OSTEOPOROSIS IN A SEVENTH YEAR OLD BOY WITH ACUTE LYMPHOBLASTIC LEUKEMIA (Case Report)

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Abstract

Osteoporosis in children is rare and usually secondary to an underlying disease process whose diagnosis may be difficult to detect. It can be a manifestation of acute lymphoblastic leukemia (ALL). About a-quarter of children with ALL will have signs and symptoms of osteoporosis. We report the case of a seventh-year-old boy with back pain. His antero-posterior pelvic radiograph showed the osteoporotic bone. The bone age study revealed six-year-old bone. Review of peripheral blood smear showed normochromic anemia with thrombocytopenia. Immunophenotyping of peripheral blood revealed no dominant marker was seen, but the bone marrow aspiration confirms the diagnosis of ALL (L2).

Keywords: osteoporosis, lymphoblastic, leukemia, antero-posterior

INTRODUCTION

Osteoporosis, ideally this term should relate to bone fragility and not just areal bone mineral density (BMD) measured by dual-energy X-ray absorptiometry. There is no consensus about definition for osteoporosis in pediatrics1. Most bone specialists make a diagnosis of osteoporosis in children and adolescents only in presence of low BMD and at least one fragility fracture.2

Childhood osteoporosis may arise from an intrinsic genetic bone abnormality (primary osteoporosis) or an underlying medical condition and/or its treatment (secondary osteoporosis). Etiological factors responsible for osteoporosis secondary to chronic illness include immobility, pubertal delay and other hormonal disturbances, under-nutrition and low body weight, inflammatory cytokines and glucocorticoid use.2,3

Leukemia is the most common form of childhood malignancy, with ALL accounting for approximately 75% of cases.4 With an overall survival rate approaching 80%, children with ALL have an excellent prognosis.4 The two major skeletal complications of leukemia are osteoporosis and avascular necrosis.5

THE CASE

A seventh year old boy referred to Sanglah General Hospital, Bali-Indonesia with differential was diagnosed of osteomalacia and osteogenesis imperfecta. He was complaining of back pain since two month ago. The pain increased when he walked, but disappeared when he had a rest. His respiratory rate was 26 breaths per minute, no cyanotic noted, his heart rate was 96 beats per minute, no grunting noted. He had pale conjunctiva, multiple lymphadenopathies on right and left of both region coli and inguinal. The lymphadenopathies were mobile and no sign of inflammations. We noticed innocents murmur on auscultation, grade II/6. No hepato-splenomegaly was found. He had no rash, petechie nor edema on extremities.

His weight was 18.5 kg (weight for age was <3 percentiles, CDC 2000), height was 118 cm (stature for age was 10-25 percentiles, CDC 2000), and head circumference was 50 cm. His nutritional stature was 84% according to Waterlow. According to his parent’s height (father’s height was 173 cm, mother’s height was 165 cm), his genetic potential height was 167-184 cm. His upper segment was 66 cm and lower segment was 52. The upper-lower segment ratio was 1.27.

The initial complete blood count revealed normal white blood count (11.59 x 10³/μL) with low hemoglobin (8.2 g/dL). The mean corpuscular volume was 80.2 fl. The platelet count was 41 x
10^7/μL. Review of peripheral blood smear showed normochromic anemia with thrombocytopenia. The FT4 and TSH were 1.56 ng/dL and 3.24 μU/ml. Parathyroid hormone was 14.09 pg/mL. The calcium = 9.10 mg/dL, sodium = 136.10 mmol/L, potassium = 4.33 mmol/L, uric acid = 4.1 mg/dL, total bilirubin = 0.22 mg/dL, direct bilirubin = 0.1 mg/dL, ALT = 21.99 U/L, AST = 10.7 U/L, albumin = 3.65 g/dL, BUN 13.2 mg/dL and creatinine serum 0.41 mg/dL. The Fe was 133.9 μg/dL, TIBC was 214 μg/dL and Ferritin was 282.7 ng/ml. The differential diagnosis was osteoporosis with chronic infection or aplastic anemia.

The tuberculin test was negative. The postero-anterior and lateral thorax radiograph showed multiple compressions on thoraces vertebral. Antero-posterior pelvic radiograph showed an osteoporosis. The thoraces vertebral MR-Imaging showed multiple wedge and biconcave compression on left thoracal corpus vertebra and fatty marrow replacement on the bone marrow which belongs to osteoporosis (Figure 1). He was treated with daily calcium 200 mg oral.

His bone age according to 8 Idell Pyle, showed the growth of metacarpal, phalange and sesmoid was belongs to six-year-old boy (normal bone age). The spine (0.482 g/cm^2) and total body BMD (0.805 g/cm^2) was normal, with 97% age-matched and z-score at -0.5 SD.

One month later, his complete blood count became pancytopenia (white blood count = 3.54 x 10^7/μL, hemoglobin = 9.9 g/dL and thrombocyt = 37.2 x 10^7/μL). The mean corpuscular volume was 86.4 fl. He had bone marrow aspiration and the results were belongs to ALL (L2). The cell was hyper-cellular, low activity on erythroid, myeloid and megakaryocytic system (Figure 2). We noticed 50% lymphoblast cell infiltration with variation in size.

