SERIAL BONE-SCAN CHANGES IN RECURRENT BONE INFARCTION

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Recurrent bone infarcts in a black man produced a changing pattern of bone-scan abnormalities. Areas initially cold at the infarction site returned to normal over a period of months. Hyperconcentration was frequently noted during the healing phase. In the acute phase scanning was specific and more sensitive than radiography.

Infarction of bone may produce severe localized symptoms with only minimal radiographic changes in the acute phase (*1,2*). The radiographic picture of bone infarction may be indistinguishable from that of osteomyelitis (*3*) and the clinical differentiation from osteomyelitis may also be difficult, particularly in sickle cell disease where a propensity for either of these complications exists.

Having had the opportunity to assess the evolution over several years of recurrent bone infarcts in a patient with sickle cell anemia, we wish to report the bone-scan findings in this condition.

CASE HISTORY

The patient was a 25-year-old black man known to have sickle cell anemia. After experiencing his first sickling crisis at the age of 4, he suffered approximately one crisis per year, but the frequency and severity of the crises had been increasing. Both parents and two cousins had the sickle-cell trait and one maternal aunt had died of sickle cell anemia. Hemoglobin electrophoresis showed a band in the hemoglobin S region. Hemoglobin F represented 8.4%

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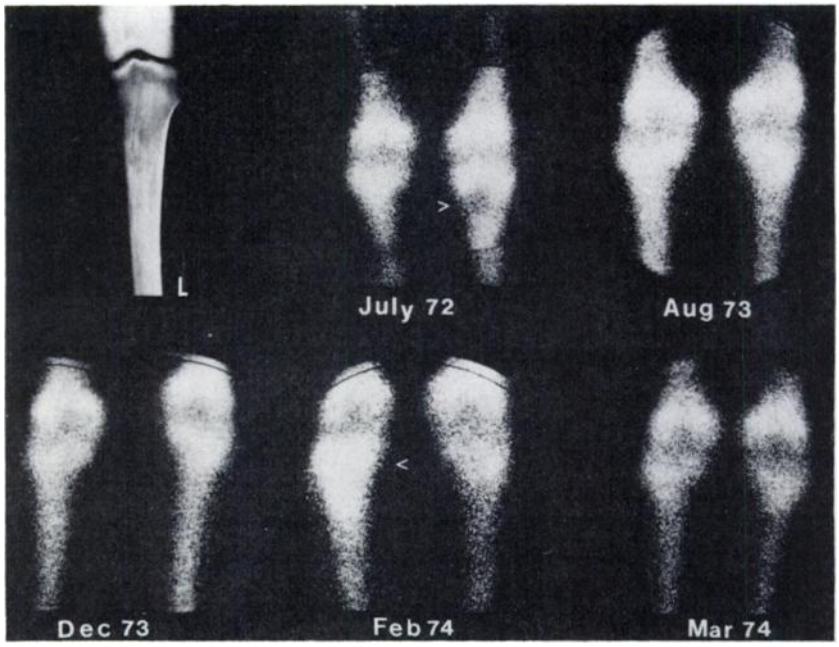

FIG. 1. Proximal tibia and tibial epiphysis infarctions. Tomogram of proximal left tibia during episode of acute pain showing spotty demineralization. July 1972: Cold area (arrow) in proximal left tibia corresponding to region of radiographic change and clinical symptoms. August 1973: Scintigram returns to normal. December 1973: Normal scintigram during period of acute pain in proximal right tibia. February 1974: Increased uptake in proximal right tibia (arrow). March 1974: Scintigram returns to normal.

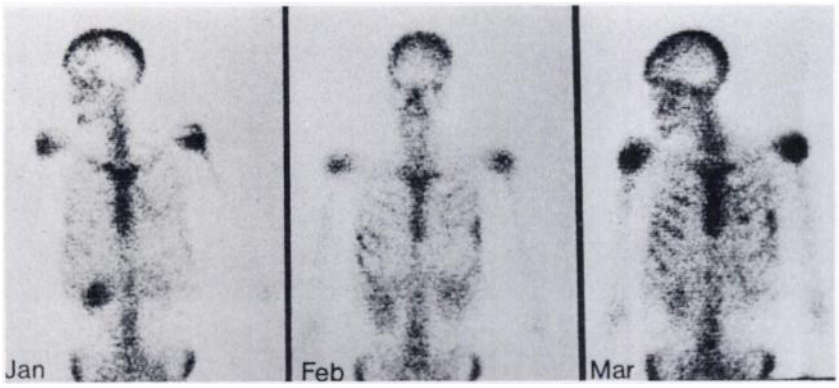

FIG. 2. Rib infarctions. January: Poor delineation of ribs with spotty uptake. February: Bilateral foci of increased uptake in ribs. March: Further increased uptake in some regions of ribs bilaterally.

of the hemoglobin present. No hemoglobin A was present.

