

# Indium-111-Labeled Leukocyte Scintigraphy in a Case of Cutaneous Sarcoidosis

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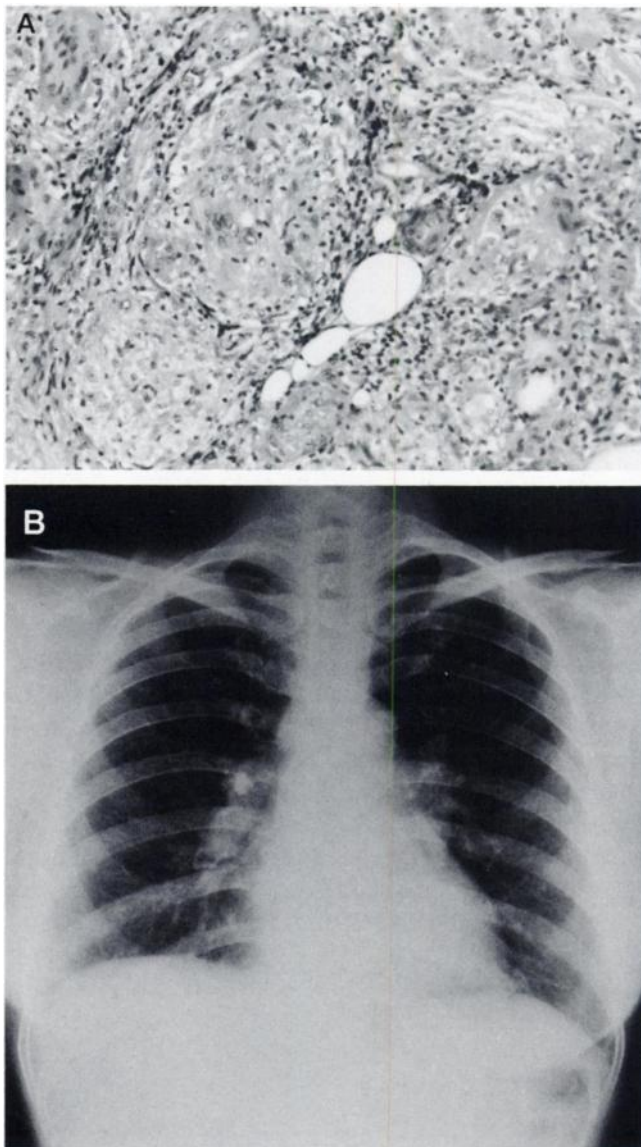
A 54-yr-old woman with cutaneous nodules showed accumulation of  $^{67}\text{Ga}$ - and  $^{111}\text{In}$ -labeled leukocytes in skin nodules, bilateral pulmonary hilar lymph nodes and the right upper mediastinum. Biopsy of the skin nodule proved epithelioid cell granuloma with moderate lymphocyte infiltration peripherally consistent with sarcoidosis. Sarcoidosis is a potential pitfall in labeled leukocyte imaging, which is performed for detecting a febrile focus.

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**S**cintigraphy with  $^{111}\text{In}$ -labeled leukocytes is a well-established clinical tool for the diagnosis and localization of inflammatory diseases (1–5). However, noninfectious diseases, such as pancreatitis, myocardial infarction, noninfected wounds, cystic fibrosis, etc., have been reported to show positive findings (6–7). We report a case of sarcoidosis which showed positive findings in both  $^{67}\text{Ga}$  and  $^{111}\text{In}$ -labeled leukocyte scintigraphy.

