Case Report

Ellis-van Creveld syndrome with facial hemiatrophy

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ABSTRACT

Ellis-van Creveld (EVC) syndrome is a rare autosomal recessive congenital disorder characterized by chondrodysplasia and polydactyly, ectodermal dysplasia and congenital defects of the heart. We present here a case of a 16-year-old short-limbed dwarf with skeletal deformities and bilateral postaxial polydactyly, dysplastic nails and teeth, also having left-sided facial hemiatrophy. The diagnosis of EVC syndrome was made on the basis of clinical and radiological features. To the best of our knowledge, this is the first report of EVC syndrome with facial hemiatrophy in the medical literature from India.

Key words: Ellis-van Creveld syndrome, Chondroectodermal dysplasia, polydactyly, facial hemiatrophy

INTRODUCTION

Ellis-van Creveld (EVC) syndrome, also known as chondroectodermal dysplasia, is a rare autosomal recessive congenital disorder with an incidence of approximately one in every 60,000 live births and equal sex predisposition.[1] A higher prevalence has been reported among certain populations like Old Order Amish and Arabs of the Gaza strip. This syndrome was first described by Richard WB Ellis of Edinburgh and Simon van Creveld of Amsterdam in 1940.[2] The genes responsible for this syndrome have been mapped to chromosome *4p16*.[3] Disproportionate dwarfism, postaxial polydactyly, ectodermal dysplasia, a small chest and a high frequency of congenital heart defects characterize this syndrome. Facial hemiatrophy is a disorder of subcutaneous tissue, muscles and bones that rarely has a genetic inheritance.[4,5] We herewith report such a case. To the best of our knowledge, this is the first report of EVC syndrome with facial hemiatrophy in the medical literature from India.

CASE REPORT

A 16-year-old short-statured Kashmiri female, product of second degree consanguineous marriage, fourth in birth order, born of full-term normal delivery, presented with asymmetry and atrophy of the left cheek for last one year. Her mother gave history of an uneventful prenatal period, slow growth since infancy, delayed eruption of teeth, difficulty in running, menarche at 13 years of age and a normal intelligence. There was no history of epilepsy or neurological deficit. There was no such history in the family but one of the siblings with polydactyly was born dead. However, no records pertaining to the cause of death in the sibling were available nor was any autopsy performed. On examination, patient had atrophy of left cheek with no alteration of skin colour or texture, hair loss, loss of power or neurological deficit. Patient had a high arched palate, peg shaped lower incisor and upper canine, absent upper lateral incisors, widely spaced teeth with dental malocclusion, enamel hypoplasia and dental caries [Figure 1]. Anterior portion of upper lip was fused to maxillary gingival margin and lower lip to frenulum of tongue by a band. Height of the patient was 133 cm with disproportionately shortened limbs compared to axial skeleton, the upper segment-lower segment ratio being 1.2: 1. The middle segments (forearm and legs) were shorter than the proximal segments, the ratio of proximal to middle segment being 1.27:1 in upper limb and 1.72:1 in the lower

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limbs. The patient had narrow thorax and mesomelic dwarfism i.e., the middle segment of the limbs (forearm and legs) was shorter than the proximal segment (arm and thighs). Patient also had bilateral genu valgum. Both the hands and left foot had postaxial polydactyly and were short and stubby with sausage shaped fingers [Figure 2]. Nails of both hands and feet were small, dysplastic and pigmented. Scalp, eyebrow and body hair were normal and there was no xerosis or keratoderma. No cardiac, genitourinary, hepatic or CNS abnormality was seen on clinical examination.

All studies including the hemogram, blood chemistry, ECG, echocardiography, abdominal ultrasonography, EEG, EMG of deltoid, calf and facial muscles and CT scan of brain were normal. Radiographs of the hands revealed bilateral bifid 5th metacarpals and duplication of little fingers [Figure 3]. Similar pattern was seen in radiographs of left foot. The distal and middle phalanges of hands and feet were disproportionately shorter than the proximal phalanges (Acromesomelia). The capitate and hamate showed complete fusion bilaterally. Knee radiographs showed genu valgum and hypoplasia of the lateral aspect of distal femur and proximal tibia with bilateral bony protuberances on medial proximal tibiae [Figure 4]. Radiograph and CT scan of paranasal sinuses showed hypoplastic left maxilla. Genetic analysis could not be made due to non-availability of the facilities.

Diagnosis of EVC syndrome was made on the basis of short limbed dwarfism, dysplastic nails and teeth, and clinical and radiological features of skeletal deformities.

