Case Report

A Rare Case Report of Ellis-van Creveld Syndrome from Northern India

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SUMMARY

Ellis-Van Creveld syndrome (EVCS) or chondroectodermal dysplasia is an autosomal recessive disorder with the highest reported prevalencein Amish population. The four principal characteristic features are chondrodysplasia, polydactyly, ectodermal dysplasia and congenital heart defects. The typical oral manifestations of EVC syndromeinclude fusion of upper lip to the gingival margin, presence of multiple frenula, congenitally absent or abnormally shaped and microdontic teeth.This syndrome has rarely been reported from India. We present a young female with the syndrome and discuss this serious and potentially fatal condition.

INTRODUCTION

EVC syndrome is a skeletal dysplasia, first described by Richard Ellis and Simon-Van Creveld in 1940 who coined the term 'Chondroectodermal dysplasia'.[1]This autosomal recessive disorder is caused by mutation(s) in the EVC and EVC 2 genes located on chromosome 4p16.[2,3,4] The syndrome is most prevalent in the Amish population in Lancaster County, Pennsylvania, occurring in 1/5000 live births.[5,6]There is parental consanguinity in 30% of the cases with 7/1,000,000 prevalence outside Amish community. Globally about 300 cases have been described in literature including very few reports from India.[4,5,7]

The characteristic tetrad of EVC syndromecomprises disproportionate dwarfism with symmetric distal limb shortening, bilateral postaxial polydactyly, ectodermal dysplasia and, congenital heart malformations.[8]

Oral manifestations in EVC syndrome are remarkable andconstant. The most common finding is a fusion of the anterior portion of the upper lip to the gingival margin, microdontic teeth and enamel hypoplasia.[9]Life expectancy of patients with EVCS is determined by the presence of congenital cardiac disease and many patients die in childhood because of cardiac complications. Some patients with EVCS may be undiagnosed because of lack of awareness and proper screening. Here we report case of a 32-year female diagnosed with EVCS on the basis of characteristic dysplastic features. To the best of our knowledge this syndrome has been reported once only from North India.[11]

CASE REPORT

A 32 yearsfemale, the second child of a native nonconsanguineous couple,was referredto Endocrinology department for short stature and abnormal facies.(figure1) She had previously visited Physicians several times for leg pains, short statureand premature decaying of teeth. Her birth history, postnatal history and family history had been normal. The patient had undergone surgical correction of polydactyly in both hands at the age of 10 yrs. She attained menarche at age of 13 years and was menstruating regularly. Physical examination revealed normal intellectual function and profound short stature,(height 130

cms; Ht. SDS 5.7). The extremities were exceptionally short with evident acromelic and mesomelic dwarfism, bowing of radius and genu valgum.(figure2,3)There was wide gap between big toe and second toe [figure 3]. Ulnar aspect of both hands had scars because of surgical repair of polydactyly. Patient's fingernails were small, dystrophic with, sausage shaped fingers [figure 2].She had prominent fleshy nose and wide nasal bridge with marked dental abnormalities. Oral examination revealed small, peg shaped hypoplastic teeth, fusion of middle portion of upper lip and gingiva, bound down by multiple frenula (labiogingival attachment) [figure 4]. Agenesis of lower incisors was noted with crossbite with upper first molars. Hair and skin were normal.Postaxial polydactyly was observed in hands and feet.

Her pubertal staging was as per age (B4PH4AH+), no ambiguity of genitalia noted. Systemic examination including cardiovascular examination was normal. Her baseline investigations were suggestive of microcytic hypochromic anaemia though rest of the baseline investigations were normal. Thorough review of cardiac, respiratory and reproductivesystems was carried out and no abnormality was detected. Echocardiography was not suggestive of any interseptal or valvular abnormality. Radiographs were suggestive of bowing of radius and short stubby metacarpals [figure 5,6]

DISCUSSION

Ellis-Van Creveld Syndrome also known as chondroectodermal dysplasia is a genetic disorder with autosomal recessive inheritance caused by mutations in a novel gene on chromosome 4p16. Parental consanguinity is present in up to 30% of the cases and does not show any gender predilection[3]. In our patient parental consanguinity was not presentand there was no history of similar illness in sibling or family member.

The primary underlying defect isdysplasia of enchondral ossification affecting long tubular bones of limbs resulting in acromesomelic dwarfism.[4,5,11,12]Distal rather than proximal segment shortening differentiates EVCS from achondroplasia phenotype.The other features include polydactyly, usually bilateral postaxial hexadactyly, most often seen in upper limbs on ulnar side as seen in our patient. Our patient also had wide hands and feet, sausage shaped fingers, dysplastic fingernails, genu valgum and bowing of radius as described characteristically in patients with this syndrome.

Congenital heart malformations aredescribed in a 50-60% of patients with EVCS.The most common cardiac anomalies includeatrioventricular canal defect (AVCD),while patent ductus arteriosus, hypoplastic left heart syndrome, defects of the mitral and tricuspid valves, can also be seen; cardiac anomalies are the leading cause of decreased life-expectancy in these patients.[4,11]No cardiovascular abnormality was evident in our patient afterscreening with echocardiography. Patients who survive infancy have a normal life expectancy, the oldest living patient so far reported was of 82 years of age.[13]

Early appearance of orodental abnormalities at birth or in childhood helps in early diagnosis. Specific features include fused upper lip to gingival margin without mucobuccal fold, multiple accessory frenula, ankyloglossia, conical microdontic teeth, hypodontia, anodontia resulting in malocclusion and associated enamel hypoplasia.[12]The typical oral manifestations help in early diagnosis at birth or later during early childhood.The most commonamong them include fusion of the upper lip to the gingival margin resulting in the absence of mucobuccal fold, multiple small accessory frenula, ankyloglossia, malocclusion, conical microdontic teeth, hypodontia, anodontia(commonly the absence of permanent mandibular central and lateral incisors) and enamel hypoplasia.[6,11,14]Our patient had similar oral manifestations as already described.

