

LETTER TO EDITOR

Osteoblasts in the Vicinity of Osteoclasts in a Case of Infantile Osteopetrosis

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ARTICLE INFO

Article History:

Received: 29.10.2015

Accepted: 20.12.2015

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Please cite this article as: Alavi S, Arabi N, Esteghamati S. Osteoblasts in the Vicinity of Osteoclasts in a Case of Infantile Osteopetrosis. IJBC 2016; 8(1): 25-26.

Dear Editor

An 18-month-old girl with failure to thrive, frontal bossing, bilateral proptosis, profound hepatosplenomegaly, severe anemia and thrombocytopenia was admitted to our pediatric oncology department. On physical examination she was a fussy baby with malformed teeth and abdominal distension. There was complete visual loss in the child. Laboratory data showed severe anemia, normal leukocyte counts with leukoerythroblastosis, and moderate thrombocytopenia (platelet counts 57000 / μ L). Liver transaminases were three times the normal values. Hemoglobin electrophoresis was normal. Skeletal survey showed remarkable sclerosis of the base of the skull, bone within bone appearance in vertebrae and metaphyseal fraying and cupping in distal long bones of the extremities which were all in favor of osteopetrosis. Bone marrow aspiration of the infant revealed a mild to moderate hypocellular marrow. There were increased number of osteoclasts (about 5 osteoclasts per 500 cells) observed in high power fields ($\times 100$). There were also osteoclasts with increased size and nucleation noticeable in some occasional fields (figure 1, 2). Another noticeable finding which prompted us to report this case was the simultaneous increase in the number of osteoblasts along with osteoclasts; some even close together in the same field (figure 2, 3).

Osteopetrosis, or marble bone disease, was initially reported by Albers-Schönberg in 1904 as a complex

disease associated with disrupted physical development and bone fragility.¹ The disease ranges from mild to severe lethal states. It is genetically determined as either an autosomal dominant benign type or an autosomal recessive malignant type.² A defect in the mechanism of bone remodelling leads to a constellation of somatic problems and hence devastating clinical picture of the disease. The basic defect in bone formation and resorption resides in osteoclastic malfunction that in turn results in an increase in bony mass, thickening of the cortical bones, and narrowing or obliteration of the medullary cavities.³ Multiple genetic mutations contribute to developing this heterogeneous disease. The pathogenetic defect may be intrinsic either to the osteoclast lineage or to the mesenchymal cells that constitute the microenvironment supporting the development and activation of the osteoclasts.⁴ Osteoclasts are the cells responsible for bone resorption that work continuously in conjunction with osteoblasts to proceed with bone strength and function.^{2,4}

Colony stimulating factor 1 (CSF-1), the growth factor for cells of the mononuclear phagocytic system, is essential for the development of osteoclasts. Altered CSF-1 production has been considered to be involved in almost complete lack of osteoclast development and as a result impaired bone resorption.⁴ In a study, light and transmission electron microscopic study of iliac crest metaphyseal bone from nine patients with infantile osteopetrosis demonstrated a variable spectrum

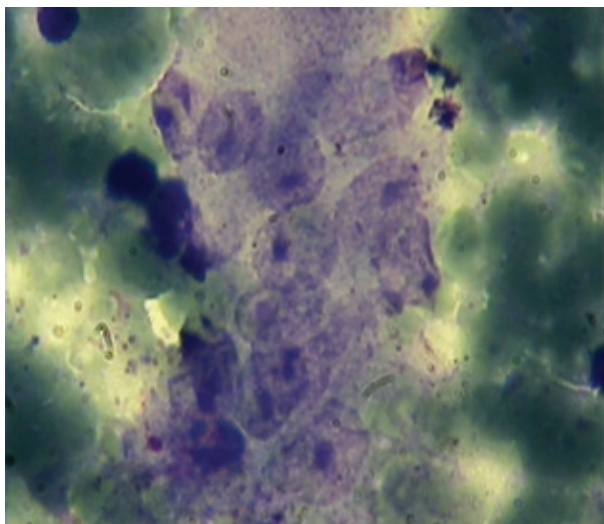


Figure 1: A large osteoclast with increased nucleation

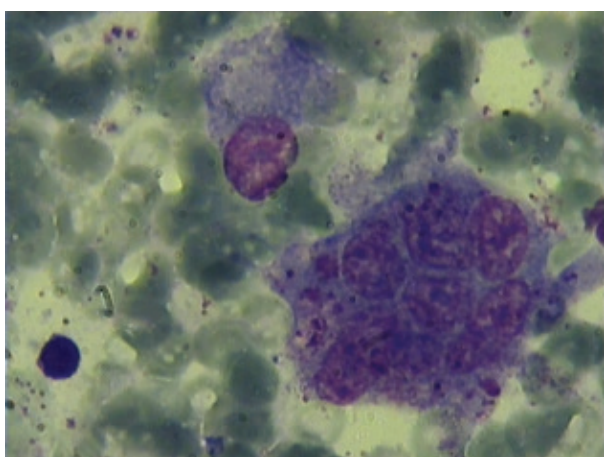


Figure 3: Osteoclast along with osteoblast in a smear

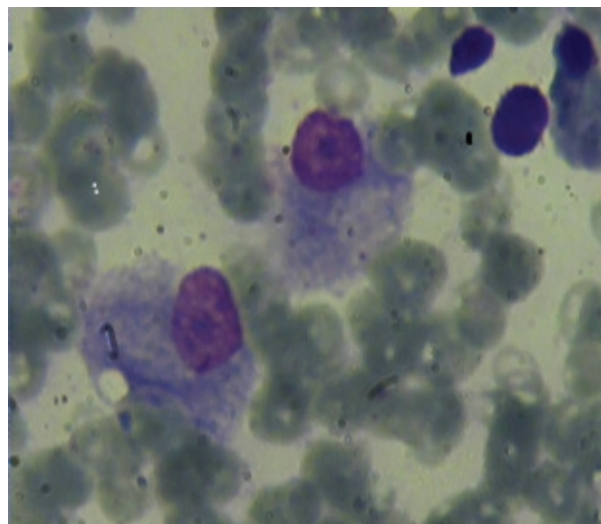


Figure 2: Increased numbers of osteoblasts

Finally, a combined defect in osteoblasts and osteoclasts in terms of number and function could be hypothesized that needs to be proved in future.

Conflict of Interest: None declared.

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of osteoclast abnormalities; osteoclast numbers were invariably increased.⁵ Osteoclast number, size, and nucleation ranged from mildly to markedly increased. In those with only a mild-to-moderate osteoclast increase, the marrow had a near-normal appearance with a good complement of hematopoietic cells. In those with markedly increased osteoclasts (hyperosteoclastic state) there were only scanty nests of hematopoietic cells.⁵ Osteoclasts are only infrequently seen in bone marrow aspirates. They become more obvious when the cellularity is depressed.⁶ In our case there was increased number of osteoclasts easily recognized on marrow smears. It has been shown that in both autosomal recessive and dominant types of osteopetrosis with different mutations bone resorption can be severely hampered despite marked elevation in osteoclast number.⁷ According to the study by Henriksen et al, in osteopetrosis, resorption is severely reduced, but the osteoclast number was increased by two to three-fold.⁸ Osteoblasts might also affect the pathogenesis of the disease, either because they are affected by intrinsic defects, or because their activity may be enhanced by deregulated osteoclasts present in large quantities in most forms.⁹ However, interestingly in the presented case osteoblasts were also increased in number.