CASE REPORT

B-acute lymphoblastic leukaemia

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SUMMARY

A 13-year-old boy presented with fever, skeletal pain, polydipsia, polyuria and multiple osteolytic lesions in pelvic bones and upper femur. There was no organomegaly or lymphadenopathy. His serum calcium levels were raised. Peripheral blood film examination was normal. Bone marrow showed presence of blast cells. Flowcytometry indicated B-acute lymphoblastic leukaemia (B-ALL). Hypercalcaemia and osteolytic lesions are rare presentations of B-ALL. This should be kept as a differential if a child presents with unexplained skeletal pain with lytic lesions.

BACKGROUND

Hypercalcaemia and osteolytic bone lesions are rare presentations of B-acute lymphoblastic leukaemia (B-ALL) in contrast to their high incidence in some other lymphoid malignancies such as myeloma, Langerhan cell histiocytosis (LCH) and T-cell lymphoblastic leukaemia/lymphoma.

We think this presentation of leukaemia needs to be reported so that B-ALL can be kept in differential whenever a child presents with skeletal pain and multiple osteolytic lesions with normal peripheral blood picture.

CASE PRESENTATION

A 13-year-old boy presented with malaise and fever associated with anorexia, pain in both lower limbs, polyuria and polydipsia, on and off for 3 months.

On examination he had pallor and bone tenderness. There was no organomegaly or lymphadenopathy.

INVESTIGATIONS

The boy was referred to the radiology department. X-rays revealed multiple lytic lesions in the pelvis and upper femur of both lower limbs (figure 1). A provisional diagnosis of LCH was made.

Biochemical parameters were: alkaline phosphatase 156 IU/L, lactate dehydrogenase 1650 IU/L, uric acid 5 mg/dL, albumin 3.4 g/dL and serum calcium 14 mg/dL.

He was referred to the haematology department for further work up. His haemogram revealed haemoglobin 9.1 g/dL, total leucocyte count 6300/mm³, differential leucocyte count: polymorphs 69%, lymphocytes 22%, eosinophil 2% and monocytes 7%.

Bone marrow aspiration showed 92% blast cells with high nuclear cytoplasmic ratio, fine nuclear chromatin and inconspicuous nucleoli (figure 2). Hence, diagnosis of ALL was made. Fine-needle aspiration cytology from the lytic lesions also showed similar blast cells (figure 3).

Figure 1 X-ray pelvis showing multiple lytic lesions.

Flowcytometry of bone marrow aspirate showed positivity for CD34, CD10, CD19, CD20 and negativity for CD7, CD2, CD3, CD13 and CD33.

As a result, confirmatory diagnosis of B-ALL was made.

DIFFERENTIAL DIAGNOSIS

Based on X-ray findings a differential diagnosis of LCH was made; however, presence of blast cells on bone marrow aspirate as well flowcytometry confirmed B-ALL as the diagnosis.

Figure 2 Bone marrow aspirate showing blast cells (Leishman stain $\times 100$).

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Figure 3 Fine-needle aspiration cytology from lytic lesions showing similar blast cells (Leishman stain $\times 40$).

TREATMENT

The patient was treated as per conventional protocol for B-ALL.

OUTCOME AND FOLLOW-UP

The patient has achieved complete remission but his bone lesions are still persisting. His serum calcium levels have normalised.

DISCUSSION

Acute lymphoblastic leukaemia (ALL) is the most common malignancy in the paediatric age group.¹ Symptoms of ALL include anaemia, fever, bleeding tendency and fatigue.² Hypercalcaemia and osteolytic lesions are rare in B-ALL in contrast to their incidence

Box 1 Factors associated with hypercalcaemia of malignancy⁸

Factor

TNF- α , TNF- β

IL-1 α , IL-1 β , IL-6

TGF- α , TGF- β

PTHrP

Ectopic PTH

1,25 dihydroxyvitamin D

PG-E1, PG-E2

RANKL

MIP-1 α

M-CSF

Lymphotoxin

IL, interleukin; MIP, macrophage inflammatory protein; M-CSF, macrophage colony-stimulating factor; PG, prostaglandin; PTH, parathyroid hormone; PTHrP, parathyroid hormone-related peptide; RANKL, receptor activator of nuclear factor κ B, ligand/osteoprotegerin system; TGF, transforming growth factor; TNF, tumour necrosis factor.

in some other lymphoid malignancies like adult T-cell leukaemia/lymphoma, myeloma and LCH.²⁻⁴ However, in our case, due to the patient's young age, myeloma was ruled out. Owing to lytic bone lesions the most likely diagnosis was LCH (eosinophilic granuloma), but bone marrow aspiration revealed the presence of blasts which on immunophenotyping by flowcytometry indicated B-ALL.

