

Isolated Muscular Sarcoidosis Causing Fever of Unknown Origin: The Value of Gallium-67 Imaging

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An unusual case of a patient with a long-standing fever of unknown origin (FUO) is presented whose gallium-67 (^{67}Ga) images revealed increased activity only in the calf muscles bilaterally. Other imaging modalities also failed to show chest or other abnormal findings. Subsequent biopsy of the right gastrocnemius muscle revealed noncaseating granulomas consistent with the diagnosis of sarcoidosis. When using ^{67}Ga to evaluate a patient with a FUO, imaging of the extremities should always be included. Also, when abnormal Ga-67 uptake is present in the extremities, sarcoidosis should be included in the differential diagnosis.

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Sarcoidosis is a chronic noncaseating granulomatous disease which involves multiple organ systems with thoracic involvement in 95% of the patients. Extrathoracic involvement is less frequent and varies widely among different organs (1-3). Although asymptomatic muscle involvement is thought to occur in 50%-80% of patients, symptomatic involvement is very infrequent (0.5%) and only rarely occurs without associated pulmonary disease (1,4). Occasionally, sarcoidosis can present as the diagnostically challenging patient with a fever of unknown origin (FUO). Scintigraphy can be helpful in determining sites of involvement and activity of disease.

We present an unusual case of a patient with a long-standing FUO whose gallium-67-citrate (^{67}Ga) images showed abnormal activity only in the lower extremities. Subsequent biopsy of a calf muscle revealed noncaseating granulomas consistent with sarcoidosis.

CASE REPORT

A 42-yr-old white male was admitted for work-up of an FUO, which he claimed had been present intermittently over the preceding 20 yr but had not been treated with either antibiotics or steroids. In addition, he complained of generalized malaise, fatigue, night sweats, and myalgia of both lower extremities. The physical examination revealed only tender calf muscles without nodularity or skin abnormalities. The lungs, liver, and spleen were all normal and there was no palpable lymphadenopathy. He was anemic with a hemoglobin of 10 g/dl and a slightly elevated white blood cell count of 13,200 without a left shift. Urine cultures, multiple blood cultures, rheumatology profiles, viral serologies, and a PPD skin test were all negative. Serum angiotensin-converting enzyme level (ACE) was normal while chest X-ray (Fig. 1), lower extremity X-rays, and computed tomography scans of the chest, abdomen, and pelvis were unremarkable. A total-body bone scan did not reveal any osseous pathology. A gallium scan was ordered to help search for an occult site of infection. This was preferred over an indium-111-WBC scan because of the chronicity of the patients' complaints.

Seventy-two hours following the i.v. administration of 5 mCi of ^{67}Ga images over the entire body were obtained. The only abnormality found was that of multiple small confluent focal areas of increased tracer activity scattered about both calf areas (Fig. 2). The lungs, mediastinum, abdomen, and lymph nodes in other areas showed a normal distribution of ^{67}Ga activity (Fig. 3). Muscle biopsy of the right gastrocnemius muscle also revealed noncaseating granulomas consistent with sarcoidosis.

The patient was placed on oral steroid therapy with resolution of both his fever and calf myalgias. A repeat gallium scan could not be obtained because the patient was subsequently lost to follow-up.

DISCUSSION

Sarcoidosis is a granulomatous disorder that primarily affects the lungs and the mediastinal lymph nodes. However, multiorgan disease is also a common manifestation with liver (70%), spleen (50%), skin (10%),

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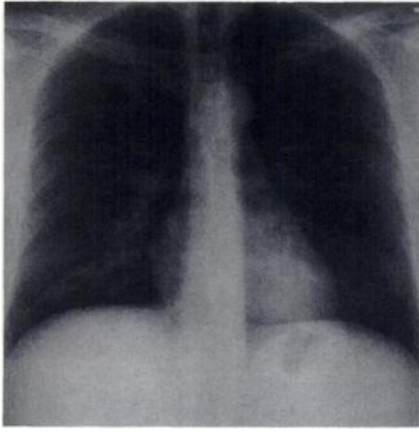


