A rare case of Ellis-van Creveld syndrome with primary immunodeficiency with recurrent and persistent pneumonia

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Introduction

Ellis-van Creveld syndrome (EVCS) is a rare autosomal recessive disorder of skeletal dysplasia.[1] This disorder was first described by Ellis and van Creveld. EVCS is an uncommon skeletal dysplasia with an incidence of approximately 7 in 10,00,000 live births in normal population.[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 EVCS cases may be undiagnosed because of lack of awareness and proper screening. Very few cases have been reported from Bangladesh and India.[4,5] Report of 4 cases with EVCS observed over a nine-year period. Most of the cases showed predisposition to develop recurrent sepsis.[6]

We are reporting here a case of Ellis-van Creveld syndrome in a 10-month-old male child presented with history of recurrent lower respiratory tract infections with an episode of persistent pneumonia and was diagnosed incidentally as a case of Ellis–van Creveld syndrome.

Written permission was given by the parents to publish the case report with patients photograph and investigation reports.

Case report

A 10-month-old male child, first issue of a non-consanguineous parents admitted at Ad-Din Medical College Hospital with the complains of fever, cough and cold with respiratory distress for 10 days. He was born by NVD, and his postnatal period was uneventful. He was vaccinated as per immunization schedule.

His milestone of development was delayed, still he cannot sit without support. He had history of repeated attack of fever, cough, and cold and respiratory distress for which he required hospitalization 6 times but never cured completely from his respiratory problem. On admission, he had fever of 103^{O}F, respiratory rate was 62 breaths per minute with severe chest indrawing. On auscultations there was vesicular breath sounds with prolong expiration, bilateral crepitation with rhonchi. His heart rate was 162 beats per minute with central cyanosis. His weight was 6.2 kg, length was 67cm, weight for height Z score - 3SD, upper segment was 41 cm and lower segment was 26 cm. upper segment lower segment ratio was 1.5:1. His OFC was 42cm. The patient also had narrow thorax and sparse hair (Fig1) He had multiple skeletal anomalies including lumber scoliosis (Fig2) and short broad hands and feet (Fig3) with distal shortening of both upper and lower limbs with dystrophic nails in both hands and feet.

Laboratory investigations revealed neutrophilic leukocytosis with microcytic hypochromic anemia. Blood culture did not grow any organism.

On chest X ray there was patchy opacities over both lung field with a pneumatocele at the lower zone of the right lung field and cardiomegaly with narrow chest and short ribs (Fig: 4). X-ray pelvis showed small, square iliac

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DOI: https://doi.org/10.3329/nimcj.v13i1.73546
Northern International Medical College Journal Vol. 13 No. 1-2 July 2021-January 2022, Page 594-597

crest, spikes of bone at the triradiate cartilage (Fig:5). X ray both hand showed dysplasia of the metacarpal bones. (Fig:6) Color Doppler echocardiography did not reveal any cardiac anomaly except cardiomegaly. For recurrent respiratory tract infections upper GI contrast X-ray was done to exclude gastro-esophageal reflux in T position which was normal.(Fig:7)

Due to history of recurrent pneumonia we send the blood for primary immunodeficiency panel to see leukocyte subtype analysis by flow cytometry. Lymphocytes were of 26.2% of the total leucocyte population. Absolute count of the CD19+ B cells, CD56+NK cells and CD3+ CD4+ were decreased with altered CD4: CD8 ratio. Serum IgG was reduced and IgA, IgE, IgM levels were normal.

During his last hospital stay, there was no significant clinical and radiological improvement for more than 1 month of treatment and was discharged home with oxygen, feeding procedure with nutritional advice, vitamins. Also trained the mother and advised for nasal and oral suction maneuver if there is aspiration. Also training on chest physiotherapy was given by the physiotherapist. Parents were counseled about the critical consequences of the child.

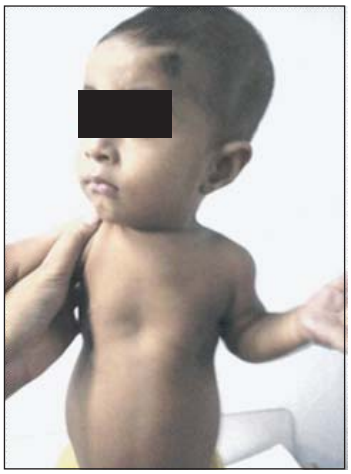


Fig 1: showing long narrow chest with sparse hair

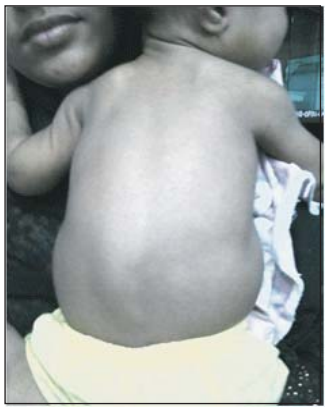


Fig 2 : Back with scoliosis

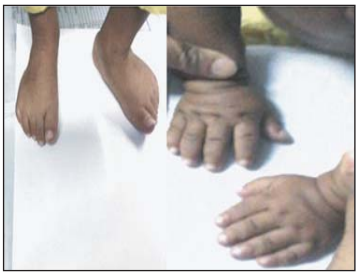


Fig 3: Hand and feet showing fingernails and toenails are markedly hypoplastic.

