American Journal of Medical Case Reports, 2013, Vol. 1, No. 1, 12-15
Available online at http://pubs.sciepub.com/ajmcr/1/1/5

DOI:10.12691/ajmcr-1-1-5

Osteopenia of Prematurity in an Extremely Low-Birth-Weight Infant

Daiva Gorczyca[1,*], Hanna Cebula[2], Elżbieta Rapior[3], Marek Michalski[3]

[1]3rd Department and Clinic of Pediatrics, Immunology and Rheumatology of Developmental Age, Wroclaw Medical University, Wroclaw, Poland
[2]Department of Clinical Immunology and Pediatrics, Gromkowski Hospital, Wroclaw, Poland
[3]Department of Neonatology, Gromkowski Hospital, Wroclaw, Poland
*Corresponding author: daiva.gorczyca@umed.wroc.pl

Received October 29, 2013; Revised November 30, 2013; Accepted December 22, 2013

Abstract Osteopenia of prematurity is a relatively frequent disease in preterm infants. In many cases it remains clinically silent and it is poorly recognized until signs of rickets and pathological fractures occur. We report a case of a preterm female infant with a gestational age of 27 weeks and a birth weight of 820 g with clinical signs of osteopenia: flattened occiput, softness of the skull, generalized hypotonia, bone fragility and fractures. Early and proper supplementation of nutrients and minerals is essential to achieve sufficient bone mineralization.

Keywords: *osteopenia, prematurity, bone, calcium, ELBW infant*

Cite This Article: Daiva Gorczyca, Hanna Cebula, Elżbieta Rapior, and Marek Michalski, "Osteopenia of Prematurity in an Extremely Low-Birth-Weight Infant." *American Journal of Medical Case Reports* 1, no. 1 (2013): 12-15. doi: 10.12691/ajmcr-1-1-5.

1. Introduction

There are comparatively significant rates of preterm births worldwide and literature reports indicate that in 2010 one in ten children was born preterm [1]. Osteopenia of prematurity can be defined as a reduction in bone mass due to decreased trabecular thickness and/or decreased thickness of the bone cortex as a result of disturbances in bone mineral metabolism [2]. It is a relatively frequent disease in preterm infants born before 32 week of pregnancy [3]. Backström et al. estimated that osteopenia of prematurity occurs in 20-30% of preterm infants with birth weight below 1500 g and in 50-60% of preterm infants with birth weight below 1000 g [4].

The article is aimed at presenting the clinical manifestations of osteopenia of prematurity in an extremely low-birth-weight (ELBW) infant and difficulties in obtaining a balanced bone turnover in the treatment of a premature neonate with many risk factors.

2. Case Report

A preterm female infant with a gestational age of 27 weeks, a birth weight 820 g and a birth length 40 cm was born to a 29-year-old healthy mother. Mother's prenatal history was unremarkable. She took vitamins and mineral supplements recommended for pregnant women, however she smoked during pregnancy. The infant was delivered by cesarean section because of threatening fetal asphyxia. Apgar score was 1 at 1st minute and 5 at 5th minute of life. The patient was intubated due to respiratory distress and transferred to the intensive care unit for further management.

Upon admission, apart from symptoms of cardiorespiratory failure, physical examination revealed symptoms of rickets, such as: enlarged fontanelles, flattened occiput, softness of the skull, generalized hypotonia. Laboratory tests showed elevated C-reactive protein (CRP) level 158 mg/l (normal range, < 5 mg/l), normal plasma calcium concentration 2.25 mmol/l (normal range, 1.8–2.8 mmol/l), low plasma phosphate concentration 1.37 mmol/l (normal range, 1.6-3.1 mmol/l), highly elevated parathyroid hormone (PTH) level 185 ng/l (normal range, 15-80 ng/l), high serum alkaline phosphatase (ALP) activity 738 U/l (normal range, 95-337 U/l), normal serum vitamin D level 330 pmol/l (normal range, 117-700 pmol/l). There was decreased urinary phosphate excretion, increased urinary calcium excretion in the urine. The X-ray of the skull showed generalized bone loss and poor calcification. Bone inflammation, osteogenesis imperfecta and hypophosphatasia were also taken under consideration in differential diagnosis. Finally the diagnosis of osteopenia of prematurity was retained.

