Pathological Case of the Month

Consolato Sergi, MD; Otwin Linderkamp, MD

A 14-MONTH-OLD GIRL, born to a German family with severe psychosocial problems, was breastfed for 4 weeks and then given cow's milk. Vaccinations and vitamin D prophylaxis were not administered. A home examination by emergency medical services revealed a dehydrated asystolic child (not breathing, blue lips, mid-wide pupils without light reaction). On admission, she was intubated, received epinephrine intratracheally, and was transported to the intensive care unit. Her heart rate was 95 bpm with no peripheral pulse or measurable blood pressure, cerebral reflexes were lost, and electroencephalograms showed no electrical activity. Laboratory analysis: white blood cell count, 21.6 × 10^3/µL; red blood cell count, 4.0 × 10^6/µL; hemoglobin, 9.5 g/dL; hematocrit, 32%; platelet count, 201 × 10^3/µL; C-reactive protein, 0.087 g/L; total protein, 4.2 g/dL; blood urea nitrogen, 84 mg/dL; creatinine, 1.9 mg/dL; prothrombin time, 49 s; partial platelet thromboplastin time, 113 s; fibrinogen, 2.52 g/L; anti-thrombin III, 48%; γ-glutamyltransferase, 26 U/L; aspartate aminotransferase, 292 U/L; alanine aminotransferase, 139 U/L; glutamatedehydrogenase, 10 U/L; IgG, 3.43 g/L; IgA, 0.36 g/L; IgM, 0.73 g/L; calcium, 11 mg/dL; phosphate, 10.3 mg/dL; alkaline phosphatase, 1240 U/L; 25-hydroxyvitamin D, 30 mmol/L (normal range [NR], 50-300 mmol/L); parathyroid hormone, 84.7 pmol/L (NR, 1.0-6.0 pmol/L); 1,25-dihydroxy vitamin D, 70 nmol/L (NR, 112-674 nmol/L). The tracheal biopsy specimen grew S. pneumoniae. No virus was detected. Chest radiography showed pneumonia. Netilmicin and cefotaxime therapy was initiated. Sodium bicarbonate was administered for metabolic acidosis, but electroencephalograms showed no cerebral activity.

Postmortem radiography showed enlargements of the costochondral junction in the chest and of the epiphyseal-metaphyseal junctions in long bones, with cupping and fraying of the distal ends and signs of double contour at the vertebral column (Figure 1). Glycol methacrylate bone sections without previous decalcification showed widening and thickening of the physeal growth plate (Figure 2A) with poor removal of cartilage, persistent hypertrophic chondrocytes in the zone of provisional ossification (Figure 2B), disordered vascular penetration of cartilage with impaired chondrocyte proliferation, and deposition of newly formed and poorly defined broad osteoid tissue (Figure 2C, D). Subperiosteal bone formation was less affected and overtook endochondral ossification.

From the Institute of Pathology (Dr Sergi) and the Department of Neonatology (Dr Linderkamp), University Hospital, Heidelberg, Germany.
Denouement and Discussion

Classic Rickets in a Setting of Significant Psychosocial Deprivation

Figure 1. Postmortem radiography of the chest and extremities showing enlargements of the costochondral junction in the chest (A) and of the epiphyseal-metaphyseal junctions in the long bones with cupping and fraying of the distal ends (B and C).

Figure 2. Glycol methacrylate bone sections without previous decalcification (A) showing poor removal of cartilage with persistent hypertrophic chondrocytes in the zone of provisional ossification (B), disordered vascular penetration of cartilage with impaired chondrocyte proliferation, and poorly defined broad osteoid seams (C and D). Subperiosteal bone formation is less affected and overtakes endochondral ossification (radiological appearance of the rachitic rosary).

A postmortem revealed poor nutritional status and dwarfism. The external examination showed craniopties, parietal bossing, and enlargements of the distal ends of long bones at the wrist, ankles, elbows, and knees. The lungs showed a consolidation of the parenchyma with infiltrates of neutrophils at the left lower pulmonary lobe, the middle pulmonary lobe, and in both upper pulmonary lobes. Brain examination showed hypoxia signs. The right heart was dilated with hypertrophic necrosis of the central regions of the lobules in the liver and hypoxic necrosis of the proximal tubules in the kidney. The cause of death was bilateral pneumonia.

Nutritional rickets affects endochondral and membranous ossification in infants and young children who may have inadequate sunlight exposure coupled with a low dietary intake of vitamin D. Rickets owing to vitamin D deficiency develops as a result of the body's attempt to maintain normal serum calcium levels because calcium is necessary for the normal function of nerve, muscle, endocrine glands, and intercellular bridging. The lowered calcium level increases the secretion of parathormone, leading to mobilization of calcium and phosphorus from the bone. The serum calcium level is thus maintained, but secondary effects occur, including bone changes, low serum phosphate concentration, and elevated serum alkaline phosphatase. Laboratory values change at advanced stages and during healing.

Clinical signs of rickets include craniopties, puffy swelling of the wrists and ankles. Diagnosis is based on nutritional history and clinical observation and confirmed by chemical analysis and radiography. Nonrachitic craniopties can occur in the immediate postnatal period but disappear before rachitic softening of the skull becomes manifest. Congenital epiphyseal dysplasia, cytomegalic inclusion disease, syphilis, rubella, and copper deficiency are further differential diagnoses. In most cases in Western countries, there is a combination of different risk factors, such as maternal vitamin D deficiency, no vitamin D supplementation, long-term breastfeeding, and insufficient sunlight exposure. Occult rickets has been reported in Asian immigrant children in the United Kingdom. Dagnelli et al compared the vitamin D metabolism in white 10- to 20-month-old children receiving a macrobiotic diet with children on omnivorous diets. The low availability of calcium in the macrobiotic diet was an independent factor in causing the high prevalence of rickets in infants with macrobiotic diets. Nutritional rickets by child neglect without signs of child abuse has received little attention. The mother of this patient was an alcoholic; alcohol abuse is present in many families with abused or neglected children. In these families, marital problems, unemployment, and drug abuse may play a role as trigger factors. Prevention and treatment measures for problems related to alcohol have been proposed, such as home visitation services.

Pneumonia is an important complication of rickets in developing countries. In Iran, 43% of 200 children with radiologically proven rickets had bronchopneumonia, and 44% of 250 Kuwaiti children with vitamin D deficiency rickets had pneumonia, and 44 (81%) of 54 Egyptian children with rickets had acute respiratory infections. Muhe et al found a 13-fold higher incidence of rickets among children with pneumonia than among controls. The association of rickets and pneumonia may be explained by effects of the hormonal form of vitamin D (calcitriol) on the immune system. Calcitriol stimulates phagocyte-dependent and antibody-dependent macrophage cytotoxicity and modulates functions of T and B lymphocytes. Constitutional factors, including the Harrison groove and asteatosis, may also contribute to pneumonia in children with vitamin D deficiency.

Accepted for publication August 25, 1999.

Reprints: Consolato Sergi, MD, Institute of Pathology, University of Heidelberg, INF 220/221, D-69120 Heidelberg, Germany (e-mail: Consolato_Sergi@med.uni-heidelberg.de).

REFERENCES


©2001 American Medical Association. All rights reserved.