# Intense Muscle Uptake of Gallium-67 in a Patient with Sarcoidosis

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Sarcoidosis has been associated with muscle involvement. In general, this involvement remains asymptomatic. The following case report demonstrates a patient with a 4-mo history of sarcoidosis who reported severe fatigue and slight muscular complaints at a regular checkup. Gallium scintigraphy indicated unexpected and unusually extensive muscular localizations of the disease. The latter findings were confirmed by examination of biopsy specimens. The importance of gallium scintigraphy lies in the possibility of whole-body screening for inflammation localizations, particularly when physical, laboratory, lung function and radiographic examinations fail to provide convincing evidence of active sarcoidosis. Furthermore, it can be helpful in the follow-up of the effect of supportive treatment.

**Key Words:** sarcoidosis; gallium-67 scintigraphy; muscular involvement

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Sarcoidosis is characterized by the formation of noncaseating epitheloid cell granulomas in various organ systems. Although the lung is the most commonly affected organ (90%–95%), many extrapulmonary manifestations, such as mediastinal and hilar lymphadenopathy (75%–90%) and skin (such as erythema nodosum), bone marrow, spleen and liver manifestations frequently occur. Sarcoidosis localized in the kidney, nervous system, heart or gastrointestinal tract is rare (*1,2*). Asymptomatic muscle involvement is also common compared with symptomatic muscle involvement. Prevalence of sarcoidosis ranges from 1 to 40 cases per 100,000 population (*3–5*).

Serum angiotensin-converting enzyme (ACE) levels, 24-hr urine and serum calcium levels, chest radiography, $^{67}$Ga scintigraphy, bronchoalveolar lavage (BAL) and, if the clinical situation justifies it, biopsies are used in the management of sarcoidosis. Gallium scintigraphy can be helpful in assessing active sarcoidosis, particularly to localize extrapulmonary lesions.

In the following case report, an unusually intense and symmetrical accumulation of $^{67}$Ga in various muscle groups, reflecting active sarcoidosis, was seen.

## CASE REPORT

A 65-yr-old man, nonsmoker, was admitted to University Hospital Maastricht. He was suffering from increasing fatigue, polyuria, polydipsia and anorexia, resulting in severe weight loss. In 1989, coronary artery bypass graft surgery was performed after he experienced a myocardial infarction. Physical examination revealed no abnormalities. Laboratory data on admission showed an erythrocyte sedimentation rate of 35 mm/hr, C-reactive protein of 2 mg/liter (reference value = 2–9 mg/liter), white blood cell count of 7.3 × $10^9$ cells/liter with a normal differentiation and a low hemoglobin level of 7.3 mmol/liter (reference value = 8.5–10.5 mmol/liter). The serum calcium level was elevated (3.42 mmol/liter; reference value = 2.10–2.60 mmol/liter) as was the serum ACE level (46 IU/liter; reference value = 9.0–25.0 IU/liter). The serum phosphorus level (1.50 mmol/liter) and parathyroid hormone level (1.1 pmol/liter) were within normal limits. Liver function tests were normal and serology for autoimmune disease was negative. The chest radiograph showed a poorly defined solitary nodule 1.5 cm in diameter in the right upper lobe. CT confirmed the presence of this lesion. Furthermore, ipsilateral hilar and mediastinal lymphadenopathy were observed. At this time, a primary bronchus carcinoma was considered as the diagnosis. Fiberoptic bronchoscopy revealed no endobronchial abnormalities. Accordingly, BAL was performed. BAL fluid analysis showed an increased total cell count (18.7 × $10^4$/liter; reference value for nonsmokers = 10.3 ± 1.5 × $10^4$/liter) with predominant lymphocytosis (39%; reference value for nonsmokers = 11.0% ± 0.3%) that was indicative of sarcoidosis (*6*). Culture of BAL fluid remained sterile and cytologic examination showed no signs of malignancy. Histologic examinations of four lymph node biopsy specimens obtained by mediastinoscopy showed noncaseating epitheloid cell granuloma compatible with sarcoidosis. Systemic treatment with corticosteroids was initiated (50 mg prednisone daily). The patient's clinical condition improved, with a concomitant normalizing of the serum calcium level. The prednisone dosage was tapered off and eventually stopped.

One month later, the patient reported increased fatigue, moderate muscular weakness and pain during his regular checkup. The serum calcium level was elevated again (2.70 mmol/liter), as were the serum ACE and serum urate levels. Although the creatinin phosphokinase level was within normal limits (136 IU/liter; reference value = 40–240 IU/liter), it was higher than previously.

To objectify the extent of sarcoidosis, $^{67}$Ga scintigraphy was performed 72 and 168 hr after intravenous injection of 148 MBq $^{67}$Ga-citrate. At both intervals, scintigraphy showed unexpected and unusually high uptake in various muscles, particularly in the major pectoral muscles (mainly on the right side), the biceps brachii muscles and the muscles of the thighs, shins and calves. Moreover, an accumulation was observed in the right rear axillary region, possibly corresponding with the lateral part of the latissimus dorsi muscle. In the thigh, the calculated muscle-to-background ratio was 2.2:1.0. In contrast, the lungs, mediastinal and other lymph nodes showed no increased uptake, although some regions were difficult to review because of the intense muscle uptake (Fig. 1a–c). Furthermore, hepatic uptake was relatively decreased. This was probably caused by increased muscle uptake, because there was no previous use of iron salts, transfusion or chemotherapy to explain this finding.

