Indium-111-Leukocyte and Gallium-67 Imaging in Acute Sarcoidosis: Report of Two Patients

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Two young women with acute sarcoidosis underwent ^{111}In-labeled autologous leukocyte imaging because of persistent fevers. Images of one of the women demonstrated faint thoracic lymph node uptake of labeled cells, but no discrete focus suggestive of infection was seen. Images of the second woman were normal. Gallium-67 imaging, performed 48 hr after the leukocyte studies, revealed multiple areas of abnormal radiotracer accumulation corresponding to regions of active sarcoid in both women. These cases suggest that leukocyte imaging is not useful for assessing the extent of disease in patients with sarcoidosis. This technique may be valuable, however, in excluding superimposed infection in these individuals.

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Indium-111-labeled mixed autologous leukocyte imaging is extremely useful for localizing foci of infection in general, and has been most successful in identifying those infections that incite a neutrophilic response. In contrast, however, this procedure has been far less successful for localizing those processes that incite other than a neutrophilic response, such as tuberculosis and pneumocystis carinii pneumonia (*1–7*). We recently imaged two young women with acute sarcoidosis and observed that while the leukocyte study correctly excluded infection, it significantly underestimated the extent of disease in both of these individuals.

CASE REPORTS

Both patients underwent labeled leukocyte imaging ~24 hr after injection of ~18.5 MBq (500 μCi) of mixed autologous leukocytes labeled with ^{111}In-oxine according to the method of Thakur et al. (*8*). Imaging was performed on a large field of view gamma camera equipped with a medium-energy, parallel-hole collimator using 20% windows centered over the 174 keV and 247 keV photopeaks of ^{111}In. Gallium imaging was performed on large field of view gamma cameras equipped with a medium-energy, parallel-hole collimators using 20% windows centered over the 93 keV, 186 keV and 300 keV photopeaks of ^{67}Ga, 48 hr after injection of ~185 MBq (5 mCi) of ^{67}Ga-citrate.

Case 1

Three months prior to undergoing leukocyte imaging, a 32-yr-old woman had noted the acute onset of polyarthralgias, intermittent cough, dyspnea and fevers to 38.5°C. She was diagnosed as having acute sarcoidosis, subsequently confirmed by skin punch biopsy after instillation of the Kveim-Siltzbach antigen, and, despite treatment with nonsteroidal anti-inflammatory agents, her symptoms persisted. A chest x-ray, performed approximately 1 mo prior to leukocyte imaging, revealed bilateral hilar and right paratracheal lymphadenopathy, with minimal bibasilar infiltrates, and was interpreted as consistent with sarcoidosis (Fig. 1A). Approximately 1 wk prior to leukocyte imaging the patient developed left-sided pleuritic chest pain. Although it was felt that all of her symptoms were due to sarcoidosis, leukocyte imaging was performed to exclude a superimposed infection. The images revealed faint bilateral hilar and right paratracheal activity thought to represent lymph node uptake of labeled leukocytes; hepatomegaly was noted. No discrete foci suggestive of infection were appreciated (Fig. 1B). Gallium imaging was then performed to evaluate the extent of organ involvement by sarcoid. Images revealed prominent ocular activity, as well as parotid gland and intense bilateral hilar, and right paratracheal lymph node uptake, the so-called panda-lambda sign which has been reported to be highly specific for sarcoid (*9,10*). Mild diffuse pulmonary parenchymal uptake was noted, as was intense uptake in an enlarged liver. The final diagnosis was that of acute sarcoidosis involving lymph nodes, skin, eyes, liver and lungs. Treatment with steroids was begun, with subsequent improvement.

Case 2

A 30-yr-old woman presented with a 3-mo history of fever to 40°C and migratory arthritis. Her left knee was swollen and tender. Laboratory tests were unremarkable. Blood and urine cultures were reported as no growth. Aspiration of the left knee yielded several cc of straw-colored fluid. The total leukocyte count in the aspirate, 360 cells per mm^3, was composed entirely of lymphocytes and macrophages, with no polymorphonuclear leukocytes present, and was interpreted as noninflammatory in

