Doi: 10.32677/IJCH.2016.v03.i02.021

Case Report

Unusual presentation of vitamin D deficiency rickets in a 6 day old extremely low birth weight baby

Neeraj Kumar Deepak[1], Kiran Meshram[1], Manjula Rupani[1], Samir Sheikh[2]

From [1]Department of pediatrics, Division of Neonatology, B J Wadia Hospital for Children, Nowrosjee Wadia Maternity Hospital, [2]NICU, Wockhardt Hospitals, Mumbai, Maharastra, India

Correspondence to: Dr Niraj Kumar Dipak, Division of Neonatology, B J Wadia Hospital for Children, Nowrosjee Wadia maternity Hospital, Acharya Donde Marg, Parel, Mumbai - 400012, Maharashtra, India. E-mail: drndipak@gmail.com

Received – 04 February 2016 Initial Review – 09 April 2016 Published Online – 25 April 2016

ABSTRACT

Clinical and biochemical signs of vitamin D deficiency in early neonatal period may be different from those of classic rickets. The most common presenting symptom in this age group is either incidental hypocalcemia or seizure, whereas skeletal deformities are minimal. This case report describes an extremely low birth weight baby who presented with clinical signs of rickets in the early neonatal period. Over a period of 6-week, his phosphorus, alkaline phosphatase, urinary calcium/creatinine, and urinary calcium/phosphorus ratio started improving. Between 1 and 4 months of age his abnormal biochemical findings showed significant improvement. This case report highlights the fact that pregnant women should be informed, at their first antenatal visit, of the importance of adequate vitamin D intake.

Key words: *Calcitriol, Costochondral beading, Congenital rickets, Extremely low birth weight baby, Vitamin D*

Inadequate mineralization of new endochondral bone at the growth plate results in the osteopenia of the growing bones; also called rickets. Clinical and biochemical signs of vitamin D deficiency in early neonatal and infancy period may be different from those of classic rickets. The most common presenting symptom in this age group is a seizure while skeletal deformities are minimal [1,2]. Rahim et al. reported 4-term newborns with an age range from 1.5 to 5 months presented with hypocalcemic seizures. All of them had hypocalcemia and low level of serum 25-hydroxyvitamin D (25(OH)D), and their mothers had not received vitamin D supplementation during pregnasncy [3]. Vitamin D deficiency as a prime reason for rickets in neonates, particularly in pre-terms, is far less frequent than calcium and phosphorus deficiency. This case report describes an extremely low birth weight (ELBW) baby with clinical signs of rickets in the early neonatal period.

CASE REPORT

A 700 g pre-term male baby was born to a 27-year-old primigravidae mother by emergency lower segment cesarean section in view of fetal growth restriction (FGR) with absent end-diastolic flow at 30.3 weeks of gestation. Pregnancy was unbooked with a very poor antenatal follow-up. She had not received calcium and vitamin D supplementation. Following birth, baby was maintained on non-invasive respiratory support after surfactant replacement therapy. On day 6, clinical examination revealed costochondral beading, wide sagittal sutures, wide anterior, and posterior fontanels (Fig. 1). Chest X-ray revealed generalized osteopenia of ribs and vertebrae (Fig. 2).

Biochemical investigations showed hypocalcemia, hypophosphatemia, very low level of 25(OH)D, and elevated intact parathormone (iPTH) and urinary calcium excretion and normal renal function tests (Table 1) [4-6]. Furthermore, ultrasound kidneys, ureters, bladder region did not reveal any abnormality. Mother had serum calcium 8 mg/dL, serum phosphorus 3.1 mg/dL, 25(OH)D 10 ng/mL, alkaline phosphatase (ALP) 300 IU/L, iPTH 48 pmol/L. Above investigations suggested vitamin D deficiency in mother and baby both and a diagnosis of rickets was made and baby was managed accordingly.