MRI of the thighs showed that the signal intensity of the adductor muscle groups and the vastus lateralis muscle was increased on T2-weighted and inversion-recovery axial images (Fig. 2). These findings on MRI were attributed to diffuse inflammation of muscle tissue. Biopsy specimens obtained from the left quadriceps muscle (adductor muscle region) showed multiple small granulomas without clustering in nodules (Fig. 3). Additionally,

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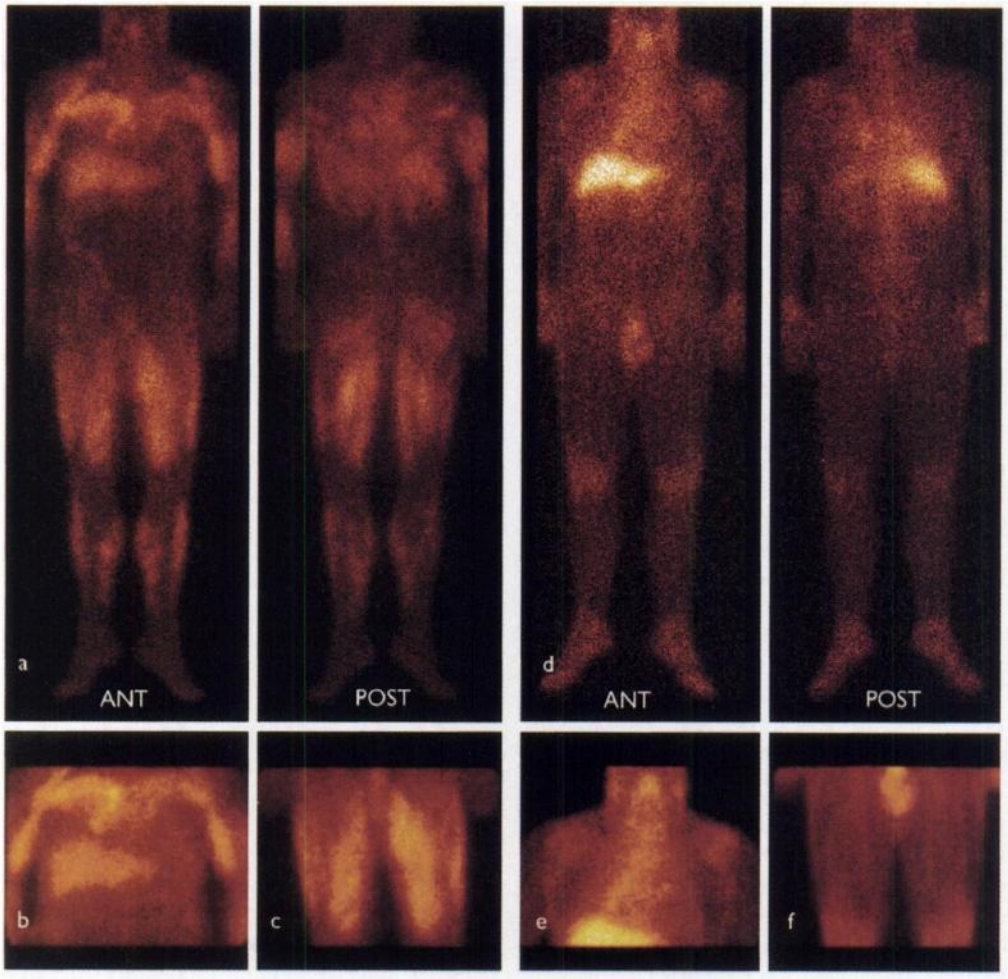


**FIGURE 1.** Gallium-67 scintigraphy of 65-yr-old man, nonsmoker, with severe sarcoidosis. (a–c) After discontinuation of first course of prednisone treatment, abnormal, increased uptake of $^{67}$Ga was observed in major pectoral muscles, both biceps muscles and muscles of the thighs, shins and calves. (d–f) After second course of prednisone treatment, normal distribution of $^{67}$Ga in muscles is seen compared with earlier observations (a–c). Abnormal uptake was observed only in mediastinal lymph nodes and right lung.

treatment with prednisone was restarted (50 mg daily) and tapered off again after improvement of the patient's clinical condition. Two months later, $^{67}$Ga scintigraphy showed no signs of the previous increased muscle uptake (Figs. 1d–f) and the muscle-to-background ratio decreased to 0.8:1.0. Furthermore, the biodistribution pattern normalized, particularly hepatic uptake. Abnormal accumulation was now observed in the mediastinal lymph nodes and the right lung.

## DISCUSSION

Sarcoidosis is a chronic, multisystem disorder characterized by noncaseating granulomas and derangements of normal tissue architecture. It is most often localized in the lungs and mediastinal lymph nodes, but many other extrapulmonary locations have been documented.

