CASE REPORT

Cleidocranial dysplasia: complete clinical, radiological and histological profiles

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SUMMARY

Cleidocranial dysplasia is an autosomal-dominant condition characterised by widely patent calvarial sutures, clavicular hypoplasia, supernumerary teeth and short stature. Though it is not a very uncommon occurrence, its histopathological features are not frequently reported. This paper presents a similar case with complete clinical, radiological, histological and treatment profiles.

BACKGROUND

Bone is an important calcified connective tissue of the body which plays an essential role not only in physical functions but also in various physiological and biochemical processes.¹ Bones together form the primary structural framework that provides support to the body, helps in locomotion in conjunction with skeletal muscles, protects the internal organs and houses the haematopoietic tissue, in addition, it takes part in calcium and phosphate metabolism and serves as the major reservoir for calcium and other vital minerals.²

Bone along with the joints which it forms may be affected by a wide variety of pathological conditions, such as, neoplasms, infections, developmental disorders, etc. Skeletal dysplasias are one such heterogeneous group, in which the disorder results in numerous disturbances of the skeletal system and most of which include dwarfism.³ Cleidocranial dysplasia (CCD) is one such condition which is a part of this large spectrum of constitutional disorders of bone. Thousands of cases of CCD have been documented since the reports of Meckel in 1760 and Martin in 1765. It was probably seen even in Neanderthal man though the syndrome was precisely explained in late 1800s.⁴ A well-preserved skeleton in the Museum of Pathological Anatomy in Vienna exhibits the typical features of CCD.⁵ This term was initially coined as 'Cleidocranial dysostosis' by Marie and Saiton in 1897. The term was intended to emphasise the prime involvement of craniomaxillofacial region and clavicles in this syndrome. But over the years numerous other features seen in this condition have been documented and the term has been modified from cleidocranial dysostosis to CCD.⁴ It is considered as one of the mesodermal dysfunctions, which directly affect many tissues and organs and results in skeletal abnormalities. The nature of its inheritance is considered as complex and capricious. Till now chromosomal alterations on chromosome 6, in the form of pericentric inversion⁶ balanced translocation between chromosomes 6p and 18q⁷ or as

microdeletion,⁴ have been implicated in the occurrence of this complex disorder. But recent studies reveal an additional mechanism for the pathogenesis of CCD, particularly with regard to the regulation of MSX2 on chromosome 5.⁸

Though this rare entity has been reported, its histology is not often discussed. This article presents a case of CCD with all its clinical and radiographic findings. Further, an emphasis is laid on the less-documented histopathological features of bone and teeth in patients affected by CCD.

CASE PRESENTATION

A 15-year-old, female patient reported to the clinic with missing teeth. From clinical history it was found that the patient had shortness of breath on mild exertion and also recurrent episodes of sinusitis.

Upon clinical evaluation the patient had brachycephaly, frontal bossing, hypertelorism, depressed nasal bridge and sloping shoulders which could be approximated towards the midline. Intraoral examination revealed retained deciduous teeth, missing permanent teeth and a high arched, narrow palate.

INVESTIGATIONS

Upon radiographic assessment, chest x-ray showed hypoplastic clavicles and sloping ribs. Intraoral and extraoral radiographs demonstrated open skull sutures, obliterated maxillary sinus and multiple unerupted and supernumerary teeth (figure 1).

After thorough assessment of the case a multidisciplinary treatment plan was framed. As a part of this the retained deciduous teeth which were extracted were sent for histopathological evaluation (one ground section + one decalcified section). In addition, a bony bit which was obtained during surgical exposure (figure 2) of the impacted permanent teeth was also sent for similar evaluation.

Figure 1 Orthopantomogram showing multiple impacted and supernumerary teeth.

To cite: Vij R, Batra P, Vij H. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-009015

Figure 2 Surgical exposure of impacted teeth and attachment of brackets for orthodontic treatment.

Upon microscopic examination both the teeth and bones showed a deviation from normal in their architecture. H&E-stained sections of bone exhibited osteocytes in lacunae, resting lines and occasional canals, but well-formed osteons could not be appreciated (figure 3). The sections of teeth illustrate distorted dentinal tubules at places, prominent interglobular dentine (figure 4), acellular cementum with conspicuous absence of cellular cementum in the apical region (figure 5).

TREATMENT

In the case under discussion, the retained deciduous teeth were extracted, the impacted teeth were surgically exposed, moved to the level of occlusion and aligned with the help of orthodontic treatment.

DISCUSSION

Though the first description of cleidocranial dysostosis is credited to Meckle in 1760, the combination of clavicular and cranial defects was identified by Scheuthauer in 1871.⁹ It has been accepted to be an autosomal disorder with a generalised involvement of bone. This is a trait with high penetrance and marked variability of expression.¹⁰ As the name implies, the most obvious characteristics are malformations of the head and clavicles, which produce a typical and striking appearance of the face and shoulders, which were noticed even in the present case.

