Cleidocranial dysplasia: A light microscope, electron microscope, and crystallographic study

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An unusual case of cleidocranial dysplasia associated with more than 60 unerupted teeth is presented and examined with light and scanning electron microscopes and crystallographic techniques. The present case revealed pseudoprognathism with facial asymmetry, the right side being larger than the left. The extracted teeth showed enamel hypoplasia in light and scanning electron microscopy, yet the crystalline composition did not differ from that of the normal teeth. The potential causes of lack of eruption and supernumerary tooth formation in cleidocranial dysplasia are discussed.
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Cleidocranial dysplasia is a rare developmental disease of bone characterized by abnormalities of the skull, jaw, and clavicles as well as by occasional stunting of long bones.[1] The oral manifestations characteristically seen in this disease are multiple unerupted teeth, many of which are supernumerary; however, cases with more than 60 unerupted teeth are rare.[2] Detailed morphologic study of the teeth and jaws in cleidocranial dysplasia has not been reported.

We report here a study, done with light and scanning electron microscopy together with crystallographic techniques, of a case of cleidocranial dysplasia associated with 63 unerupted teeth.

CASE REPORT

In November 1977 a 26-year-old Japanese woman visited Nihon University Dental Hospital at Matsudo with anterior maxillary gingival pain. About 4 years previously eight erupted carious teeth had been extracted and she had been provided with full dentures. Subsequently, however, she suffered from mucosal ulceration of the upper right gingiva and consulted a private dentist who detected multiple unerupted teeth and referred her to our dental hospital.

Her medical history disclosed that she had been born of nonconsanguineous parentage as a premature baby. At the time of her initial visit in1977, her father was 73 years old and healthy, and her mother had died of cerebral embolism 2 years earlier. The patient was the seventh child of seven children and the only one in her family of short stature. At the age of 9 years she had been suspected of having rickets, yet no treatment had been rendered.

Examination, revealed that she was of short stature, 139 cm in height and 40 kg in weight. Wrinkling of her forehead and perioral region was noticed. She was wearing full dentures although coronal portions of the lower right molar and upper right incisor and molar were erupted. Mucosal redness of the upper right maxillary region was also observed.

Laboratory data such as hematologic and serologic studies, urinalysis, and blood chemistry values, including calcium and alkaline phosphatase levels, showed almost no remarkable change, with the exception of slight anemia and occult hematuria.

Radiographically, a total of 63 unerupted teeth were identified by orthopantomography (Fig. 1). The unerupted teeth were present in various positions: vertical, mesioangular, horizontal, and distoangular although no cyst formation around these uncrupted teeth was seen. Comparison of normal adult bone with the lateral X-ray photographs of the jaws showed that development of the premaxilla was retarded and that the mandible was better developed, a situation that created a relative "pseudoprognathism." The area of the right jaws was larger than that of the left. Wormian bones were present in the region of the lambdoid and coronal sutures. A chest radiograph showed bilateral absence of the clavicles with associated funneling of the thoracic inlet.

A diagnosis of cleidocranial dysplasia was made. Three teeth, including the lower right deciduous molar and the

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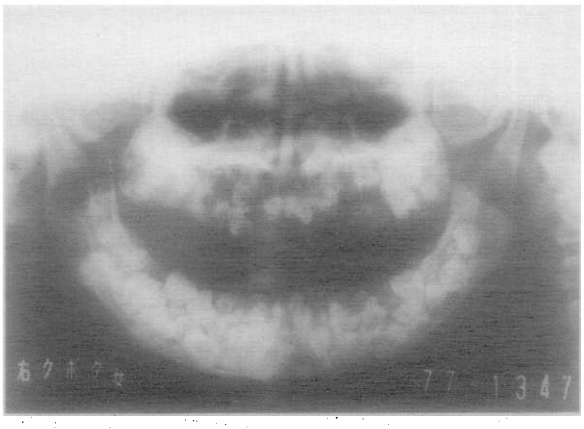

Fig. 1. Orthopantomograph reveals 63 unerupted teeth (37 in the mandible and 26 in the maxilla) and asymmetric right and left sides of jaws.

upper right incisor and molar, were extracted. In July 1985 she returned to our hospital because a supernumerary tooth in the lower right molar region had begun to erupt and cause inflammation of the surrounding mucosa. The tooth was extracted at that time.

