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Prematurity and Rickets

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Summary

Iroha EO, Oduwole AO. Prematurity and Rickets. *Nigerian Journal of Paediatrics* **2000; 27:20** This is a case report of a premature infant who developed rickets. The neonate was a female born at 29 weeks gestation with a birth weight of 1250grammes. She was exclusively breast-fed and by 77 days of life developed rickets which was confirmed by radiological, biochemical and clinical features. The rickets responded to vitamin D, calcium and phosphate supplementation as was verified by improvement in clinical features and biochemical parameters. The infant had a turbulent period during her 68 days on the unit characterised by respiratory distress syndrome, recurrent apnoeic attacks, anaemia and septicaemia.

Introduction

THE increased survival amongst the extreme preterm infants achieved in the last two decades following improvement in neonatal intensive care has increased awareness of rickets in this group of patients. The tendency for developing rickets in thriving preterm infants has been well documented, over the years in the developed countries while they are few in the sub Saharan part of Africa.[1-5] Rickets in preterm infants is usually sub-clinical. Often it is diagnosed after the development of severe complications such as fractures or overt late onset respiratory distress syndrome.[3 4 6]

The incidence of rickets in infants of low-birth weight is said to be more than 57 percent in some centres.[7] The incidence of this disorder in Nigeria is unknown. However, over a 5 year period at a Nigerian teaching hospital, with an incidence of babies with low birth weight being 20 per 1,000 live births, three cases observed were reported.[4] The reason for a small number of reported cases is conjectural and may relate to poor perinatal and neonatal outcome of these infants and/or the lack of awareness by healthcare providers.

The contributing factors for development of rickets in preterm infants are interwoven and complex. These factors could be deficiency of the bone substrate mainly calcium, phosphate and magnesium and an incompetent vitamin D metabolism causing hormonal deficiency.[3 8-10] Other factors such as the immaturity of the infants system, the rapid growth that it is experiencing and possible associated debilitating illness may also contribute to the development of rickets of prematurity.

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The present case is reported to create awareness among practitioners and highlight the roles of bone substrate deficiency and vitamin D in the pathogenesis of rickets of prematurity.

Case Report

Baby YY (hospital no. 331479) was born prematurely at Lagos University Teaching Hospital by spontaneous vertex delivery to non-consanguineous Nigerian parents. The mother was an 18 year old housewife primigravida and father was a 30 year old soldier. Both parents had no history of,metabolic bone disease or overt rickets. Pregnancy was uneventful until the second trimester when mother developed ante-partum haemorrhage. She went into spontaneous labour at 29 weeks gestation and gave birth to a female infant. At birth baby had a Apgar scores of 7 and 9 at 1 and 5 minutes respectively. The birth weight was 1250gms, the length 39cm and the occipitofrontal circumference was 28.50cm. All these were appropriate for gestational age. The infant was nursed in the incubator with head box oxygen. The baby developed respiratory distress with grunting, substernal recession and tachypnoea with respiratory rate of 70 cycles per minute at age of 4 hours. Chest X-ray done showed diffuse reticulo-granular pattern with air bronchogram consistent with idiopathic respiratory distress syndrome. She had the first series of apnoeic attacks within 60hours of life, which lasted for a few hours. Investigations were done to rule out metabolic causes of apnoea such as hypoglycaemia and results were within normal range. A reoccurrence of apnoeic attacks were observed by 18days of age lasting two days. She had photo-therapy for jaundice that was observed on her second day of life and had cleared by the seventh day of life. Serum bilirubin results are shown on the table. She thrived and on observation of weight loss of 50grams over two consecutive days she was commenced on expressed breast milk from the fifth day of life at 5mls two hourly with continuous intravenous 10% dextrose fluid at appropriate rate to maintain her calorie intake. She was carefully monitored for any intolerance to the oral feed and having tolerated the expressed breast milk it was gradually increased to 200mls/kg body weight per day by the end of two and a half weeks of life with appropriate reduction of intravenous fluid. She was given ABIDEC drops 0.60ml (Parke Davis multivitamin with a vitamin D content 400iu/ 0.60mls), mist ferri 25mg and folic acid 0.50mg daily from the second week of life as a routine supplement by the unit for all premature infants. She had three episodes of sepsis while on admission. The first episode was at age 18 days, which was characterised