He was initially on total parenteral nutrition (TPN) for 10 days with increasing enteral feeds afterward. On reaching full enteral feeds by day 16, he was continued on enteral supplementation of calcium 160 mg/kg/day, phosphorus 80 mg/kg/day, calcitriol (1,25(OH)2D3) 0.25 µg/day which was given for 6 weeks along with cholecalciferol (vitamin D3) 800 IU/day. Gradually, over a period of 6-week his phosphorus, ALP, urinary calcium/creatinine, and urinary calcium/phosphorus ratio started improving (Table 1). During his stay in NICU, he required non-invasive ventilator support for

initial 14 days followed by invasive ventilation for late-onset sepsis for 4 days. He had failure of extubation attempts twice before successful transition to non-invasive support and room air. He was discharged at 38 weeks of post-menstrual age with outpatient follow-up. Between 1 and 4 months of age his abnormal biochemical findings showed significant improvement (Table 1).

DISCUSSIONS

Origin of osteopenia of growing bones lies in either calcipenia or phosphopenia. Calcipenic rickets result due to deficiency of calcium or vitamin D (either dietary deficiency, abnormalities in metabolism, or end-organ resistance to its biologically active metabolite), whereas deficient intake of phosphorus as in premature neonates with extended stay in NICU, prolonged TPN, and hereditary hypophosphatemic rickets account for phosphopenic rickets [8]. In infancy, early development of rickets involves upper limbs (swollen epiphyses of the wrists), ribs (rachitic rosary, Harrison's sulcus), and skull (craniotabes, widened cranial sutures, frontal bossing). Maternal vitamin D deficiency, hypoparathyroidism, and prolonged magnesium therapy in mother can give rise to neonatal vitamin D deficiency and congenital rickets [7].

Vitamin D deficiency due to other etiologies like neonatal cholestasis, short bowel syndrome or chronic renal failure usually presents few weeks after birth [8]. Similarly, clinical and

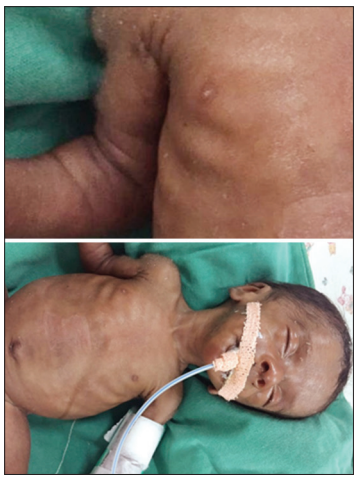

Figure 1: Costochondral beading noted on day 6

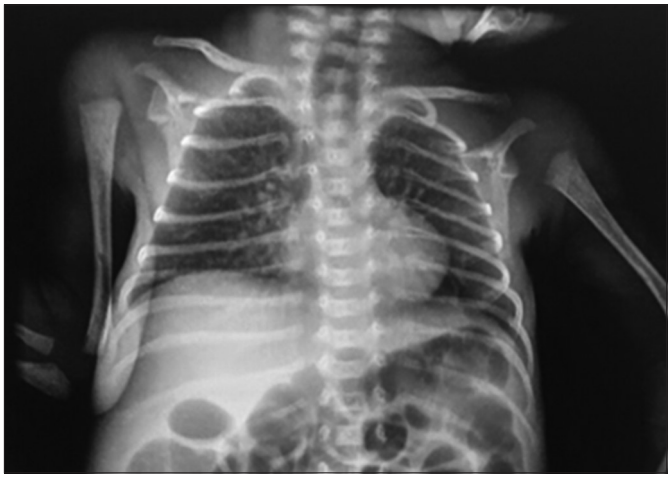

Figure 2: Chest X-ray showing generalized osteopenia of ribs and vertebrae

Table 1: Abnormal bone metabolic profile of the baby [4-7]

Serum/urine values with range	1 week	11 weeks	15 weeks
Serum calcium (9.2±1.1 mg/dL) [4]	7	7.9	9
Serum phosphorus (7.6±1.1 mg/dL) [4]	3.5	6	5
Serum alkaline phosphatase (48-406 U/L) [5]	500	326	171
iPTH (1-84) (67±9 pmol/L) by CMIA method [6]	100	150	68
25(OH)D (30.01-100 ng/mL) by CMIA method [7]	<3.1	10	32
Urine calcium/creatinine (<2.4 mmol/mmol) [6]	5	3	0.58
Urine phosphorus/createnine (1.2-19 mmol/mmol) [6]	0.15	0.2	0.68