The immunophenotyping of peripheral blood revealed no dominant marker was seen.

The bone marrow aspiration showed ALL (L2)

Based on bone marrow aspiration, a diagnosis of ALL (L2) was made. He had a serial chemotherapy for 109 weeks, with calcium and vitamin D supplementations.

**DISCUSSION**

Normal bone mass is defined by the World Health Organization as BMD within one standard deviation (SD) of the young adult mean; osteopenia as increased bone loss, with bone mass between 1 and 2.5 SDs below normal; and osteoporosis as bone mass ≥2.5 SDs below normal. Osteoporosis in younger patients is defined by the presence of both a clinically significant fracture history and low bone mineral content or BMD. In this case, the whole body BMD was decreased by 0.5 SD. Prospective studies have shown that a decrease in BMD by 1 SD is associated with a 1.5- to 3-fold increase in the relative risk of fracture.

There are some forms of primary and secondary osteoporosis typically observed in the young. The primary forms are relatively rare, while secondary forms of osteoporosis are increasingly observed in many chronic conditions.

Kaste et al sign an accumulation process of bone mineral during the period corresponding to onset of most childhood ALLs. Haddy et al noted that osteopenia/osteoporosis was observed in all phases of the disease: at diagnosis, during treatment, and throughout the post-treatment period for as long as 20 years. Among the findings that have been described are musculoskeletal pain, disturbed gait, fractures, kyphosis, lordosis and growth failure. Pathologic fractures and vertebral collapses may
occur secondary to severe osteopenia (leukemic osteopathy). 9

Strauss et al. 5 reported a 5-year cumulative fracture incidence in children with ALL of 28%. Rogalsky et al. 10 reported fractures in 25% of children with acute leukemia, 12% pathological, and 13% following trauma, during the course of their disease. By completion of therapy, Halton and Atkinson 11 reported that 39% of children with ALL had fractures. An increased fracture frequency was also reported by van der Sluis et al. 12, who found a fracture rate in children with ALL six times that of healthy controls, up to 12 months following chemotherapy. Bone mass is often reduced at diagnosis in ALL and falls significantly during the first 6 months of chemotherapy. 12, 13 Risk factors for the development of skeletal complications in ALL include poor nutrition, reduced mobility, impaired bone mineralization, older age at diagnosis and male sex. 5, 11 Despite this initial skeleton insult, the long-term follow-up of children with ALL, who had not received cranial irradiation, indicates that bone health tends to fully recover. 14, 15

About two-thirds of children with ALL will have had signs and symptoms of disease for less than 4 weeks at the time of diagnosis. However, a history of some months is also compatible with the diagnosis of ALL. The first symptoms are usually nonspecific and include lethargy, unrelenting fatigue, bone pain or loss of appetite. More specific symptoms such as anemia, hemorrhage and infections are a consequence of lymphoblast occupying the bone marrow and disturbing the residual normal hematopoiesis. 9

Bone pain is one of the initial symptoms in 25% of childhood ALLs, as confirmed in our case. It may result from direct leukemic infiltration of the periosteum, bone infarction, or expansion of marrow cavity by leukemic cells. In normal hematopoiesis, hematopoietic stem cells are in balance with components of the hematopoietic microenvironment including osteoblastic cells, osteoclasts, mesenchymal cells, and vascular structures. In leukemia, invasion of leukemia cells results in osteopenia mediated by an expansion of osteoclasts causing increased bone resorption and a concomitant reduction of osteoblastic activity. 17

Radiologic changes seen most frequently include osteolytic lesions involving medullary cavity and cortex, transverse metaphyseal radiolucent bands, transverse metaphyseal lines of increased density (growth arrest lines), and subperiosteal new bone formation. 16 In our case, the bone age confirmed growth failure of the metacarpal, phalanges and sesmoids. Multiple compressions were seen in the postero-anterior and lateral thorax radiograph, the antero-posterior pelvic radiograph, and the thoraces vertebral MR-Imaging which belongs to osteoporosis. For childhood ALLs, the white blood cell (WBC) count may be low, normal, or increased. Our case had an initially normal WBC count, but then dropped to 3.54 x 10^9/uL. The hemoglobin usually moderate to marked reduction, with normocytic normochromic red cell morphology. The blood smear for ALLs with leucopenia usually have very few to no blast, but when the WBC is greater than 10^9/mm^3, blasts are usually abundant. The first blood smear in our case showed normochromic anemia with thrombocytopenia. Both the blood smear and immunophenotyping in this case had no blast. Almost 92% of childhoods ALLs have platelet counts below normal. 16

The bone marrow is usually replaced by 80-100% blasts. Megakaryocytes are usually absent. Leukemia is suspected when the bone marrow contains more than 5% blasts. The hallmark of the diagnosis of acute leukemia is the blast cell, a relatively undifferentiated cell with diffusely distributed nuclear chromatin, one or more nucleoli, and basophilic cytoplasm. Special studies such as histochemistry, immunophenotyping and cytogenetic, will help in detailed leukemic subtypes classification. Unfortunately, because of the leucopenia, we didn't find any dominant marker on immunophenotyping of this case to classify the ALL. 9, 16

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