Along with intensive treatment of the cardiorespiratory insufficiency and sepsis, including mechanical ventilatory support with endotracheal intubation, surfactant therapy, management focused on fluid and electrolyte balance, antibiotic therapy (cefepime and vancomycin), and total parenteral nutrition. The patient received supplementation of calcium, phosphorus, vitamin D. For the first 10 weeks of life patient required total parenteral nutrition, with administration of calcium in a dose of 2.5 mmol/kg/day and phosphorus in a dose of 2 mmol/kg/day. Once enteral feeding was tolerated, formula feeding enriched with

calcium (100 mg/100 ml) and phosphate (50 mg/100 ml) was given. Vitamin D (800 IU per day) was also administered. In addition, 5 up to 10 minutes of daily passive physical exercise of upper and lower limbs were conducted through the whole period of hospitalization.

At 9 weeks of age a swelling was noted on the neonate's right thigh. The X-ray of the proximal right femoral metaphysis disclosed areas of osteolysis and massive periosteal reaction (Figure 1). Asymmetry of tracer accumulation at the base of the proximal right femur was noted on scintigraphy. These was regression of biological signs of inflammation with CRP < 5 mg/l, but abnormalities of markers of bone turnover were still observed: calcium 2.45 mmol/l, phosphorus 1.07 mmol/l, PTH 342 ng/l, ALP 771 U/l, vitamin D 447 pmol/l. At 11 weeks of age the respiratory signs had regressed, and he was haemodynamically stable, with a body weight of 2320 gms. She was then transferred to the Department of Neonatology.

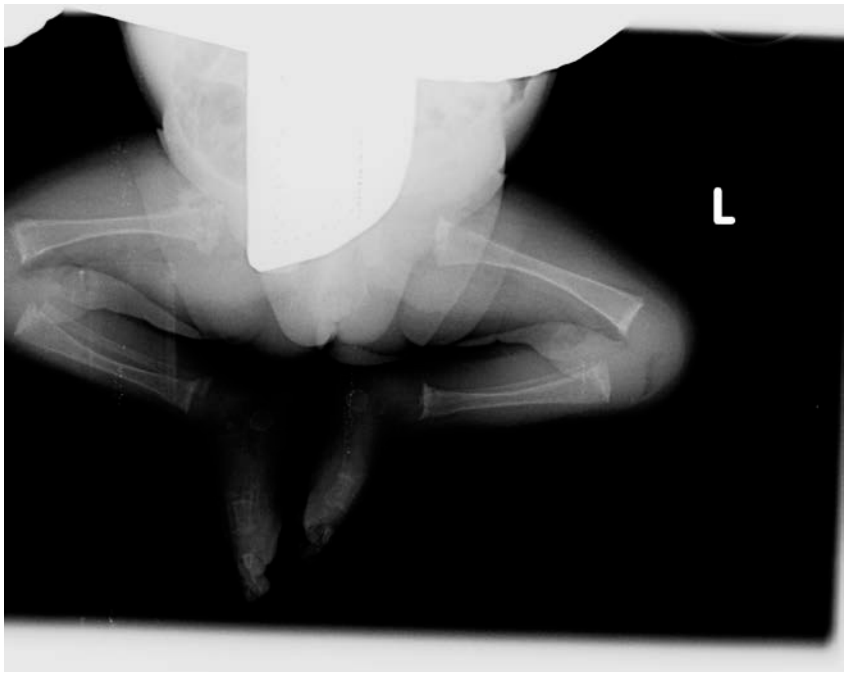

Figure 1. The X-ray of the proximal right femoral showing areas of osteolysis and massive periosteal reaction