## CASE REPORT

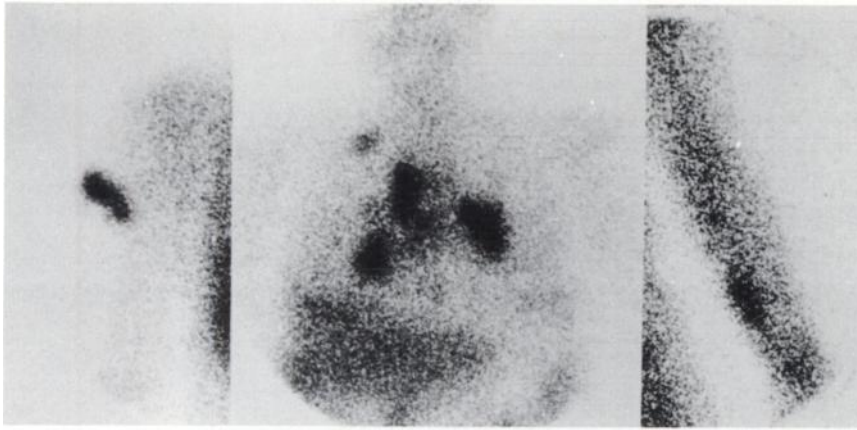
A 54-yr-old female visited the dermatology service for evaluation of multiple skin nodules. Skin biopsy showed epithelioid cell granuloma with moderate peripheral lymphocyte infiltration and chest x-ray demonstrated bilateral pulmonary hilar lymphadenopathy (Fig. 1). The appearance of both were consistent with sarcoidosis. To assess the sites of involvement and pulmonary sarcoidosis activity, scintigraphy was performed 72 hr after administration of 74 MBq of  $^{67}\text{Ga}$ -citrate. Increased uptake was seen in the right upper arm, left forearm, right supraclavicular fossa, right upper mediastinum and both pulmonary hilar regions. Uptake in both lower lung fields was slightly increased in comparison to the region of the heart (Fig. 2). The  $^{67}\text{Ga}$  scintigram was highly suggestive of sarcoidosis. Seven days after  $^{67}\text{Ga}$  scintigraphy, an  $^{111}\text{In}$ -WBC study was performed to evaluate the migration of peripheral leukocytes to the sarcoidosis lesion. Mixed autologous leukocytes (18.5 MBq) labeled with  $^{111}\text{In}$ -oxine were injected and scintigraphy was done 24 hr after administration using a LFOV gamma camera with a medium-



**FIGURE 1.** (A) Microscopic appearance of a skin lesion. There are many epithelioid cell granulomas with a moderate admixture of lymphocytes. (B) Posterior, anterior chest radiograph demonstrates bilateral hilar lymphadenopathy and no definite abnormal finding in both pulmonary parenchyma.

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**FIGURE 2.** Anterior view of the chest and upper extremities at 72 hr after  $^{67}\text{Ga}$  administration. Intense activity is seen in the regions of both pulmonary hilar, right upper mediastinum and right upper arm. Moderate uptake is noted in the left forearm and right supraclavicular fossa. Activity in both lower lung fields is a little higher than that in the heart region.

energy, parallel-hole collimator. Accumulation of  $^{111}\text{In}$ -labeled leukocytes was seen in many of the sites that concentrated  $^{67}\text{Ga}$  except for lung fields (Fig. 3). On examination of the  $^{111}\text{In}$  scintigrams, the peripheral leukocytes counts were  $4000/\text{mm}^3$ , consisting of 17% lymphocytes, 7% monocytes and 76% granulocytes. Angiotensin-converting enzyme (ACE) was 113 IU/liter/ $37^\circ\text{C}$  (NI = 8.3 – 21.4) and lysozyme was  $22.5 \mu\text{g}/\text{ml}$  (NI = 5.0 – 10.2).

## DISCUSSION

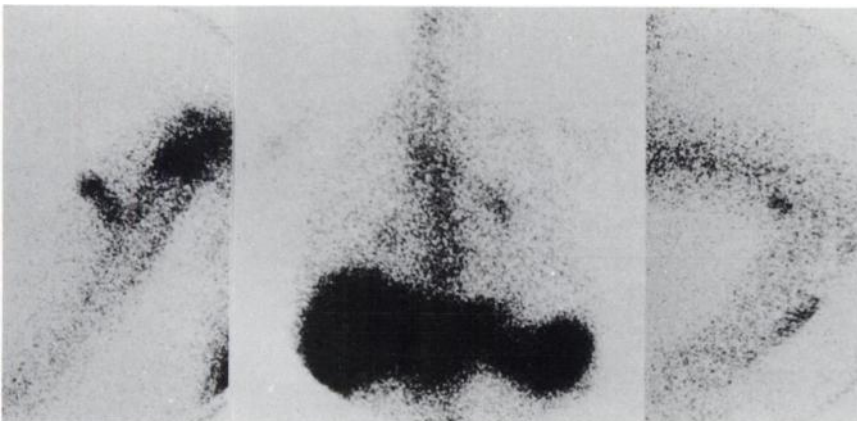
Sarcoidosis is an idiopathic disease characterized by multiple noncaseating granuloma which is a compact nodule of epithelioid cells with a few lymphocytes, monocytes, and macrophages. In typical lesions of sarcoidosis of the skin, a slight to moderate admixture of lymphoid cells is usually present, particularly at the margins of the epithelioid cell granuloma (8,9). Mixed autologous leukocytes labeled with  $^{111}\text{In}$ -oxine administered to the patient contained lymphocytes as well as granulocytes. In this patient, from skin biopsy results which proved the presence of moderate amounts of lymphocytes, we speculate that some of the cells in the lesions were lymphocytes labeled with  $^{111}\text{In}$ . Pozzilli and colleagues reported that

