Pictorial Essay

Skeletal scintigraphy manifestations of hematologic disorders

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ABSTRACT

Skeletal manifestations are common in hematologic disorders. Benign entities such as Sickle cell disease develop microvascular embolization causing skeletal crisis. Leukemia, acute myeloblastic or lymphoblastic may develop bone marrow infarcts. Compromised immunity makes them susceptible to secondary infection leading to osteomyelitis or septic arthritis. Exposure to steroids may lead to osteonecrosis in these cases. Presented here is an atlas of various scintigraphic skeletal manifestations encountered over the past 10 years, in hematologic disorders.

Keywords: Acute myeloid leukemia, bone infarct, bone scan, chronic myeloid leukemia, osteonecrosis, Sickle cell anemia

INTRODUCTION

Skeletal symptoms are common in day to day practice. Elderly patients with mineral deficiency, degenerative changes, osteoarthritis etc may account for a large proportion of these cases. However, young patients or grown up patients with progressive skeletal manifestations may be specifically evaluated to rule out some systemic conditions. Hematologic disorders may also present with such symptoms and critical review of bone scan in such cases may help in early settlement of diagnosis. Present study highlights some important hematologic condition in pictorial essay.

MATERIALS AND METHODS

Skeletal scintigraphy was performed in the presented cases using Technetium 99 m-methylene diphosphonate. A dose of 150–750 MBq was used depending upon the age. Imaging was performed three to 4 h post-radiopharmaceutical administration E-Cam or Symbia gamma camera (Siemens, Erlangen, Germany) systems using a low-energy high resolution collimator. Matrix size used was 512 × 512.

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Three phases scanning was done in patients with clinically localizing symptoms. Images were interpreted using dicom studies.

CASES AND DISCUSSION

Sickle cell anemia

Sickle cell anemia was first described in 1910.[1] It is an autosomal recessive hemoglobinopathy. Hemoglobin electrophoresis and chromatography studies have demonstrated substitution of thymine for adenine in the glutamic acid codon of DNA, which, results in substitution of valine for glutamic acid in the sixth position on the beta globin chain of hemoglobin molecule.[2,3] The major genotypes are Sickle cell (SS homozygous), Sickle cell C (SC Sickle hemoglobin C), Sickle beta thalassemia disease. Sickle cell trait is seen in a small population. Diagnosis is made by demonstration of various migration pattern of normal and hemoglobin S during electrophoresis. The difference in migration patterns of normal and hemoglobin S seen during electrophoresis is due to substitution of valine for glutamic acid resulting in two fewer negative charges in the abnormal molecule.

When a cell repeated Sickles because of deoxygenation, its membrane is permanently altered.[4,5] These end-stage cells are responsible for clinical manifestations of Sickle cell anemia such as recurrent painful episodes, chronic organ dysfunction and chronic hemolytic anemia. Gall stones, hemolytic jaundice, poorly healing ulcers of shin are some other complications.

Case 1

Illustration of avascular necrosis, cortical bone infarct, soft tissue infarct in Sickle cell anemia [Figure 1].

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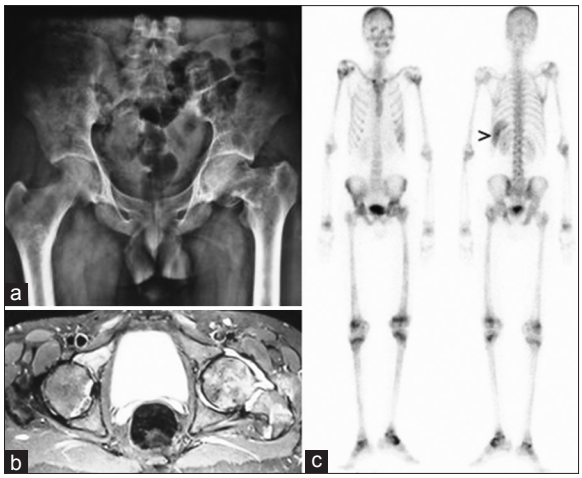

Figure 1: A 24-year-old man presented with pain in the hip. His hemoglobin was 8 g per deciliter, hemoglobin electrophoresis result: Hemoglobin (Hb) Ao 49% (reference range 80-99%), Hb A 2 2.9% (reference range <2-3.5%), Hb F 0.5% (<2.5%), Hb S 41.9% (<0.9%), Hb D nil, Hb C nil. Plain radiograph; (a) Revealed osteolytic lesion in the superolateral quadrant of head of left femur,(b) Magnetic resonance imaging revealed osteonecrosis in the head of left femur. Bone scan; (c) Showed increased inhomogeneous tracer distribution in the shaft of long bones bilaterally, pelvis bilaterally suggesting cortical infarcts. The head of left femur shows cold area with increased inhomogeneous uptake within, that is compatible with osteonecrosis. There is soft tissue tracer localization in the spleen (>) typical of Sickle cell anaemia