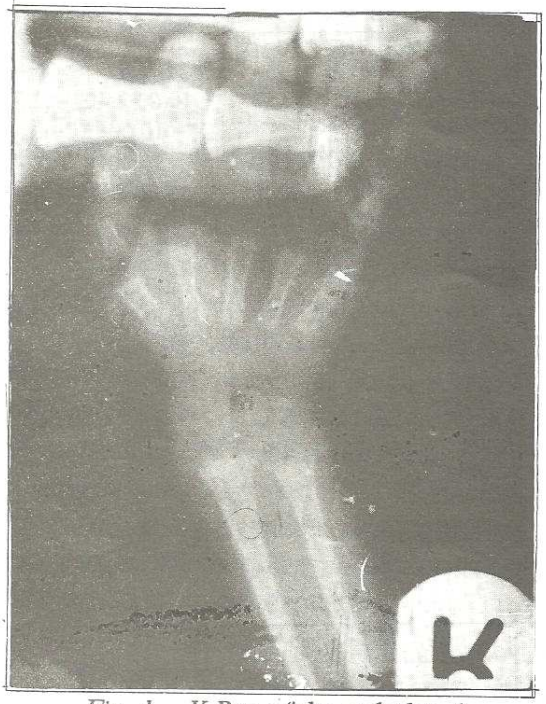

Fig. 1 X-Ray of the right hand

by hypothermia, lethargy and recurrent apnoeic attacks. Other episodes of recurrent sepsis were at 33 and 47 days. She responded well at each instance to antibiotics therapy. Other problems she developed during the neonatal period included recurrent anaemia of prematurity for which the infant received four top up transfusions at 38, 41, 48 and 77 days of life. After the third blood transfusion she had malaria fever with positive thick and thin blood film for *plasmodium falciparum.* She had episodes of severe metabolic acidosis (see table I) that required treatment with oral sodium bicarbonate by 10th, 15th and 47th day of life. She was discharged home for the first time at nine weeks of life weighing 1750gms.

When reviewed at the follow up clinic

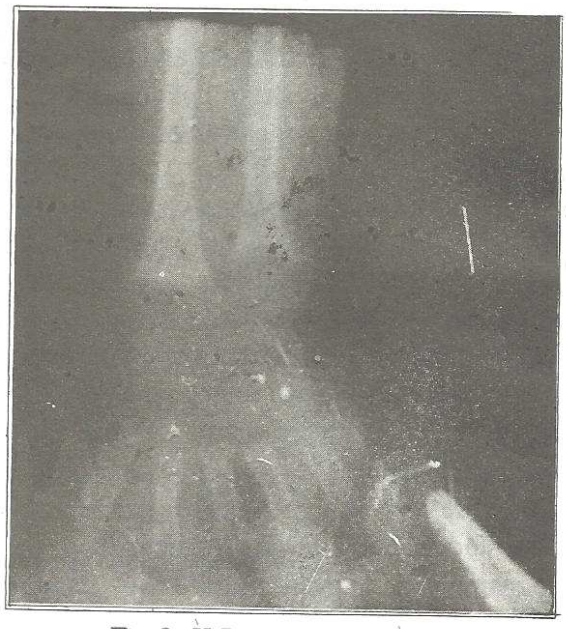

Fig 2 X-Ray of the left hand

Table I

Laboratory Profile

Age (day)	*PCV (%)*	*HB (gm%)*	*WBC*	*HCO_3^- (mmol/L)*	*Ca^{2+} (mmol/L)*	*PO_4 (mmol/L)*	*$AlkPO_4$ U/L*	*MP*	*BCul*	*XRay*
2	-	13.50	-	10.00	-	-	-	-	-	
8	18.00	-	170	10.00 2.40	1.70	-	-	-		
10	-	14.30	-	<10.00**	-	-	-	-	-	
15	30.00	-	8200	6.00**	-	-	-	-	-	
18	27.00	-	14000	7.00 2.70	1.40	-	-	-	NG	
24	20.00	8.90	-	-	-	-	-	-	-	
26	-	5.90*	-	-	-	-	-	-	-	
28	-	13.20	-	16.00 2.80	-	-	-	-	-	
33	17.00	7.40	-	18.00 2.20	2.70	-	-	-		
37	11.00*	-	-	-	-	-	-	-	-	
47	-	-	-	11.00**	-	-	-	-	-	
68	21.00*	-	-	-	-	-	-	+	-	
78	-	-	-	-	2.10	0.50	-	-	-	Cupping, flaying fraying and generalised oesteopeania of the lower end of the ulna and radius
-	-	-	-	-	-	-	-	-	-	
-	-	-	-	-	-	-	-	-	-	
-	-	-	-	-	-	-	-	-	-	
102	-	10.30	-	-	2.70	-	156.00		-	
150	-	9.80	-	-	2.70	1.90	-	-	-	