lymphocytes labeled with  $^{111}\text{In}$  accumulated in the thyroid in patients with Hashimoto's thyroiditis and primary myxedema in which histologically documented lymphocytic infiltrates were predominant (10).

The peripheral lymphocyte count usually remains within the normal range or decreases in patients with sarcoidosis and elevation in ACE occurs more often in those with active disease. In this patient, the count of peripheral lymphocytes was slightly decreased and the level of ACE was extremely high.

Distribution of  $^{111}\text{In}$ -leukocytes was similar to that of  $^{67}\text{Ga}$ . However, the pulmonary hilar and right mediastinal findings were less impressive on the  $^{111}\text{In}$ -labeled leukocyte study than on the  $^{67}\text{Ga}$  study and accumulation in the right supraclavicular fossa was very faint on the leukocyte study. Only the cutaneous abnormalities were similar in intensity on both studies. The degree of intensity in the sarcoidosis lesion on the leukocyte study may be related to the degree of infiltration of lymphocytes.

Investigation into the use of  $^{111}\text{In}$ -leukocytes has demonstrated that sarcoidosis could result in the increased uptake observed in this patient and is a potential pitfall in labeled leukocyte imaging.



**FIGURE 3.** Anterior view of the chest and upper extremities at 24 hr after administration of  $^{111}\text{In}$ -labeled autologous leukocytes. Intense uptake is seen in the right upper arm. There is moderate to faint accumulation of leukocytes in both pulmonary hilar, right upper mediastinum and the left forearm. In the right supraclavicular fossa, activity is very faint.

## REFERENCES

1. Segal AW, Arnot RN, Thakur ML, Lavender JP. Indium-111-labeled leukocytes for location of abscess. *Lancet* 1976;2:1056-1058.
2. Thakur ML, Lavender JP, Arnot RN, Silvester DJ, Segal AW. Indium-111-labeled autologous leukocytes in man. *J Nucl Med* 1977;18:1014-1021.
3. McDougall IR, Baumert JE, Lantieri RL. Evaluation of In-111-leukocyte whole body scanning. *AJR* 1979;133:849-854.
4. Knochel JQ, Koehler PR, Lee TG, Welch DM. Diagnosis of abdominal abscess with computed tomography, ultrasound, and In-111 leukocytes scan. *Radiology* 1980;137:425-432.
5. Goodwin DA. Clinical use of In-111-leukocyte imaging. *Clin Nucl Med* 1983;8:36-38.
6. Anderson JR, Spence RAJ, Laird JD, Ferguson WR, Kennedy TL. Indium-111 autologous leukocyte imaging in pancreatitis. *J Nucl Med* 1986; 27:345-352.
7. Coleman RE, Welch D. Possible pitfalls with clinical imaging of indium-111 leukocytes: concise communication. *J Nucl Med* 1980;21:122-125.
8. Rosai J. Sarcoidosis. In: Stamathis G, ed. *Ackerman's surgical pathology*, 7th edition. St. Louis: CV Mosby; 1989:978-981.
9. Lever WF, Schaumburg-Lever G. Noninfectious granulomas. In: Cooke DB, ed. *Histopathology of the skin*, 7th edition. Philadelphia: JB Lippincott; 1990:252-256.
10. Pozzilli P, Pozzilli C, Pantano P, Negri M, Andreani D, Cudworth AG. Tracking of indium-111-oxine labelled lymphocytes in autoimmune thyroid disease. *Clin Endocrinol* 1983;19:111-116.

