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An Unusual Presentation Of Acute Myeloid Leukemia As Diffuse Osteolytic Lesions

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Abstract

Acute myeloid leukemia (AML) accounts for 20% of all childhood leukemia. AML presenting as osteolytic lesions is an unusual presentation and have been seldom described in literature. We describe a 13 year old child who presented with osteolytic lesions with hypertension and was subsequently diagnosed as AML, treated with chemotherapy. He went into relapse and succumbed to sepsis due to profound neutropenia.

Keywords: Leukemia, osteolytic, tumour lysis syndrome, pediatric

Introduction

Lytic bone lesions are well known to occur in disseminated bone tumours like Ewing's sarcoma, osteosarcoma, metastatic neuroblastoma and Langerhans cell histiocytosis but are uncommon in leukemia and lymphoma. There are only a handful of reported cases of AML presenting with osteolytic lesions. The following case describes a 13 year old child presenting with hypertension, bone pain and diffuse osteolytic lesions. His blood investigations were suggestive of hypercalcemia and tumour lysis syndrome. He was diagnosed with Acute myeloid leukemia on bone marrow biopsy. The patient went into clinical remission on induction chemotherapy but was readmitted with relapse 10 months later and died of neutropenia. This presentation of acute leukemia needs to be reported so that it can be kept in differentials whenever a child present with skeletal pain, multiple lytic lesions and hypertension.

Case Presentation

A 13 years old male child presented on December, 2020 with chief complaints of pain in multiple joints, fever, generalised weakness and weight loss since 3 months and progressive paleness of the body since 2 weeks with no significant past medical history.

On examination, child was hypertensive (BP: 170/110 mm of Hg) and underweight (25.5kg) with a BMI of 12.12 kg/m^2. He also had pallor, hepatomegaly, splenomegaly and bilateral knee joint swelling associated with tenderness and decreased range of motion. There was no spinal tenderness or bony deformity and rest of the systemic examination was normal.

His Skeletal survey showed multiple diffuse lytic permeative lesions in skull, vertebral spine, hip, lower and upper limbs and scapula. Initial laboratory investigations with complete blood count revealed severe anemia, neutrophilic leucocytosis and thrombocytopenia. Also the biochemical parameters revealed tumour lysis syndrome (acute kidney injury with hyperuricemia, hyperphosphatemia) and of note hypercalcemia. Child was also investigated for additional aetiologies of hypercalcemia which were normal. CECT thorax was done which showed

multiple lytic lesions in vertebrae, ribs, scapula, bilateral hypodense enlarged kidneys and multiple ground glass centrilobular nodules. Laboratory investigation reports are summarized in the given table 1.1

Table 1.1 : Summary of lab investigations

Initial Investigations	
Haemoglobin	6.8 gm/dl (N:12.5-16.1)
Total leucocyte count	36,920/mm^3 (N: 4,000/mm^3 -10,500/mm^3)
Differential leucocyte count	N_{84} L_{11}
Platelet count	0.8 lakh (N:1.5 lakhs-4 lakhs)
Biochemical Parameters	
Serum creatinine	2.1 mg/dl(N: 0.3-0.8)
Serum phosphate	6.5 mg/dl(N: 2.9-4.5)
Serum uric acid	15.3 mg/dl(N:2.7-6.7)
Serum calcium	14.0 mg/dl(N: 8.8-10.8)
Serum LDH	3133.2 U/l(N: 150-450)
Investigations for hypercalcemia	
Serum iPTH	14.5 ng/l(N: 12-72)
Serum 25-(OH) Vitamin D	22ng/ml (N: 20-100)
Urine routine microscopy	Ph : 6,Protein : trace, Pus cells : 5/ HPF
Urine calcium creatinine ratio	0.54 (Normal : < 0.20)

He was managed for hypertension, hypercalcemia and tumour lysis syndrome and a bone marrow aspiration was performed. It resulted in dry tap, following which a bone marrow biopsy was performed. It had 39% myeloblasts and occasional Auer rods (> 3% blasts were SBB positive) consistent with a diagnosis of acute myeloid leukemia. Immunophenotyping was positive for MPO, CD13 and CD33 markers suggestive of Acute myeloid leukemia.