FIGURE 1
Normal PA chest X-ray without hilar or paratracheal lymph node enlargement or interstitial lung disease.

and salivary glands (5%) being frequently involved (1). Although muscle granulomas are also thought to be common, generally the majority do not produce symptoms and nearly all have concomitant pulmonary disease (8). Our patient presented with a FUO, normal chest findings, and tenderness of his leg muscles. The ^{67}Ga scan convinced the clinicians that a calf muscle biopsy might be helpful. This subsequently led to the diagnosis of sarcoidosis.

There are three different forms of skeletal muscle involvement by sarcoidosis. The main type is painful or painless nodules consisting of noncaseating granulomas of various sizes. A second less common form is that of diffuse infiltration of muscle causing the clinical picture of an acute or subacute polymyositis. The third type presents as a chronic myopathy characterized by symmetrical weakness and atrophy of proximal muscle groups (1). Edan et al. described a patient with muscular sarcoidosis with associated mediastinal adenopathy which most likely represents the polymyositis form of the disorder (8). Our patient, however, had the nodular

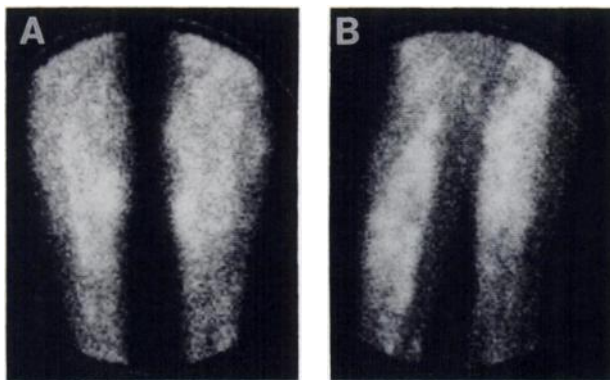


FIGURE 2
Anterior (A) and lateral (B) ^{67}Ga images of the lower extremities obtained 72 hr after administration of 5.0 mCi of gallium. There is diffuse as well as multiple small focal areas of increased uptake scattered throughout both calf regions.



FIGURE 3
Anterior chest ^{67}Ga images show mild accumulation at the costo-chondral junctions bilaterally. There is no evidence of ^{67}Ga accumulation to suggest sarcoidosis in these regions.

form of muscular sarcoidosis, which was isolated to the calf muscles and produced severe symptoms. Gallium-67 imaging is a highly sensitive examination for detection of disease activity in patients with known sarcoidosis. Although this is well documented for patients with chest involvement, the true sensitivity of gallium imaging in muscular sarcoidosis is not known. Serial examinations, however, in patients with known muscular sarcoidosis have been shown to be helpful (8,9).

There are many inflammatory disorders as well as tumors that can involve the extremities and cause avid ^{67}Ga uptake (7,10). It is often difficult to separate skin from muscle uptake in this type of study because of their close proximity and the relatively poor resolution of current camera systems. However, physical examination may help differentiate the two.

Many disorders that cause FUO will also cause abnormal ^{67}Ga accumulation and, therefore, correlation with clinical findings and other imaging modalities is necessary before making a final diagnosis. Nevertheless, ^{67}Ga imaging can direct one to an appropriate biopsy site as it did with our patient. With this in mind, one should always include an evaluation of the extremities during ^{67}Ga imaging in patients with FUO. Also, when abnormal ^{67}Ga accumulation is seen in the extremities, sarcoidosis should be included in the differential diagnosis.