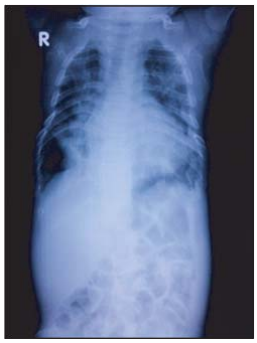


Fig 4: X ray both hands showed dysplasia of the metacarpal bone

Fig 5 : X-ray pelvis showing small, square iliac crest with spikes of bone at the triradiate cartilage and scoliosis

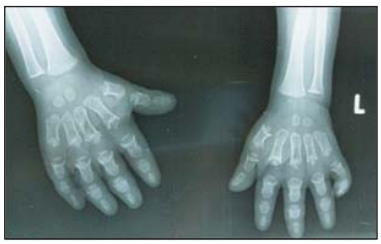


Fig 6 : X ray chest and abdomen : showing long narrow chest with small ribs and cardiomegaly

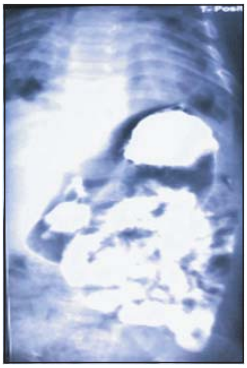


Fig 7 : Upper GI contrast X-ray in T position with no reflux

Discussion

Ellis-Van Creveld (EVC) syndrome is a rare disease[7] that is a result of mutations in two non-homolog genes EVC1 and EVC2 on chromosome 14p16.[7,8,9] The syndrome was first introduced by Ellis and Van Creveld in 1940.[10] Another name for this syndrome is meso-ectodrmal dysplasia or chondroectodermal dysplasia. This syndrome is a tetrad of chondrodystrophy, polydactyly, ectodermal dysplasia and congenital heart defects.[11,12] Chondrodystrophy means disproportionate dwarfism i.e. normal trunk with symmetrical shortening of middle and distal extremities.[13] All four classical signs were present in our patient but no history of consanguinity among the parents were present though it is an autosomal recessive disorder.

Ellis-van Creveld syndrome presents a characteristic tetrad as follows:

1. Disproportionate dwarfism due to chondrodysplasia of the long bones and an exceptionally long trunk. The severity of short limbs increases from the proximal to the distal portions. Our patient had chondrodysplasia and long trunk as calculated with upper segment and the lower segment ratio.

2. Bilateral postaxial polydactyly of the hands, with the supernumerary finger usually being on the ulnar side. Occasionally a supernumerary toe may be present. These were absent in our patient.

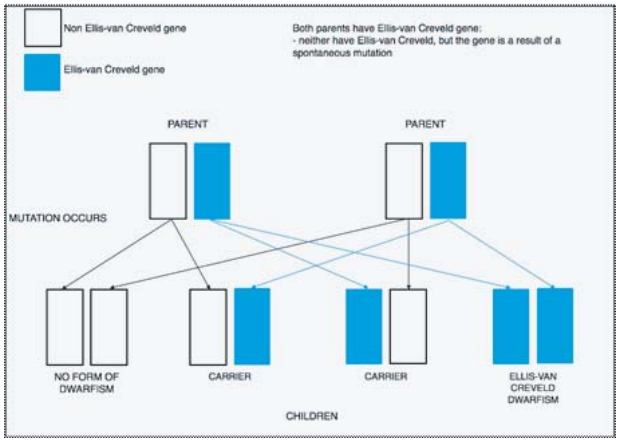
3. Ectodermal dysplasia with dystrophic, small nails, thin sparse hair were present in this patient, and hypodontic and abnormally formed teeth is other features of EVCS and here our patient did not have teeth eruption.

4. Congenital heart malformations in 50% to 60% of cases, the most common being a single atrium and a ventricular septal defect. Our case did not have cardiac anomaly but rather had cardiomegaly. Other skeletal anomalies such as genu valgum have occasionally been reported.[14] Patient's intelligence is usually normal.[15] Polydactyly, which is usually bilateral and post axial, most often found in the upper limbs and involves the lower limbs in about 10% of the cases.[14,16]

Ectodermal dysplasia is present in almost 93% of cases of EVC syndrome and includes hypoplastic, dystrophic nails which may sometimes totally absent. Hair and eyebrows may be sparse.[16]

Recurrent bacterial infection and sepsis was observed in three cases (75%) in a case series of 4. Early onset sepsis was present in both the neonates in the case series, one of which was due to Escherichia coli (isolated on blood culture). Another child of this series admitted with pneumonia had previous history of four episodes of lower respiratory tract infection and failure to thrive within the first four months of life. Screening for immune deficiencies with total leukocyte count, immunoglobulin profile and parental antiretroviral antibodies were found to be negative in all these patients.[6] Our case had recurrent episode of pneumonia with one episode of persistent pneumonia with evidence of combined immunodeficiency.

As it is an autosomal recessive disorder genetic counseling is necessary to prevent recurrence of the disease.[17] Genetic counseling could be done with the following chart.



EVCs present with oro-dental problems like multiple broad labial frenula with abnormal attachments, congenital missing incisors, anomalous teeth, bilateral partial clefts of the alveolar bone, and malocclusion.[18] Our patient did not show oral malformation and had no teeth eruption.

Conclusion

This syndrome is diagnosed mainly by its clinical features and supported by X-ray and echocardiographic findings. Ellis-van Creveld syndrome with primary immunodeficiency is a rare association, Genetic counseling is necessary to prevent recurrence of the disease. Multidisciplinary approach is needed to manage these patients according to the need of the child.

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