Localization of Ga-67 in Inflammations in the Absence of Circulating Polymorphonuclear Leukocytes

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Two cases are reported in whom there were no circulating polymorphonuclear leukocytes, on peripheral blood smears, at the time when Ga-67 citrate studies were carried out. In both of these women, Ga-67 accumulated at sites of inflammation. This shows that nonpolymorphonuclear pathways are sufficient to deliver Ga-67 and to allow its accumulation. The possible roles of lymphocytes or of noncellular pathways (such as transferrin to tissue lactoferrin) are mentioned.

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The relative importance of various mechanisms in the localization of Ga-67 citrate in inflammatory lesions is not yet defined. Accumulation of the radiolabel by polymorphonuclear leukocytes, and by microorganisms, may be reasons for the concentration in or around abscesses (*1*). Indeed leukocytes labeled in vitro with Ga-67, and then washed to rid them of noncell-bound activity, are effective in localizing experimentally induced abscesses (*2*). A distinct pathway not mediated by leukocytes may exist for transfer of Ga-67 to the site of lesions. Radiogallium is known to bind to transferrin. Recent evidence suggests that transferrin-bound Ga-67 can be taken up by the tissue protein lactoferrin (*3*). This assumes added interest when it is noted that human lactoferrin can exert a bacteriocidal effect (*4*). We have recently encountered two patients, with no demonstrable circulating polymorphonuclear leukocytes, in whom Ga-67 did localize at inflammatory sites. This suggests that a pathway via lymphocytes or noncellular elements may be sufficient for radiogallium delivery and uptake.

CASE REPORTS

Case 1. A 43-year-old white woman developed aplastic anemia following gold therapy for rheumatoid arthritis. There had been an unsuccessful bone-marrow transplant. She was admitted with a history of epistaxis, vaginal bleeding, and petechiae over the extremities. Her medications included prednisone. She was afebrile, pale, and in acute distress. Aside from the petechiae there were no pertinent physical findings. Laboratory findings included a hemoglobin of 8.6 g/dl. The white cell count was 800/mm^3. The differential count showed 86% lymphocytes, 5% bands, and 9% polymorphonuclear leukocytes. Repeat white cell counts indicated 500–800/mm^3 with 96% lymphocytes and 4% bands. The platelet count was 20,000/mm^3. Bone-marrow biopsy revealed hypocellularity, especially of the granulocyte series. The patient was maintained on transfusions of packed cells and platelets and predisone was continued. A right middle lobe pneumonia, which developed during antibiotic therapy, was thought to be due to an opportunistic fungus infection. A lung biopsy revealed infarcted tissue and mycelia, likely representing *Aspergillus* (this was confirmed by culture). There was no evidence of polymorphonuclear or mononuclear cells in the biopsy. A radiogallium

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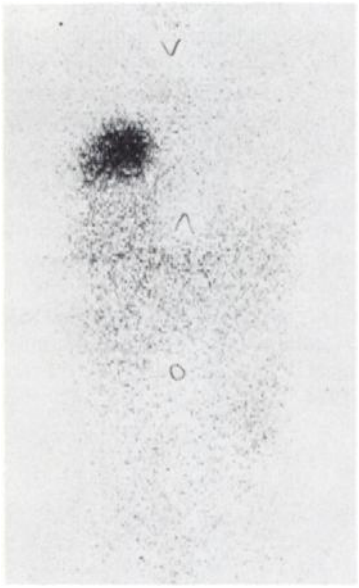

FIG. 1. Anterior rectilinear scan, performed 72 hr after i.v. administration of Ga-67 citrate in Case 1. Accumulation in right pulmonary lobe can be seen. Markings are at sites of sternal notch, xyphoid, and umbilicus.

study was performed following i.v. administration of 2.5 mCi of Ga-67 citrate. At that time there were no demonstrable polymorphonuclear leukocytes in the blood smear. Rectilinear scans at 24 and 72 hr (Fig. 1) revealed intense radioactivity in the area corresponding to the pulmonary fungal infection. Her condition deteriorated, despite supportive therapy and she died. An autopsy was not obtained.

Case 2. A 49-year-old white woman was in good health until 3 mo before admission, when she noted easy bruising. For 1 mo she had felt weak and short of breath. She was afebrile, pale, and not in acute distress. There were pinpoint erythematous papules over the nasal mucosa. Petechiae covered all extremities. The hemoglobin was 11.5 g/dl. The white cell count was 1,100/mm^3. The differential count was lymphocytes 86%, bands 7%, and polys 7%. The platelet count was 76,000/mm^3. Bone-marrow biopsy showed hypocellularity of the normal elements, with infiltration of primitive mononuclear cells, consistent with acute lymphatic leukemia. The patient was started on vincristine and prednisone. Packed red cells and platelet transfusions were given. One week later, while on chemotherapy, she began spiking a high fever and had chills. In an effort to locate an occult infection, she was injected with 2.5 mCi of Ga-67 citrate. At that time the white cell count was 800/mm^3. The differential count showed 89% lymphocytes, 10% atypical lymphocytes, and 1% bands; no polymorphonuclear leukocytes were seen on repeated examinations. Rectilinear scanning at 24 and 48 hr after radiogallium administration (Fig. 2) revealed an intense focus in the perirectal area (loose stools indicated that this was not rectal retention). Repeated urine examinations did not reveal any abnormality. The patient was placed on antibiotics and a perirectal abscess was surgically drained. Despite this, her condition deteriorated and she died. Permission for autopsy was denied.

FIG. 2. Posterior rectilinear scan in Case 2, obtained at 48 hr. Intense perirectal activity can be seen.

DISCUSSION

These two patients shared the feature of having essentially no circulating polymorphonuclear leukocytes. In each case, Ga-67 showed discrete localization that corresponded to an inflammatory site. This means that there must be at least one pathway for radiogallium deposition that is not polymorphonuclear-dependent. Gelrud and coworkers (6) had made monkeys leukopenic by use of cyclophosphamide, and then induced sterile lesions with turpentine. In one of the two monkeys, Ga-67 did localize at the inflammatory site. However, the cyclophosphamide may have had effects beyond those on leukocytes. The lesser avidity of lymphocytes for Ga-67 might account for the delivery of the radionuclide in our two cases when polymorphonuclear leukocytes were absent. Perhaps the noncellular pathway (transferrin to tissue lactoferrin) accounts for the observation. It has been suggested that Ga-67 bound to lactoferrin might be an intracellular agent involved in the localization of radiogallium (*5*). Lactoferrin is known to be present in high concentrations in grannulocytes and a number of normal tissues such as colonic mucosa, bone marrow, spleen, salivary

glands, and nasal secretions. Although still other mechanisms must be sought, the two patients reported here clearly establish that the nonpolymorphonuclear pathway is sufficient to enable radiogallium delivery and accumulation to occur in inflammatory sites.

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