Multiple Fractures in Neonates and Osteogenesis Imperfecta

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Introduction

Fractures in a neonate commonly result from a genetic predisposition and birth trauma. A generalized defect in collagen/connective tissue manifests as osteogenesis imperfecta (OI), which remains the commonest cause of genetic osteoporosis. Approximately 1 in 20000 cases of OI are detectable during infancy [1]. We report 3 cases of OI detected in early neonatal period in a span of one year.

Case Report

Details of the 3 cases are given in Table 1. All 3 babies were products of nonconsanguinous marriage. Pregnancy had to be terminated in case 2 because of antepartum hemorrhage. Serum alkaline phosphatase, radiological survey and cranial USG were carried out apart from routine investigations. The alkaline phosphatase levels were 450IU/L,

380IU/L and 360 IU/L in case 1,2 and 3 respectively. All cases were managed conservatively with splinting and minimal handling. Cases 1 & 3 were regularly reviewed clinically for evidence of hearing deficit, respiratory and neurological complications till they were lost to follow up after 04 and 02 months respectively. Case 2 died at 34 weeks due to sepsis.

Discussion

OI is an inherited autosomal dominant disorder characterized by the triad of fragile bones, blue sclera and deafness [1]. Clinical picture, radiological evidence and positive family history form the basis of diagnosis and classification. Sillence classification is the commonest one used in prognostication - Type I is usually detected in childhood due to its mild phenotype, Type II is perinatally lethal, Type III is progressively deforming and Type IV is of variable severity [2]. Temporal profiling

Table 1
Clinical characteristics of the cases

Characteristics	Case 1	Case 2	Case 3
Obstetric history	Unbooked 30 yrs, G4P3A0 (3 living female issues)	Booked 30 yrs, G3P1A1 (previous FTND, 6 year old male); had PIH	Booked 21 yrs, G2P0A1 (Spontaneous abortion at 12 weeks)
Antenatal USG	No fetal anomaly detected	Fracture femur (Rt) ? skeletal dysplasia	No fetal anomaly detected
Delivery	LSCS (breech)	LSCS (vertex)	Vaginal
Gestation (wks)	40	29	40
Birthweight (kg)	2.4	1.36	3.1
Sex	M	F	M
Presenting Symptoms	Multiple limb deformities; paradoxical irritability		Respiratory distress at 30 min
Clinical findings	Frog-leg attitude, protuberant abdomen, macrocephaly, large anterior fontanel, craniotabes, short limbs with marked bowing. Blue sclera (Fig 1a)	Shortening of lower limb (Above knee); no tenderness, movements intact White sclera	Small "bell shaped" thorax; Short limbs with multiple skin creases with paucity of movements, tenderness & crepitus of right forearms & thigh. White Sclera (Fig 1c)
X-rays	Marked osteopenia Fractures - Ribs, humerus, radius ulna (Fig 1b)	Mild osteopenia; Healing fracture shaft femur with callus formation	Mild osteopenia Narrow thorax Fractures - right radius and ulna, proximal end right femur (Fig 1d)
Final diagnosis	OI Type III	OI Type III	OI Type III / IV

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Fig. 1 (a) Frog-leg attitude with short limbs with marked bowing under splint. (b) Marked osteopenia with fractures – Ribs, humerus, radius ulna (c) Small “bell shaped” thorax Short limbs with multiple skin creases (d) osteopenia with narrow thorax and fractures - right radius, ulna and proximal metaphysis right femur.

of the cases is vital since the phenotype in the early neonatal period may be similar between the various subtypes. A loss to follow up common in our population compounds the difficulties of subclassification and may account for underreporting of these cases. Congenital hypophosphatasia and battered baby syndromes are common differential diagnoses in the early neonatal period [3].

Decreased bone mass, disturbed organization and altered bone geometry resulting from abnormal collagen lead to bone fragility in OI. Molecular diagnosis depends on demonstration of abnormal incorporation of radioactive amino acids in collagen in fibroblast cultures. Genetic localization can be done by DNA probes [1]. Molecular genetics reveals at least seven discrete types – majority (Sillence Class I-IV) have mutations in one of the two genes encoding type I collagen; the recently recognized Types V-VII do not have such mutations. In two other forms, (Bruck, and osteoporosis - pseudoglioma syndromes) defects in other proteins have been characterized [4].

Follow up includes a good orthopedic management and rehabilitation. Regular hearing assessment is vital for early detection of hearing deficit. Respiratory infections and neurological complications like basilar invagination and brainstem compression are frequent [1,3]. Dentinogenesis imperfecta, a common association, important in subclassification becomes apparent only after a few months. Cutaneous and ligamentous laxity and occasional bleeding diathesis are also reported [5].

No curative therapy exists and using bisphosphonates in order to reduce osteoclast mediated bone resorption has targeted increased bone turnover in OI. Cyclical intravenous pamidronate and calcitriol administration reduces bone pain and fracture incidence, with increased bone density and level of ambulation, with minimal side effects [4,6]. Growth hormone therapy has also been tried with variable results depending on type of OI [7]. Gene therapy may be the answer in the future.

Genetic screening and counselling is of paramount importance since the risk of an affected individual passing the gene to the offspring is 50% and the recurrence risk for an apparently unaffected couple of having a subsequently affected offspring is 5-7 % [1]. Antenatally, lethality can be predicted at 14-16 weeks of gestation by ultrasonography with severe shortening of the long bones, femur length-abdominal circumference ratio of less than 0.16, hypoplastic thorax and marked bowing or fractures [1,8]. Chorionic villous biopsy can be done for recurrent cases [1]. Fetal MRI using ultra fast imaging technique, half-Fourier single-shot turbo spin-echo (HASTE) has been used to improve imaging conspicuity and spatial resolution [9].

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