Chest radiograph showed bell-shaped rib cage and hypoplastic clavicles [Figure 7]. Based on the clinical and radiographic findings, a diagnosis of CCD was made. She was referred to otolaryngologist for opinion and audiometry revealed conductive deafness of right side of the ear. Multidisciplinary approach with dental and medical team of doctors will aid in the treatment of this rare CCD.

DISCUSSION

The membranous calvarial bones at birth display severely reduced calcification, and with advancing age, mineralization of the calvaria increases, but the fontanelles and the metopic suture persist beyond the normal time of fusion. The combination of frontal bossing and metopic suture further accentuates resulting in a more noticeable deformity. The fontanelles will often exhibit secondary ossification centers, thereby resulting in the formation of wormian bones. These changes contribute to the frontal and parietal bossing. There is typical delayed closure of the fontanelles and some adults have open fontanelles. The conservative cranioplasty technique can be performed for the reduction of the frontal bossing and subsequent filling of the metopic

suture defect with the autogenous bone chips.[4] Although unusual, platybasia (developmental deformity of base of the skull in which the lower occiput is pushed by the upper cervical spine into the cranial fossa) and basilar impression may lead to crowding of the brain stem and upper cervical spinal cord, which would be an absolute contraindication for cervical manipulation.[5]

Other changes of the skull include small or absent nasal bones, segmental calvarial thickening, underdevelopment of the maxilla, delayed union of the mandibular symphysis, a small cranial base with reduced sagittal diameter, and a large foramen magnum. The skeletal changes include a large, brachycephalic head with parietal and marked frontal bosses separated by a metopic groove, a depressed nasal bridge, and hypertelorism with possible exophthalmia.[6,7]

The neck appears long and the shoulders are narrow and down sloping. The maxilla, accessory sinuses, and mastoid air cells are hypoplastic and together with the hypoplastic development of the facial bone and paranasal sinuses, give the mandible a prognathic appearance. The skeletal gnathic relationship tends to exhibit a Class III malocclusion due mainly to maxillary hypoplasia.[2]

Individuals with CCD often have abnormalities of the teeth and many have extra or supernumerary teeth. The teeth may be unusually formed or positioned. Delayed eruption of teeth, especially the permanent teeth, is common. Individuals with CCD having identical *RUNX2* gene mutations showed a wide variation in the supernumerary tooth formation, and many of the supernumerary teeth occurred asymmetrically in the maxilla and the mandible, implying that the number and position of supernumerary teeth are not solely governed by *RUNX2* mutation. Other non-genetic factors, such as epigenetic factors, modifier genes, copy number variations, as well as environmental factors, may also be involved in the formation of supernumerary teeth in CCD.[8-10] Supernumerary teeth, lack of cellular cementum, lack of appropriate inflammatory response, an inadequate expression of some cytokines , increased bone density that impedes resorption, and the underlying defects in bone resorption have been noted to be the factors for delayed tooth eruption in cleidocranial dysostosis.[11]

The clavicles may be completely absent on one or both sides, but more commonly are underdeveloped, usually deficient at the end closest to the shoulders. Occasionally the clavicles are normally formed on each end with a gap in the middle which allows bringing their shoulders together in front of their bodies and the muscles attached to the clavicles may be unusually formed and placed. Occasional abnormalities that are associated with CCD include scoliosis, extra ribs, tendency to have bone fractures, cleft palate, small pelvis, hearing loss, and respiratory problems such as recurrent sinus infection or pneumonia.

The pelvis is invariably involved and shows characteristic changes. The widened symphysis pubis results from a delay in ossification during adulthood. Other changes include hypoplasia and anterior rotation of the iliac wings and wide sacroiliac joints. The femoral epiphyses are large, the femoral necks broad, and there is frequently coxa vara.[7] It is important that all women with CCD have adequate evaluation of their pelvic diameter prior to giving birth as cesarean section may be the preferred method of delivery.[12]

It is also important to monitor regularly for evidence of conductive hearing loss, and sensorineural hearing loss which may not only be due to the structural and functional changes of the temporal bone, bones of the ear, together with unusual or abnormal formation of the palate and/or Eustachian tube dysfunction which may necessitate the placement of tympanostomy tubes, but can also be due to abnormal function of the nerves of hearing. The significant points concerning hearing loss are as follows:[13]

- The hearing deficit is predominantly a middle ear conduction problem secondary to structural abnormalities of the ossicles.
- There is sometimes a small bone conduction deficit indicating either a cochlear or an eighth nerve problem.
- There is dense sclerosis of the temporal bone.

Therefore, patients with CCD should be evaluated routinely by an otolaryngologist and should undergo complete audiological testing.[14] Deregulated transforming growth factor-b (TGFb) or *RUNX2* function compromises the distinctly hard cochlear bone matrix and causes hearing loss in CCD.[15] Management for the patient with CCD is quite challenging. The earlier the treatment is initiated, the better is the prognosis.[16] Comprehensive dental and craniofacial management involves the team work of radiologists, pedodontists, oral maxillofacial surgeons, prosthodontists, and orthodontists to achieve better facial aesthetics.[17] For further management of skeletal abnormalities, the patient was referred to an orthopedic surgeon.

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