DISCUSSION

EVC is an autosomal recessive disorder and an *EVC*

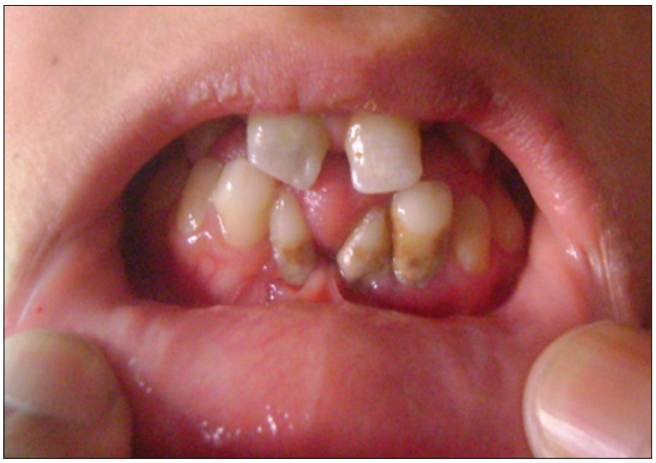

Figure 1a: Peg shaped widely spaced teeth and a band attaching lower lip to frenulum

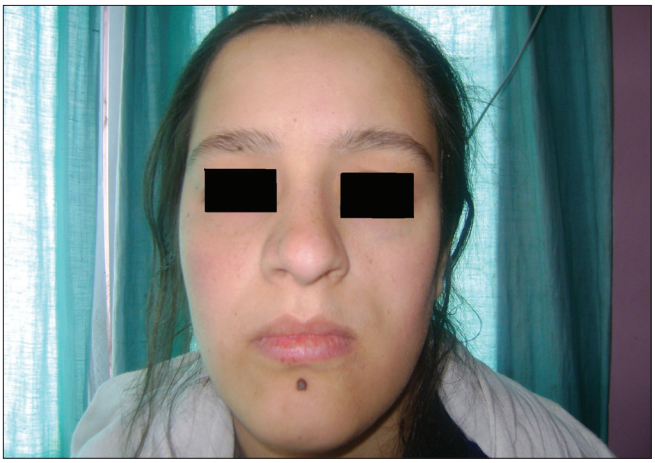

Figure 1b: Left facial hemiatrophy

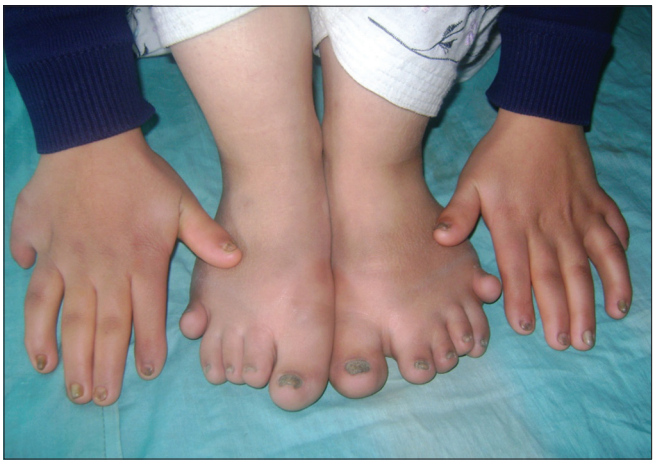

Figure 2: Polydactyly, short stubby fingers and dysplastic nails

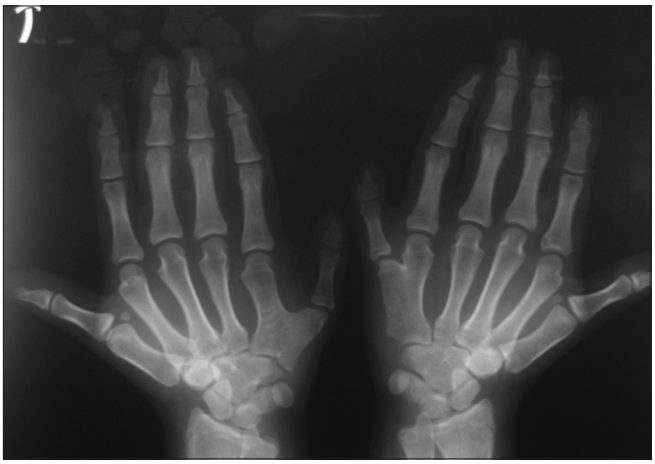

Figure 3: AP radiograph depicting post-axial polydactyly, bifid 5th metacarpals, complete duplication of fingers and fusion between capitate and hamate

