ELLIS-VAN CREVELD SYNDROME

INTRODUCTION

The disorder formerly termed chondroectodermal dysplasia, now known as Ellis-van Creveld syndrome (EVC) was first described completely in 1940 by Richard WB Ellis of Edinburgh and Simon van Creveld of Amsterdam. It is a rare genetic disorder of the skeletal dysplasia type, occurring in approximately 7/100000 births; it demonstrates autosomal recessive inheritance and there is parental consanguinity in approximately 30% of the cases. After birth, the cardiac features usually present are disproportionate small stature with increase in severity from the proximal to the distal portions of the limbs. Short stature is seen uniformly in adult patients (average height of 139 centimeters, with wide variations). Shortening of middle and distal phalanges, polydactyly affecting hands (uni or usually bilateral) and occasionally the feet, hydroptic ectodermal dysplasia mainly affecting the nails, hair and teeth, congenital heart malformation occurring in about 50 to 60% of the cases and comprising single atrium, defects of mitral and tricuspid valves, patent ductus, ventricular septal defects, atrial septal defects and hypoplastic left heart syndrome. The presence of congenital heart disease may support the diagnosis of Ellis-van Creveld syndrome and hence its importance to dentists.

Keywords: Autosomal recessive, bilateral postaxial polydactyly, chondroectodermal dysplasia, ectodermal dysplasia, skeletal anomalies.

CASE REPORT

A 24-year-old female patient reported to the department of Oral Medicine and Radiology, AECs Maaruti College of Dental Sciences and Research Center, Bangalore, with a chief complaint of missing upper and lower front teeth since childhood and wanted replacement of the same. The patient is the first child of healthy parents of consanguineous marriage, and has a younger sister with features similar to her. The medical history revealed that the patient has had repeated respiratory infections and dyspnea on exertion for the past 1 to 2 years and was not under any medication. General examination revealed that the patient was of short stature, moderate build and acromesomelic shortening of upper and lower limbs (Fig. 1), with marked bilateral genuvalgum, resulting from bone dysplasia. The examination of the hands revealed extra digit on the ulnar side of both the hands as well as on the feet. Closer examination revealed finger and toenails to be markedly hypoplastic with longitudinal ridges and the nail completely absent in the fifth and the sixth digits bilaterally. The examination also revealed bifid hallucal clefts and cleft lateral malleoli bilaterally.

The medical history of the patient revealed that the patient was born prematurely. Prenatal abnormalities may be discovered as early as the 13th week of gestation as increased first trimester fetal nuchal translucency thickness in association with the syndrome. After birth, the cardinal features usually present are disproportionate small stature with increase in severity from the proximal to the distal portions of the limbs. Short stature is seen uniformly in adult patients (average height of 139 centimeters, with wide variations). Shortening of middle and distal phalanges, polydactyly affecting hands (uni or usually bilateral) and occasionally the feet, hydroptic ectodermal dysplasia mainly affecting the nails, hair and teeth, congenital heart malformation occurring in about 50 to 60% of the cases and comprising single atrium, defects of mitral and tricuspid valves, patent ductus, ventricular septal defects, atrial septal defects and hypoplastic left heart syndrome. The presence of congenital heart disease may support the diagnosis of the Ellis-van Creveld syndrome and appears to be the main determinant of longevity. For the diagnosis of Ellis-van Creveld syndrome to be established, a minimum of 3 of the 4 principal anomalies must be present.

The oral manifestations spectrum is wide, including malocclusion, labiogingival adherences and gingival hypertrophy, labiogingival frenulum hypertrophy, accessory labiogingival frenula, serrated incisal margins, dental transposition, diastema, conical teeth, enamel hypoplasia and hypodontia. The teeth may be prematurely erupted at birth or exfoliate prematurely.
Ellis-van Creveld Syndrome

presence of several restorations in relation to 16, 17, 26, 27, 28, 37 and 47 (Figs 2 and 3). Orthopantomograph reveals the presence of deciduous canine in the right lower quadrant with missing 12, 22, 31, 32, 41, 42, 43 and impacted 35 and hypoplasia of left condyle (Fig. 4). The hand-wrist radiograph (Fig. 5) shows bilateral postaxial hexadactyly, shortening of the middle phalanges of hands, polymetacarpalism, syncarpalism and fusion of hamate and capitate bones. The anteroposterior view of the lower limbs (Fig. 6) reveals the mesial angulation and hypoplasia of the proximal tibial epiphysis resulting in genuvalgum and shortened tibia and fibula.