MATERIAL AND METHODS

Specimens were obtained from the lower right deciduous molar and lower right supernumerary teeth. They were fixed in 10% neutral formalin and cut into several pieces with Buehler Isomets (Buehler Ltd., Evanston, Ill.). Some of these specimens were decalcified by means of the Plank-Rychlo method (Sehnellentkalkungsmethode), embedded in paraffin, sectioned, and subsequently stained with hematoxylin and eosin. The remainder were ground to about 60 μm for optical examination, scanning electron microscopy, and crystallographic analysis.

For scanning electron microscopy the ground sections were then immersed in a 0.14 mol/L solution of sodium hypochlorite for 1 minute. They were subsequently washed in distilled water for 10 minutes and dehydrated in ascending grades of ethanol. The sections were air dried and coated with carbon and gold. They were examined in a JEOL T-200 (JEOL, Tokyo, Japan) scanning electron microscope.

X-ray crystallographic analysis was performed by a microdiffractometer (Rigaku, Tokyo, Japan). The X-ray beam (Cu Kα. 1.542 Å) was collimated to 100 μm in diameter. Diffraction patterns obtained were similar to those of the powder diffraction method, but the instrument had lower intensity and angular precision.

FINDINGS

Macroscopically, the lower right deciduous molar was 11 and 8 mm in mesiodistal and buccolingual

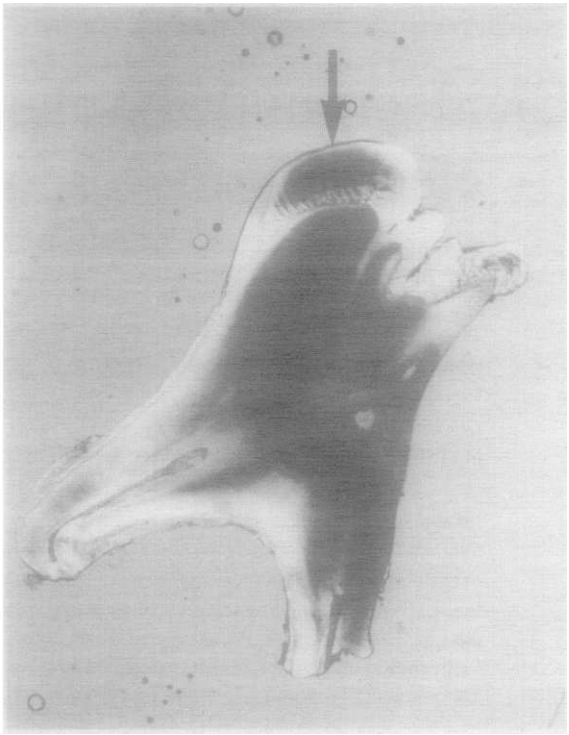

Fig. 2. Polarizing microscopy of the deciduous molar reveals a dark zone of enamel *(arrow)* that indicates hypocalcification. (Original magnification ×8.)

width, and 4 and 10 mm in crown and root length, respectively. The lower right supernumerary tooth was 9 and 5 mm in mesiodistal and buccolingual width, and 5 and 6 mm in crown and root length, respectively. The crowns of both teeth had 6 cusps with Y-shaped grooves. The roots exhibited moderate to marked resorption. The size of the molar conformed to the average size for Japanese deciduous teeth as described by Fujita.[3]

Microradiographs of the ground sections of both teeth showed hypocalcification along the walls of the grooves, at the cusp tips, and in the cervical regions.