Table 1 Different types of bony lesions in acute lymphoblastic leukaemia/lymphoma

Author	Case number	Age/sex	Presenting symptoms	PBS/BMA*	Radiological findings
Shahnazi <i>et al</i> ¹	Case 1	4 year/F	Back pain	No blasts in PBS; BMA revealed blasts	Multiple dorsolumbar collapsed vertebrae
	Case 2	4 year/F	Pallor, weakness, wrist tenderness	PBS and BMA had blasts	Wrist X-ray revealed metaphyseal lucent band in radial and ulnar metaphyses and lucent bony lesions of the first and third metacarpal
	Case 3	8 year/M	Cough and musculoskeletal pain	Blasts in PBS and BMA	CXR reveals permeative bone lesion in the right humerus
	Case 4	8 year/M	Fever, back pain and limping	Blasts in PBS and BMA	Thoracolumbar AP and Lat X-rays revealed multiple collapsed vertebrae, knee X-ray revealed hypodensity around the knee joint with metaphyseal translucency
	Case 5	6 year/F	Pallor, weakness, pain in knee joint and elbow	Blasts in PBS and BMA	Periosteal reaction of radial proximal metaphysis with distal metaphyseal translucency (arrow); AP X-ray of knee joints revealed metaphyseal translucency in distal femurs and proximal tibiae
	Case 6	9 year/M	Groin pain and limping	Blasts in PBS and BMA	Reduced height of femoral epiphysis with osteochondral fracture on the left side due to avascular necrosis
	Case 7	13 year/F	Pallor, fever, headache and bone pain	Blasts in PBS and BMA	Skull X-ray revealed multiple lytic lesions; lumbosacral AP X-ray revealed permeative bony lesions in iliac bones with reduced vertebral height of L5; knee X-ray revealed reduced bone density with permeative appearance; CXR revealed permeative bony lesions in bilateral scapular bones
Sirelkhatim <i>et al</i> ⁴	Case 8	17 year/M	Fever and backache	Blasts in PBS and BMA	Diffuse osteolytic lesions of lumbosacral area and pelvis
	Case 9	12 year/F	Compression fracture of thoracic vertebrae	Blasts only on BMA	Osteolytic lesions in thoracic vertebrae and femur
Chaudhary <i>et al</i> ⁵	Case 10	7 year/M	Pain in lumbosacral area	Blasts only on BMA	Dorsal MRI showed atypical changes on MRI
	Case 11	3 year/F	Knee pain and swelling	No blasts on PBS and BMA showed occasional abnormal cells	Expansile lytic lesion at the right supracondylar region and multiple lytic areas in the diaphyseal and metaphyseal regions of both femora and tibia

*PBS is peripheral blood smear and BMA is bone marrow aspirate.

Lytic bone lesions with hypercalcaemia can be the initial signs even in the absence of blasts from peripheral blood smears. Hence in such cases bone marrow aspiration is mandatory (table 1). Hypercalcaemia in such cases is due to TNF (alpha and beta), IL-2, IL-6, TGF beta, 1-25(OH)₂ and direct invasion by the tumor cells or due to PTHrP and PGE₂ secretion by the tumor cells.⁴⁻⁷

Our patient presented with multiple osteolytic lesions with hypercalcaemia and a normal total leucocyte count without any blasts in peripheral blood. It is not uncommon to find osteolytic lesions without circulating blasts in peripheral blood in patients of ALL (box 1). Many such cases have been reported in the literature.^{1 3 5 9} Therefore, ALL should always be kept as a differential in any child having multiple osteolytic lesions and hypercalcaemia even in the presence of normal peripheral blood findings.

Learning points

- Unexplained skeletal pain in children can have multiple aetiologies like trauma, infection and, rarely, leukaemia. So once trauma and infection are ruled out, leukaemia should be considered in differential.
- Lymphoblastic leukaemia should be considered in differential diagnosis whenever a child presents with osteolytic lesions and hypercalcaemia with normal peripheral blood film.

Contributors RK undertook manuscript preparation, analysis, data collection and will act as guarantor. AK, MJ and USS helped in manuscript editing and manuscript review.

Competing interests None.

Patient consent Obtained.

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