Author's response to reviews

Title: Osteoporosis resulting from acute lymphoblastic leukemia in a 7-year-old male: a case report

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Author's response to reviews: see over
Author’s response to reviews

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Version: 2  Date: 19 January 2014

Author’s response to reviews: see over
Reviewer’s report
Title: Osteoporosis resulting from acute lymphoblastic leukemia in a 7-year-old male: a case report
Version: 2 Date: 19 January 2014
Reviewer: Sumadiono -
Which of the following following best describes what type of case report this is?: Unexpected or unusual presentations of a disease
Has the case been reported coherently?: Yes
Is the case report authentic?: Yes
Is the case report ethical?: Yes
Is there any missing information that you think must be added before publication?: Yes
Is this case worth reporting?: Yes
Is the case report persuasive?: Yes
Does the case report have explanatory value?: No
Does the case report have diagnostic value?: No
Will the case report make a difference to clinical practice?: Yes
Is the anonymity of the patient protected?: Yes
Comments to authors:
- Complete the other data of clinical/laboratory results (organomegaly, petechiae/bleeding, frequent fever, hemoglobin, leukocytes and platelets, etc.)

We have completed the data of clinical/laboratory results on page 3:

“A 7-year-old Asian Balinese male was referred to our hospital because of persistent back pain over a 2-month period. The pain increased when he walked, but disappeared when he rested.

His respiratory rate was 26 breaths per minute, no cyanotic was noted, his heart rate was 96 beats per minute, and no grunting was noted. His axillaries temperature was 37°C. He had pale conjunctiva. He also had multiple lymphadenopathies to the right and left of both the abdominal and inguinal regions. The lymphadenopathies were mobile, with no sign of inflammation. There was no retraction on thorax region. We noticed an innocent murmur on auscultation, grade II/6. No enlargement of the hepar or spleen was found. He had no rash, petechia nor edema on his extremities.

The initial complete blood count revealed a normal white blood cell count \(11.59 \times 10^3/\mu L\), with low hemoglobin level (8.2 g/dL). The mean corpuscular volume was 80.2 fL. The platelet count was \(41 \times 10^3/\mu L\). A review of a peripheral blood smear showed a normochromic anemia with thrombocytopenia. The free T\(_4\) and thyroid stimulating hormone levels were 1.56 ng/dL and 3.24 uIU/ml, respectively. The parathyroid hormone level was 14.09 pg/mL. 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, ureum = 13.2 mg/dL and creatinine serum = 0.41 mg/dL. The serum iron was 133.9 ug/dL, total iron binding capacity was 214 ug/dL and ferritin was 282.7 ng/ml.
One month later, his complete blood count showed pancytopenia (white blood count = 3.54 \times 10^3/uL, hemoglobin = 9.9 g/dL and thrombocyte = 37.2 \times 10^3/uL). The mean corpuscular volume was 86.4 fL.”

- Described morphology of blast cells in the BMP
  We have described the morphology of blast cells on page 4 and figure 2:
  “The child had a bone marrow aspiration and the results revealed ALL (L2). The sample was hyper-cellular, with round and oval nucleus shape, smooth-homogeneous chromatin, and high nuclear-cytoplasmic ratio. There were low activities in the erythroid, myeloid and megakaryocytic system (Figure 2). We noticed a 50% lymphoblast cell infiltration, with size variations. The immunophenotyping of peripheral blood revealed no dominant markers.”
  “Figure 2. Histological examination of a bone marrow aspiration, taken 1 month after admission, revealed acute lymphoblastic leukemia (L2). The cytological feature revealed large-heterogeneous cells, with homogeneous nuclear chromatin, one or more nucleoli, and low activity in the erythroid, myeloid and megakaryocytic system.”