The child was subsequently started on Children oncology group AAML0531protocol[17] to which child responded clinically, morphologically (Bone marrow aspiration showing 3% blasts) and radiologically. But he had to be readmitted with relapse (Bone marrow aspiration showing 82%blasts) 10 months later. Salvage chemotherapy with modified FLAG regimen[18] was initiated but the child died due to profound neutropenia.

Discussion

Acute myeloid leukemia (AML) is characterized by the abnormal proliferation and differentiation of myeloid precursors in the bone marrow and constitutes 20% of childhood leukemia.[1]The Incidence of osteolytic lesions varies from 10.5% to 39% in acute leukemias[2] but majority of them have been described with lymphoid types. Literature searches on PubMed revealed only 9 published cases of AML with osteopenia so far,[3-11] and among them only two cases were of pediatric age group.[10, 11]Lytic lesions are especially localized in the metaphysis of long bones but may also occur in flat or small bones with/without periosteal reaction[12] and are believed to be due to abnormal production of parathormone[13]however its pathogenesis is poorly defined. In fact in our case iPTH was normal.The optimal management and outcome of patients of AML presenting with osteolytic lesions has not been

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critically assessed and no guidelines exist for the same and because of the rarity of the disease, prognosis of patients presenting with extensive osteolytic lesions in AML is still unclear.

Hypercalcemia occurs in less than 1% of children with cancer[14] due to direct invasion of the skeleton by tumor cells and ectopic production of parathyroid hormone related protein (PTHrP). Its symptoms are non-specific and if left untreated may lead to cardiac arrhythmias, severe hypertension, renal failure, acidosis, dehydration, and coma.

Tumor lysis syndrome as defined by Cairo-Bishop criteria[15] is found in 3-5% of the patients of AML[16]. It usually develops in patients of non-hodgkins lymphoma or acute leukemias and occurs when tumor cells release their contents into bloodstream, either spontaneously or in response to therapy, leading to characteristic findings of hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia. These electrolyte and metabolic disturbances can progress to clinical toxicity, including renal insufficiency, cardiac arrhythmias, seizures, and death due to multiorgan failure.

Conclusion

AML presenting as osteolytic lesions is an extremely rare phenomenon. It poses a diagnostic and therapeutic dilemma and only a handful of cases have been reported in literature. The optimal management, outcome and prognosis of such patients is yet to be defined.This report is our humble attempt to emphasize that the possibility of acute myeloid leukemia may be kept in a child presenting with osteolytic lesions.

Abbreviations

AML- acute myeloid leukemia, iPTH- intact parathormone, PTHrP- parathyroid hormone related protein, FLAG- fludarabine, cytosine arabinosidase, doxorubicin and G-CSF.

Additional Information

Disclosures

Human subjects: Consent was obtained by all participants in this study.

Payment/services info: No financial support was received from any organization for the submitted work.

Financial relationships: No financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work.

Other relationships: No other relationships or activities that could appear to have influenced the submitted work.

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Figures

A. Trephine biopsy showing adequate erythropoiesis

B. Trephine biopsy showing Blast cells

C. Trephine biopsy showing adequate megakaryopoiesis

D. CT CHEST showing ‘tree in bud’ appearance in bilateral lobes and centrilobular nodules

E. CT chest showing osteolytic lesions in spine

F. Bulky kidneys (parenchymal leukemic infiltration)

G,H,I - Pre chemotherapy bone scan showing osteolytic lesions

J,K,L – Post chemotherapy bone scan showing resolution of lesions.

