

Ellis-van Creveld syndrome: report of two cases

Sumit Mehndiratta, Amita Tyagi, Veena Devgan

Delhi, India

Background: Ellis-van Creveld syndrome (EVC syndrome, MIM 225500) or chondroectodermal dysplasia is a rare, autosomal recessive disorder. This syndrome is characterized by a tetrad of chondrodystrophy, post axial polydactyly, and hidrotic ectodermal dysplasia, mostly involving teeth and nails and a high frequency of congenital cardiac anomalies, most frequently a common atrium. The genetic basis of this disorder has been identified as mutations in the *Evc* and *Evc2* genes. We present a report of two affected siblings with features consistent with those of the syndrome.

Methods: A 2-month-old child with features of lower respiratory tract infection was admitted to the pediatric emergency department. Detailed examination revealed skeletal anomalies such as limb shortening and polydactyly in both hands. On cardiac evaluation, ventricular septal defect was found. There were no neonatal teeth. A diagnosis of EVC syndrome was made based on the findings.

Results: Screening of family members revealed that the elder sibling had features consistent with those of EVC syndrome. He was 4 years old, yet undiagnosed with short bones, polydactyly, partial anodontia and ventricular septal defect. The third child and the parents were unaffected. The treatment of this disorder is primarily supportive particularly for associated cardio-respiratory problems. The parents were extensively counseled for regular follow-up.

Conclusions: The diagnosis of this syndrome is based on clinical grounds supported by radiological evaluation. Prenatal diagnosis is possible by ultrasonography and genetic testing. Genetic counseling is required to make the parents aware of the risk of recurrences.

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Key words: chondrodystrophy;
chondroectodermal dysplasia;
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polydactyly

Introduction

Ellis-van Creveld syndrome (EVC syndrome, MIM 225500) is a rare autosomal recessive disorder of skeletal dysplasia.^[1] This disorder was first described by Ellis and van Creveld.^[2] The gene for EVC syndrome has been mapped (Locus: 4p16, 4p16).^[3] The genetic basis of this disorder has been identified as mutations in the *EVC* and *EVC2* genes. The phenotype is identical in either of the mutations and the incidence is equal in both genders. This disorder is characterized by short limbs, short ribs, postaxial polydactyly, and dysplastic nails and teeth. It is associated with a high frequency of congenital cardiac defects. Survivors have short adult height and suffer from frequent dental problems, though most of them have intelligence in the normal range.

The EVC cases may be undiagnosed because of lack of awareness and proper screening. Very few cases have been reported from India.^[4,5] We here present a report of two siblings with features consistent with EVC syndrome.

Case reports

Case 1

A 2-month-old girl was brought to the pediatric emergency with complaints of cough, fever and breathing difficulty. On examination, the child was febrile with a respiratory rate of 75/min with chest indrawing and a heart rate of 140/min. There was no cyanosis. On auscultation bilateral crackles and wheezing were present with a systolic murmur of grade IV, best heard in the parasternal area. Weight was 3.2 kg, length 52 cm, head circumference 39 cm and chest circumference 30 cm. The rest of the systemic examination were normal.

The patient had multiple skeletal anomalies in the form of short broad hands, polydactyly in both hands

Author Affiliations: Department of Pediatrics, LN Hospital, Delhi, India (Mehndiratta S); Department of Pediatrics, SDN Hospital, Delhi, India (Tyagi A); Department of Pediatrics, Hindu Rao Hospital Hospital, Delhi, India (Devgan V)

Corresponding Author: Sumit Mehndiratta, MBBS, DCH, DNB (Pediatrics), MNAMS, B-246 Yojna Vihar, Delhi, India (Email: drsmehndiratta@gmail.com)

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(with 7 digits each) and 6 digits in left foot. Also noted was syndactyly of 5th and 6th finger in the left hand and 6th and 7th finger in the right hand. There was proximal migration of the great toe of the left foot. Both limbs had rhizomelic shortening. The patient also had low set ears and a high arched palate, and a narrow thorax (Fig. 1).