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## SELF-STUDY TEST

### Skeletal Nuclear Medicine

#### QUESTIONS (continued)

16. The finding, at the end of a 6-week course of appropriate antibiotic treatment for acute osteomyelitis, that  $^{67}\text{Ga}$  uptake has decreased from pretreatment levels, but not to normal, is a strong indication of an unsatisfactory response.
17. Low-grade  $^{67}\text{Ga}$  concentration is often seen in chronic osteomyelitis in a distribution that is anatomically similar to that of  $^{99\text{m}}\text{Tc}$  MDP.
18. Osteosarcoma and acute osteomyelitis generally can be distinguished by their differential accumulation of  $^{67}\text{Ga}$  and  $^{99\text{m}}\text{Tc}$  MDP.

## SELF-STUDY TEST

### Skeletal Nuclear Medicine

#### ANSWERS

#### Item 1: "Flare" Phenomenon

Answer: A

The term "flare phenomenon" was originally used by Gillespie et al. to describe the increase in activity seen on  $^{87\text{m}}\text{Sr}$  bone scans during treatment of patients with metastatic disease who were responding to chemotherapy. This phenomenon was further characterized by Rossleigh et al. in patients undergoing  $^{99\text{m}}\text{Tc}$  MDP bone scintigraphy for evaluation of therapy for breast cancer metastases. They defined the "flare response" as: (1) an increase in tracer uptake or in the apparent size of known metastatic lesions and/or the appearance of new lesions within 6 months of commencing therapy, in the absence of increasing bone pain (in practice, however, pain occurs in some patients responding to therapy); and (2) subsequent decreased uptake in these lesions, without a change in therapy, on repeat scintigraphy within 2-3 months. In this series, ten patients showed a healing "flare response" 6 weeks to 6 months after therapy. Five of the ten patients showed increased uptake in previously demonstrated lesions. In the other five patients, new lesions were identified that previously were undetected. In all of the patients, therapy was not altered during the course of the serial studies, there was a reduction in bone pain or objective tumor responses in other sites, and later follow-up studies showed decreased uptake in the known lesions. In only one of the patients was a radiographic change (sclerosis of a lytic lesion) seen in association with the healing flare. The "flare phenomenon" has been seen in patients with prostate carcinoma and other tumors as well. It also may occur locally in regions undergoing irradiation for metastatic disease. The likelihood of observing the "flare phenomenon" depends on the type of tumor, the type of therapy, the interval after onset of treatment and the frequency of bone scintigraphy.

The "extended pattern" seen with primary bone tumors in long bones is not related to the "flare phenomenon." Patients with primary bone tumors may show increased activity in adjacent joints or along the entire extremity. This increase in activity is usually mild to moder-

ate in degree and is thought to be due either to generalized increased blood flow to the extremity or to a change in the patient's gait. The "extended pattern" is one reason that bone scintigraphy may overestimate the extent of osseous involvement by a primary bone tumor. Similar "extended" findings also occur with inflammatory lesions of the long bones.

When Paget's disease involves long bones, the process may involve the entire bone or it may extend from one end of the bone for a variable length into the diaphysis. Radiographically, the leading edge of the lytic phase of Paget's disease in a long bone has been described as a "flame-like" rarefaction. This also has been characterized as a "blade of grass" appearance.

The persisting minimal uptake seen in regressing metastases is not the "flare phenomenon." This uptake likely reflects continued remodeling of bone after the local tumor deposit has been reduced or eradicated.

On oblique scintigrams of the skull, an area of increased activity in the anterior temporoparietal region is occasionally seen. This has been called a calvarial flame and probably is due to the increased bone thickness of the lateral orbital ridge or the pterion viewed on end in this projection.

#### References

1. Gillespie PJ, Alexander JL, Edlestyn GA. Changes in  $^{87\text{m}}\text{Sr}$  concentrations in skeletal metastases in patients responding to cyclical combination chemotherapy for advanced breast cancer. *J Nucl Med* 1975;16:191-193.
2. Goldman AB, Braunstein P. Augmented radioactivity on bone scans of limbs bearing osteosarcomas. *J Nucl Med* 1975;16:423-424.
3. Levenson RM, Sauerbrunn BJL, Bates HR, Newman RD, Eddy JL, Ihde DC. Comparative value of bone scintigraphy and radiography in monitoring tumor response in systemically treated prostatic carcinoma. *Radiology* 1983;146:513-518.
4. Pollen JJ, Witzum KF, Ashburn WL. The flare phenomenon on radionuclide bone scan in metastatic prostate cancer. *AJR* 1984;142:773-776.
5. Rossleigh MA, Lovegrove FTA, Reynolds PM, Byrne MJ, Whitney BP. The assessment of response to therapy of bone metastases in breast cancer.

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