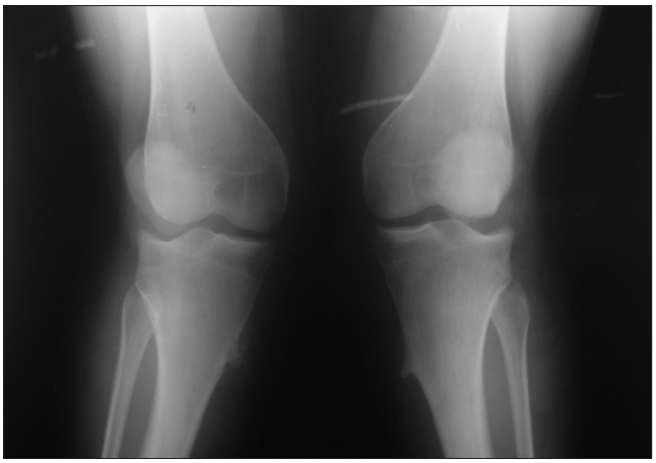

Figure 4: Knee radiograph shows genu valgum, hypoplasia of femoral condyles and bilateral osteochondromas

gene has been mapped to chromosome band *4p16,* which codes for a 992 amino acid protein.[3] EVC is also caused by mutations in a second gene, called *EVC 2*, which is also located on chromosome 4p16, the transcription sites of EVC and EVC2 genes being separated by only 2624 base pairs. EVC2 codes for a 1228 amino acid protein.[6,7]

The features of EVC are the tetrad of chondrodysplasia, polydactyly, ectodermal dysplasia and cardiac anomalies. Cardiac anomalies, although part of the tetrad, are seen in only 50-60% patients, the commonest anomaly being a common atrium.[8,9] The absence of the cardiac anomalies in our patient may account for her survival as opposed to her sibling. EVC is classified among subgroup 1-2-3 in the modified Freire-Maia and Pinheiro classification of ecodermal dysplasia.[10] Hidrotic ectodermal dysplasia is observed in 93% patients. The nails are hypoplastic, dystrophic, friable and ridged, and may even be absent in some cases. Our patient had small, pigmented, ridged dysplastic nails. The hair in EVC is usually normal, but may be sparse and brittle.[10] Our patient had normal scalp and eyebrow hair, although body hair was sparse.

Intra-orally, there may be presence of natal and neonatal teeth, congenital absence of teeth, delayed eruption and the enamel hypoplasia may result in abnormal shaped teeth with frequent malocclusion.[11] Other oral manifestations include the absence of the normal sulcus between the upper lip and the gum. Our patient was having most of these features. Skeletal manifestations in EVC are profound and involve the appendicular skeleton more than the axial skeleton, resulting in disproportionate dwarfism. The dysplasia in EVC is of acromesomelic type which is well demonstrated in the hand radiographs of our patients which demonstrate disproportionately shorter middle and distal phalanges than the proximal ones. Polydactyly involving the hands is the constant feature of EVC, seen in all the patients.[1,11] The polydactyly involves the ulnar side of the hands, as opposed to asphyxiating thoracic dystrophy wherein the extra digit lies on the lateral aspect. The polydactyly may be just extra soft tissue not adherent to skeleton and devoid of bone or, as in our patient, show bifid metacarpal with duplication of the phalanges. Fusion between hamate and capitate, like the one seen in the hand radiographs of the patient, has been reported to be the commonest intercarpal fusion seen in EVC. Some authors have also reported the presence of a 9th carpal bone in the distal row.[12] Our patient also had polydactyly in the foot, an association seen only in 10% of EVC patients.

A number of uncommon findings seen in EVC include Dandy Walker malformation, congenital cataracts, cryptorchidism and hypospadiasis. The facial hemiatrophy seen in the patient is an association not reported in literature so far. Progressive facial hemiatrophy (Parry-Romberg syndrome) is a rare condition which usually starts within the first two decades with altered pigmentation, premonitory muscle spasms or neuralgia at the affected site and may involve skin, subcutis, muscle and bone.[13] Our patient had no premonitory symptoms and the hemiatrophy seems to be due to hypoplastic maxilla.

EVC needs to be distinguished from a number of closely related entities. Weyers's acrofacial dystosis is an autosomal dominant condition with clinical features similar to EVC, but a milder phenotype. EVC and Weyer's syndrome are allelic forms of the EVC gene. However, the patients are often of normal stature and cardiac defects and thoracic dysplasia are generally absent. The form of EVC syndrome presenting in neonatal period has skeletal changes similar to those of asphyxiating thoracic dystrophy (Jeune syndrome). Jeune syndrome is an autosomal recessive disorder characterized by small chest (which is the major cause of death due to respiratory distress), renal anomalies, retinal degeneration and short distal and middle phalanges. Most of the patients do not survive beyond the early years, respiratory distress due to thoracic abnormality, and thereby, account for most of deaths.

About one-third of patients with EVC die in the first two weeks of life, however, those who survive have a normal life expectancy, except those with severe cardiac defects. The surviving patients, however, have significant morbidity, which requires a multidisciplinary approach involving orthopaedic surgeons, cardiac surgeons, cardiologists and dentists. The management must be started at early age to achieve a good functional outcome.

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