Case Report

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Osteogenesis Imperfecta: A Case Report

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Abstract

Three year old girl child born out of non consanguious marriage, 4th by birth order presented with sever respiratory distress and was unable to walk since the age of 1.5 years due to multiple recurrent fractures following minor trauma. Her 3 siblings died due to similar complaint. On examination she was malnourished, frontal bossing was present, oral examination dentition normal, sever respiratory distress with b/l crepitations and gallop rhythm heard. X-ray long bones showed multiple fractures with osteopenia. 2d echo-suggestive of dilated cardiomyopathy with cardiac failure. *Results:* Based on clinical examination and radiological features, and on ruling out other differentials: metabolic bone disease,fanconi syndrome,child abuse diagnosis is osteogenesis imperfecta.

Keywords: Osteogenesis imperfect; Recurrent fractures; Dilated cardiomyopathy.

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Introduction

Osteogenesis imperfecta (brittle bone disease) is the most common genetic cause of osteoporosis. It is a connective tissue disorder exhibiting a wide range of clinical severity ranging from multiple fracture in utero and perinatal death to benign nearly asymptomatic with mild predisposition to fracture and normal life span. Most of them are autosomal dominant inheritance although there are variants of autosomal recessive and de novo mutation. Mutation in one of the Type I collagen genes is commonly associated with osteogenesis imperfecta.

Case History

Three year old girl child born out of non consanguineous marriage to healthy parents, fourth by birth order presented with sever respiratory distress. She was complaining of fever, cough and difficulty in breathing since 10 days. She was unable to walk since the age of 18 months due to multiple recurrent fractures following minor trauma. She had tenderness on touching both upper and lower limbs for which no medical help was taken. She was born full-term by spontaneous vaginal delivery without fetal distress or asphyxia, birth weight 2.5 kg. At birth no fractures were present. History of repeated lower respiratory tract infection was given. She was breastfed. With no delayed teeth eruption, and was able to sit at eight months and walk independently at 16 months and has normal cognitive development. Her 3 siblings died due to similar complaint. First girl child died at the age of 9 months, it was a sudden death, she had history of repeated lower respiratory tract infection and fractures. Second male child had history of fractures following minor trauma since the age of 1 year, developmentally he was normal, died at the age of 2 years due to severe pneumonia, was sudden death. Third girl child had similar history died at the age of 3 years.

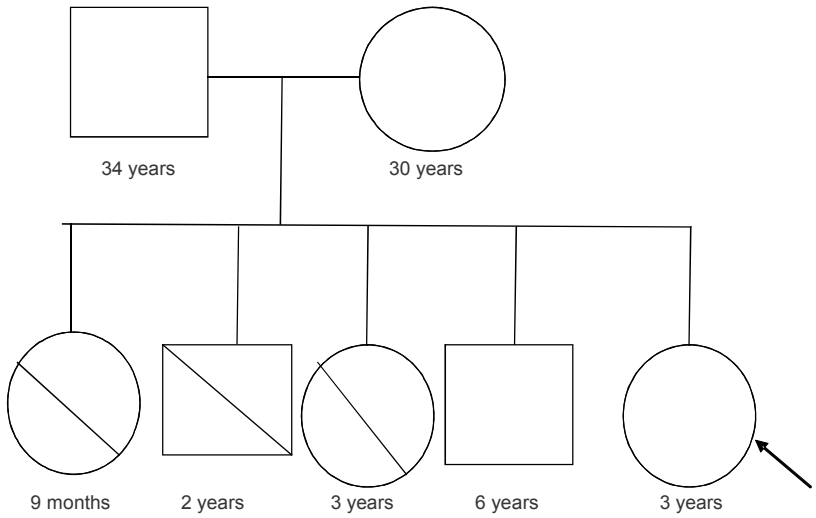

Fig. 1: Pedigree Chart

Clinical findings

- She was short stature with stunted growth; conscious, oriented to time, place and person.
- Frontal bossing present.
- On oral examination,dentition is normal.
- Barrel shaped rib cage-Pectus carinatum leading to the presenting complain of respiratory distress.
- Harrison groove and pallor seen.
- Pitting edema present on lower limbs.
- Repeated fractures followed by healing resulting in severe limb deformities present.