25(OH)D: 25 hydroxyvitamin D, iPTH: Intact parathyroid hormone, CIMA: Chemiluminescent microparticle immunoassay

Table 2: Types of nutritional rickets related to prematurity

Investigations	Vitamin D deficiency rickets	Calcium deficiency rickets	Osteopenia of prematurity
Calcium	Low	Very low	Normal/elevated/low
Phosphorus	Low	Low	Very low
Alkaline phoshatase	Elevated	Elevated	Elevated
25(OH)D	Very low	Normal	Normal
1,25(OH)D	Normal/elevated	Elevated	Elevated
PTH	Elevated	Elevated	Normal/low

25(OH)D: 25 hydroxy cholecalciferol, 1,25(OH)2D: 1,25 dihydroxycholecalciferol, PTH: Parathyroid hormone

biochemical manifestations of osteopenia of prematurity (OOP) is seen between 4 and 12 weeks of age. It affects 20-30% of very low birth weight babies and 60-70% of ELBW babies [9]. In our case, costochondral beading (rachitic rosary), wide anterior and posterior fontanels, and wide sagittal suture were noted on day 6 of life making OOP less likely diagnosis. Secondary hyperparathyroidism and near normal or low phosphorus level differentiates vitamin D deficiency from OOP [10] (Table 2).

Research indicates that adequate vitamin D intake in pregnancy is optimal for maternal, fetal and child health. Adverse health outcomes during pregnancy are preeclampsia; gestational diabetes mellitus and cesarean section. Consequences in newborns are FGR, neonatal rickets, a risk of neonatal hypocalcemia, asthma and/or type 1 diabetes [11]. In developing countries, most women at childbearing age have vitamin D deficiency which is an important risk factor for congenital rickets.

Vitamin D deficiency is prevalent in India, a finding that is unexpected in a tropical country with abundant sunshine. A study in pregnant women in South India assessed maternal vitamin D status by measuring serum 25(OH)D in stored serum samples and found that more than 60% of the women had low 25(OH)D concentration (<50 nmol/L) at 30 weeks gestation [12]. At present, vitamin D supplementation is not a part of antenatal care programs in India.

Women of Indian origin, especially pregnant women, are known to have a high prevalence of vitamin D deficiency due to low calcium intakes and increased demands on calcium economy because of repeated cycles of pregnancy and lactation [13]. The currently recommended supplementation amount of vitamin D is not sufficient to maintain a value of 25(OH)D vitamin above 30 ng/ml, during pregnancy [14]. The Canadian Pediatric Society recommends 2000 IU of vitamin D3 for pregnant and lactating mothers with periodic blood tests to check the levels of 25(OH)D and calcium [15]. The American Academy of Pediatrics recommendations focuses on supplementing the infant and make no specific recommendations about universally supplementing breastfeeding mothers.

If a mother is vitamin D deficient, breast milk is not a good source of vitamin D, so infants need to be given vitamin D supplementation until they are weaned. It was recently shown that a maternal supplementation of 2100 IU vitamin D/day was needed, when administered during the period of lactation, to observe an increase in serum levels of 25(OH)D in the breastfed infants comparable to that observed in children given 400 IU/day [16]. It also suggests vitamin D supplementation of 400 IU/day to breastfed infants is the most secure way of preventing rickets in infants [16].

Plasma 25(OH)D3 concentration is a useful vitamin D biomarker reflecting vitamin D supply and use over a period [17]. Presently, there is no consensus regarding the cutoffs of 25(OH)D level in neonates, infants and children to define deficient state, but many experts accept a range 75 nmol/L (≥30 ng/mL) as optimal [17]. Vitamin D deficiency rickets responds to oral vitamin D3. The earliest response may be a rise in serum phosphorus and fall in alkaline phosphatase and decrease in hypercalciuria (calcium/creatinine ratio <2.0 in a spot sample). Urinary calcium phosphorus ratio (mmols/L) less than 1 by 3 months of age indicates that the infant is phosphorus repleted [18]. It is important to check these biochemical variables, at 3 monthly intervals so that dose of vitamin D can be adjusted according to response, and to guard against inadvertent hypervitaminosis D (leading to hypercalcemia, hypercalciuria, and nephrocalcinosis). If there is hypercalcemia or hypercalciuria, vitamin D should be temporarily stopped until urinary calcium excretion returns to normal.