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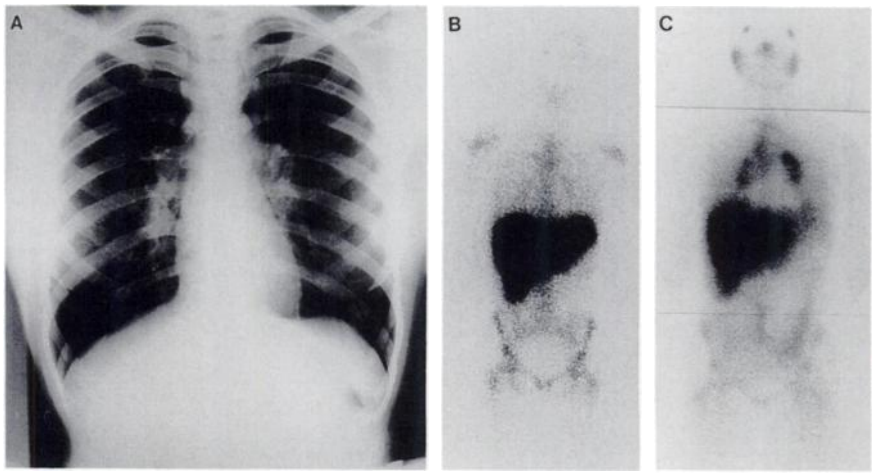

FIGURE 1. (A) Posteroanterior chest x-ray of a 32-yr-old woman with acute sarcoidosis, There is bilateral hilar and right paratracheal lymphadenopathy. Minimal bibasilar infiltrates are present. (B) Anterior total body labeled leukocyte image demonstrates faint bilateral hilar and right paratracheal activity. The liver is enlarged. (C) Anterior gallium image demonstrates moderately increased ocular activity. The increased parotid gland activity together with intense bilateral hilar and right paratracheal uptake illustrates the panda-lambda sign which has been reported to be highly specific for sarcoid. Faint bilateral pulmonary parenchymal uptake is present. There is intense uptake in an enlarged liver. (Although these images were acquired as static images, they have been reconstructed in a total-body format to facilitate comparison with A.)

nature. Cultures of the aspirate were reported as no growth. Leukocyte imaging was interpreted as normal except for bone marrow expansion into the distal femurs (Fig. 2A). A chest x-ray performed 24 hr after the leukocyte study demonstrated widening of the mediastinum (Fig. 2B). Because the chest x-ray raised the possibility of sarcoidosis, gallium scintigraphy was ordered. Gallium images performed 48 hr after the chest x-ray (72 hr after the leukocyte study) revealed extensive lymph node uptake of radiotracer in the mediastinum, right and left paratracheal regions, and both hila. Prominent ocular uptake was present as well (Fig. 2C). Skin punch biopsy after instillation of the Kveim-Siltzbach antigen demonstrated large epithelial granulomata with giant cells, and the final diagnosis was acute sarcoidosis.

DISCUSSION

Indium-111-labeled leukocyte scintigraphy is a very useful procedure for localization of infection (*1–7*). The success of the procedure is based upon the fact that foci of infection attract leukocytes via chemotaxis. Such foci appear as areas of increased uptake of radiolabeled cells on leukocyte images. The chemotactic response of leukocytes, upon which the success of this very useful study is based, also limits the utility of the procedure. When a mixed population of leukocytes is employed, the majority of the cells labeled are usually neutrophils. Noninfectious conditions that induce an intense neutrophilic response, such as inflammatory arthritides and drug-induced pneumonitis, may therefore result in false-positive studies (*11–14*). Inflammatory conditions in which the predominant cellular response is other than neutrophilic, however, may result in false-negative studies, probably due to the small number of these other cell types labeled or to their relatively long residence time in the circulation or both (*6,7*).

It is this latter explanation that we believe accounts for the minimal abnormalities present on the leukocyte images in these two patients with acute sarcoidosis. Sarcoidosis is a multisystemic disease of unknown etiology, characterized by a noncaseating epithelioid granuloma which is composed of a focal, compact, interdigitating collection of macrophages and epithelioid cells, which often coalesce forming multinucleated Langhan's type giant cells and closely admixed lymphocytes. Central necrosis is rare. The epithelioid cell itself is derived from bone marrow monocytes and is in fact a modified macrophage, which differs from ordinary macrophages by, among other factors, a paucity of phagocytic activity (*15*).

While the monocytes and lymphocytes that comprise the cellular response in sarcoid are labeled with radiotracer, their numbers in the peripheral circulation are probably too few, and their residence in the circulation (up to several days) is too long for imaging, typically performed 24 hr after injection, to be successful, as these cases illustrate.

