Case Report

Pediatric patient with cleidocranial dysostosis: case report and literature review

Abstract

Cleidocranial dysostosis, a rare autosomal dominant disorder classified under osteochondrodysplasias, exhibits a prevalence of 1 in 1,000,000. This syndrome arises from haploinsufficiency in the RUNX2 gene, initially documented in 1765 and formally characterized in 1871. Recognizing its clinical and radiological features promptly is crucial for optimal management. This article presents a literature review and a case report of a pediatric patient diagnosed with cleidocranial dysostosis.

Keywords: dysostosis, syndrome, dental exfoliation, autosomal

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Introduction

Cleidocranial dysostosis, a dominant autosomal disorder categorized as osteochondrodysplasia.[1] Manifests primarily due to haploinsufficiency in the RUNX2 gene1. This condition is typified by congenital skeletal anomalies such as clavicular hypoplasia or aplasia, delayed cranial fontanelle closure, brachycephalic morphology, delayed dental deciduous dentition shedding, postponed eruption of permanent teeth, presence of multiple supernumerary teeth, and maxillary morphological aberrations.[2]

Historically, its earliest documentation traces back to around 1765 with the inaugural report on clavicular aplasia, followed by Scheuthauer's comprehensive delineation of its clinical features in 1871 1. Subsequently, in 1898, Marie and Sainton coined the term "hereditary cleidocranial dysostosis.[1] "Noteworthy is Jackson's 1940 report, notably the "Arnold case," wherein a genealogical study identified 70 descendants exhibiting the syndrome's hallmark traits.[1] In 1988, this syndrome was classified as skeletal dysplasia within the osteochondrodysplasia spectrum.[2] Further genetic elucidation by Ramesar in 1996 revealed a shared genetic lineage among 100 patients traced back to the Arnold case.[2]

Etiologically, cleidocranial dysostosis is linked to the RUNX2 gene on chromosome 6, locus p21, belonging to the RUNX transcription factor family, which encodes the CBFA1 protein.[2] This protein's expression in oral tissues, notably the dental follicle mesenchyme, regulates growth and differentiation, crucial for epithelial-mesenchymal interactions, morphogenesis control, and enamel epithelial organ histodifferentiation.3,4 Additionally, its expression in the periodontal ligament influences osteoclast differentiation, potentially contributing to observed delayed dental eruption in cleidocranial dysostosis.[2]

Mundlos describes three putative pathobiological mechanisms of cleidocranial dysostosis:[1]

1. Non-functional protein: Despite appropriate protein encoding, functional deficiency due to haploinsufficiency occurs.[1]
2. Premature synthesis halt: Premature termination of protein synthesis, despite adequate gene and protein encoding, leads to impaired bone formation.[1]
3. Total gene absence. [1]

Characteristic clinical features include delayed cranial suture closure, hypoplastic or aplastic clavicles, and dental anomalies like supernumerary teeth and delayed permanent tooth eruption. Radiographically, open sutures and fontanelles, delayed skull ossification, absent or deficient paranasal and frontal sinuses, impacted and retained supernumerary teeth are observed. Additionally, dysplastic scapulae, clavicular anomalies, delayed pelvic bone ossification, hip bone hypoplasia, sacral fusion, coxa vara, and digital anomalies may be present.[3]

Case report

A 13-year-old male presented to the maxillofacial surgery department for retained dental organ extraction. Clinical examination revealed dolichocephaly, a rectangular face, underdeveloped facial skeleton, flattened frontal bone, acro-osteolysis, and a triangular torso. There was no reported family history of similar conditions.

Radiographic studies including posteroanterior (PA) and lateral skull radiographs, PA chest radiograph, PA and lateral spine radiograph, and maxillary tomography were obtained (Figure 1).

Following radiographic evaluation, the characteristic cleidocranial dysostosis triad—supernumerary teeth, total or partial clavicular agenesis, and cranial alterations—was evident (Figure 2 & 3).