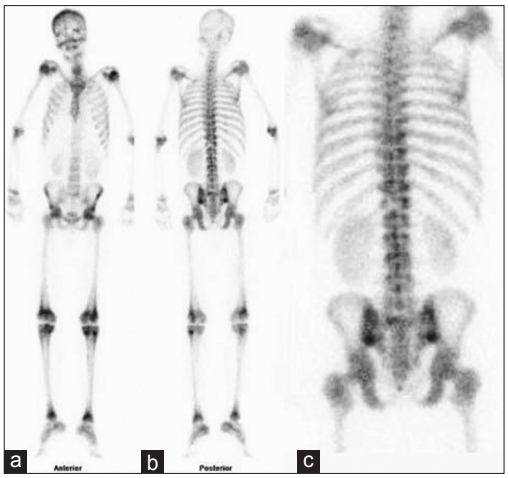

Figure 2: A known case of congenital hemolytic anaemia, this 52-year-old man had backache of 10 days duration. Plain radiograph (not shown here) was normal. Bone scan revealed photon deficiency in D12 vertebra suggesting bone infarct. The distal metaphysis of long bones were expanded (remodeled) as a result of prolonged hemolytic anemia

Musculoskeletal manifestation is the most common cause of morbidity in Sickle cell anemia.[6] Painful crisis usually affects the meta-diaphyseal region and can involve multiple sites. Juxta-articular involvement may cause joint effusion.[7,8] Onset is usually at 5 years and progress until 30 years.[9] Precipitating factors include fever, dehydration, infection, acidosis, hypoxia and pregnancy.[10]

Presented is a known case of hemolytic anemia with hip pain. Bone scan revealed features of osteonecrosis of head of the left femur, the long bones revealed linear cortical uptake at multiple sites suggestive of cortical infarcts. Spleen revealed soft-tissue localization because of recurrent microvascular infarcts.

Case 2

Illustration of infarct, remodeling in hemolytic anemia had a backache of 10-day duration at presentation. He was a known case of congenital hemolytic anemia. Bone scan revealed cold area in D12 vertebra suggesting infarction. The distal metaphysis of femur and proximal metaphysis of tibia appear to be expanded. This is a manifestation of persistence of hematopoiesis in long bones in view of recurrent hemolysis [Figure 2].

Acute myeloid leukemia

Skeletal manifestations have been described in acute leukemia. These are osteolysis, osteopenia, metaphyseal bands, pathological fractures, osteosclerosis, periosteal reaction, mixed lysis-sclerosis. It has been suggested that unexplained persistent skeletal pain and radiologic alterations should be investigated for acute leukemia.[11] Massive periosteal reaction has been reported in a variant of acute myeloid leukemia.[12] Post-bone marrow transplantation graft versus host disease related myositis has also been reported.[13]

Osteonecrosis can occur because of steroids or chemotherapy (all trans-retinoic acid). Alterations in fat metabolism with vascular occlusion due to fat embolization, as well as microtraumata and osteoporosis are etiologic factors. Multifocal aseptic osteonecrosis has been reported in acute leukemia.[14,15]

Plain radiogram is usually the first investigation to be performed. It is less sensitive in detecting early changes. Bone scintigram and magnetic resonance imaging show early changes with variable sensitivity and specificity.[16] Both early and delayed phase of bone scan must be acquired to increase the sensitivity of the test.[17]

Case 3

Illustration of cortical infarcts in acute leukemia. A 4-year-old boy presented with weakness in lower limbs. Plain radiograph was normal. Three phase bone scan showed diffuse uptake of tracer in the shaft of femur bilaterally suggesting cortical infarcts. Hematologic work up revealed acute myeloid leukemia [Figure 3].

Case 4

Illustration of osteonecrosis of humeral head secondary to steroid treatment was a known case of T cell lymphoblastic leukemia, which had allographic stem cell transplant. He was on long-term steroid therapy and complained of pain in the shoulder joint bilaterally. Bone scan revealed diffuse increased tracer uptake in the head of humerus bilaterally suggesting osteonecrosis [Figure 4].

Superselective angiographic study in patients at risk for osteonecrosis with steroid therapy has shown obliteration of branches of the superior retinacular arteries as well as failure of revascularization.[18-20]

Chronic myeloid leukemia

Chronic myeloid leukemia is a myeloproliferative disorder with clonal expansion of transformed primitive hematopoietic progenitor cells. It comprises 15% of all adult leukemias. The

