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Ellis-Van Creveld Syndrome. Case report and literature review

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Abstract
Ellis-van Creveld syndrome is a genetic disorder that was first described by Richard Ellis and Simon van Creveld in 1940. The four principal characteristics are chondrodysplasia, polydactyly, ectodermal dysplasia and congenital heart defects. The orofacial manifestations include multiple gingivolabial musculofibrous fraenula, dental anomalies, hypodontia and malocclusion. The disease can be diagnosed at any age, even during pregnancy. The differentiation should be made between Jeune syndrome and other orofaciodigital syndromes.

Key words: *Ellis-van Creveld syndrome, chondrodysplasia, orofacial anomalies.*

Introduction
Ellis-van Creveld syndrome (EVC) or chondroectodermal dysplasia is a rare autosomal recessive disease resulting from a genetic defect located in chromosome 4p16 (1-3). It was first described in 1940 by Richard Ellis and Simon van Creveld (4). The exact prevalence of this illness is unknown. Around 150 cases are described in the literature (3).
The principal features of this syndrome are chondroectodermal dysplasia, polydactyly and congenital heart defects. The patients have small stature, short limbs, fine sparse hair and hypoplastic fingernails. Oral manifestations include multiple musculofibrous frenula, dental transposition, conical teeth, hypoplasia of the enamel, hypodontia and malocclusion. The teeth can erupt and exfoliate prematurely (1-5).
This review of the clinical and radiographic features of EVC syndrome provides the dentist with the possibility of making an early diagnosis and treatment, and to establish a differential diagnosis with other clinically similar entities.
We describe a clinical case of a patient who visited the Odontological Clinic of the University of Barcelona presenting the typical clinical features of EVC syndrome.

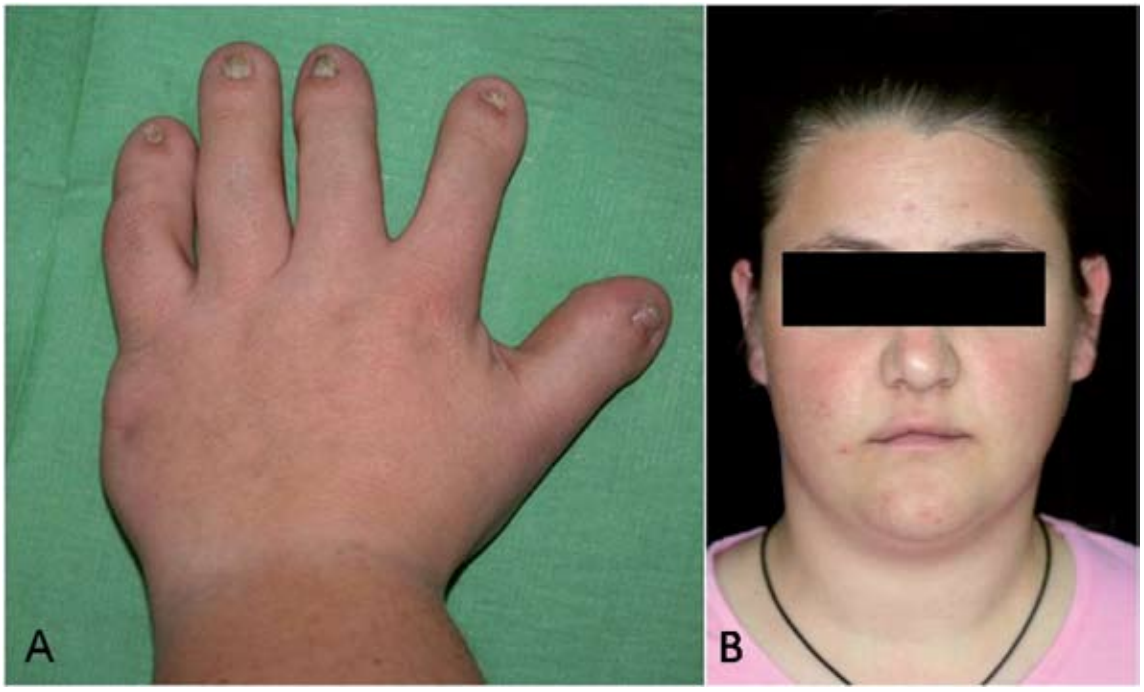

Fig. 1.
A) The presence of a surgically operated sixth finger is perceived on both hands and the hypoplastic fingernails are observed.
B) Frontal photographs. Facial symmetry, fine and lip seal.