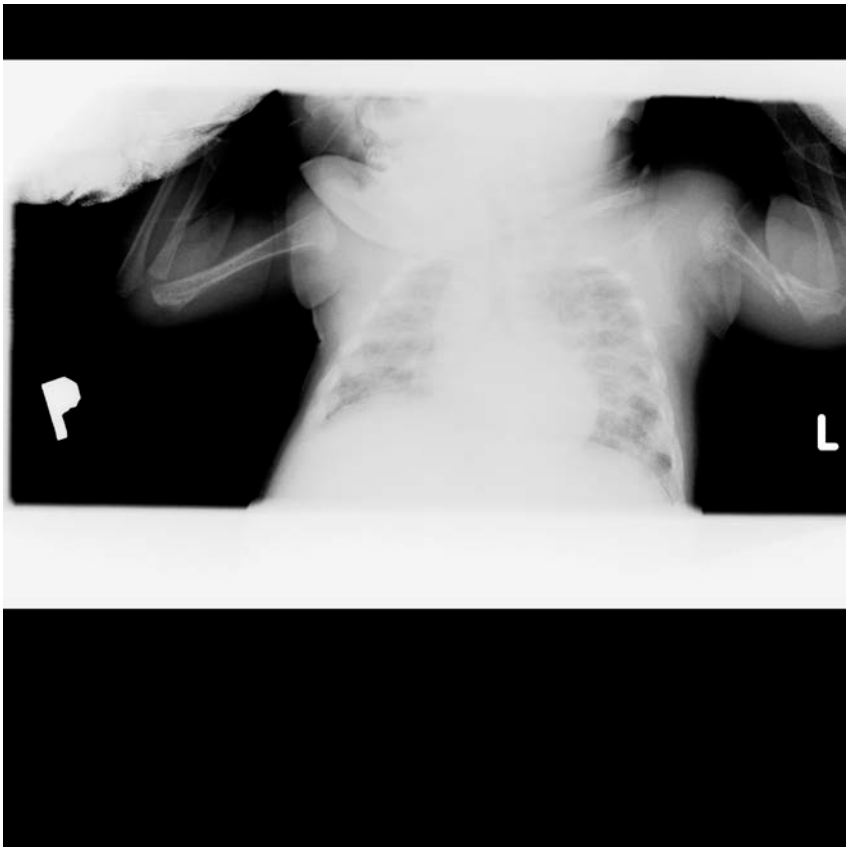

Figure 2. The X-ray revealed the fracture of the humerus with bone displacement

At 12 weeks of age physical examination revealed a swelling of the left upper extremity. An X-ray of the limb revealed a fracture of the humerus with bone displacement (Figure 2). Additionally, the chest X-ray showed mutifocal hazy pulmnary opacities, reflecting atelectasis, typical for bronchopulmonary dysplasia. The laboratory studies showed a CRP< 5mg/l and still abnormal serum biochemical markers (calcium 2.33 mmol/l; phosphorus 1.02 mmol/l; PTH 592 ng/l; ALP 886 U/l). The fracture was treated with shoulder brace. Control X-ray of the fractured limb at 18 weeks of age showed normal healing of the left humerus but still apparent bone loss (Figure 3).

The infant was discharged at 20 weeks of age in good general condition with body weight of 3930g. The laboratory investigations short before discharge showed CRP 6.8 mg/l, calcium 2.50 mmol/l, phosphorus 1.38 mmol/l, PTH 149.5 ng/l, ALP 662 U/l.

Mineral supplementation was continued at the recommended doses and a child was to be followed up at the neonatal clinic and then by a family physician. Two years follow up revealed normal development and adequate nutritional status of the child. No rickets symptoms or fractures were observed.