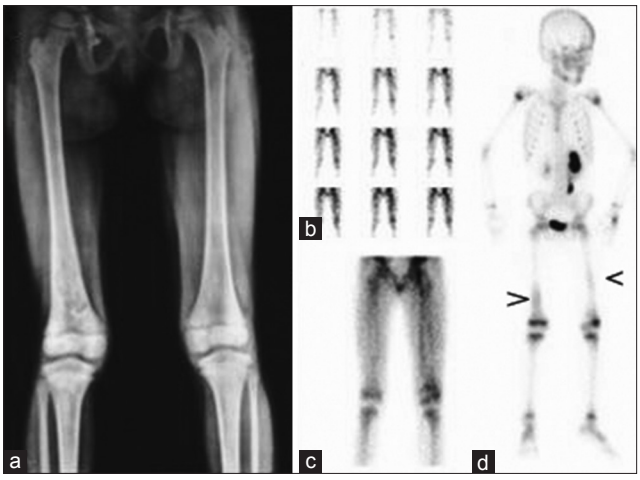

Figure 3: A 4-year-old male child presented with weakness of few days in lower extremities and inability to bear weight. There was mild fever. Plain radiograph was unremarkable; (a) A working diagnosis of osteomyelitis of femur was made clinically. Three phase bone scan revealed diffuse increased tracer localization in the distal shaft of right femur (>) and mid shaft of left femur (<); (d) Perfusion and blood pool images did not favor the diagnosis of osteomyelitis; (b,c) Hematologic work up was suggested suspecting this to be bone cortical infarcts. Subsequent work up revealed acute myeloid leukemia

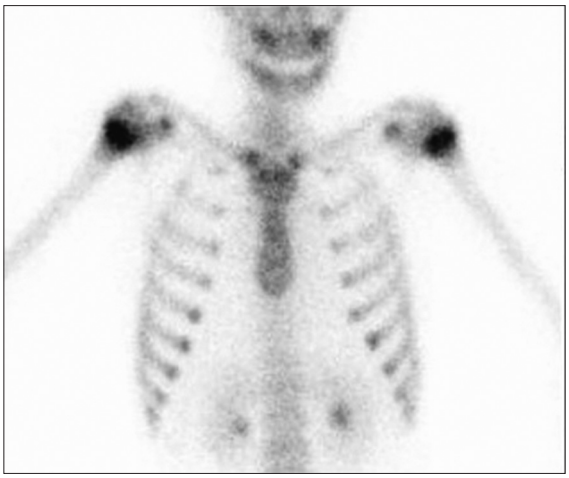

Figure 4: A known case of acute T cell lymphoblastic leukemia on treatment underwent allographtic stem cell transplantation. His hemogram was as follows: Hemoglobin 10.2 g/dL, red blood cell 2.22 10^6/uL (N 4.50-6.50), white blood cells=200/cmm (N 4000-10000) Neutrophils 21.6% Lymphocytes 47.4%, Monocytes 30.6%, Eosinophils 0.4%, Basophils 0%. He was on steroid therapy. He presented with pain in the shoulders bilaterally. Bone scan revealed diffuse uptake of radiotracer in the head of shoulder bilaterally suggesting osteonecrosis

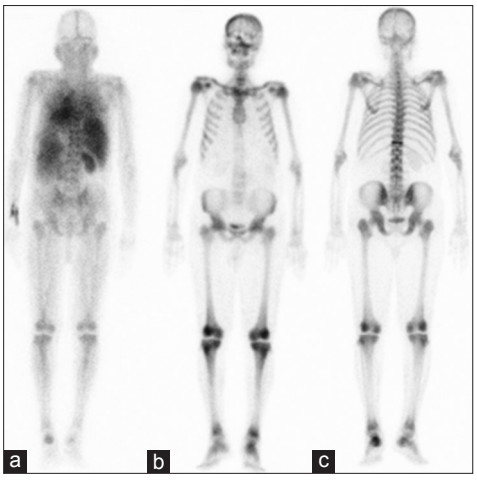

Figure 5: A 67-year-old known case of chronic myeloid leukemia had backache. Plain radiograph was normal. Bone scan revealed D12 vertebra showed linear uptake suggesting osteoporotic collapse. Whole body study revealed diffuse increased tracer localization in the axial and appendicular skeleton. Hyperactive bone marrow was probably responsible for such a pattern that simulated metabolic bone disease. Please note diminished tracer localization in the kidneys

Philadelphia chromosome (Ph), which results from a translocation between the long arms of chromosomes 9 and 22, *t* (9; 22) (q34; q11), can be demonstrated in 90% of patients with chronic myeloid leukemia (CML).

The condition may be diagnosed incidentally in asymptomatic patients as there are two phases of the disease-an indolent benign (chronic) phase or the acute blast phase. Exposure to steroids can make the skeleton osteoporotic and susceptible to fractures.

Case 5

Illustration of osteoporotic collapse Early whole-body images show increased tracer pooling in the metaphysis of long bones as well as the dorsolumbar vertebrae. Delayed images show linear uptake in thoracic 12 vertebra suggesting osteoporotic collapse. In addition diffuse uptake in axial and appendicular skeleton indicating high turnover of minerals in the skeleton. This is related to diffusing bone marrow involvement or underlying metabolic bone disease [Figure 5].

CONCLUSION

Skeletal manifestations in various hematologic disorders are described. Bone scan is a non-specific investigation. Any insult that interferes with osteoblastic activity of the skeleton will appear to be hot. However, critical evaluation of scintigrams along with judicious review of clinical manifestations can help in making the diagnosis of underlying hematologic disorders. Some of these are subtle and the interpreter must be aware of these to avoid delay in diagnosis and management.

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