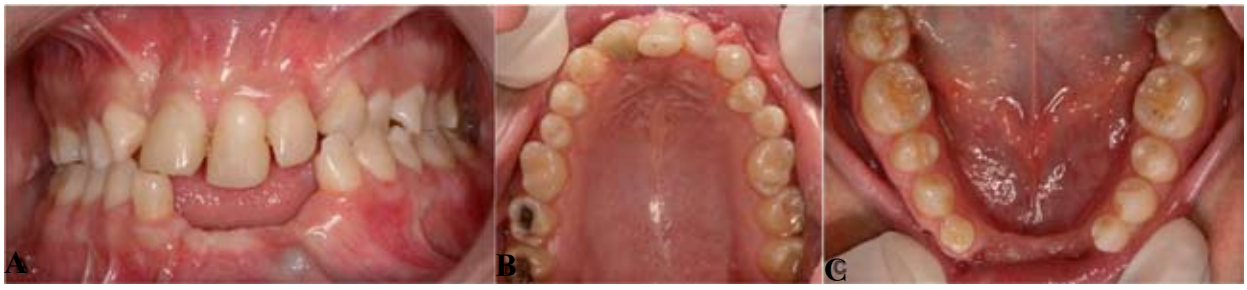

Fig. 2. View of occlusion and dental arcades.
A) Frontal view of the mouth. Multiple musculofibrous frenula, diverse morphological anomalies of the teeth and malocclusion are observed.
B) Occlusal image of the upper dental arcade.
C) Occlusal view of the lower dental arcade showing agenesis of the 4 lower incisors.

Case Report

The patient attended the Pathology and Periodontal Surgery Unit of the Department of the Oral Surgery of the University of Barcelona, Spain, referred by the Orthodontic Service. The objective was to assess the periodontal condition and to control the Plaque Index in preparation for orthodontic treatment to align and level the teeth for subsequent prosthetic rehabilitation.

The patient, a 21-year-old woman with no toxic habits or known allergies. No family history of interest, and a personal pathological history of having been diagnosed at birth with EVC syndrome without heart involvement. At 18 months of age the polydactyly had been surgically corrected (fig.1A).

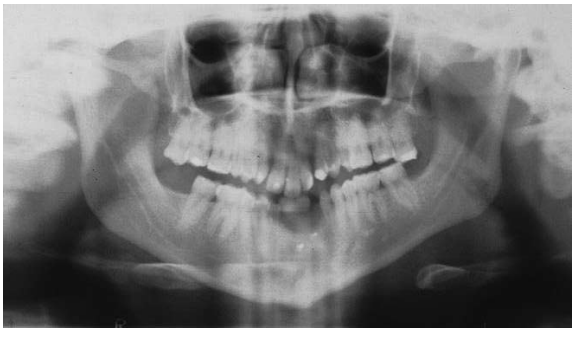

Fig. 3. The orthopantomography reveals extruded upper third molars, agenesis of the lower third molars and the 4 incisors and an anteroinferior radiopacity due to the presence of a bone graft fixation screw.

The patient is generally healthy (fig.1B) although with very short stature (1.35 m). The hands are deformed and the presence of a sixth finger can be perceived (Fig. 1A). At orofacial level, no anomalies are detected on examination of the temporomandibular joint. Regarding soft tissues, the appearance of gingivolabial fibrous bands or multiple muscular frenula is highlighted. Mid-line deviation presents, also malocclusion with posterior crossbite in the second and third quadrants, and extrusion of teeth 1.1, 2.1, 2.2 and upper third molars. Dental morphologic anomalies of number (hypodontia with agenesis of the 4 incisors and the lower third molars), of size (microdontia of the canines and premolares) and in shape (conical canines and incisors) (Fig. 2 and 3) are observed. The patient wears no prosthesis and presents good oral hygiene. The orthopantomography (Fig.3) shows extruded upper third molars, altered dental morphology, dental agenesis and a radiopacity in the anteroinferior sector due to a fixation screw from a previous bone graft made for later implant rehabilitation.