Anthropometry

- Head circumference - 44 cm below 3rd percentile.
- Height - 72 cm, below 3rd percentile.
- Upper Segment - 39 cm, Lower Segment - 33 cm;
- Chest circumference - 37cm.
- Weight - 5.7 kg, Grade IV PEM according to IAP classification.

Systhemic examination

- On inspection trachea is cental in position, barrel shaped chest, tachypnea (RR-38/min), subcoast and intercostal retraction with nasal flaring seen. Apical impulse seen in 6th IC space lateral to mid clavicular line.
- On palpation hyperdynamic apical impulse and parasternal heave felt.
- On percussion left heart border 2 cm lateral to mid clavicular line.
- On auscultation bilateral crepitations, tachycardia with gallop rhythm heard.
- Liver was 6 cm palpable below the subcostal margin.
- No evidence of hearing impairment, scoliosis and neurological examination was unremarkable.

Laboratory Investigations

- Hb - 6.3 mg/dl; MCV - 65; MCH - 20; MCHC-32
- suggestive of Nutritional Anemia.
- ESR- 25, CRP- 1.3 mg/dl (up to 6.0 mg/dl)
- Liver function test and kidney function test was normal.
- Serum Calcium - 7.8 mg/dl (9.0–11.0).
- Alkaline Phosphatase - 325IU/L (30–300).
- Serum Phosphorous - 4.1 mg/dl (2.5–5)
- Parathyroid Hormone (PTH) - 33.4 pg/ml (12–95 pg/ml)
- 1, 25-Dihydroxyvitamin D-51.8 ng/ml (sufficient 21–100)
- Thyroid profile, phosphorous-inorganic urine spot, calcium urine spot were within normal range.
- Urine analysis for detecting glycosuria and aminoaciduria (positive dipstick for protein) was normal.

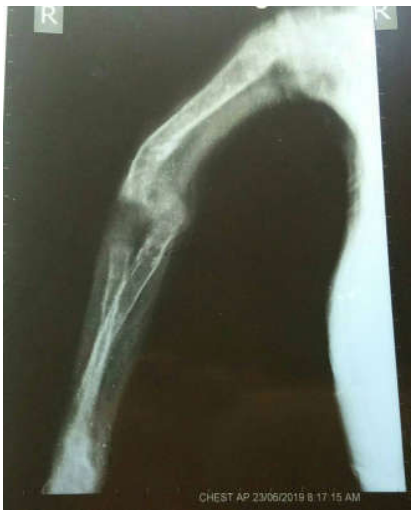

Fig. 2: X-ray right upper limb-osteopenia and displaced fracture of radio ulnar joint with multiple linear fractures.

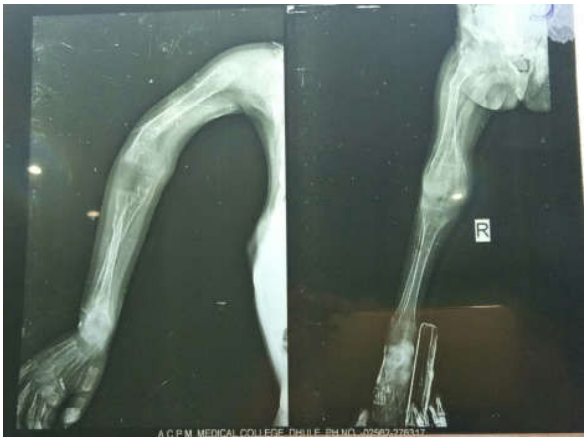

Fig. 3: X-ray of Right lower limb shows- Multiple non-displaced linear fractures with osteopenia. Sclerosis seen with callus formation in lower one third of diaphysis of right femur suggestive of previous fractures.

