

# Ellis-Van Creveld Syndrome: Radiological Findings of a Case and Review of the Literature

## Ellis-Van Creveld Sendromu: Bir Olgunun Radyolojik Bulguları ve Literatürün Gözden Geçirilmesi

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Geliş Tarihi/Received: 11.12.2013  
Kabul Tarihi/Accepted: 22.11.2014

Presented as a poster presentation in  
34<sup>th</sup> National Radiology Congress,  
November 6-10, 2012; Antalya

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**ABSTRACT** Ellis-Van Creveld syndrome is a rare autosomal recessive genetic disorder with an incidence of 7/1 000 000 in general population. The syndrome includes many anomalies like postaxial polydactyly of both hands, bell-shaped thorax with hypoplastic lungs, multiple cardiac malformations, short limb dwarfism, gingival malformations and hypoplastic nails. Polydactyly, where distal and middle phalanges are affected more than the proximal ones, is always present. Ellis-Van Creveld syndrome should be included in the differential diagnosis of skeletal dysplasia and dwarfism cases with cardiac malformations. There are a limited number of cases reported in literature and almost none are basically focused on the radiological findings which are in fact the key to the diagnosis. In this manuscript we aimed to review the clinical and roentgenographic findings of this rare syndrome by presenting a case.

**Key Words:** Ellis-Van Creveld syndrome; dwarfism; polydactyly; radiography

**ÖZET** Ellis-Van Creveld Sendromu genel populasyonda 7/1 000 000 oranında görülen nadir bir otozomal resesif genetik hastalıktır. Sendrom postaksiyel polidaktili, konjenital kalp defekti, kısa kollu dwarfizm, hipoplastik akciğer ve çan şeklinde toraks, maliforme dişler, hipoplastik tırnaklar gibi birçok anomaliyi içerir. Distal ve orta falanksların proksimal falankslardan daha çok etkilenen polidaktili her zaman mevcuttur. Ellis-Van Creveld Sendromu, kardiyak anomalilerin de eşlik ettiği dwarfizm ve iskelet displazisi olgularında ayırcı tanıya dahil edilmelidir. Literatürde sınırlı sayıda bildirilmiş Ellis-Van Creveld Sendromu olgusu birlikte bu sunumların hemen hiçbiri tamda çok önemli olan radyolojik bulgulara odaklanmamıştır. Bu çalışmada bir olgu nedeni ile sendromun radyolojik ve klinik bulgularını gözden geçirmek amaçlanmıştır.

**Anahtar Kelimeler:** Ellis-Van Creveld sendromu; cücelik; polidaktili; radyografi

Turkiye Klinikleri J Case Rep 2015;23(4):431-5

doi: 10.5336/caserep.2013-38395

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**E**llis-Van Creveld (EVC) syndrome which is also known as 'chondroectodermal dysplasia' is a rare genetic disorder with four major characteristics: chondrodysplasia, polydactyly, ectodermal dysplasia and congenital heart defects.<sup>1,2</sup> It was first described by Richard W.B. Ellis of Edinburgh and Simon van Creveld of Amsterdam in 1940. Its incidence in general population is low: 7/1 000 000, however the incidence may be higher in small, closed societies with marriages between relatives like the American Amish society.<sup>3</sup> There seems to be no sexual predilection but a 30% rate of parental consanguinity is reported.<sup>4,5</sup> The prognosis of the disease depends on the severity of the cardiac and respiratory problems.<sup>6,7</sup>

Two adjacent genes called EVC and EVC2 which were identified on chromosome 4 in the year 2000 and 2002, are considered to be responsible for the development of the disorder.<sup>8,9</sup> However no mutations can be identified in either gene in 31% of the cases and more genetic research is needed to find out possibly further genetic heterogeneity.<sup>9</sup> Therefore practically the diagnosis of EVC syndrome is generally based on clinical grounds supported by radiological evaluation.

There are a limited number of cases reported in literature and almost none are basically focused on the radiological findings which are in fact the key to the diagnosis. Here we represent the radiological findings of a case with typical phenotypical appearance of EVC syndrome.

## CASE REPORT

A 29 day-old female new-born was presented to our radiology department for a bone survey. She had been born term via normal vaginal delivery with a birth weight of 2460 g. She was the 3<sup>rd</sup> child from the 3<sup>rd</sup> pregnancy of 32 year-old mother. She was hospitalized right after delivery secondary to meconium aspiration and multiple congenital anomalies. She had two older siblings with no congenital abnormalities. Her parents were related as first degree cousins.

Patient's medical history revealed that she had a prenatal sonogram depicting polydactyly, short extremities and macrocephalia at 29<sup>th</sup> week. TORCH markers of the mother came out negative at the time.