In contrast, gallium imaging is very useful in evaluating the extent of disease in patients with sarcoidosis (*9,10,16–18*). Gallium is bound to lactoferrin, and both B-lymphocytes and mononuclear cells possess lactoferrin surface receptor sites. Activated macrophages may engulf cellular debris and accumulate gallium. Cellular activation of lymphocytes and macrophages associated with chronic inflammatory changes such as those found in sarcoid may explain gallium uptake (*19*). A similar disparity of results between gallium and labeled leukocyte imaging also has been observed in *pneumocystis carinii* pneumonia and tuberculosis, conditions in which the cellular immune response, as in sarcoidosis, is predominantly monocytic (macrophage) and lymphocytic, rather than neutrophilic (*6*).

In summary, these two cases suggest that leukocyte imaging is not useful for evaluating the extent of disease in patients with acute sarcoid. This lack of uptake of labeled leukocytes in acute sarcoidosis, however, may actually be useful when the clinical question is whether or not infection coexists with this entity in a particular patient.

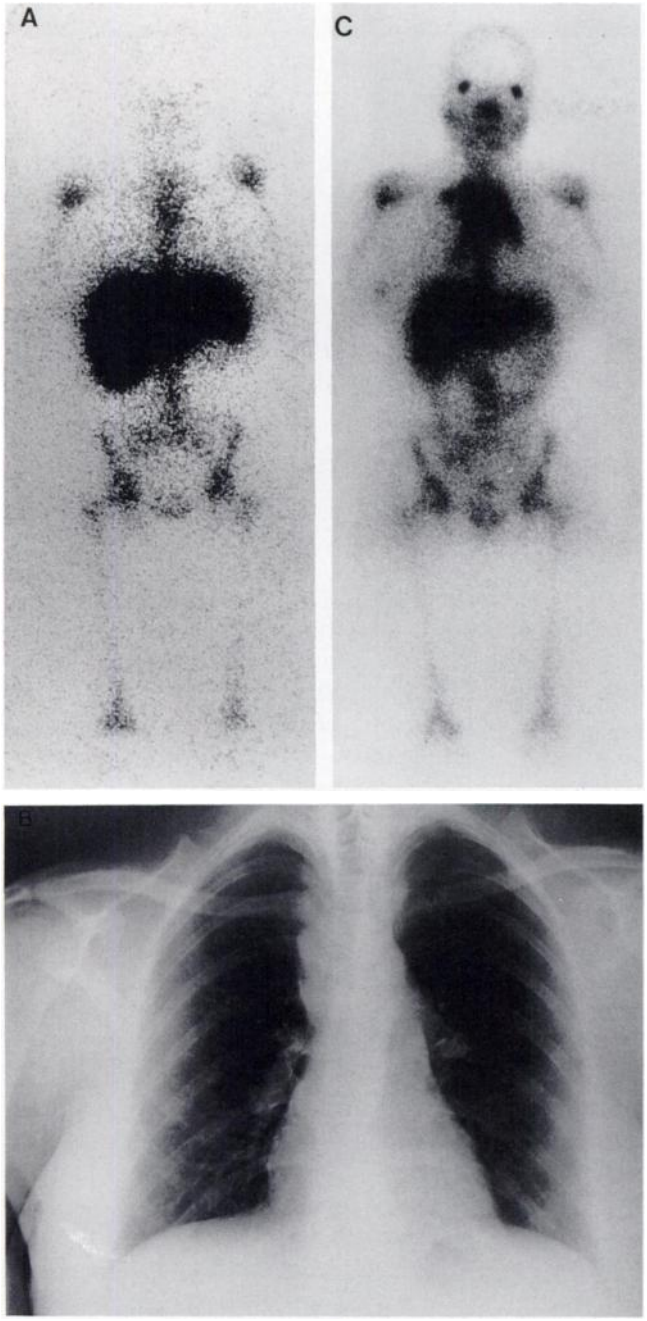

FIGURE 2. (A) Anterior total-body labeled leukocyte image study demonstrates moderate bone marrow expansion, but is otherwise normal. (B) Posteroanterior chest radiograph demonstrates mediastinal, paratracheal, and left hilar lymphadenopathy. There is a suggestion of minimal right hilar enlargement as well. The pulmonary parenchyma is unremarkable. (C) Anterior total-body gallium image demonstrates intense mediastinal, bilateral paratracheal and hilar lymph node uptake. Bilateral supraclavicular lymph node uptake is seen. Prominent ocular activity is also present.

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