



Neonate presenting with Polydactyly - Think of Ellis Van Creveld Syndrome

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ABSTRACT

Ellis-van Creveld syndrome (EVCS) or meso/chondroectodermal dysplasia is a rare congenital, autosomal recessive disorder. It is caused by mutation of EVC gene (both EVC1 and EVC2) on locus 4p16. The incidence of EVCS in general population is low but a high prevalence has been reported among Amish community of USA. There are more than 300 cases of EVCS reported in the literature. The characteristic features are bilateral postaxial polydactyly, chondroectodermal dysplasia, congenital heart defects and hypoplastic nails and teeth. Here we describe a case of EVCS in a newborn male child with the tetrad of cardinal features along with additional systemic features. The diagnosis of EVCS is important because it is transmitted by autosomal recessive manner, so genetic counselling has to be offered to make the parents aware of the risk of recurrence.

KEYWORDS: *Ellis-van Creveld syndrome, polydactyly, Chondroectodermal dysplasia*

INTRODUCTION

Ellis Van Creveld syndrome (EVCS) or chondroectodermal dysplasia was described in 1940 by Richard W.B. Ellis and Simon Van Creveld. ^[1] In 1964, McKusick et al, reported a large number of cases in the Amish community of Lancaster country, Pennsylvania USA with prevalence rate of 1/50,000 live birth. ^[2] In non-Amish population, the estimated birth prevalence is 7/1,000,000. Around 150 cases are described in literature and not more than 25 cases have been reported in India. ^[1]

EVCS is caused by mutations of the *EVC1* and *EVC2* genes and inherited by autosomal recessive mode with parental consanguinity in about 30% of cases. ^[3] EVCS is considered a part of an emerging class of diseases called ciliopathies. The proposed hypothesis is dysfunction in chondrocyte ciliary structures which are crucial organelle for skeletal development. The ciliary defect affect 'numerous signaling pathway essential to cellular development and thus explains multisystem involvement in this syndrome. ^[4] EVCS presents with a characteristic tetrad of disproportionate

dwarfism, bilateral postaxial polydactyly, ectodermal dysplasia and congenital heart defects. ^[1]

CASE REPORT

A preterm male baby was born to a 32 year old G5P4L3 mother by vaginal delivery in the hospital. Baby was a product of non consanguineous marriage with no antenatal or perinatal complications, but family history was significant. Baby had four elder siblings with comorbidities and mortalities. First girl child (who was born 8 years ago and survived till 6 months of age) and another 4 year old girl (alive) had similar features. Only a 6 year old boy is completely healthy, while 2 year old girl died at 7 months of age due to some unrelated complications. This male baby cried immediately after birth with APGAR scores 7 and 9 at 1 and 5 minutes respectively. Baby developed respiratory distress after birth which improved after oxygen therapy. Head to toe examination of the baby revealed certain dysmorphic features including bilateral postaxial polydactyly in all four limbs with wide gap between fifth and sixth finger (Figure 1 & 4). Distal shortening was noticed in lower limbs; nails were also hypoplastic in toes (Figure 1 & 3).



Figure1: Baby showing polydactyly in both hands, low set ears & shortened distal lower limb.



Figure 2: Bifid tongue with natal teeth



Figure 3: Polydactyly in left foot with hypoplastic nails.



Figure 4: Characteristic wide gap between fifth and sixth finger

Intraoral examination revealed large bifid tongue, absent mucobuccal folds and two natal teeth in lower jaw (Figure 2). Facial dysmorphism was appreciable in the form of microcephaly, large open anterior fontanel, short neck, low set ears and bilateral micro-ophthalmia (Figure 1). Genital examination revealed hypoplastic penis and

cryptorchidism. A provisional diagnosis of chondroectodermal dysplasia was kept after reviewing the literature.

Detailed investigations were done to find out internal organs defects. Neurosonogram showed a cystic lesion in the pineal gland region. An echocardiogram revealed a patent ductus arteriosus with normal left and right ventricular function. Chest X-Ray and abdominal ultrasound didn't reveal any anomalies. Due to the lack of availability of genetic studies, diagnosis of EVCS was made clinically and with the aid of additional cardiac and radiological investigations [7]

After stabilization of vitals, baby was attached with multispecialty departments including cardiology, orthopedics dental and pediatrics with regular 6 monthly follow up examination.

DISCUSSION

EVCS is a rare genetic disorder of skeletal dysplasia and belongs to short rib-polydactyly group of disorders. EVCS most oftently described in families with a history of consanguinity and transmitted by autosomal recessive mode. The cardinal features usually present as tetrad of: a) disproportionate small stature with increasing severity from the proximal to distal portions of the limbs b) polydactyly, affecting hands (100%) and occasionally the feet (10%) c) hydrotic ectodermal dysplasia mainly affecting the nails, hair and teeth in 93% d) congenital heart malformations occurring in about 50%–60% of cases. [5] Cardiac defects include patent ductus arteriosus, single atrium, defects of the mitral and tricuspid valves, ventricular septal defect, atrial septal defect and hypoplastic left heart syndrome. [6] Our case demonstrated characteristic features of EVCS like polydactyly, cardiac defect, nail hypoplasia and limb shortening. Additionally facial dysmorphism, orodontal findings and cryptorchidism have been described.

Oral manifestations of EVCS include submucous clefts, absent vestibular sulcus, multiple musculofibrous frenula, dystrophic philtrum, hypodontia, enamel hypoplasia, delayed eruption,

natal teeth (as in our case) microdontia, conical teeth, malocclusion and diastema. [5] Skeletal features include genu valgum, talipes equinovarus, talipes calcaneovalgus and pectus carinatum with a long narrow chest. Genitourinary abnormalities are seen in about 22% of the cases and include vulvar atresia, megaureters, nephrocalcinosis and renal agenesis. Several additional clinical findings are described, including strabismus, hypospadias, cryptorchidism (as in our case), thoracic wall and pulmonary malformations. Exceptionally, hematological anomalies such as dyserythropoiesis and perinatal myeloblastic leukemia have been reported. [7] Approximately 50% of patients of EVCS die in infancy due to thoracic dysplasia leading to respiratory insufficiency and cardiac anomalies. Patients who survive in infancy have a normal life expectancy. [6]

EVCS can be suspected during the antenatal period, starting from the 18th week of gestation, by ultrasonography. [7] Molecular genetic testing (DNA mutation analysis) can be done by amniocentesis or chorionic villi biopsy. [8] The definitive diagnosis is established by molecular studies showing homozygosity for a mutation in the EVC 1 and/or EVC 2 genes. [7]

Differential diagnosis includes Jeune syndrome and Orofaciodigital syndromes. Jeune syndrome is a rare, potentially lethal, autosomal recessive disease. It is 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. The orofacioidigital syndromes are limited to women due to dominant sex-linked inheritance. It is characterized by multiple gingivolabial frenula, hypoplasia of the nasal cartilages, moderate mental retardation and fissured tongue or ankyloglossia. [8]

A multidisciplinary approach is advocated involving a clinical geneticist, cardiologist, pulmonologist, orthopedic surgeon, physical and occupational therapist, dentist, psychologist, developmental pediatrician and pediatric neurologist for proper management and rehabilitation.

CONCLUSION

To conclude, diagnosis of EVCS is important because it is transmitted as autosomal recessive manner so genetic counselling is required to make the parents aware of the risk of recurrence. Further a multidisciplinary team approach is always required for suitable diagnosis, management and rehabilitation of such patients.

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