On physical examination she was found to have bilateral postaxial polydactyly of the hands, short upper extremities with short fingers showing overriding. In both feet clinodactyly was present. Nail hypoplasia was noted in the upper and lower extremities. She had micrognathia, retrognathia, macrocephaly, megalocornea, a flat nasal bridge and a short bell-shaped thorax. A first degree cardiac murmur was also noticed as one of the initial physical exam findings. Oral examination revealed gingival malformation.

Initial routine blood investigations were unremarkable and thyroid function tests were within normal limits. Echocardiography (ECHO) revealed single atrioventricular (AV) leaflet, single atrium, complete AV septal defect, ventriculoseptal defect (VSD) and patent ductus arteriosus (PDA). Abdominal and cranial sonographic findings were normal.

Bone survey graphies consisting of X-rays of the skull, entire spine, chest, pelvis, bilateral upper and lower extremities were obtained. Cranial radiograms revealed frontal bossing and micrognathia (Figure 1a, b). There was postaxial polydactyly of both hands with short distal and middle phalanges compared to the proximal ones. Carpal development was delayed. Shortening and thickening was



**FIGURE 1:** Frontal bossing and micrognathia is seen in anterior-posterior (a) and lateral cranial (b) radiograms.

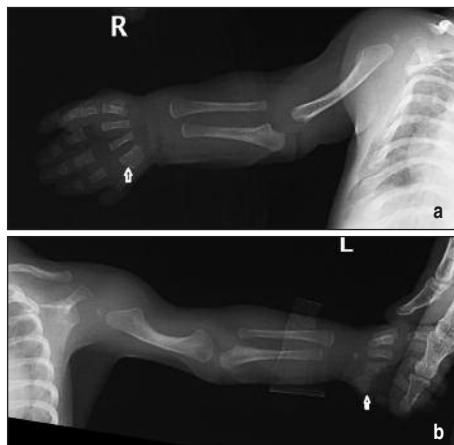
noted in the long bones of the upper extremities with dislocation of the radial heads secondary to the shortening of ulnae (Figure 2a, b). Pelvic radiograms depicted square shaped iliac bones with reduced horizontal dimension and horizontal acetabulum with medial spurs (trident acetabulum). In the lower extremities all long bones were short and thick, being most prominent in fibula than tibia (Figure 3). Though not typical chest X-ray revealed a narrow thorax resembling a bell-shaped thorax with short ribs and cardiomegaly (Figure 4).

This study is in accordance with the ethical standards of the World Medical Association (Declaration of Helsinki). Informed consent was taken from the parents of the patient.

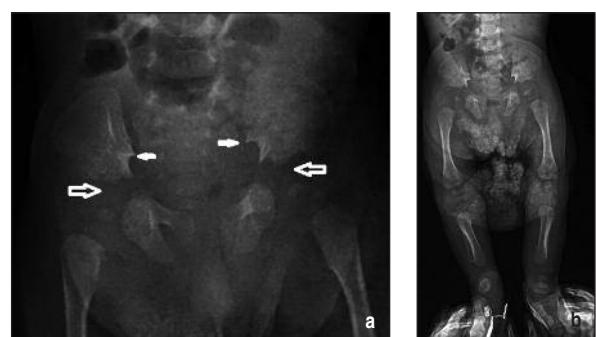
In our case, presence of most of the classical clinical and radiological features were strongly suggestive of EVC. The family was given genetic consultation and the patient was scheduled for follow-up.

## DISCUSSION

EVC syndrome is a rare chondroectodermal dysplasia with autosomal recessive inheritance. Family history can include other affected family members or marriage between relatives. In our case, parents



**FIGURE 2:** X-rays of upper extremities reveal bilateral (a. right; b. left) posteroanterior polydactyly with shortening of distal and middle phalanges as compared to proximal ones. Bifid metacarpals due to fusion of fifth and sixth metacarpal bones are noted (arrows). Similarly shortening of the long bones are more prominent in bilateral radii and ulnae than humeri. Dislocation of the radial heads is seen secondary to the shortening of ulnae.



**FIGURE 3:** a) Bilateral short iliac wings and horizontal acetabulum (big arrows) with medial spurs (small arrows) -trident acetabuli- are seen in pelvis. b) X-ray of the lower extremities show short and thick long bones, being more prominent in fibula and tibia. The superimposed opacities are artefacts from unremoved diaper.



**FIGURE 4:** PA chest radiogram shows a narrow thorax resembling a bell-shaped thorax with short thick ribs, underdeveloped lungs and an enlarged heart.