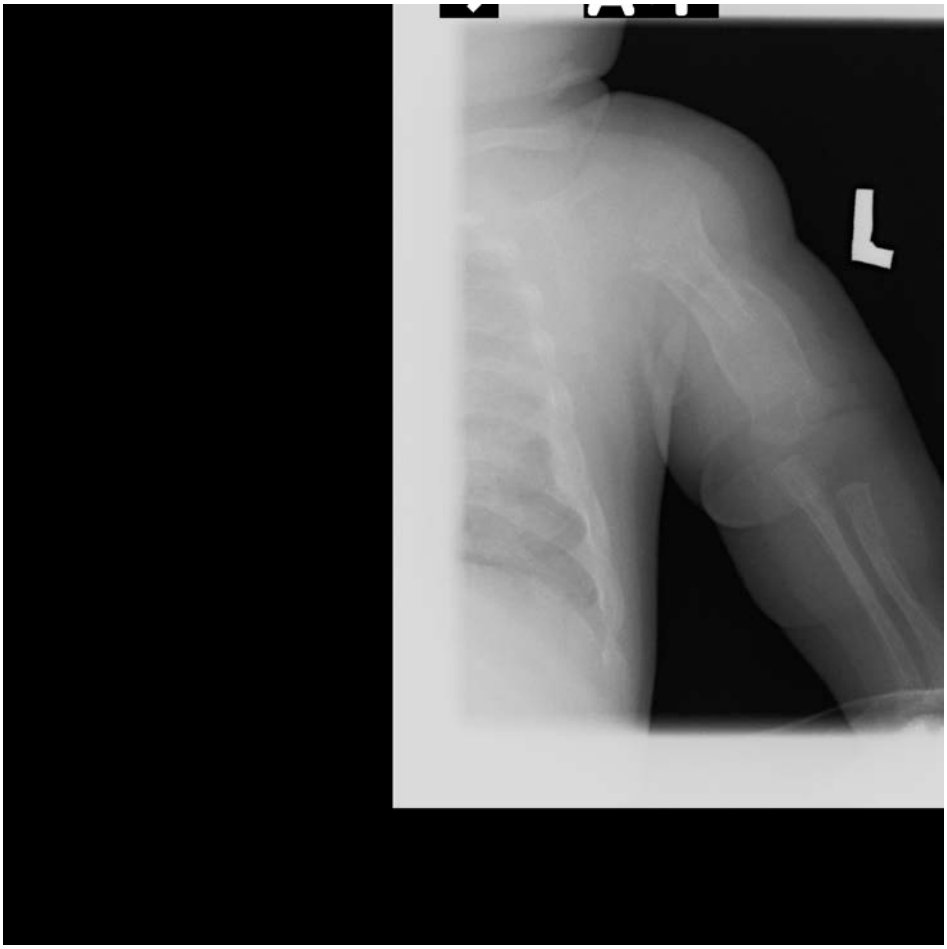

Figure 3. Control X-ray showed normal healing of the left humerus but still apparent bone loss

3. Discussion

This case presents a patient with osteopenia of prematurity. Birth weight below 1500g, gestational age less than 28 weeks, total parenteral nutrition over 4 weeks, use of diuretics or steroids carry the risk of development of osteopenia of prematurity [5]. However, chronic disease e.g. bronchopulmonary dysplasia contribute to the increasing incidence of osteopenia of prematurity. Our patient had many risk factors of osteopenia and she developed classic clinical symptoms of this disease: flattened occiput, softness of the skull, generalized hypotonia, bone fragility, and pathological fractures along with typical laboratory abnormalities. To diagnose osteopenia of prematurity it is useful to determine calcium and phosphorus concentrations and serum alkaline phosphatase activity. Elevated ALP activity (in our case 738 U/l) and low serum inorganic phosphate concentrations (in our case 1.37 mmol/l) strictly correlate with low bone mineral density in preterm infant.

The main cause of osteopenia of prematurity is a calcium deficiency and / or phosphorus deficiency. The bioavailability of these minerals in the gastrointestinal tract of a premature infant is diminished [6]. This is a reason why in many cases enteral supplementation is not sufficient to ensure proper mineralization. In our case, we used parenteral supplementation of calcium and phosphorus in the first stage of treatment, in the recommended doses (calcium dose of 2.5 mmol/kg/day, phosphorus dose of 2 mmol/kg/day) [7]. Then a mixture of milk enriched with calcium and phosphate was used in enteral feeding, in the recommended doses (calcium 100 mg/100 ml, phosphate 50 mg/100 ml) [8]. Patient also received vitamin D at a dose of 800 IU a day according to the ESPGHAN guidelines [8].

Studies have noted that regular movements of a fetus against the uterine wall are essential for normal fetal bone development. Reduced muscle tone outside the uterus, low physical activity of the preterm infant contribute to the imbalance between the processes of formation and resorption of a bone, which in turn leads to a reduction of osteoid [9,10]. That is a reason why physical rehabilitation of the patient was conducted as an essential part of treatment [11].

The differential diagnosis for osteopenia of prematurity versus rickets or osteomyelitis is determined lab test and imaging. In the diagnostic imaging of osteopenia of prematurityDual Energy X-ray Absorbtiometry and Quantitative Ultrasound are currently recommended to estimate bone density and they have become more widely used recently [12,13]. In the case of our patient these methods in the first stage were not possible to perform due to the heavy general condition of the child and the further course of infant's disease did not require expanding diagnostic imaging. It is know that X-ray examination is not sensitive enough to detect early stage of a disease, but it is still used to disclose bone loss, fractures and rickets features. Therefor, it was very useful in our diagnostic process.