Orofacial findings of this disorder are very significant. Extraoral findings include an increase in the transverse

Figure 4 Photomicrograph showing prominent areas of interglobular dentine (H&E, $\times 10$).

dimensions of the cranium (brachycephalic head) and sagittal shortening of the cranial base. Frontal and parietal bossing may be associated along with metopic depression. Closure of fontanelles and cranial sutures is delayed and wormian bones may be present. The nasal bridge is depressed with deficiencies in the nasal and lacrymal bones. To this may be added the effect on the long bones, phalanges, spine, pelvic muscles and the CNS. The middle-third of the face is hypoplastic both in the antero-posterior and vertical dimensions. Absence of zygomatic arches is seldom reported and the bridge of the nose is often wide and flat. There is an incomplete fusion of the symphysis menti.^{11–13} Most of these characteristic features were noticed in the present case but open sutures were most prominent.

Varying degrees of aplasia of the clavicles cause an elongated appearance of the neck and permit near approximation of the shoulders with internal rotation. The clavicles are usually asymmetrically deficient at their outer ends or they may be absent all together, thus accounting for the sloping shoulders and the classic trick of shoulder tip approximation,^{14–16} as were discerned even in our case. The case under discussion also exhibited hypoplastic clavicles and sloping shoulders. Additional skeletal defects are spina bifida, failure of union of neural arches to the body of the vertebrae, failure of union of the pubic bones

Figure 3 Photomicrograph showing ill-defined osteons and multiple reversal lines (H&E, $\times 10$).

Figure 5 Photomicrograph showing absence of cellular cementum in apical region ($\times 4$).

with a 'chef's hat appearance', with sacroiliac joints and wide spaces between ossified ribs and vertebrae. Most individuals show delayed and deficient ossification of long bones, which account for somatotypically short and broad body builds, which is an attribute common to this disorder and was also observed in the case presented in this paper. These defects are brought about by derangement in ossification of long bones especially expressing itself in bones ossifying in membrane.^{13 17 18}

Multiple abnormalities have a typical appearance in relation to the dentoalveolar complex in CCD. Supernumerary teeth are localised in both the jaws especially in the areas of the premolars. Some authors however state that cases may be present with all the classical symptoms but no supernumerary teeth. Retention of deciduous teeth for a long period may cause failed eruption of the permanent dentition.¹⁹ The alveolar processes are underdeveloped since the eruption pattern is altered. Therefore the vertical height of the middle third of the face decreases. The case under consideration too illustrated retained deciduous teeth along with multiple impacted and supernumerary teeth. Prolonged retention of deciduous teeth and poorly developed jaws may cause difficulty in mastication. The combined abnormalities of the dentoalveolar complex and middle third of the face result in a characteristic prognathic appearance of the mandible.^{20–22} Although submucosal or complete clefting of the palate is rare, the hard palate is generally high and narrow. The other intraoral manifestations are ectopic eruption of permanent teeth and the formation of cysts associated with impacted teeth. The roots of unerupted teeth are spindly and dilacerated and the crowns of unerupted teeth seem compressed and show enamel hypoplasia. Dentigerous cysts are common but are thought to be a result rather than a cause of delayed eruption.^{21 22}

It is interesting to note that the development of primary dentition in these patients is normal, hence most of the patients with cleidocranial dysplasia are unaware of any problem until the lack of eruption of the permanent teeth causes difficulty in mastication and a serious psychosocial problem. The formation of permanent teeth is normal with a delay of about 3–4 years. A disturbance of bone resorption along with an interposed fibrous tissue between the dental follicle and the mucosa or a lack of cellular cementum can be the cause of the unerupted teeth.²³ Similar conspicuous absence of cellular cementum in the apical region was seen in the present case. Along with it prominent areas of globular dentine were also noted as were also reported by Fukuta *et al*.²³ These authors also observed enamel hypoplasia, predominant Tomes' granular layer, obscure incremental lines of von Ebner and counter lines of Owen and lower quantities of calcium and phosphate in the enamel and dentine than those of the control sample. The associated bone in the present case showed irregular osteons suggestive of abnormal bone remodelling as has been put forth by Lukinmaa *et al*.²⁴

It has been suggested that the incomplete or marked delay in the resorption of the dental lamina which are reactive in the course of crown completion explained the development of supernumerary teeth.^{19 20 24 25} The lack of space in the jaws at the time of development of the supernumerary teeth causes malformed crowns and roots.^{9 19}

In patients with this condition dental treatment planning should aim at correction of the dentofacial deformity both aesthetically and functionally. In cases where diagnosis is made early the supernumerary teeth are surgically exposed and orthodontic traction is applied to bring them in occlusion, as was performed in the present case. Some authors advocate extraction of all primary and permanent teeth followed by prosthesis. Orthognathic surgery for

correction of the midfacial deformity is also advocated. Some authors state that only erupted teeth should be extracted as this would minimise the alveolar bone loss.²² In the present case too retained teeth were extracted, the impacted teeth were surgically exposed and moved to the level of occlusion and aligned with the help of orthodontic treatment.

Learning points

- ▶ Presence of any oral abnormalities should instigate us for through systematic evaluation to detect or rule out a generalised pathology.
- ▶ Clinically identifiable disorders can show abnormality in histological profile, which may not have been previously reported. This in turn will prompt newer studies to find a definitive pathogenesis as well as cure for numerous mysterious diseases.
- ▶ Clinic–pathological correlation is essential for reaching a definitive diagnosis, to enhance our knowledge regarding age/gender/racial predilection of various rare and common pathologies and also to build the database of number of cases reported of a particular pathology.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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