PA: Posteroanterior.

were first degree cousins. 50-60% of the patients have congenital cardiac malformations, most frequently a single atrium or a atrioventricular (AV) defect, and the prognosis depends on the severity of cardiac defects along with respiratory insufficiency.<sup>10</sup> Our patients also received oxygen treatment and respiratory support after birth for a combination of meconium aspiration and underdeveloped lungs. She had multiple cardiac defects including single atrium and atrioventricular septal defect (AVSD) depicted by ECHO.

The definitive diagnosis of EVC can lately be made by depicting EVC gene (EVC and EVC2) defects by molecular diagnostic methods. Thomson et al. reported that they have not identified mutations in either gene in 31% of cases in their study group of 65 affected individuals.<sup>9</sup> Therefore it seems that more research is needed on genetical grounds and

meanwhile the diagnosis of EVC syndrome is practically based on clinical and radiological findings.

Radiological findings of EVC syndrome are typical. Polydactyly is always present and is seen as postaxial hexadactyly of the hands, and in 10% of the cases the feet.<sup>3,8</sup> Polydactyly is seen as a sixth finger at the ulnar side of the hands and may be in the form of extra soft tissue without cartilage, joint or tendon; or a complete formation of a digit with its own metacarpal and complete soft tissue.<sup>11</sup> There may be bifid metacarpals or carpal fusion. Bone age is delayed.<sup>12</sup>

Tubular bones and particularly the distal and middle segments of the limbs are more prominently affected by chondrodystrophy which is one of the major components of EVC syndrome. This results in acromesomelia (shortening of the extremities; particularly striking in the distal portions) and a disproportionate dwarfism is seen symmetrically affecting the forearms, fingers of the upper extremity, lower legs and toes of the lower extremity. Shortening of the distal and middle phalanges more than the proximal phalanges results in square shaped hands.<sup>10,13</sup>

Bell-shaped short and narrow chest can be seen on chest X-ray secondary to short poorly developed ribs, and underdeveloped lungs are present. A pectus carinatum may be present and the heart is usually enlarged. Bilateral short iliac wings, small sacral notches and trident acetabula (horizontal acetabula with medial and lateral 'spurs') are noted on pelvic radiograms.<sup>14</sup>

Our case shows almost all of these typical radiologic findings described (Figures 1-4). Valgus deformity of the knees, lumbar lordosis or kyphosis can occasionally be seen on roentgenograms.

As EVC is a chondroectodermal dysplasia not only bone and cartilage but also other tissues derived from ectoderm such as nails, hair and teeth are affected resulting in malformed and missing teeth, hypoplastic nails, thin and sparse hair. Urinary tract anomalies, strabismus, congenital cataracts, cryptorchidism, and epi- and hypoplasias are some other uncommon anomalies that can be seen in EVC syndrome.<sup>15</sup>

Short limb polydactyly syndrome type III (SLP Type III-VermaNaumoff syndrome) is considered in the prenatal differential diagnosis of EVC syndrome and is characterized by hypoplastic thorax due to short ribs, short limbs, frequent polydactyly and visceral abnormalities.<sup>7</sup> Postnatally the essential differential diagnosis includes Weyers acrofacial dysostosis, Jeune syndrome (asphyxiating thoracic dysplasia), and McKusick-Kaufman syndrome.<sup>3,7,15</sup> Weyers syndrome is a autosomal dominant genetic disease and the heterozygous manifestation of the EVC gene. Postaxial polydactyly and oral manifestations are common with EVC syndrome however disproportionate dwarfism, thoracic dysplasia and cardiac defects are only seen in EVC syndrome. Unlike EVC syndrome the polydactyly in Jeune syndrome is not symmetrical. The narrow, long appearance of the chest and respiratory distress decreases as the child grows. Additionally these patients develop renal insufficiency in early adulthood. Ectodermal dysplasia and cardiac malformations are suggestive of EVC. Postaxial polydactyly and congenital cardiac defects are common findings in McKusick-Kaufman syndrome and EVC, but in McKusick-Kaufman syndrome hydrometrocolpos is seen in girls.<sup>7,10</sup>

There is no definite cure for this rare genetic disease. Treatment of EVC is usually symptomatic and a multidisciplinary approach including Pulmonologist, Cardiologist, Orthopedist, Psychiatrist, Plastic surgeon and Dentist is needed. Early treatment can prevent various orthopedic and dental complications. However, a high mortality rate is reported in early life due to cardiopulmonary insufficiency.<sup>7,15</sup>

In conclusion EVC syndrome is a rare autosomal dominant disorder which can be diagnosed based on clinical grounds supported by radiological evaluation. There are a limited number of case reports in the literature, mostly focused on clinical aspects rather than radiological findings. Some of the reported clinical and radiological features are constant, but some may be variable in different patients. Pediatric radiologists should be familiar with the roentgenographic findings in EVC syndrome which are of major importance for the diagnosis and differentiation of the disease.

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