Delineation of Peripheral Bone Infarcts in a Child with a Rare Hemoglobinopathy (SO_{Arab}) and Purpura Fulminans: Case Report

William C. Klingensmith III, Elizabeth H. Danish, George J. Dover, and Henry N. Wagner, Jr.

Johns Hopkins Medical Institutions, Baltimore, Maryland

A 27-month-old patient with SO_{Arab} hemoglobinopathy complicated by purpura fulminans was studied with ^{99m}Tc-pyrophosphate. The study showed an absence of radiotracer in the bones of both feet and the distal portions of both hands, along with an increased concentration of radiotracer proximal to the regions of absent radiotracer. Subsequent amputation of the distal portions of all four extremities was necessary because of dry gangrene. The amputation site in each extremity (selected on clinical grounds only) corresponded closely to the junction of absent and increased bone radiotracer, suggesting that bone imaging may be used as an aid in determining the extent of nonviable tissue in similar patients.

J Nucl Med 17: 1062–1064, 1976

We have studied a patient with a rare hemoglobinopathy (SO_{Arab}) complicated by pneumococcal sepsis and purpura fulminans; he eventually required amputation of the distal ends of all four extremities for dry gangrene. This patient illustrates: (A) how bone infarcts can appear as areas of absent radiotracer in bone imaging studies; (B) how the increased concentration of radiotracer usually seen in osseous lesions in bone imaging depends on preservation of blood flow; and (C) how bone imaging may be useful in determining amputation sites.

CASE REPORT

A 27-month-old black boy with known hemoglobin SO_{Arab} presented with a 20-hr history of fever and grunting respirations. His past medical history was remarkable for several episodes of the "hand–foot" syndrome and at least three pneumonias. On physical examination there was a generalized morbilliform rash and cyanosis of the nail beds. All pulses were present. Initial laboratory data included a hematocrit of 24%, reticulocyte count of 12.8%, and a white blood cell count of 22,900/mm^3, with a differential of 32 bands, 52 neutrophils, 14 lymphocytes, and 2 monocytes. A chest radiograph showed an enlarged heart and normal lungs. The patient was started on intravenous antibiotics for probable sepsis, and blood cultures grew *Streptococcus pneumoniae* within 24 hr.

Several hours after admission, the distal cyanosis spread to involve both feet, the entire left hand, and parts of the right hand. Purpuric lesions appeared on the knees, axillas, and upper arms. The dorsalis pedis pulses became weak and then nonpalpable as the feet and left hand lost motor function and became black, painful, and cold. At that time the platelet count was 64,000/mm^3, prothrombin time was 33 sec (control, 12 sec), fibrin split products were positive at 1:128, fibrinogen was 155 mg% (normal, above 200 mg%), and partial thromboplastin time was 70 sec (control, 34 sec). The diagnosis of purpura fulminans was made and the patient was treated with packed red blood cells, fresh plasma transfusions, and corticosteroids. Within 24 hr his vital signs had returned to normal, but evidence of dry gangrene involving both feet, the entire left hand, and parts of the right hand had developed.

Received Dec. 26, 1975; revision accepted June 1, 1976.

For reprints contact: William C. Klingensmith III, Nuclear Medicine Service, Veterans Administration Hospital, 1055 Clermont St., Denver, CO 80220.

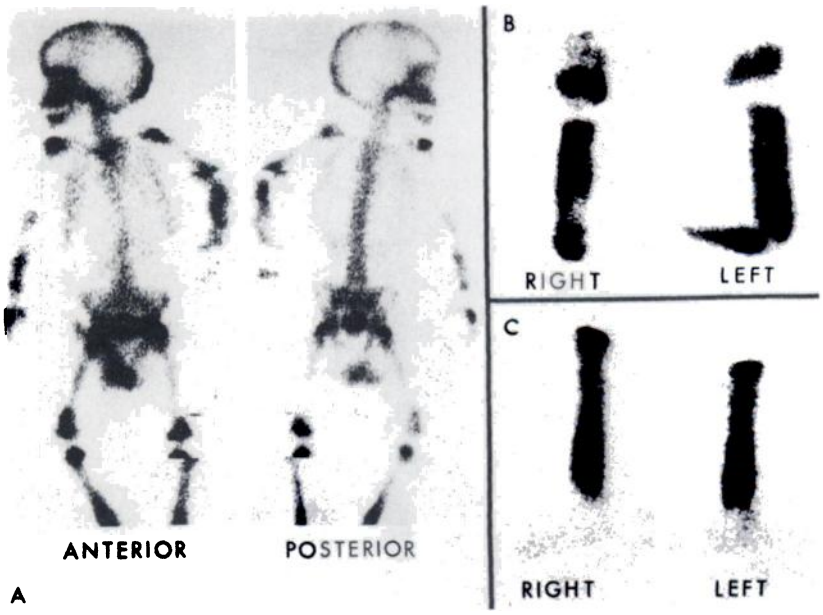

FIG. 1. Preoperative bone-imaging study with ^{99m}Tc-pyrophosphate: (A) whole body, (B) hands and forearms, (C) feet and legs. Radiotracer is absent from bones of fingers of left hand, distal portion of right index finger, and both feet, along with increased radiotracer concentration proximally in tibias, radii, ulnas, and metacarpal bones. Usual amount of soft-tissue radiotracer is present adjacent to areas of both absent and increased bone radiotracer.