The patient was the product of a non-consanguineous marriage, 3rd in birth order, born by normal vaginal delivery in a hospital with an apparently uneventful neonatal period. Ultrasonography at 8-month gestation had revealed limb deformities and lung defects. Laboratory evaluation showed leucocytosis. The child was treated for chest infection as per standard protocols and responded well. Echocardiography revealed a membranous ventricular septal defect. Cranial and abdominal ultrasonography was normal. A diagnosis of EVC syndrome was made based on clinical and radiological findings.

A detailed family history revealed that an elder sibling of the patient also had skeletal defects.

Case 2

The elder sibling was 2nd in birth order, developmentally normal and 4 years old. He had an uneventful perinatal

period and subsequent course till date. This child had a weight of 15 kg, height 89 cm, upper segment 51 cm, lower segment 38 cm, chest circumference 35 cm, head circumference 49 cm, arm span 78 cm, and mid-arm circumference 13.5 cm. Both knees had valgus deformity. Both hands had polydactyly with 7 digits in the left hand and 6 digits in the right hand. This child also had dysplastic teeth with anodontia. Bilateral testicles were descended and genital examination was normal. A systolic murmur was present in the parasternal area which was confirmed as membranous ventricular septal defect by echocardiography. Ultrasonography of the abdomen did not reveal any renal abnormalities. Skeletal survey revealed shortening of distal extremities and bilateral shortened fibulae, along with short ribs. Thus this child was also determined to have features consistent with EVC syndrome (Fig. 2).

The eldest child of the family was evaluated and found to be normal. The parents were average in stature and detailed examination and evaluation did not reveal any cardiac or skeletal deformity. The parents were counseled and explained risk of recurrence. Despite repeated requests, the parents failed to return for follow-up.

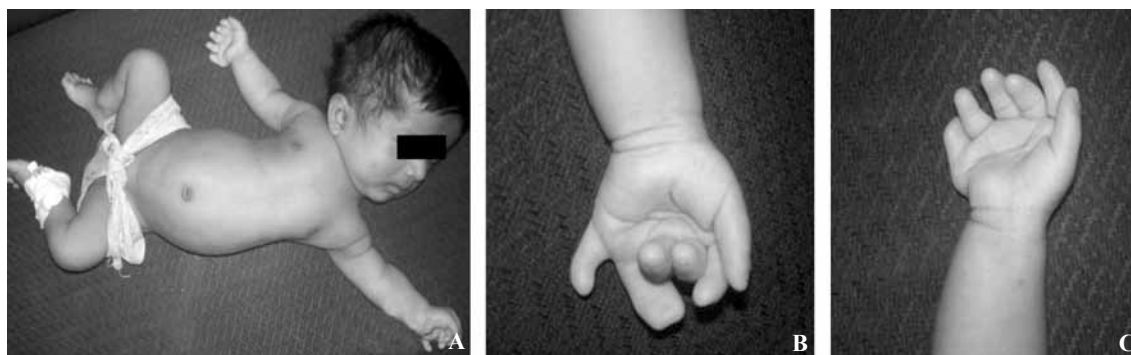


Fig. 1. Case 1. A: narrow thorax and limb shortening; B: left hand polydactyly and syndactyly; C: right hand polydactyly and syndactyly.