The patient has been followed at our hospital since 1969. Initially radiographs were used to assess the patient's complaints. Prior to 1972, despite skeletal pain in various areas, repeated radiographic examinations showed no abnormalities at the onset of symptoms although evidence of bone infarction was established later. Since 1972 both radiographs and bone scans have been used concomitantly to assess the musculoskeletal crises. Bone scanning was performed on a General Electric dual 5-in. rectilinear scanner in the 5:1 minification mode, 2 hr after intravenous injection of 15 mCi of ^{99m}Tc-polyphosphate. Abnormal areas were also scintigraphed with a Pho/Gamma HP camera with a low-energy parallel-hole collimator.

In July 1972 the patient experienced acute pain in the proximal left tibia. A radiograph (Fig. 1) revealed an ill-defined central radiolucency with spotty demineralization and irregular areas of slight sclerosis in that region. The appearance was compatible with either bone infarction or osteomyelitis. The initial bone scan (July 1972) showed decreased activity in this area, suggesting bone infarction. The activity had returned to normal when the patient was rescanned about 1 year later (August 1973).

In January 1974 the patient experienced bilateral rib pain. The bone scan (Fig. 2) showed areas of diminished uptake in the anterior ribs. The condition resolved approximately 2 weeks later; scanning then (February 1974) showed areas of increased activity. Seven weeks after the initial symptoms, the bone scan showed persistent osteoblastic activity in several ribs bilaterally. A similar sequence of changes was noticed in the right upper femur (Fig. 3) and proximal right humerus (Fig. 4). These show decreased uptake at the onset of the acute symptoms; uptake increased later, indicating osteoblastic activity.

The possible exception to this usual sequence occurred in the right upper tibia (Fig. 1), studied in December 1973 at the time of severe pain in the proximal right tibia. Two months later (February 1974), scanning showed increased uptake in the epiphyseal region and proximal right tibia. This was transient, however, and in March 1974 the activity in both tibiae was symmetric. No "cold phase" was recorded.

Significant laboratory investigations included negative blood cultures. Alkaline phosphatase levels remained within normal limits. Hemoglobin levels varied over 8–11 gm% with a hemoglobin fall of 1–2 gm% during a crisis. White blood cell counts rose from 15,000 to 18,000 cells/mm^3 during a crisis.

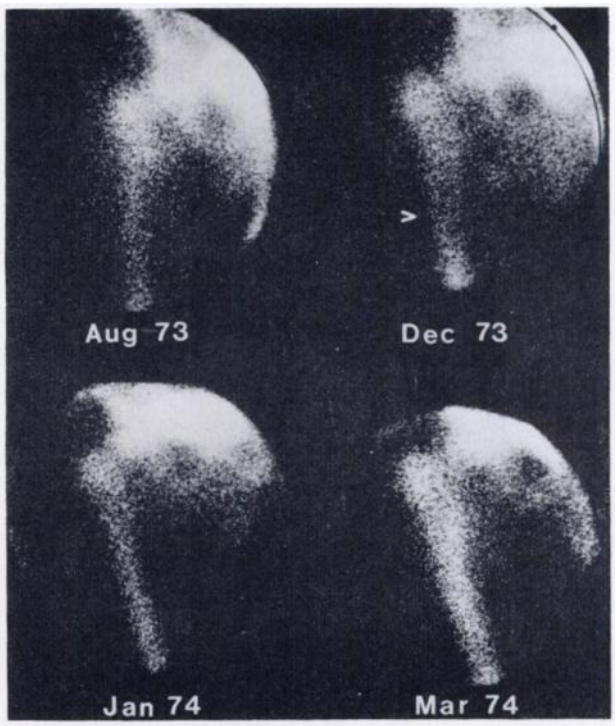

FIG. 3. Proximal right femur infarction. August 1973: Baseline study; patient asymptomatic. December 1973: Decreased uptake in proximal femur (arrow) during period of acute regional pain. January 1974: Homogeneous uptake now noted. March 1974: Generalized increased uptake in proximal right femur.