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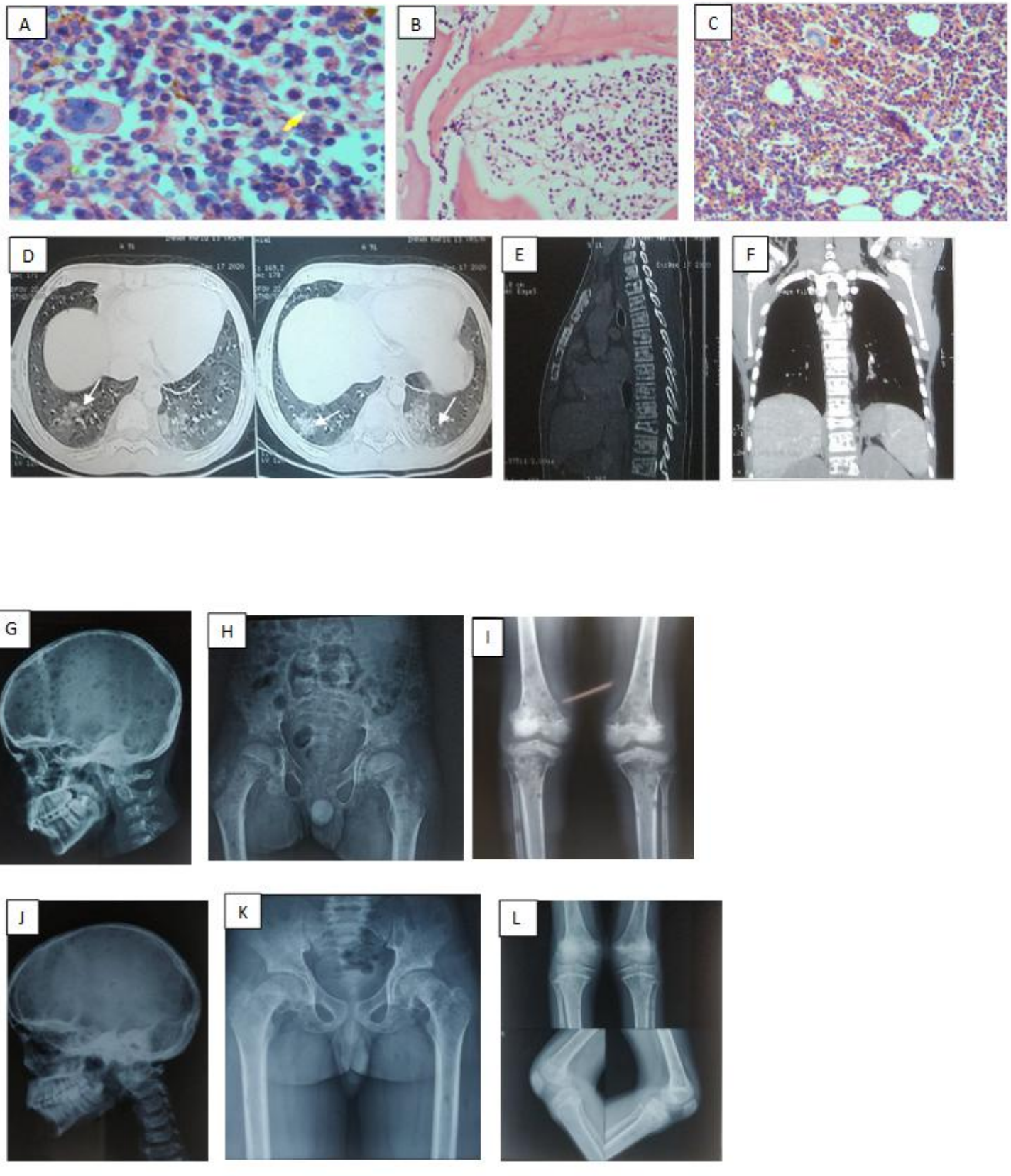

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