

Abnormal Gallium-67 Skull Uptake: A Sign of Peripheral Marrow Activation in HIV-Positive Patients with Disseminated Mycobacterioses

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The purpose of this study was to investigate the significance of abnormal ^{67}Ga -citrate skull uptake in AIDS patients with mycobacterioses. **Methods:** Gallium-67 scans of 39 HIV-positive patients who had been diagnosed with mycobacterioses were analyzed; the scans of 15 consecutive HIV-positive patients without mycobacterioses were also reviewed as a control group. The skull was chosen to assess bone marrow uptake because of the absence of overlapping structures. **Results:** Twenty-nine of 39 (74%) patients with mycobacterial infections had disseminated disease. Gallium-67 uptake in the skull was visualized in 24 of these 29 patients (82%). One of the patients without disseminated disease and one patient in the control group ($n = 15$) showed skull uptake. **Conclusion:** Abnormal ^{67}Ga skull uptake appears to be a sensitive (82%) and specific (92%) indicator of disseminated mycobacterial infection in HIV-positive patients.

Key Words: gallium-67 imaging; skull activity; disseminated mycobacterioses; AIDS

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The incidence of mycobacterioses related to HIV infection in developed countries is increasing, due in part to improved life expectancies in HIV-positive patients (1). The diagnosis of AIDS-related mycobacterial infection is frequently difficult because there may be nonspecific clinical symptoms due to disseminated, rather than focal, disease.

The role of ^{67}Ga -citrate scans in tuberculosis and *Mycobacterium avium* (*M. avium*) complex infection has been assessed elsewhere (2-5). The aim of this study was to investigate whether there is alteration of the usual ^{67}Ga distribution in the bone marrow in HIV-positive patients suffering from disseminated mycobacterial infection.

MATERIALS AND METHODS

Patients

We prospectively analyzed the scans of 39 HIV-positive patients with mycobacterioses (30 men, 9 women, aged 20-42 yr). Thirty-one were drug abusers and nine were homosexuals. Diagnosis was established by culture of *M. avium* complex or *M. tuberculosis*, chest roentgenogram showing a miliary nodular pattern, or biopsy-proven noncaseating or caseating epithelioid granulomas. Disseminated disease was assessed if bone marrow culture was positive, mycobacteria were cultured from more than one source or a biopsy demonstrated epithelioid granuloma in more than one organ. These patients exhibited clinical symptoms of fever ($n = 25$), respiratory symptoms ($n = 18$), palpable lymphadenopathies ($n = 111$), constitutional syndrome ($n = 6$) and others ($n = 13$). Samples for microbiologic study were taken within 7 days of the ^{67}Ga scan. Bone marrow samples of 30 patients were cultured and those of 24 patients underwent cytological studies.

Gallium-67 Scan

Each patient received 185 MBq (5 mCi) ^{67}Ga -citrate intravenously. Scanning was performed 48 and, if necessary, 72 hr after tracer injection. Imaging was performed with a large field of view gamma camera and a medium-energy, parallel-hole collimator. Images were obtained with a triple photopeak of ^{67}Ga (20% window centered in 93, 185 and 300 keV). Anterior and posterior views of the whole body were taken. The scans were interpreted by at least two experienced nuclear medicine physicians. Small uptake was graded as increased or normal.

Results were compared with the control group, which consisted of 15 consecutive HIV-positive patients who were studied in our institution the first six months of 1994 for fever of unknown origin. Mycobacteriosis was excluded in these patients.

RESULTS

Twenty-eight patients had tuberculosis and the remaining 11 had *M. avium* complex infection. Of the 29 patients diagnosed with disseminated mycobacterioses, 11 yielded positive culture for *M. avium* complex infection and 18 for *M. tuberculosis*. Skull uptake in the ^{67}Ga scan was visualized in 24 of the 29 patients with mycobacterioses (82%) (Fig. 1). Of these 24 patients, 13 had been diagnosed with tuberculosis and 11 with *M. avium* complex infection.

