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Cleidocranial dysplasia in a mother and her daughter within the scope of neurosurgery

Report of two cases

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✓Cleidocranial dysplasia is an autosomal-dominant disorder characterized by late closure or nonclosure of the anterior fontanelle, late ossification of cranial sutures, defective clavicle, and delayed eruption of permanent teeth. In this article, two cases of cleidocranial dysplasia involving a mother and her daughter are reported, and a case management policy is suggested. The 1-year-old daughter was macrocephalic and brachycephalic, and had midface hypoplasia and hypertelorism. Plain radiographs revealed aplasia of the clavicles. Three-dimensional computerized tomography scanning demonstrated a large anterior fontanelle, a patent posterior fontanelle, and bone defects at the pterion and asterion, together with nonfused metopic and sagittal sutures. The mother was 22 years of age. She had an open anterior fontanelle, aplastic clavicles, and unerupted permanent teeth.

Although it is a rare disorder, cleidocranial dysplasia should be recognized by neurosurgeons. A protective helmet can be provided in early childhood, and craniofacial remodeling can be undertaken at a later age, when the final size and shape of the skull become apparent.

Key Words • **cleidocranial dysplasia** • **craniofacial abnormality** • **pediatric neurosurgery**

Cleidocranial dysplasia is an autosomal-dominant disorder characterized by late closure or nonclosure of the anterior fontanelle, late ossification of cranial sutures, defective clavicle, and delayed eruption of the permanent teeth.[5] Although more than 500 cases have been reported, only one paper appears in the neurosurgical literature, and suggestions regarding the neurosurgical treatment of these patients are missing.[11] In this paper, two cases of cleidocranial dysplasia, one involving a mother and the other her daughter, are reported, and a case management policy is suggested.

Case Reports

Case 1

History. This 1-year-old girl was admitted to the Department of Pediatrics with complaints of fever and respiratory distress. Bronchiolitis was diagnosed and appropriate medical treatment was initiated. During her general examination, she was noted to be macrocephalic (Fig. 1 *upper left)*. Plain radiographs revealed a large anterior fontanelle and aplasia of the clavicles (Fig. 1 *upper right*). A clinical diagnosis of cleidocranial dysplasia was established, and the patient was referred for neurosurgical consultation after completion of medical treatment for bronchiolitis.

Presentation and Examination. The patient was macrocephalic and brachycephalic, with midface hypoplasia and hypertelorism. Computerized tomography scanning revealed dilation of the subarachnoid space (Fig. 1 *lower left*). Three-dimensional CT scanning demonstrated a large anterior fontanelle, a patent posterior fontanelle, and bone defects at the pterion and asterion, together with nonfused metopic and sagittal sutures (Fig. 1 *lower center* and *right*).

Treatment. A protective helmet was fitted to the infant's head, and future craniofacial remodeling was recommended. Follow up was initiated for the subarachnoid dilation, and the patient was referred for orthodontic consultation.

Case 2

This 22-year-old woman, the mother of the patient in Case 1, was noted to have the same clinical picture as her daughter. The woman's anterior fontanelle was seen to be open on 3D CT scans (Fig. 2 *left*). On plain radiographs of the chest, the clavicles were aplastic (Fig. 2 *upper right*). Panoramic dental radiographs demonstrated unerupted permanent teeth (Fig. 2 *lower right*), and the woman was using a prosthesis. She was found to be the first person in her family with such an anomaly. A cranioplasty to close the skull defect was offered to this patient, but she refused.

Abbreviations used in this paper: CT = computerized tomography; 3D = three-dimensional.