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FEBRUARY 1961

Superimposed Optical and Gamma-Ray Scanner Images

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Whole-body gamma-ray scanning has been used for some time to locate functioning thyroid tissue in patients suspected of metastatic thyroid disease. The patient is given a tracer dose of ^{131}I and at 24-96 hr later is scanned to detect any lesions that may take up the isotope. When the gamma-ray image shows an area that concentrates ^{131}I , the site of the uptake should be located as accurately as possible. One method is to superimpose the gamma-ray

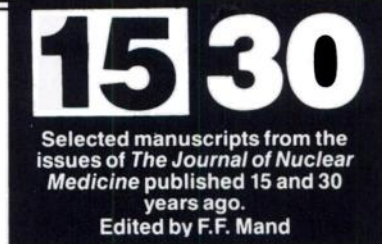


image of an X-ray radiograph, as reported by West. The area of iodine concentration is thereby located with respect to the X-ray anatomy of the patient. However, this procedure increases the radiation dose received. Therefore, we have built an apparatus that automatically superimposes an optical photograph of the patient on the gamma-ray image.

The gamma-ray scanner used for this purpose employs ten scintillation counters mounted in a lead shield that moves over the patient. Each counter is connected to a glow lamp, which flashes with every count detected. As the counters move slowly over the patient, a moving image of the glow lamp is projected onto photographic film. The pattern of radioactivity is reproduced as a pattern of dots on the film. We have added a telephoto lens and mirror system to this, which allows photographing the patient on the same film. Magnification and location of the photographic image are such that it coincides exactly with the size and location of the gamma-ray image. ■



FEBRUARY 1976

Inadvertent Iodine-131 Therapy for Hyperthyroidism in the First Trimester of Pregnancy

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Although it is well known that [^{131}I] sodium iodide therapy after the 12th week of pregnancy may result in an hyperthyroid child, clinical data regarding such administration are lacking. This information would be useful, since inadvertent administration is most likely to occur early in pregnancy. As thyroid consultants, we are contacted 3-4 times each year by anxious physicians who have administered ^{131}I for hyperthyroidism only to discover subsequently that the patient was a few weeks pregnant. The advisability of therapeutic abortion is the primary concern. The literature is surprisingly silent on this point.

Letters of inquiry (963) were sent to members of the American Thyroid Association and the Endocrine Society, who were selected based on their likelihood of treating thyroid patients. The physicians were asked:

1. How many of their thyroid patients had received therapeutic doses of ^{131}I during the first trimester of pregnancy?
2. How many of these patients were advised to seek a therapeutic abortion?
3. How many of these patients carried to term under observation?
4. Of the deliveries, how many babies were observed with fetal abnormalities upon birth?

For the babies with abnormalities, the physicians were further asked to provide:

1. The estimated week of pregnancy of the ^{131}I administration.
2. Urine pregnancy test results (if performed).
3. The date and dosage of ^{131}I therapy.
4. Thyroid function tests results (if performed) in hyperthyroid infants, the age at which hyperthyroidism was diagnosed, indications of mental deficiencies (if any), and the child's current age.

Of the 963 physicians surveyed, 517 (54%) responded. A total of 237 patients inadvertently treated with ^{131}I while pregnant were reported by 116/517 physicians.

When this survey was planned, we assumed that by this time everyone admin-

istering ^{131}I therapy would routinely perform a pregnancy test for patients of child-bearing age. Therefore, we did not request this information. However, 22 physicians offered comments indicating that our expectations were incorrect. For example, one physician said that he administered ^{131}I therapy upon the request of the attending physician and was not a participant in the patient's clinical evaluation. Another physician indicated he was not concerned with pregnancy testing because it was his understanding that the fetal thyroid does not concentrate ^{131}I in the first trimester, and that after the first trimester the diagnosis of pregnancy should be obvious.

The survey data suggest that the majority of physicians do not recommend therapeutic abortion for pregnant patients who inadvertently receive ^{131}I therapy in the first trimester. This conservative approach seems justified by the finding that the rate of fetal and neonatal abnormalities was no greater than that reported for uncomplicated pregnancies. Of perhaps greater concern was the discovery that urine pregnancy tests are still not performed routinely, even in major medical centers. ■