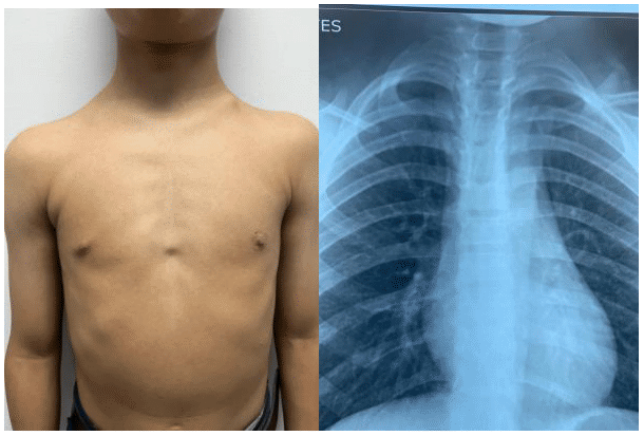

Figure 1 Frontal photograph depicting the triangular torso and posteroanterior (PA) chest radiograph showing a triangular shape of the thoracic cage and partial development of the clavicles.

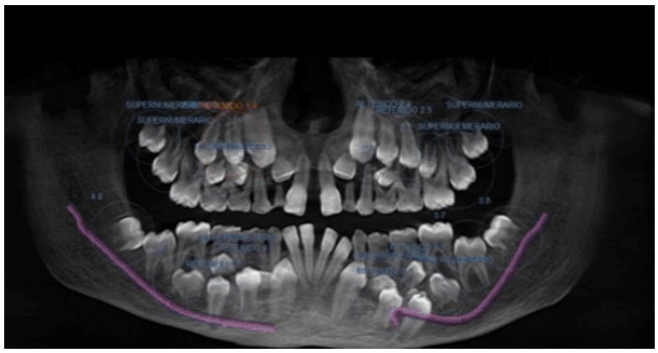

Figure 2 Axial computed tomography revealing numerous retained supernumerary teeth in both jaws.

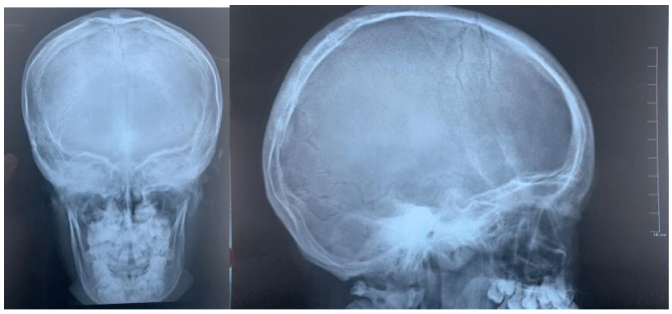

Figure 3 Posteroanterior (PA) and lateral skull radiograph depicting incomplete closure of the anterior fontanelle and absence of the frontal sinus.

Discussion

Cleidocranial dysplasia was initially documented by Martin in 1765. Following this, Marie and Sainton independently delineated the disease criteria. Subsequently, over 700 instances of this syndrome have been cataloged in the literature, predominantly within European and American contexts. Additionally, more than a hundred cases have been elucidated in Japanese Scholarly works.[3]

Cleidocranial dysostosis manifests as a genetically inherited disorder with a pattern correlated to the RUNX2 gene, situated on chromosome 6 at the p21 locus.1 It pertains to the RUNX family of transcription factors.1 The gene encodes the CBFA1 protein, expressed notably in oral tissues such as the mesenchyme of the dental follicle, exerting regulatory control over growth and differentiation processes.[4,5] Furthermore, it serves as a pivotal determinant in the orchestration of mesenchymal-epithelial interactions, morphogenesis regulation, and histodifferentiation within the enamel epithelial organ.[3,4] Moreover, CBFA1 finds expression within the periodontal ligament, wherein cells of this tissue exhibit diminished capacity for inducing active osteoclast differentiation under conditions of cleidocranial dysostosis, thereby partially elucidating the clinically observed phenomenon of delayed dental eruption.[2,6,7]

As per Tanaka et al.[8] the diagnostic triad for cleidocranial dysostosis encompasses the complete or partial absence of clavicles, supernumerary teeth, and cranial anomalies including dysostosis of cranial sutures, failure of fontanelle closure, incomplete formation of the facial skeleton, and the absence of frontal and maxillary sinuses.

Conclusion

A profound understanding of the syndromic manifestations of cleidocranial dysostosis is paramount for the timely identification of this congenital anomaly. Both dentists and physicians must adeptly discern the clinical presentations, necessitating a multidisciplinary approach for optimal management and improved patient outcomes.

Acknowledgments

None.

Conflicts of interest

The authors declare no conflicts of interest.

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