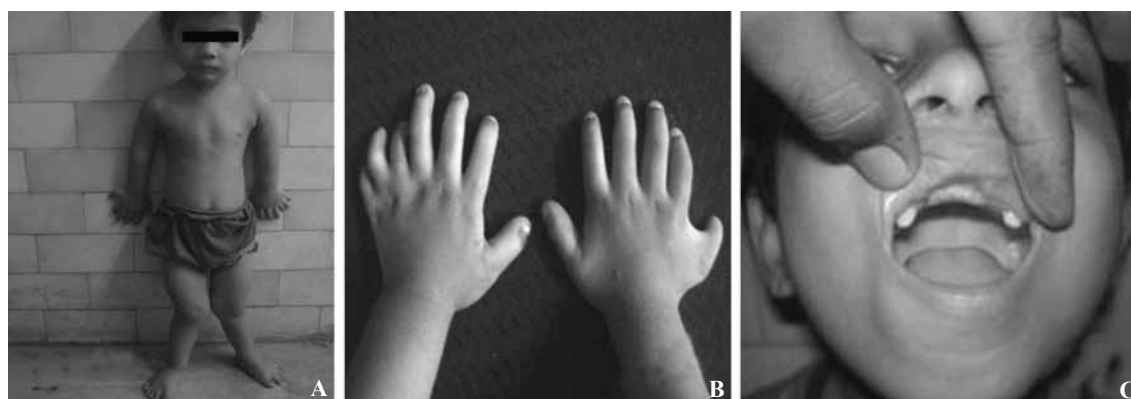


Fig. 2. Case 2. A: bilateral limb shortening and genu valgum; B: polydactyly of both hands; C: anodontia.

Discussion

EVC syndrome also known as chondroectodermal dysplasia or mesoectodermal dysplasia, occurs with a higher incidence within founder-effect populations like the Amish group due to lack of genetic variability.^[2] In most parts of the world, EVC syndrome occurs in 1 of 60 000 to 200 000 live births with almost similar frequency in males and females. It is difficult to estimate the exact prevalence because the disorder is very rare in the general population though a wide variation has been reported in cases worldwide.^[1,5]

The largest pedigree of EVC syndrome has been described in one particular inbred population, the old order Amish community in Lancaster County, Pennsylvania.^[6] It is an autosomal recessive disorder (Gene map locus 4p16, 4p16) of bone growth that results in short stature and a variety of skeletal abnormalities, i.e., short forearms and lower legs, narrow chest with short ribs, polydactyly, unusually formed nails and teeth, and cardiac defects.^[7] Both our cases had features suggestive of this syndrome, i.e., limb anomalies, polydactyly and cardiac defects. There were no neonatal teeth in the first case but dental anomalies were present in the second case. However both cases were devoid of any renal or central nervous system anomalies.

Clinically, EVC syndrome consists of a tetrad of chondrodystrophy affecting the tubular bones, post axial polydactyly (a constant finding), hidrotic ectodermal dysplasia and cardiac anomalies. Chondrodystrophy leads to progressive limb shortening and disproportionate dwarfism. Cardiac defects are present in almost half of the cases, the most frequent one being a common atrium. Other cardiac defects reported are atrial septal defect, ventricular septal defect and patent ductus arteriosus. Less frequently, genitourinary and central nervous system anomalies may also be associated. Diagnosis is based on clinical and radiological findings supported by genetic studies like gene sequencing and mutation analysis.^[3,8]

Respiratory insufficiency due to thoracic dysplasia and cardiac anomalies are responsible for the majority of deaths in infancy. The management of patients with EVC syndrome requires comprehensive care involving pediatrician, orthopedist, cardiologists, pulmonologists, dentists and occupational therapists. Treatment is mainly symptomatic for cardio-respiratory problems along with supportive dental care. Surgical intervention may be required to correct orthopedic malformations and cardiac defects. Intervention of a

clinical psychologist may be required in cases of mental retardation and developmental delay.

Genetic counseling also plays an important role. Parents must be made aware of the risk of recurrence which is 25%. Prenatal diagnosis is possible by Level II ultrasonography after 18 weeks' gestation which would reveal skeletal deformities. Fetal echocardiography may be used in combination to ascertain cardiac anomalies.^[9] Molecular genetic testing (DNA mutation analysis) can be done by amniocentesis or chorionic villi biopsy.^[3]

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Contributors: Mehndiratta S formulated the diagnosis, conceptualized the idea, reviewed the literature and wrote the draft of this paper. Tyagi A and Devgan V provided advice on medical aspects and diagnostic work up. All authors contributed to the intellectual content and approved the final version.

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