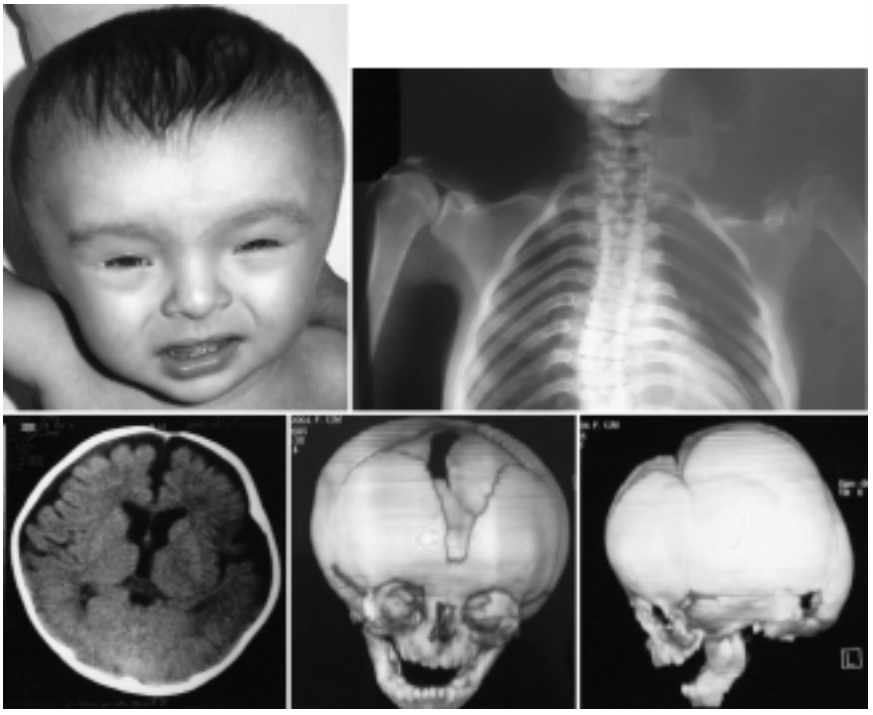

FIG. 1. *Upper Left:* Photograph of the daughter, who was macrocephalic, with midface hypoplasia and hypertelorism. *Upper Right:* Radiograph illustrating aplastic clavicles. *Lower Left:* A CT scan showing dilation of the subarachnoid space. *Lower Center:* A 3D CT scan depicting open anterior and posterior fontanelles and nonfused metopic sutures. *Lower Right:* A 3D CT scan depicting the brachycephalic skull and bone defects at the pterion and asterion.

Discussion

Cleidocranial dysplasia is an autosomal-dominant disorder characterized by late ossification of cranial sutures, defective clavicle, and delayed eruption of permanent teeth.[5] Although similar cases have been reported, the condition was first named by Marie and Sainton as "dysostose cléidocrânienne héréditaire" in 1898.[7] It arises from a microdeletion in chromosome 6p21 that leads to a haploinsufficiency of core binding factor transcription factor A1 (CBFA1, also known as RUNX2).[8] Although cleidocranial dysplasia has an autosomal-dominant inheritance, one third of the cases are fresh mutations. The result is defective intramembranous and altered endochondral ossification.[13]

Craniofacial anomalies include brachycephaly with bossing of frontal, parietal, and occipital bones; late closure or nonclosure of the anterior fontanelle and late mineralization of sutures; incomplete development of air sinuses; midfacial hypoplasia; hypertelorism; and wormian bones.[5] Eustachian tube dysfunction and conductive and sensorineural hearing loss can occur due to the skeletal changes in the temporal bone.[12] The chest is small, with oblique ribs, and there is partial or complete aplasia of the clavicles. Dental anomalies include retention of deciduous teeth, the presence of supernumerary teeth, and noneruption of permanent teeth.[1] Although the birth length is within normal limits, children between the ages of 4 and 8 years do not maintain a normal rate of growth, and their heights are below the third percentile.[7] Mental acuity is usually normal.

More than 500 cases have been described, including reports of three generations in a single family[2] and a series of 90 cases.[3] Only one paper in the neurosurgical literature mentions the association between cleidocranial dysplasia and syringomyelia.[11] Published studies are generally concentrated in the fields of genetics and orthodontics. Therefore, suggestions regarding the neurosurgical treatment of these patients are nonexistent in published form.

Children suffering from cleidocranial dysplasia are susceptible to cerebral injury following head trauma due to their large fontanelles and bone defects. Because of the defective ossification, craniofacial remodeling in such a child requires repair of the skull defects together with rigid fixation; yet such repairs are not appropriate during the period of brain development and rapid skull growth. Therefore, these children should be followed up, at least until preschool age. A protective helmet can be provided in the meantime.