This case report illustrates the important role of $^{67}$Ga scintigraphy in the management and follow-up of sarcoidosis.

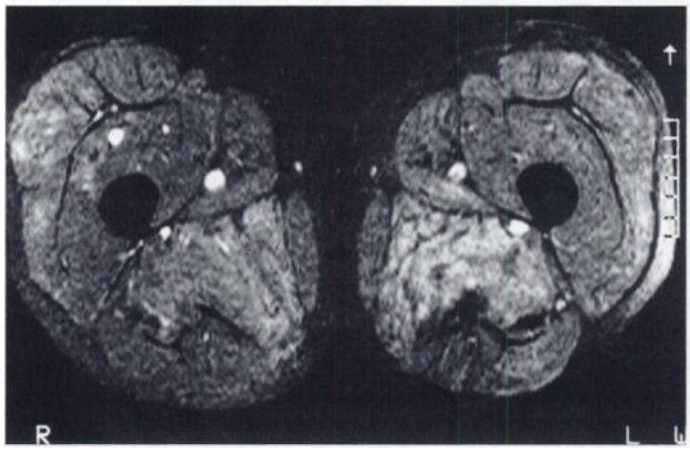


**FIGURE 2.** Axial inversion-recovery MR image through proximal third of thigh demonstrates bilateral, mildly increased signal intensity in adductor muscle groups and vastus lateralis muscle.

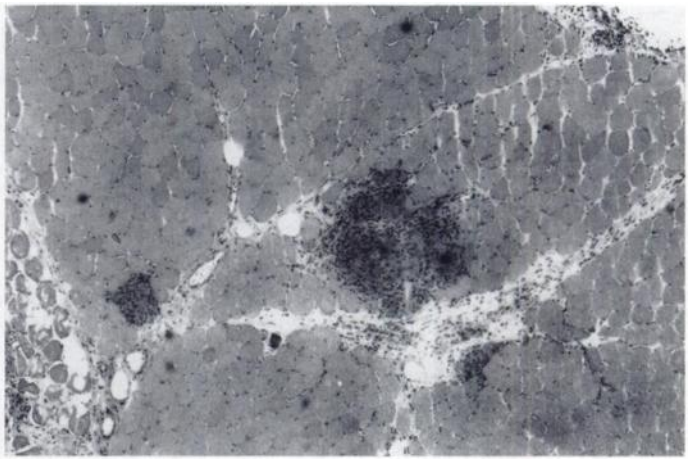

**FIGURE 3.** Conventional (hematoxylin-eosin) staining of biopsy sample from adductor muscle region of thigh shows granuloma surrounded by normal muscle tissue.

Particularly, the combination of the "panda appearance" (symmetrical lacrimal and parotid gland uptake) and the "lambda sign" (distinctive intrathoracic lymph node uptake) is considered highly specific for sarcoidosis (*7,8*).

Asymptomatic granulomatous muscle involvement in sarcoidosis has been reported with a prevalence of 80%, whereas symptomatic muscle involvement is much less common (range 1.4%–2.3%) (*1,3,9*). The symptomatic involvement that has been described varies from a palpable nodular type to an acute myositis and a chronic myopathic type. Patients usually suffer from pain, weakness, fatigue and muscle atrophy, including respiratory muscles, and sometimes fever (*4,10,11*).

The techniques useful in assessing the extent and severity of clinically suspected muscle involvement in sarcoidosis are serum markers, including creatinin phosphokinase levels (*11*); gallium scintigraphy; MRI; and muscle biopsy.

High muscle uptake of $^{67}$Ga has been reported in sarcoidosis (*3,12–15*), in a few other conditions such as Lyme disease (*16*) and aplastic anemia (*17*) and in a patient with a hypercoagulable state after exercise (*18*). Israel et al. (*13*) reported that in a group of 172 sarcoidosis patients, 4 (2.3%) had abnormal muscle uptake of gallium. Otake (*14*) compared CT, MRI and $^{67}$Ga scintigraphy for detecting nodular and myopathic muscular sarcoidosis. He found gallium scintigraphy to be superior for whole-body screening. Moreover, it was the only modality that showed myopathic sarcoidosis. MRI, however, was preferred for detecting the nodular form. Israel et al. (*13*) reported three specific indications for $^{67}$Ga scintigraphy in sarcoidosis: as an adjunct to diagnosis by increased uptake, to guide an appropriate localization for biopsy and to evaluate a suspected relapse.

## CONCLUSION

In this patient with sarcoidosis, $^{67}$Ga scintigraphy showed severe and extensive muscle uptake. Additionally, the localization for a muscle biopsy was made. The patient seemed to suffer from an early stage of sarcoid polymyositis with only moderate weakness and fatigue. The discrepancy between clinical presentation and scintigraphic findings was remarkable, and this observation provides additional arguments for $^{67}$Ga scintigraphy as an essential adjunct to diagnosis in sarcoidosis. This case report shows that gallium scintigraphy can be useful in guiding therapy and in monitoring the effect of supportive treatment.

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