REFERENCES

1. Bereket A. Rickets in developing countries. Endocr Dev. 2003;6:220-32.
2. Taha SA, Dost SM, Sedrani SH. 25-Hydroxyvitamin D and total calcium: Extraordinarily low plasma concentrations in Saudi mothers and their neonates. Pediatr Res. 1984;18(8):739-41.
3. Saeidi M, Vakili R, Khakshour A, Taghizadeh Moghaddam H, Zarif B, Nateghi S, et al. Iron and multivitamin supplements in children and its association with growth rate. Int J Pediatr. 2013;1(1):13-7.
4. Thomas JL, Reichelderfer TE. Premature infants: Analysis of serum during the first seven weeks. Clin Chem. 1968;14:272-80.
5. Rosenthal P. Assessing liver function and hyperbilirubinemia in the newborn. National Academy of Clinical Biochemistry. Clin Chem. 1997;43(1):228-34.
6. Salle BL, Delvin EE, Lapillonne A, Bishop NJ, Glorieux FH. Perinatal metabolism of vitamin D. Am J Clin Nutr. 2000;71 5 Suppl:1317S-24.
7. Kaplan W, Haymond MW, McKay S, Karaviti LP. Osteopenic effects of MgSO4 in multiple pregnancies. J Pediatr Endocrinol Metab. 2006;19(10):1225-30.
8. Hatun S, Ozkan B, Orbak Z, Doneray H, Cizmecioglu F, Toprak D, et al. Vitamin D deficiency in early infancy. J Nutr. 2005;135(2):279-82.
9. Mitchell SM, Rogers SP, Hicks PD, Hawthorne KM, Parker BR, Abrams SA. High frequencies of elevated alkaline phosphatase activity and rickets exist in extremely low birth weight infants despite current nutritional support. BMC Pediatr. 2009;9:47.
10. James JR, Congdon PJ, Truscott J, Horsman A, Arthur R. Osteopenia of prematurity. Arch Dis Child. 1986;61(9):871-6.
11. Hsu SC, Levine MA. Perinatal calcium metabolism: Physiology and pathophysiology. Semin Neonatol. 2004;9(1):23-36.
12. Harinarayan CV, Ramalakshmi T, Prasad UV, Sudhakar D, Srinivasarao PV, Sarma KV, et al. High prevalence of low dietary calcium, high phytate consumption, and vitamin D deficiency in healthy south Indians. Am J Clin Nutr. 2007;85(4):1062-7.
13. Sachan A, Gupta R, Das V, Agarwal A, Awasthi PK, Bhatia V. High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. Am J Clin Nutr. 2005;81(5):1060-4.

14. Kaushal M, Magon N. Vitamin D in pregnancy: A metabolic outlook. Indian J Endocrinol Metab. 2013;17(1):76-82.
15. Vitamin D supplementation: Recommendations for Canadian mothers and infants. Paediatr Child Health. 2007;12:583-98.
16. Wagner CL, Greer FR. American Academy of Pediatrics Section on Breastfeeding; American Academy of Pediatrics Committee on Nutrition. Prevention of rickets and vitamin D deficiency in infants, children, and adolescents. Pediatrics. 2008;122:1142-52.
17. Salle BL, Glorieux FH, Lapillone A. Vitamin D status in breastfed term babies. Acta Paediatr. 1998;87(7):726-7.
18. Rigo J, Pieltain C, Salle B, Senterre J. Enteral calcium, phosphate and vitamin D requirements and bone mineralization in preterm infants. Acta Paediatr. 2007;96(7):969-74.

Funding: None; Conflict of Interest: None Stated.

How to cite this article: Deepak NK, Meshram K, Rupani M, Sheikh S. Unusual presentation of vitamin D deficiency rickets in a 6 day old extremely low birth weight baby. Indian J Child Health. 2016; 3(2):174-177.