Microscopically, both teeth revealed similar findings. The occlusal surface of the crown and cusps was covered with membranous cuticle-like substances. The structure of enamel rods revealed a relatively clear arrangement with Hunter-Schreger bands and growth lines in both teeth (Figs. 2 and 3). Enamel and, to a small extent, dentin growth of the mesial side of the lower right deciduous molar was severely altered (Fig. 2). Large enamel tufts were seen in some areas. The area of interglobular dentin and calcospherites was widely distributed from crown to root apex, especially in the cervical region (Fig. 4). The layer of predentin was thick with regard to the patient's age. The mantle dentin, granular layer of Tomes, and some areas of grooves corresponded with

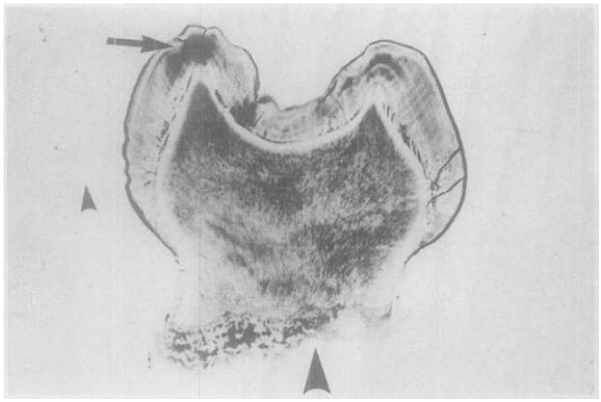

Fig. 3. Polarizing microscopy of the supernumerary tooth shows root resorption *(arrowhead)* and some enamel hypocalcification *(arrow)*. (Original magnification ×20.)

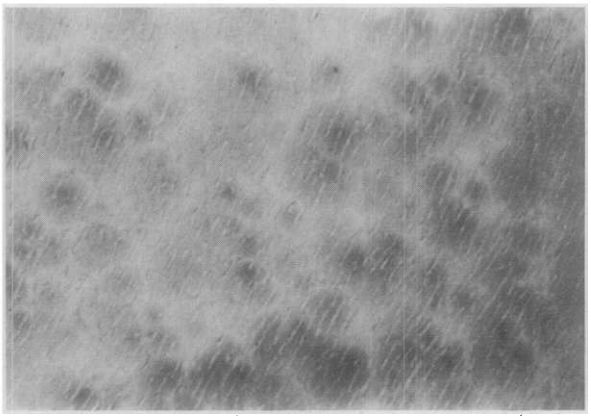

Fig. 4. High-power view of interglobular dentin. (Hematoxylin and eosin stain. Original magnification ×200.)

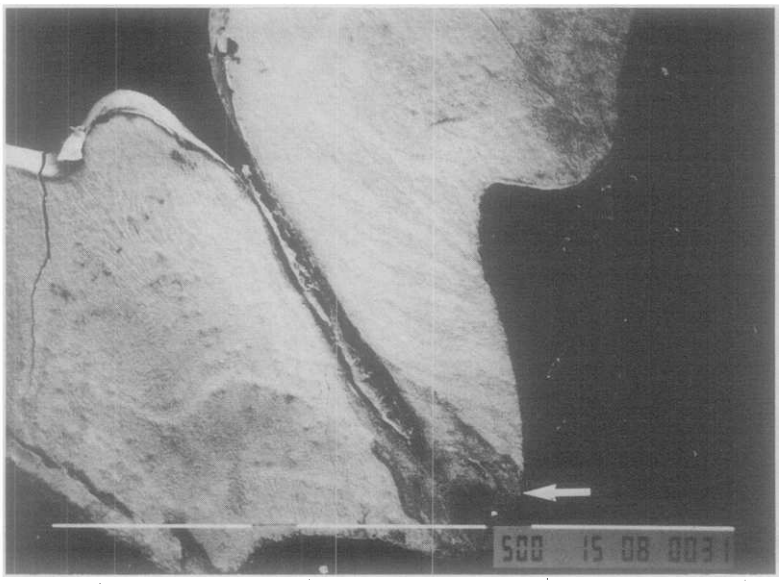

Fig. 5. Scanning electron micrograph reveals hypocalcification in the enamel groove *(arrow)*. (Original magnification ×35.)

hypocalcified areas as mentioned above. Thick acellular cementum covered the distal side of the lower third of the deciduous tooth root. The pulp chamber was narrow and contained dilated capillaries.

