CASE REPORT

Cleıdocranıal Dysplasıa: A Rare Skeletal Dysplasıa

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ABSTRACT

Cleidocranial dysplasia (CCD) is a rare autosomal dominant skeletal dysplasia. Hypoplastic clavicles, delayed closure of the cranial sutures, dental abnormalities, and short stature are main features in this syndrome. RUNX2 is the responsible gene for CCD. Here we reported two cases with CCD; they are admitted to clinic for short stature and dental abnormalities. We report these cases to increase the awareness of clinicians

Keywords: Hypoplastic clavicles, dental abnormalities, skeletal dysplasia.

INTRODUCTION

Cleidocranial dysplasia (CCD) is a rare congenital skeletal disorder that affects the intramembranous ossification of the bones and teeth. It is an autosomal dominant genetic disease. The disorder is characterized by hypoplasia or aplasia of the clavicles, delayed closure of the fontanelles, supernumerary teeth, and short stature. RUNX2 gene is responsible for the pathogenesis of CCD (1–4).

The syndrome is characterized by the delayed closure of fontanelles, hypermobility of the shoulders, wormian bones, and wide pubic symphysis. The teeth and vertebral bones are affected in varying degrees. Dental abnormalities are the typical main features of CCD, and the permanent dentition is severely disturbed (5, 6).

CASE 1

A 10-year-old girl was admitted to Department of Pediatric Endocrinology, School of Medicine, Kocaeli University, Turkey. She presented with open anterior fontanelle and severe tooth anomalies. These dental problems were especially the complaints of delayed eruption of the permanent anterior teeth. She was born at 38 weeks, and weighed 3600 g from healthy parents. Her mental and motor developments were in the normal range. In her first examination, her height was 126 cm (–0.49 standard deviation (SDS)), her weight was 24.5 kg (–0.63 SDS) and her head circumference was 52 cm. Her anterior fontanel diameter was 0.5 × 1 cm. She had frontal bossing, hypertelorism, hypoplastic zygomatic bones, flattened nasal root, prognathism (Fig. 1), severe dental problems (Fig. 2), and easily close-up shoulders (Figs. 3 and 4). She had palpable claviculas but abnormal facility in opposing her shoulders due to hypoplastic clavicles and pectus carinatus.

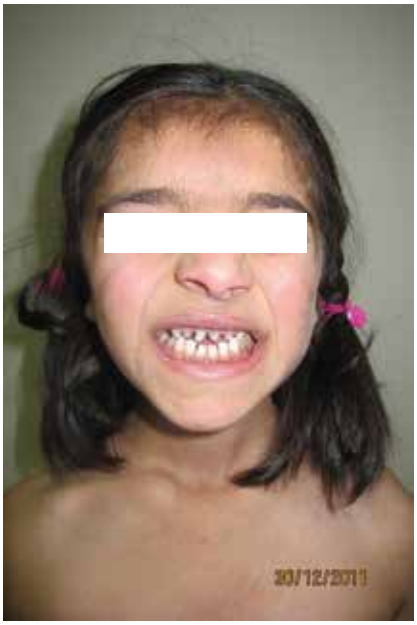

Fig. 1: Appearance of face and mild prognathism.

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DOI: 10.7727/wimj.2015.267

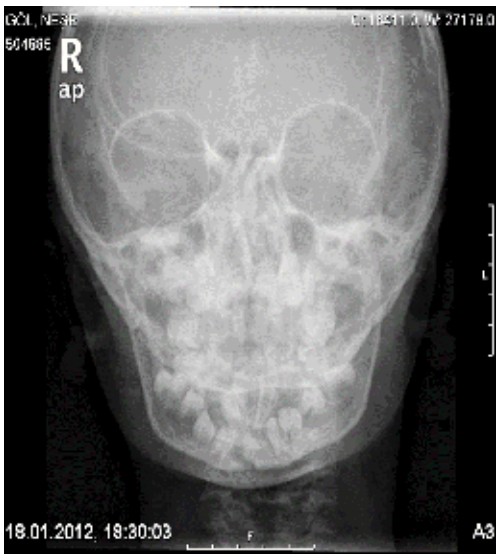

Fig. 2: Supernumerary teeth.

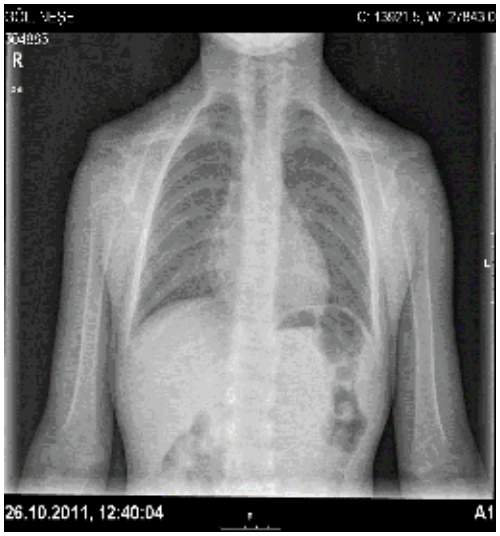

Fig. 3: Hypoplasia of distal side of clavicles.