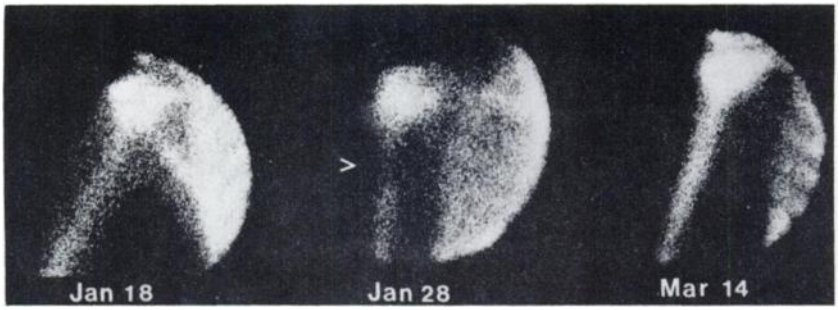

FIG. 4. Infarct in proximal right humerus. January 18: Baseline scintigram; patient asymptomatic. January 28: Decreased uptake in proximal humerus (arrow) corresponding to location of acute pain. March 14: Increased uptake in proximal humerus during period of resolution of infarction.

DISCUSSION

Under conditions of deoxygenation or acidosis, the abnormal hemoglobin in sickle cell disease undergoes a conformational change which distorts the red blood cells to produce sickle cells. In the homozygous individual, except for small quantities of hemoglobin F, all of the hemoglobin is hemoglobin S. Because of the high concentration of hemoglobin S in these individuals, sickling of the erythrocytes may occur under normal physiologic conditions (*4*). The sickled red corpuscles become trapped in small vessels and erythrostasis occurs. Plugs or masses of irreversibly sickled cells become solid enough to occlude vessels (*5*). Thrombosis and infarction readily follow. Bone pain in crises may be due to ischemia or to distension of the intramedullary cavity by vascular engorgement (*5*).

Radiographs are generally of little benefit in assessing an acute episode. When bone changes occur early in the course of symptoms, the spotty demineralization of the bone is difficult to differentiate from osteomyelitis. Later changes include periosteal reaction and irregular calcification within the infarcted area. Frequently radiographs show no abnormalities at any time. The same response to infarction incites connective-tissue cells to differentiate into bone cells. In young individuals new bone formation may be detected as early as 48 hr after injury (*6*).

Brookes (*7*) has noted massive cortical death in bones due to venous obstruction. This initiates the proliferation of cells from the periosteum and ultimate differentiation of osteoblasts in the vascular granulation tissue infiltrating the periphery of the infarct. Eventually the necrotic area becomes the focus of hyperemic inflammatory reaction and osteogenic activity.

Profound ischemia of the bone marrow may also occur independently of ischemia to the cortex (*7*). DeNardo (*8*) used bone-marrow scanning to show infarcts in bone marrow. However, he found no resolution of infarcts in serial bone-marrow scans. The reaction of compact bone to medullary ischemia is a widening of cortical vascular channels and the appearance of numerous bone-forming cells to replace the infarcted bone-marrow elements (*7*).

Bone scanning has been shown to be a very sensitive technique of assessing osteoblastic activity and bone perfusion (*9,10*). We have noted sequential changes following bone infarction using ^{99m}Tc-polyphosphate. Initially a focal area of decreased activity appears, corresponding to the local ischemia. Later increased activity, corresponding to the phase of hyperemia and osteoblastic repair, is shown. This later hyperactivity subsides as the infarct heals. The exception to this sequence may occur at the epiphyseal location if epiphyseal collaterals are adequate. No true infarct would occur in this situation, but the ischemia is sufficient to stimulate osteoblastic repair, shown by increased uptake without an initial "cold" area being demonstrable.

In osteomyelitis, on the other hand, our experience has been that the initial hyperemia of the involved area is detectable by blood pool studies and, except in areas of extreme osteolysis, the bone scan is consistently hot.

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