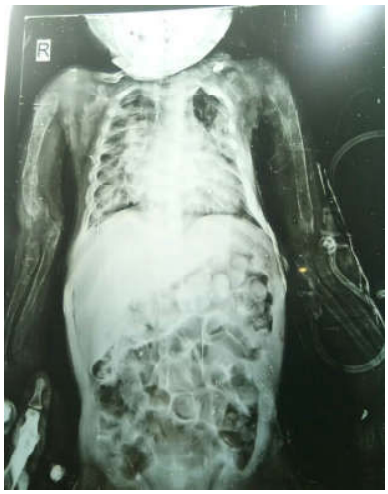

Fig. 4: Chest X-ray - AP view:

- Cardiomegaly
- Prominent right superior mediastinum.

On 2D Echo –

- Ejection fraction 35%,
- Left ventricular wall thickening with irregular wall hypokinesia with Increased end-diastolic diameter.
- severe pulmonary hypertension.

Above findings are suggestive of features of Dilated Cardiomyopathy with heart failure.

Discussion

Three year old girl child presented to us in severe respiratory distress with cardiac failure due to underlying dilated cardiomyopathy. On the basis of clinical features and laboratory investigation serum calcium, phosphorus, alkaline phosphatase and parathyroid hormone (PTH); 1,25 dihydroxy vitamin D, S.creatinine and electrolytes all appeared to be within the normal range hence metabolic bone disease-rickets due to Vitamin D deficiency, phosphorus deficiency, tumor induced rickets, calcium defiency, fanconi syndrome was ruled out. Patient is suffering from osteogenesis imperfecta with dilated cardiomyopathy, which can also be suspected in other siblings as they also had similar complaints and history of sudden death which may be due to cardiac cause.

Osteogenesis imperfecta (brittle bone disease) is the most common genetic cause of osteoporosis. The incidence is 1:20,000 and occurs in all races and ethnicity.[1] It is a connective tissue disorder exhibiting a wide range of clinical severity ranging from multiple fracture in utero and perinatal death to benign nearly asymptomatic with mild predisposition to fracture and normal life span. Most of them are autosomal dominant inheritance although there are variants of autosomal recessive and de novo mutation.[2,3]

Osteogenesis imperfecta (OI) occurs due to mutation in one of the Type I collagen genes. Since Type I collagen is one of the main structural components of connective tissues; this disease can have various extra skeletal clinical manifestations.[4] In general, Type I collagen is the most important constituent of different parts of the cardiovascular system, including the heart valves, chordae tendineae, fibrous rings of the heart, the interventricular septum, aorta, and most other arteries.[5,6] The collagen fibers in the ventricular myocardium contribute to the tensile stiffness and maintain the architecture of the myocytes.[7]

Several studies have reported the association of OI with various cardiovascular abnormalities, such as abnormalities of the aortic root and valve, mitral valve abnormalities, systemic hypertension, and tetralogy of Fallot.[8–10] Crosssectional studies have reported increased aortic root diameter, increased prevalence of diastolic dysfunction, and valvulopathies in patients with OI, but most of the included patients were asymptomatic despite cardiovascular pathology.[10]

In a study carried out by Vetter and colleagues, 58 children aged 1 to 16 years with various forms of OI were evaluated and found the septal hypertrophy and posterior left ventricular wall thickening in 40% and 68% of cases, respectively.[9] Dilated cardiomyopathy (DCM), formerly termed congestive cardiomyopathy, is characterized by enlargement of the cardiac chambers, contractile dysfunction of the myocardium, and, in later stages, by diminished cardiac output and symptoms of congestive heart failure. Familial dilated cardiomyopathy can occur secondary to an underlying inherited disease process, such as in osteogenesis imperfecta.[11–13]

Hence in this case death of all 3 siblings can be attributed to familial dilated cardiomyopathy due to Osteogenesis Imperfecta as all of them had history of recurrent fractures and lower repiratory tract infection and sudden death. Out of 5 siblings 4 were affected with osteogenesis imperfecta with dilated cardiomyopathy.

Conclusion

Patient is suffering from osteogenesis imperfecta with dilated cardiomyopathy, which can also be suspected in other siblings as they also had similar complaints and history of sudden death which may be due to cardiac cause. Hence it is essential for every patient of osteogenesis imperfecta screened for cardiovascular disease.

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