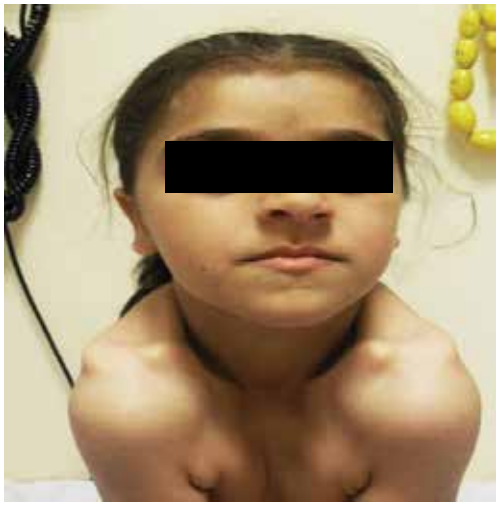

Fig. 4: Dropping shoulders.

In the laboratory evaluation, her calcium metabolism and vitamin D level (16 ng/dl) were in normal range. Her bone age was appropriate for 8 years old. The anterior–posterior (AP) and lateral cephalogram showed open sutures of the skull, large fontanelles, small maxillary sinuses, numerous wormian bones in the lambdoidal suture, a hypoplastic maxilla, a prognathic mandible, and bilateral clavicular hypoplasia on X-ray. Capitis humeri was below where it should be, and she had bilateral coxa vara. Her thoracic kyphosis and lumber lordosis were flattened. The patient was diagnosed as CCD according to her facial appearance, hypermobile shoulders, dental problems, and X-ray findings.

CASE 2

An 11-year-old girl was referred to Department of Pediatric Endocrinology, School of Medicine, Kocaeli University, Turkey, from a dentist for short stature. She was delivered by cesarean section from healthy parents, at 38 weeks weighing 3300 g. Her motor development was appropriate for her age. When she was first admitted, her height was 136 cm (–2.02 SDS), and her weight was 39.2 kg (–0.3 SDS). Her general examination revealed significantly short stature, hypertelorism, frontal bossing with brachycephalic skull, depressed and flattened nasal bridge, malar hypoplasia, and an underdeveloped maxilla with a prognathic mandible. The bone age was 8 years.

Wechsler Intelligence Scale for Children was performed for her mental assessment and mild mental retardation (MR) was detected. Intraoral examination revealed erupted upper right permanent first molar, retained deciduous teeth and high arched and narrow palate. Her panoramic radiograph revealed few impacted teeth (Fig. 5) and multiple retained deciduous teeth. Antero-posterior view of pelvis demonstrated a widened pubic symphysis. Her skull AP and lateral views showed the presence of multiple wormian bones with open fontanelles (Fig. 6). Her chest radiograph showed bell-shaped rib cage and hypoplastic clavicles (Fig. 7). Based on the clinical and radiographic findings, a diagnosis of her CCD was made. The second case could also approximate her shoulders in midline as an important sign for CCD.

In the laboratory evaluation, her calcium metabolism and vitamin D level were normal. Her bone age was appropriate for 8 years old. The AP and lateral cephalogram of the patient showed open skull sutures, large fontanelles, small maxillary sinuses, numerous wormian bones in the lambdoidal sutures, a hypoplastic maxilla,

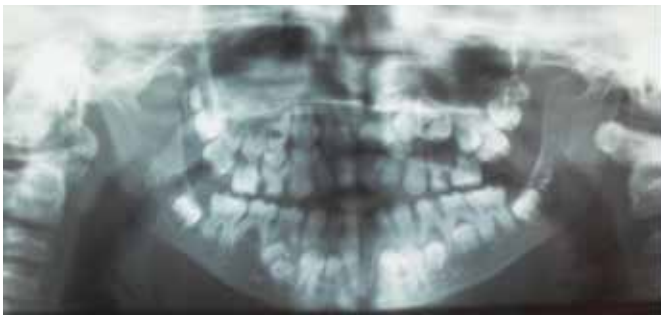

Fig. 5: Orthopantomogram supernumerery teeth

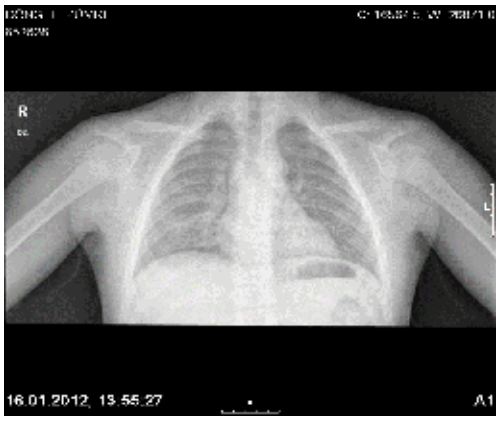

Fig. 6: Hypoplasia of distal clavicles.