As the child becomes older, the final shape and size of the skull will be apparent, the calvaria will be ready for split grafts, and it will be possible to harvest autografts from other sites.[9] Preoperative evaluation should be performed using 3D CT scanning. Plain radiographs will be unable to provide the necessary information regarding the open fontanelle due to increased calvarial bone thickness, increased mineralization of the cranium, and the prominence of occipital bone in the anteroposterior view.[10] On the other hand, radiological follow up can be performed by routine CT investigations to avoid the high radiation exposure that accompanies 3D CT scanning.

In a previous study, Jensen[4] described the craniofacial morphology of cleidocranial dysplasia in 35 adult patients. The findings were as follows: open anterior fontanelle (> 60% of patients), increased width of calvaria, prominent frontal bone, frontal groove (due to incomplete ossification of the metopic suture), decreased width of cranial base, ab-

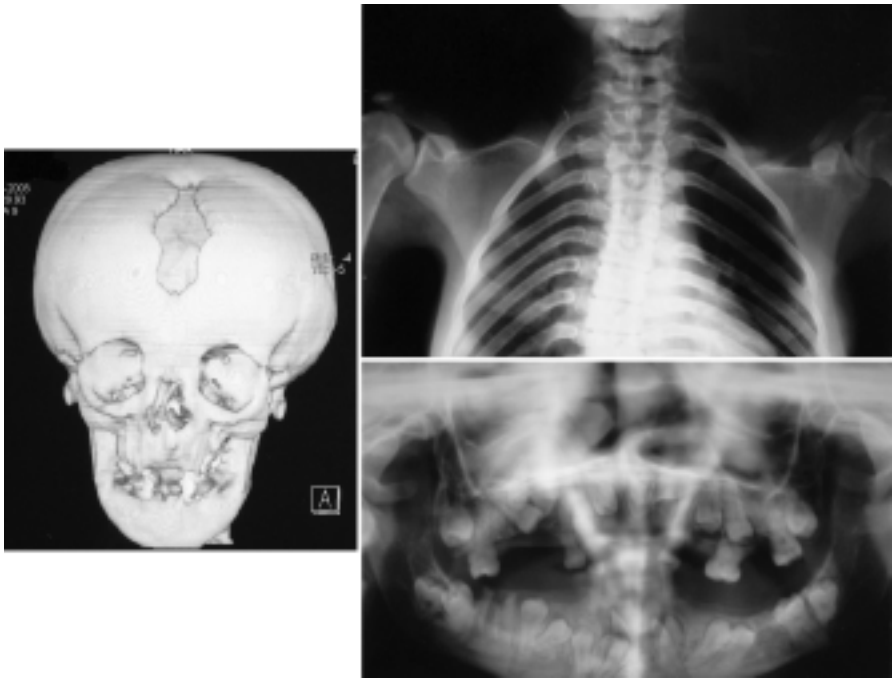

FIG. 2. *Left:* A 3D CT scan showing how the mother's anterior fontanelle was open along the metopic suture. *Upper Right:* Plain x-ray film demonstrating aplastic clavicles. *Lower Right:* Dental radiograph demonstrating that the permanent teeth were unerupted.

sent or diminished paranasal sinuses, displacement of clivus and sella turcica, anteversion of foramen magnum, hypertelorism, hypoplasia of nasal bones, and decreased height and width of maxilla and mandible.

As skull growth ceases, the child should undergo craniofacial remodeling. During closure of the skull defects, methylmethacrylate is preferable to bone grafts. Healing and incorporation of the bone graft requires a healthy osteogenic bed; however, failure of the fontanelle to close in the first place indicates that the site of the skull defect is unlikely to support a satisfactory incorporation of the graft.[9] Methylmethacrylate provides immediate and permanent mechanical protection. The patient should also receive orthodontic treatment, which consists of surgical removal of the deciduous teeth and the imbedded supernumerary teeth, followed by orthodontically aided eruption and meticulous alignment of the permanent teeth.[1] Although the absence of the clavicle causes no functional disturbance, scapulothoracic arthrodesis is indicated if scapular winging is present so that the pain associated with movement and function of the joint may be eliminated.[6]

Although it is a rare disorder, cleidocranial dysplasia should be recognized by neurosurgeons, and they should always be involved in the management team.

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