Twelve days after admission, radiographs of the extremities revealed distal osteoporosis and soft-tissue swelling of the right leg and left distal forearm. A ^{99m}Tc-pyrophosphate bone study on the 16th hospital day showed absence of radiotracer in the bones of both feet, the fingers of the left hand, and the distal portion of the right index finger (Fig. 1). Proximal to the regions of absent radiotracer there were regions of increased radiotracer concentration involving the distal tibias, radii, ulnas, and metacarpal bones. The usual amount of radiotracer was present in the soft tissues surrounding the regions of absent and increased bone radiotracer. On the 22nd hospital day there was sufficient demarcation between gangrenous and viable skin so that amputations of both feet just above the ankle joints and of the fingers of the left hand just proximal to the proximal interphalangeal joints were performed. The pathologic diagnosis was gangrene of all specimens and osteomyelitis of the distal ends of the tibia and fibula bilaterally.

A followup study with ^{99m}Tc-diphosphonate on the 46th hospital day showed amputations of both feet and fingers of the left hand at a level corresponding closely to the junctions between absent and increased concentration of radiotracer on the first bone-imaging study. The more proximal areas of increased radiotracer were unchanged from the first study. An image of the right hand with a pinhole collimator confirmed the absence of radiotracer in the distal phalanx of the index finger. Following this study, this phalanx was amputated and the pathologic diagnosis was gangrene and osteomyelitis. The patient was discharged on prophylactic penicillin and was to have prostheses made at a later date.

DISCUSSION

The most interesting finding in this unusual patient was the striking correlation between the junction of absent and increased bone radiotracer and the subsequent amputation site in each extremity. This correlation probably reflects the major role that perfusion plays in determining both the distribution of the radiotracer and the viability of bone. Localization of most radiotracers is a function of blood flow as well as metabolic factors governing extraction efficiency. Most osseous lesions appear as areas of increased radiotracer concentration on bone imaging, but areas of decreased radiotracer occur in association with decreased or absent blood flow, or replacement of bone by tumor that does not extract the radiotracer (*1–3*). In the patient reported here the absence of radiotracer in the bones of the feet and the distal phalanges of the hands was attributable to intravascular coagulation secondary to the underlying hemoglobinopathy, with complete bloodflow obstruction. The increased concentration of radiotracer in the more proximal bone was attributable to increased blood flow or metabolic activity of bone as a result of injury to the microcirculation and osteomyelitis. The normal concentration of radiotracer and the development of swelling in the soft tissues of the hands and feet suggest that blood flow to the distal soft tissues was partially preserved.

Only ten previous patients with SO_{Arab} hemoglobinopathy have been reported, and of these none developed purpura fulminans (*4*). Both hemoglobin S ($\alpha_2\beta_2^{6Glu\rightarrow Val}$) and hemoglobin O_{Arab} ($\alpha_2\beta_2^{121Glu\rightarrow Lys}$) are inherited as independent Mendelian traits. Most patients with this hemoglobin combination are clinically indistinguishable from SS hemoglobinopathy

(homozygous sickle cell disease) (*4*). Purpura fulminans is characterized by confluent painful purpuric lesions on the extremities, face, and lower back and is almost always preceded by a bacterial or viral infection. It is usually associated with disseminated intravascular coagulation and often results in gangrene of the extremities (*5*).

While purpura fulminans is an unusual complication, other complications involving the distal extremities are not. Young children (1–4 years) with sickling hemoglobinopathies often present with the relatively benign "hand–foot" syndrome (*6*). This syndrome is characterized by fever accompanied by pain and swelling of the hands and feet; all resolve spontaneously in 2–4 weeks. Radiographs are initially normal except for soft-tissue swelling, but 1–2 weeks later transient osteoporosis, lytic lesions, and periosteal new-bone formation are frequently observed (*6*). We know of no reports of bone imaging in patients with the "hand–foot" syndrome.

Although decreased radiotracer concentration on bone imaging with ^{99m}Tc-phosphate compounds has been described previously in bone infarcts in patients with sickling hemoglobinopathies, none of these patients developed purpura fulminans or required amputation (*1–3*). In the present patient amputation was delayed for several weeks to await better demarcation between gangrenous and viable skin. Our tentative conclusion is that bone imaging in similar patients with peripheral gangrene may be helpful in the earlier delineation of demarcation sites.

ACKNOWLEDGMENTS

Aid in characterizing hemoglobin SO_{Arab} was provided by Samuel Charache, Department of Medicine, Johns Hopkins Hospital.

Dr. Klingensmith is supported in part by USPHS Grant GM 10548 and NIH Fellowship 1 F 22 HL 0014-01 RAD. Dr. George J. Dover is supported by NHLI Research Grant T 32 HL-07143-01 TEC.

REFERENCES

1. GOERGEN TG, ALAZRAKI NP, HALPERN SE, et al.: "Cold" bone lesions: A newly recognized phenomenon of bone imaging. *J Nucl Med* 15: 1120–1124, 1974

2. SY WM, WESTRING DW, WEINBERGER G: "Cold" lesions on bone imaging. *J Nucl Med* 16: 1013–1016, 1975

3. MAJD M, FRANKEL RS: Radionuclide imaging in skeletal inflammatory and ischemic disease in children. *Am J Roentgenol Radium Ther Nucl Med* 126: 832–841, 1976

4. MILNER PF, MILLER C, GREY R, et al.: Hemoglobin O Arab in four Negro families and its interaction with hemoglobin S and hemoglobin C. *N Engl J Med* 283: 1417–1425, 1970

5. HJORT PF, RAPAPORT SI, JØRGENSEN L: Purpura fulminans: Report of a case successfully treated with heparin and hydrocortisone: Review of 50 cases from the literature. *Scand J Haematol* 1: 169–192, 1964

6. WATSON RJ, BURKO H, MEGAS H, et al.: The hand–foot syndrome in sickle cell disease in young children. *Pediatrics* 31: 975–982, 1963