Alk P04: Alkaline Phosphatase
MP: Malaria Parasite
NG: **No Growth**

* : Blood Transfusion
** : Aklalinisation
B Cul : Blood Culture

at age 78days her growth parameters were satisfactory with a weight of 2450gms that was twice her birth weight. However her wrist joints were expanded and she had craniotabes with patent anterior and posterior fontanelles and sutural diasthesis. Chest or limb deformity were not observed and the tone was normal globally. Review of the serum phosphate and calcium estimates done while on admission up to age 33 weeks showed that they were within normal limit for age. While the serum phosphates and calcium done on the 78th day was 0.5mmol/L and 2.0mmol/L respectively, which were abnormal. The X-ray of the wrist joint showed generalised osteopaenia, cupping, flaying and fraying of the lower end of the ulna and radius (fig 1) which was consistent with the diagnosis of rickets. She was commenced on cholecalciferol (vitamin D3) 1,500 I.U daily oral, calcium gluconate and potassium hydroxyphosphate. Her rickets improved remarkably and the serum calcium and phosphate level were 2.70mmol/L and 1.90mmol/L respectively by 72 days post commencement of replacement therapy. Her anaemia (table) also improved without a need for blood transfusion top up. For financial reasons, we could not have a serial serum calcium and phosphate level estimation as expected for monitoring and a repeat X-ray before six months after commencing therapy (when she was lost to follow up).

Discussion

Rickets refers basically to failure to calcify osteoid tissue in a growing child with resultant limb deformities and typical radiological features. In neonates the pathogenesis of rickets in premature infants is complex and multi-factorial involving insufficient intake or absorption of phosphate, calcium or vitamin D. The role of abnormal vitamin D metabolism or reduced level of the active vitamin D metabolites has also been highlighted by Japanese workers who demonstrated the impaired activity of the 1 alpha hydroxylase enzyme in preterm infants.[12]

The diagnosis of rickets was entertained in this neonate when craniotabes, expansion of the wrist joints were observed at age 11 weeks. The diagnosis was further supported by the radiological and biochemical results. Factors that may have contributed to the development of rickets in this neonate are that she was exclusively breast fed, rarely had any exposure to sunlight, prematurity, vitamin D supplement from ABIDEC drops not enough, recurrent metabolic acidosis, recurrent and severe sepsis. These suggest that the aetiology of the rickets was multifactorial.

Though the infant was exclusively breast fed, the presence of a water-soluble vitamin D in the aqueous phase of the milk in concentration about 6 times that in the fat phase has raised a question if this form of vitamin D could account for the low incidence of rickets in exclusively breast fed infants. This is in spite of the fact that breast milk vitamin D is known to be low and considered insufficient to meet the needs of a rapidly growing child especially a preterm[13] who has missed the opportunity to lay down her store in the last trimester. It is now understood that the gastrointestinal tract is not the optimal route for vitamin D absorption, instead it is the skin in the presence of sunlight that manufactures it and it takes only a brief period in the sun to produce adequate vitamin D to last a week.[14] This neonate had a turbulent period and she was nursed inside the ward mostly well covered for 73 days without direct

exposure to the sunlight. This was continued on discharge home. The vitamin D supplement from ABIDEC drop, which gives him 400U daily was obviously not enough to prevent development of rickets. It is documented that a breast-fed low birth weight infant would need an average of 1000U/day with a range of 800-1600U/day.[13 15] The above mentioned also suggest that the rickets was the nutritional type, which was further buttressed by the improvement noticed on placing her on increased vitamin D, calcium and phosphate supplementation.

Sodium bicarbonate is known to increase loss of calcium in the urine.[16] The use of sodium bicarbonate solution for the treatment of metabolic acidosis on three different occasions with treatment lasting between 4-10 days on the various times might have added to the risk of her developing rickets. The recurrent infection and anaemia, which the neonate had, has also been associated with Vitamin D deficiency Rickets. Vitamin D deficiency rickets is associated with an impaired phagocytosis by neutrophils, decreased cellularity of bone marrow and extramedullary heamatopoieis causing anaemia with an increase frequency of infections.[17 18] The administration of vitamin D is known to correct these irregularities because its metabolite $1,25(0H)_2VitD_3$ has a regulatory effect on immunological and haemopoietic cells.[16] This was corroborated in our patient by the improvement in the infants' anaemia without a need for blood transfusion.

On a dose of vitamin D 1500U/day, the infant recovered from rickets completely and this excluded the possibility of autosomal recessive vitamin D dependent rickets or other types of vitamin D resistant rickets. The cause of rickets in this infant cannot be categorically defined as being nutritional as there may be other underlying factors that we could not readily identify.

Recent studies have shown that high serum alkaline phosphate activity, which occurs in rickets in the neonatal period is associated with a reduction in the body length at age 18 months post term, even after adjustment for other factors affecting length[19]. These findings suggest that sub-clinical rickets may have insiduous consequences that can be prevented by active preventive measures and early diagnosis.

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