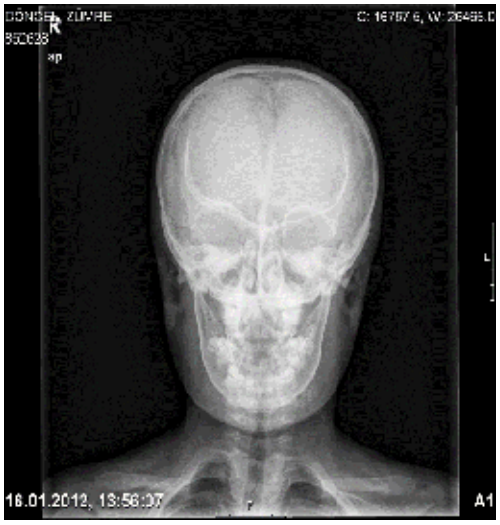

Fig. 7: Open anterior fontanelle.

and a prognathic mandible. X-ray revealed bilateral clavicular hypoplasia, and she had bilateral coxa vara. Facial appearance, hypermobile shoulders and severe dental problems with other skeletal abnormalities were diagnosed as CCD in the two patients. We have presented these cases because of very low incidences. The features of the patients are shown in the Table.

Table: Characteristics of our patients

	Case 1	Case 2
Age (years)	10	11
Family history	–	–
Sex	Female	Female
Open anterior fontanelle	+	+
Brachycephaly	+	+
Hypertelorism	+	+
Prognathism	+	+
Midface deficiency	+	+
Teeth abnormalities	+	+
Dropping shoulders	+	+
Narrow thorax	+	+
Hypoplastic iliac wings	+	+
Delayed bone age	+	+
Extra findings	–	MR/short stature
Hearing defects	–	–

MR, mental retardation

DISCUSSION

Cleidocranial dysplasia is a very rare disease, and the responsible gene for the pathogenesis of CCD had been mapped on the short arm of chromosome 6p21. This transcription factor is responsible for the proliferation of osteoblasts, dental cells, bone and teeth formation (4). The affected bones, which have intramembranous ossification (1–3), and they are the skull, clavicula and flat bones.

Aplastic or hypoplastic clavicles are the characteristic and pathognomonic features of CCD that are responsible for the appearance of narrow, dropped shoulders and for the wide range of shoulder movements, resulting in the ability of the patient to approximate his or her shoulders in front of the chest. However, aplasia is seen in only 10% of CCD patients (3, 4). Two patients had hypermobile shoulders and in the first case, distal sides of clavicles were hypoplastic.

Up to 94% of the patients with CCD had dental findings, including supernumerary teeth (they often do not lose their primary teeth) and eruption failure of the permanent teeth. The most consistent dental findings in the individuals with CCD are the presence of the second permanent molar with the primary dentition (80%) (5), and supernumerary teeth in the two patients in this study on panoramic X-ray.

These patients had typical faces: triangle face, hypertelorism, that are usually associated with frontal and biparietal bone bossing , prominent front, broad and flattened nasal root, narrow maxillary area with premaxilla, maxilla, and zygomatic developmental defects. Their

paranasal sinuses could not develop correctly due to maxillary hypoplasia. The patients rarely had deafness. They have small and elevated scapulas with narrow pelvis and thorax (1–6). Our patients had prominent front, hypertelorism, maxillary hypoplasia, prognathism, narrow thorax, and small scapulas.

Our patients' underdeveloped maxilla with overall deficient growth of the midface combined with the direction of mandibular condylar growth and its anterior rotation give the impression of relative or actual mandibular prognathism.

Other features seen in their CCD were deformities of the thoracic region, pelvic and pubic bones, and fingers. More specifically, their finger abnormalities included short, tapered fingers, and the anomalies of the phalangeal, tarsal, metatarsal, carpal, and metacarpal bones. There were significant findings on the X-rays in their CCD. There were open and wide sutures, open fontanelle, wormian bones, the retardation of the ossification of the skull, hypoplastic or absent sinuses, and supernumerary teeth on head X-rays (5). There was conic thorax with decreased AP diameter, and hypoplastic or aplastic clavicles on thorax X-rays. Pubic symphysis was broad and iliac wings were undeveloped (6). Our patients had all of the above findings on X-ray.

Mental retardation association with CCD pathogenesis is not known clearly. However, some patients were reported. A patient in a study had insertion in the 6th chromosome of CCD. In our second case, mild MR was detected and it could be related to chromosome 6 structure (7). Orthodontic and maxillofacial operations for temporary and supernumerary teeth are necessary for patients who have social difficulties because of their appearance.

CONCLUSION

If this rare disease was recognized with delayed closure of fontanelle and teeth problems earlier, the severe teeth problems might be prevented with surgical operations. The overall treatment goal is to establish functional occlusion, and an aesthetic facial and dental appearance of such patients.

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