In the treatment of our patient we used early bioavailable mineral supplementation, vitamin D administration and physical rehabilitation [11,12] Although we used proper and recommended treatment, bone fracture occured ad 9th and 12th weeks of infant's life while the hospital treatment lasted for 20 weeks. An achievement of a sufficient bone mineralization in an ELBW infant with many risk factors was therefore a challenge, ended with successful completion.

4. Conclusions

Osteopenia of prematurity can occur in extremely low birth weight infants. Management of metabolic bone disease in preterm infant with many risk factors may be difficult despite correct supplementation. The early diagnosis and management of osteopenia will prevent bone fractures that may impair the child's growth.

5. Consent

Written informed consent was obtained from the mother of the patient for publication of this report and images.

The authors declare that we have no conflict of interest (financial and others).

List of Abbreviations

ELBW: extremely low-birth-weigh

References

[1] Blencowe H, Cousens S, Oestergaard M, Chou D, Moller AB, Narwal R, Adler A, Vera Garcia C, Rohde S, Say L, Lawn JE, "National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications." *Lancet*, 379 (9832). 2162-2172. Jun. 2012.

[2] Rauch F, Schoenau E, "Skeletal development in premature infants: a review of bone physiology beyond nutritional aspects." *Arch Dis Child Fetal Neonatal Ed*, 86(2):F82-5. 2002.

[3] Pieltain C, de Halleux V, Senterre T, Rigo J, "Prematurity and bone health." *World Rev Nutr Diet*, 106. 181-188. Feb. 2013. 4.

[4] Backström MC, Kuusela AL, Mäki R, "Metabolic bone disease of prematurity."*Ann Med*, 28 (4). 275-282. Aug.1996.

[5] Harrison CM, Johnson K, McKechnie E, "Osteopenia of prematurity: a national survey and review of practice." *Acta Paediatr* , 97 (4). 407-413. Apr.2008.

[6] Rigo J, Pieltain C, Salle B, Senterre J, "Enteral calcium, phosphate and vitamin D requirements and bone mineralization in preterm infants." *Acta Paediatr*, 96 (7). 969-974. Jul.2007.

[7] Tudehope D, Fewtrell M, Kashyap S, Udaeta E, " Nutritional needs of the micropreterm infant. " *J Pediatr*, 162 (3 Suppl). S72-80. Mar.2013.8.

[8] ESPGHAN Committee on Nutrition, Aggett PJ, Agostoni C, Axelsson I, De Curtis M, Goulet O, Hernell O, Koletzko B, Lafeber HN, Michaelsen KF, Puntis JW, Rigo J, Shamir R, Szajewska H, Turck D, Weaver LT, "Feeding preterm infants after hospital discharge: a commentary by the ESPGHAN Committee on Nutrition." *J Pediatr Gastroenterol Nutr*, 42 (5). 596-603. May.2006.

[9] Bozzetti V, Tagliabue P,"Metabolic Bone Disease in preterm newborn: an update on nutritional issues. " *Ital J Pediatr*, 35. 20. Jul.2009. Available:

[10] Miller ME, "The bone disease of preterm birth: a biomechanical perspective." *Pediatr Res*, 53 (1). 10-15. Jan.2003.

[11] Schulzke SM, Trachsel D, Patole SK, "Physical activity programs for promoting bone mineralization and growth in preterm infants." *Cochrane Database Syst Rev*, 18(2). CD005387. Apr.2007.

[12] Godang K, Qvigstad E, Voldner N, Isaksen GA, Frøslie KF, Nøtthellen J, Henriksen T, Bollerslev J, "Assessing body composition in healthy newborn infants: reliability of dual-energy x-ray absorptiometry." *J Clin Densitom*, 13 (2). 151-60. Apr-Jun.2010.

[13] Pereda L, Ashmeade T, Zaritt J, Carver JD, "The use of quantitative ultrasound in assessing bone status in newborn preterm infants." *J Perinatol*, 23 (8). 655-659. Dec. 2003.