The patient was referred to Sri Jayadeva Institute of Cardiology, Bangalore for investigation of her cardiac condition, where 2D color Doppler echocardiogram and electrocardiogram was advised. It revealed the presence of mitral valve prolapse with mild mitral regurgitation and rheumatic heart disease. Based on the clinical examination and the result of the investigations, we arrived at a diagnosis of Ellis-van Creveld syndrome.

The treatment consisted of extraction retained 83 and impacted 35 and frenectomy of hyperplastic maxillary labial frenum, under prophylactic antibiotic coverage, restoration of carious teeth, and replacement of maxillary and mandibular missing teeth with fixed prosthesis or implants following closure of midline diastema.

DISCUSSION
Ellis-van Creveld syndrome is a rare autosomal recessive disorder, caused due to mutation of EVC1 and EVC2 genes,
numerary teeth have been reported in some cases. In the case region is a consistent finding in this syndrome, though super-
other criteria are inconclusive. Based on these signs, the
are pathognomonic and should be used in primary diagnosis as
the alveolar processes, partial harelip and continuous frenum
oral manifestations, mainly the combination of partial clefts of
show mild enamel hypoplasia with high caries rate. The fusion
maxillary and mandibular anterior teeth. The teeth that are erupted
is usually retarded. A variety of radiological skeletal features may be observed,
including retarded bone maturation, fusion of the hamate and
capitates bones of the wrist, defect of the lateral aspect of the
proximal part of the tibia, cubitus valgus, hypoplastic cubitus,
supernumerary carpal bone center, clinodactyly of the fifth
finger, fusion of the fifth and sixth metacarpals, disturbance in
bone modelling of the metacarpals and/or phalanges. Bone age
is usually retarded.

Hypodontia involving the maxillary and mandibular incisor
region is a consistent finding in this syndrome, though super-
umerary teeth have been reported in some cases. In the case
reported here, the patient presented with hypodontia involving
maxillary and mandibular anterior teeth. The teeth that are erupted
show mild enamel hypoplasia with high caries rate. The fusion
of the middle portion of the upper lip to the maxillary gingival
margin, eliminating the maxillary labial vestibule or the presence
of numerous frenula tethering the upper lip to the gingiva is a
consistent feature of this syndrome. The clinical variabilities of
the oral abnormalities in Ellis-van Creveld syndrome could be
due to the fact that its genetic effect on the teeth and other oral
structure development occurs during a relatively long period
and could be the result of other genetic and environmental
phenotype modifying factors. It has been suggested that some
oral manifestations, mainly the combination of partial clefts of
the alveolar processes, partial harelip and continuous frenum
are pathognomonic and should be used in primary diagnosis as
other criteria are inconclusive. Based on these signs, the
differential diagnosis with other syndromes that include short
stature, polydactyly and orofacial abnormalities, such as
McKusick Kauffman syndrome, Juene Dystrophy and Weyer’s
acrofacial dysostosis can be considered. The clinical diagnosis
is based on observation of the symptoms and manifestations
of the syndrome and supported by skeletal survey. The
definitive diagnosis is molecular, based on homozygosity for a
mutation in the EVC and EVC2 genes by direct sequencing.
Ellis-van Creveld syndrome is caused by mutation of EVC and
EVC2 genes, located in a head-to-head configuration on
chromosome 4p16. EVC is associated with the genetic
heterogeneity and EVC and EVC2 do not account for the totality
of EVC cases.

Further studies are needed to elucidate other genes involved
in the EVC manifestations. They could also contribute to
unraveling specific molecular processes that lead to the
phenotypic manifestations of Ellis-van Creveld syndrome,
although PP2ABR remains a candidate gene for human disease
genes linked to chromosome 4p16, which is associated with
this syndrome. The management of EVC is multidisciplinary;
symptomatic management is required in neonatal period,
including treatment of respiratory distress due to narrow chest
and heart failure. In infancy and early childhood, general and
specialized pediatric and orthopedic follow-up is required. Oral
Physicians play an important role in identification of dental and
oral manifestations. Dental treatment must be performed under
prophylactic antibiotic coverage with consideration for high
incidence of cardiac defects in EVC patients. EVC syndrome is
an autosomal recessive disorder, with a Mendelian risk of 25%
for subsequent pregnancies, hence requiring genetic counseling.

REFERENCES