Skull uptake was present in one patient with ganglionic tuberculosis and without evidence of disseminated disease. This patient had peripheral leucocythroblastosis, but died

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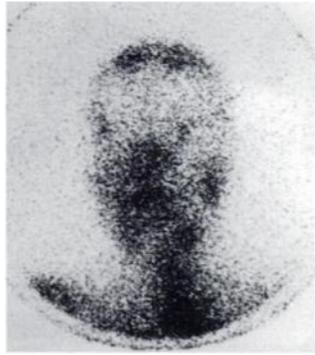


FIGURE 1. Abnormal ^{67}Ga skull uptake in an AIDS patient with fever of unknown origin. Bone marrow culture was positive for *M. avium*.

before bone marrow biopsy was performed. No other patient with mycobacterioses without disseminated disease showed ^{67}Ga skull uptake.

One patient in the control group exhibited intense ^{67}Ga skull uptake but no evidence of mycobacterioses. In this patient, who also showed focal uptake in the left axillary region, a diagnosis of Burkitt's lymphoma with bone marrow involvement was made. Skull uptake was not seen in any other patient in this group (Table 1).

Hematological findings in the peripheral blood of patients with mycobacterioses were as follows: for all 39 patients, anemia occurred in 25 (64%), leukocytosis in 2 (5%), neutropenia in 11 (28%) and lymphocytopenia and thrombocytopenia in 37 (94%) and 9 (23%), respectively. The patient with peripheral leukoerythroblastosis had anemia, leukocytosis with neutrophilia and lymphocytosis. No other patient showed evidence of hematological disease.

Bone marrow aspiration was performed in 24 patients. Sixteen had hypercellular bone marrow with granulomata, giant cells and megaloblastic changes. Bone marrow culture for mycobacteria was positive in 22 patients.

Skull uptake yielded a high sensitivity (82%) and specificity (92%) in assessing disseminated disease in HIV-positive patients with mycobacterioses.

DISCUSSION

The most common mycobacteria located in AIDS-related mycobacterioses vary according to the different epidemiologic conditions in each region and risk group. With a high prevalence of tuberculosis in the Mediterranean area, the incidence of AIDS-related tuberculosis is greater. Dis-

TABLE 1
Comparison of HIV-Positive Patients with and without Mycobacterioses

	No. of patients
HIV-Positive Patients with Mycobacterioses	39
Disseminated disease	29
Skull uptake	24
No evidence of disseminated disease	10
Skull uptake	1
Control Group	15
Skull uptake	1

seminated disease caused by *M. avium* complex, however, is progressively increasing, and, in 1992, was the cause of 6% of admissions at our institution. That this entity has been diagnosed at necropsy in a high proportion of AIDS patients (6) suggests that many cases of *M. avium* complex disease remain undiagnosed.

Patients with tuberculosis and HIV infection are likely to suffer extrapulmonary involvement, which appears in approximately 50%–72% of patients (7,8). These subjects show both unusual radiographic features and nonsignificant tuberculin test reactivity. Because of all these atypical features and nonspecific symptoms, diagnosis is more difficult in HIV-immunosuppressed patients than in immunocompetent patients (9).

Bone marrow examination is a useful method to diagnose infections in AIDS patients. In *M. avium* complex infection, it is the best indicator of early dissemination (10). Nevertheless, it has been shown that bone marrow cultures are positive in only 42% of AIDS patients with unexplained fever, and there are no predictive clinical parameters to distinguish patients with positive bone marrow culture (11). Although ^{67}Ga scans are frequently performed in AIDS patients with fever of unknown origin to identify a site for a more invasive diagnosis, the degree of skull uptake is generally not assessed as a useful finding. We now observe, however, that increased skull uptake in ^{67}Ga scans occurs in patients with disseminated mycobacterioses, without evidence of primary hematological disease. As previously described in disseminated mycobacterioses (12), our patients showed a trend toward peripheral blood cytopenia and increased cellularity in bone marrow aspirate with granulomata, giant cells and plasmacytosis, but no evidence of hematological disease.

The ^{67}Ga skull uptake may be a sign of peripheral marrow activation and could reflect the presence of expanded bone marrow. Hypothetically, this abnormal ^{67}Ga uptake may reflect bone marrow involvement in other conditions, such as primary hematological disease or leishmaniasis. The skull uptake seen in one patient with Burkitt's lymphoma and in another with peripheral leucorythroblastosis would support this hypothesis.

CONCLUSION

Assessment of bone marrow involvement by ^{67}Ga scans may be a helpful tool in diagnosing AIDS patients with fever of unknown origin in whom mycobacteriosis is suspected. In our study, the appearance of ^{67}Ga skull uptake in HIV-positive patients suffering from mycobacterioses is strongly related to disseminated disease.

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