Quality of written English: Needs some language corrections before being published
Done
Reviewer's report

Title: Osteoporosis resulting from acute lymphoblastic leukemia in a 7-year-old male: a case report

Version: 2 Date: 19 January 2014

Reviewer: Soetjiningsih Budiarsa

Which of the following best describes what type of case report this is?: Unexpected or unusual presentations of a disease

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is the case report ethical?: Yes

Is there any missing information that you think must be added before publication?: Yes

Is this case worth reporting?: Yes

Is the case report persuasive?: Yes

Does the case report have explanatory value?: Yes

Does the case report have diagnostic value?: No

Will the case report make a difference to clinical practice?: No

Is the anonymity of the patient protected?: Yes

Comments to authors:

1. The differential diagnosis of the symptoms must be explained

   We have now explained the differential diagnosis of the symptoms on page 4:
   
   “At first, the differential diagnosis was either osteoporosis with chronic infection or aplastic anemia. A tuberculin test was performed, and the result was negative. A posteroanterior and a lateral thorax radiograph showed multiple compressions of thoracic vertebrae. An anteroposterior pelvic radiograph showed osteoporosis. The thoracic vertebrae MR-Imaging showed multiple wedge and biconcave compressions of left thoracal corpus vertebra and fatty marrow replacement in the osteoporotic bone marrow (Figure 1). He was treated daily with a 200 mg oral dose of calcium for the osteoporosis.

   One month later, his complete blood count showed pancytopenia (white blood count = 3.54 × 10^3/μL, hemoglobin = 9.9 g/dL and thrombocyte = 37.2 × 10^3/μL). The mean corpuscular volume was 86.4 fL. The child had a bone marrow aspiration and the results revealed ALL (L2). The sample was hypercellular, with round and oval nucleus shape, smooth-homogeneous chromatin, and high nuclear-cytoplasmic ratio. There were low activities in the erythroid, myeloid and megakaryocytic system (Figure 2). We noticed a 50% lymphoblast cell infiltration, with size variations. The immunophenotyping of peripheral blood revealed no dominant markers.

   Based on the bone marrow aspiration, a diagnosis of ALL (L2) was made, excluding aplastic anemia and chronic infection anemia. He had serial chemotherapy for 109 weeks, with calcium and vitamin D supplements for the leukemia and secondary osteoporosis.”

2. The pathogenesis of osteoporosis as an early manifestation of ALL must be explained, because in the first examination of the peripheral blood smear was in normal limit, but on bone marrow aspiration the results was revealed ALL.
We have included the pathogenesis of osteoporosis on page 4-5:

“There is a difference between normal hematopoiesis and leukemia in bone homeostasis. In normal hematopoiesis, hematopoietic stem cells (HSCs) 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. The effect, if any, on other components of the HSC niche has yet to be determined [13].”

Quality of written English: Acceptable
Declaration of competing interests: I declare that I have no competing interests
Reviewer's report
Title: Osteoporosis resulting from acute lymphoblastic leukemia in a 7-year-old male: a case report
Version: 2 Date: 19 January 2014
Reviewer: Ângela Cristina Malheiros Luzo
Which of the following best describes what type of case report this is?: Unreported or unusual side effects or adverse interactions involving medications
Has the case been reported coherently?: Yes
Is the case report authentic?: Yes
Is the case report ethical?: Yes
Is there any missing information that you think must be added before publication?: Yes
Is this case worth reporting?: Yes
Is the case report persuasive?: Yes
Does the case report have explanatory value?: Yes
Does the case report have diagnostic value?: Yes
Will the case report make a difference to clinical practice?: Yes
Is the anonymity of the patient protected?: Yes
Comments to authors:
The case report is coherently, authentic and ethical. Moreover osteoporosis being a rare adverse effect previously to the beginning of LLA treatment, the authors could advice and highlight that a hemogram bipenia (anemia and platelet diminishing) with back pain in childhood must be investigated with at minimum a mielogram and a bone marrow biopsy due to investigated haematological disease. The is persuasive, worth being reported but the authors deserves highlight that a hemogram bipenia and back pain with osteoporosis in children are not normal and demand a mielogram and bone marrow biopsy. The case report has explanatory and diagnostic values and could make a difference in clinical practice. The authors preserve the anonymity of the patient identity. The case report is very illustrative as it demonstrates the importance of haemotopoiesis investigation in the presence of bipenias. The authors also could cite the new publications that are released in PUBMED researches; some of them published during last year. So the case report should be accepted after minor revisions I declare that I have no competing interests’ below.

Quality of written English: Acceptable