No parental consanguinity nor anomalies in the analytic tests were present. No genetic study had been made.

Discussion

EVC syndrome is a genetic disorder with autosomal recessive transmission most often described in families with a history of consanguinity (1). In our case this has not been verified. The gene responsible for this syndrome was identified in the short arm of the chromosome 4 with five different mutations (6). It is described in all the ethnic groups, however it is most prevalent in the Amish population of Lancaster in Pennsylvania, U.S.A. (3,6).

The syndrome can be diagnosed during the prenatal period, starting from the 18th week of gestation, by ultrasonography, or later by clinical examination after birth (3).

Chondrodystrophia is the most common clinical feature, affecting the tubular bones producing a serious ossification defect (1,7). In consequence, the distal extremities of the limbs are short and the patients small in stature (1). Aldegheri (8) recommends osteogenic distraction to lengthen the limbs. Baujat et al. (3) have demonstrated that growth hormone treatment with these patients is not effective. However, it is important to highlight that there is one case published in the literature in which a favorable result in growth is described following hormonal treatment (9).

The thorax is usually narrow with pectus excavatum, lumbar lordosis and genu valgum, the hair is sparse and fine. The polydactyly, wide hands and feet, sausage-shaped fingers, and dysplastic fingernails are also typical features of EVC syndrome (1).

Congenital heart malformations are described in a 50 to 60% of patients affected by this syndrome. Defects of the mitral and tricuspid valves, patent ductus arteriosus, ventricular septal defects and atrial septal defects are some of the malformations described as the principal cause of decreased life-expectancy in these patients (1,3,6).

We coincide with all published studies in regard to the oral features presented in these patients. We highlight the malocclusion, the hypodontia, the appearance of conical teeth, hypoplasia of the enamel and multiple musculofibrous frenula as constant clinical features (1, 3-5, 10,11). However, additional clinical findings affecting other organs (lungs, kidneys, liver, pancreas and central nervous system) may occasionally be observed, (1,3,12) although these were not diagnosed in our case.

Genitourinary anomalies such as agenesis and renal dysplasia, ureterectasia and nephrocalcinosis usually present in 20% of cases (13). Exceptionally, hematological anomalies have been reported. In the literature, one case with dyserythropoiesis is described and another with associated perinatal myeloblastic leukemia (3,14). Digoy et al. (13) reported a unique case of a patient with EVC syndrome presenting congenital stridor due to the appearance of a cyst in the upper airway that impeded autonomous breathing on displacing the larynx.

Other infrequent features include: strabismus, epi- and hypospadias, cryptorchidism and malformations in the thoracic or lung walls (3).

The cognitive and motor development of patients affected by EVC syndrome are normal (1,3).

EVC syndrome requires multidisciplinary therapeutic planning. The odontologist plays a fundamental role in the control of the oral and dental manifestations. A combination of orthodontics-surgery-prosthetics is essential to correct the craniofacial morphology and dental defects, aiming to achieve satisfactory functional and aesthetic results (1). Dental treatment should be made under low antibiotic prophylaxis due to the high incidence of heart pathology in these patients (3,15).

The prognosis for this syndrome is related to the difficulty in breathing during the first months of life which derives from potential heart problems and a narrow thorax (3).

The differential diagnosis includes Jeune syndrome and orofaciodigital syndromes (2,3,5,6).

Jeune syndrome is a rare, potentially lethal, autosomal recessive disease; characterized by thoracic dystrophy, short limbs, small stature, polydactyly and generalized bony dysplasia. There are anomalies in pigmentation of the retina, renal involvement and hypoplastic lungs (3,5).

The orofaciodigital syndromes result from dominant sex-linked inheritance, they are limited to women and clinically characterized by multiple gingivolabial frenula, hypoplasia of the nasal cartilages, moderate mental retardation, fissured tongue and in a third of the cases ankyloglossia (5,6).

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