Genotourinary abnormalities are seen in approximately one fourth of patients varying from nephrocalcinosis to renal agenesis.[4,12,13]Hematological abnormalities may rarely include perinatal myeloblastic leukemia or dyserythropoiesis. Confirmation of diagnosis can be done by direct sequencing for evident mutations in EVS1 and EVS2 gene but they are positive in only two third of patient. So aforementioned clinical features along with laboratory findings, radiological and cardiac imaging are sufficient to clinch diagnosis of this rare disorder especially in centers where genetic testing is not available as in our case

Ellis-Van Creveld syndrome should be differentiated fromother syndromes with overlapping features like asphyxiating thoracic dystrophy (Jeune syndrome), achondroplasia, chondroplasiapunctata, orofaciodigital syndromes and Morquio's syndrome.[12]

Management of patients with EVCS requires a multidisciplinary team including pediatric, orthopedic, orthodontic, cardiac, and possibly pulmonary care.

CONFLICTS OF INTEREST

All authors have none to declare

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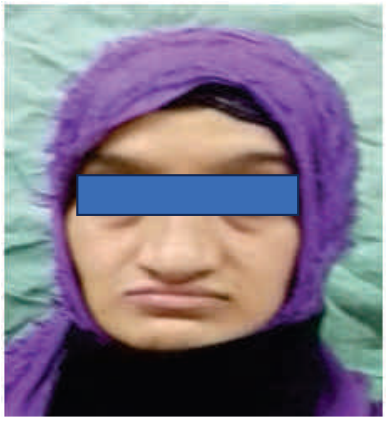

Figure1 Facial photograph

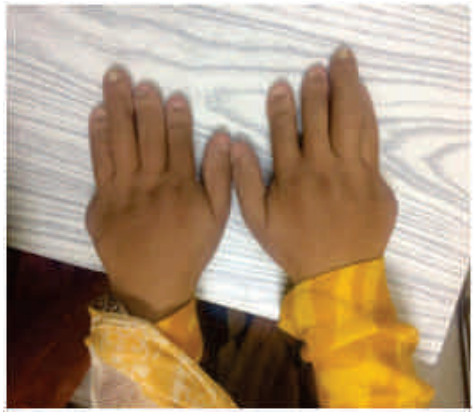

Figure 2 Postaxial polydactyly

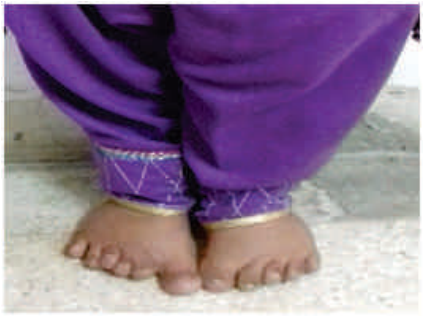

Figure 3 Polydactyly of lower limbs

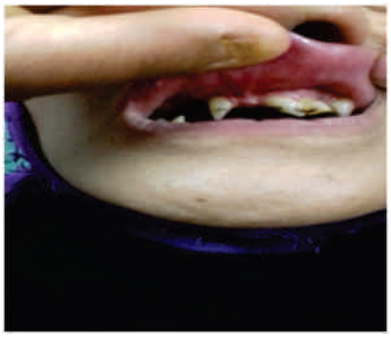

Figure 4
Multiple accessory labiogingival frenula and adontia of permanent incisors

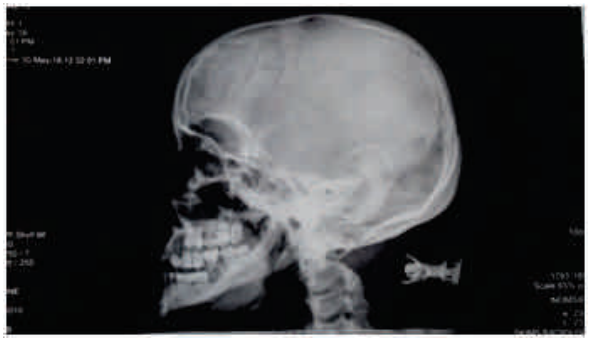

Figure 5 Radiograph showing anodontia and malocclusion of teeth

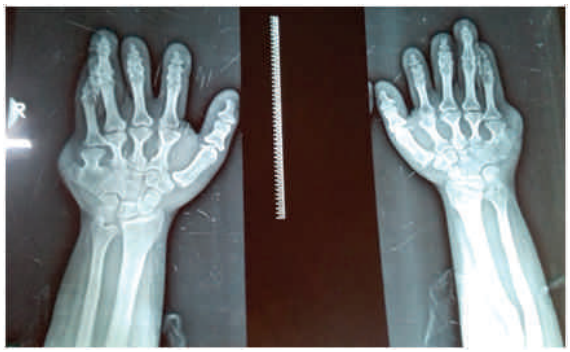

Fig 6 Radiograph of upper limb with postaxial polydactyly