Scanning electron microscopy disclosed some hypocalcified areas of enamel, in the bottom of the grooves of the deciduous molar and the supernumerary tooth (Figs. 5 and 6). These areas were covered with inorganic material (Fig. 6). The dentinal tubules were almost regularly arranged and normal in number. The resorbed areas were devoid of cementum, but the lateral side of the root possessed a cemental layer. The pulp chamber was small and narrow.

X-ray diffraction patterns of the enamel and dentin were obtained from 30 points over the specimens. The diffraction pattern shown in Fig. 7 was identified as apatite. Comparison of the X-ray diffraction patterns of enamel and dentin revealed that the crystalline composition was slightly decreased in dentin.

DISCUSSION

Cleidocranial dysplasia was first reported by Martin[4] in 1765. Subsequently, Marie and Sainton[5] independently documented the criteria of the disease. Since then over 700 cases of this syndrome have been described, mainly in the European and American literature.[6] Over one hundred cases of this disease have also been reported in the Japanese literature.[7]

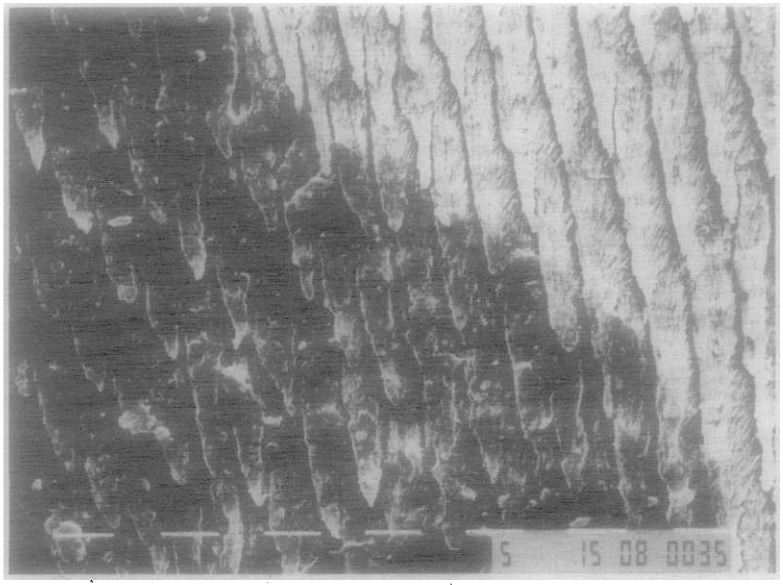

Fig. 6. Scanning electron microscopy shows hypocalcification of enamel with an overlying layer of organic material *(dark)*. (Original magnification ×1000.)

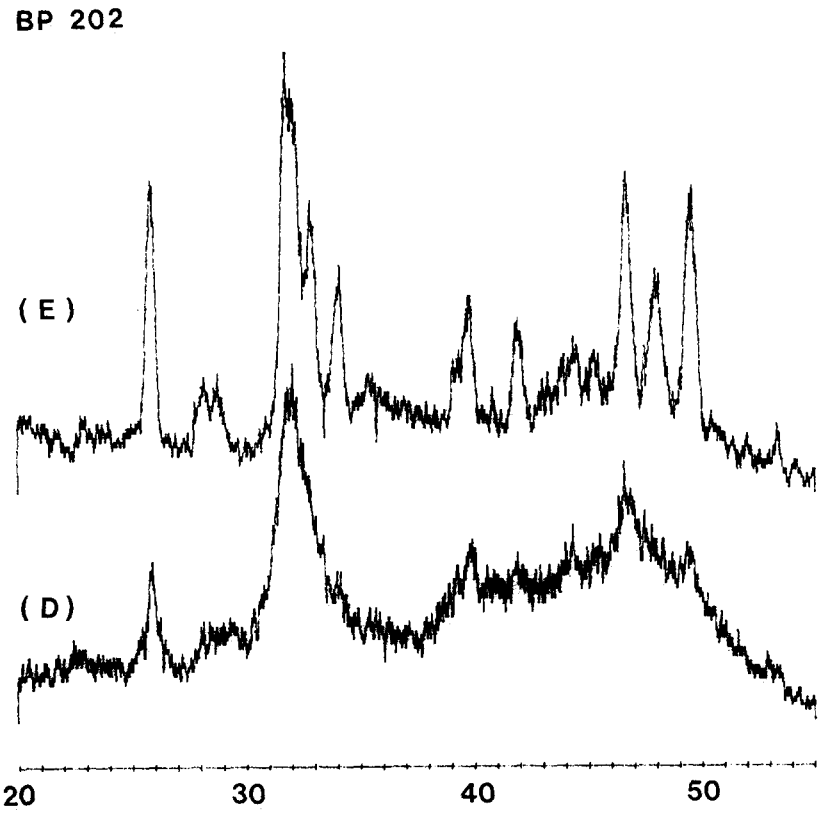

Fig. 7. X-ray diffraction patterns of enamel *(E)* and dentin *(D)* are identified as apatite. The horizontal axis of the graph represents the diffraction angle, and the height is the intensity.

The clinical features including oral manifestations have been described in detail by many authors.[1-7] Multiple unerupted teeth is one of the oral manifestations of cleidocranial dysplasia.[8-14] The present case had 63 unerupted teeth, the greatest number thus far reported.

The cause of unerupted teeth in cleidocranial dysplasia is said to be (1) a disturbance of bone

resorption,[15-17] (2) a lack of cellular cementum,[18, 19] or (3) a lack of union between the dental follicle and the mucosa due to interposed fibrous tissue acting as a barrier to eruption.[20] The tooth roots in this case revealed resorption, but there was no bone specimen in our pathologic materials. In the present case there was no identifiable osseous disease process that would account for a resorption defect. Light and scanning electron microscopy showed acellular cementum; however, a lack of cellular cementum is also seen in normal teeth and therefore is unlikely to have any influence on eruption. The numerous unerupted teeth in the present case occurred in anomalous positions and resulted in crowding of both dental arches. This mechanical obstruction is probably the chief factor contributing to failure of eruption. Early loss of the gubernacular cord or canal has been described as a cause of lack of eruption, although no evidence is provided here to support or refute this contention.[20, 21]

As for the number of teeth in cleidocranial dysplasia, the mechanism and reason for this patient's multiple supernumerary teeth are unclear. Supernumerary teeth are thought to evolve by hyperplasia or by segmentation of tooth germs.[22] Cleidocranial dysplasia is generally an autosomal dominant syndrome,[20, 23] although in the present case we were unable to identify hereditary factors; the presence of supernumerary teeth is thought to be genetically controlled.[20]

The crown form of the supernumerary teeth in this disease is similar to that of premolars, although somewhat flattened.[6] Fröhlich[24] reported that the number of molars is less than that of normal individuals. Stewart and Prescott.[20] stated that the teeth are severely deformed with hypoplastic enamel. The teeth of the present case also showed some enamel hypocalcification as demonstrated by both light and scanning electron microscope observations. Enamel calcification slowly proceeds after enamel matrix formation, but dentin and cementum immediately calcify after their matrix formation.[25] Therefore hypocalcification more often affects enamel than it affects dentin or cementum. In the present case both enamel and dentin growth were disturbed on the medial side of the deciduous molar, although the crystalline composition of both tissues, as assessed by X-ray microdiffraction, was almost the same as normal.[26]

In cleidocranial dysplasia the premaxilla is hypoplastic, yet the growth of the mandible is usually normal. Bone development may be endochondral or intramembranous.[21] In jaw bones of children endochondral growth is mainly found at the mandibular condyle. On the other hand, the maxilla develops intramembranously. Cleidocranial dysplasia is originally believed to involve only bones of membranous origin.[20] The mandible is an intramembranously derived bone for most of its bulk, at least during the development of the tooth germs. The appearance of the secondary cartilage of the condylar and coronoid processes is a later development. Therefore the difference of bone development between both jaws in this instance is partly because of pseudoprognathism.

In addition, the present case revealed asymmetry between right and left sides of both jaws, the right side being larger than the left. This asymmetry has not been previously described in the literature and may represent an imbalance resulting from altered jaw development itself, or the difference of odontogenic activity within the jaw bone may have been a factor.

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