Evaluation of Extrapulmonary Ga-67 Uptake in Sarcoidosis: A Retrospective Analysis

Sarkoidozda Ekstrapulmoner Ga-67 Tutulumunun Değerlendirilmesi: Retrospektif Bir Analiz

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ABSTRACT Objective: To evaluate the sites of extrapulmonary Ga-67 uptake. **Material and Methods:** A total of 113 patients (49 male, 64 female; mean age 38±7 years) with clinically and radiologically diagnosed sarcoidosis were retrospectively analyzed. Whole body planar images were obtained 48-72 hours after the intravenous administration of a mean dose of 185 MBq Ga-67. Scintigrams were evaluated visually by three blind experienced nuclear medicine specialists reaching a final consensus. **Results:** Eighty-two oft of 113 patients (73%) showed abnormal findings as a sign of intrathoracic involvement. Thirty-six patients had hilar and mediastinal uptake (lambda sign) (44%), 20 had only hilar uptake (24%), 6 had only mediastinal uptake (8%) and 20 had diffuse parenchymal uptake (24%). In 113 patients, 168 sites of extrapulmonary involvement were observed. Fifty-nine patients had panda sign (52%), 45 had salivary or lacrimal gland uptake (40%), 37 had lymph node uptake (33%)-11 inguinal, 11 supraclavicular, 7 axillary, 4 epitrochlear, 3 paraaortic and 1 cervical region-7 patients had articulary uptake (6%), 16 patients had breast uptake (14%), 2 patients had focal liver uptake (2%) and 2 had cutaneous uptake (2%). Four patients had normal Ga-67 scintigraphy (4%). **Conclusion:** Ga-67 scintigraphy has been used to evaluate the extent of sarcoidosis. It demonsrates not only intrathoracic but also extrathoracic involvement.

Key Words: Sarcoidosis; gallium citrate; radionuclide imaging

ÖZET Amaç: Sarkoidozda ekstrapulmoner Ga-67 tutulum alanlarının değerlendirilmesi. **Gereç ve Yöntemler:** Klinik ve radyolojik olarak sarkoidoz tanısı koyulmuş olan 113 hasta (49 erkek, 64 kadın, ortalama yaş 38 ± 7 yıl) retrospektif olarak analiz edildi. Ortalama 185 MBq Ga-67'nin intravenöz uygulanmasından 48-72 saat sonra tüm vücut planar görüntüleme yapıldı. Sintigrafiler deneyimli üç nükleer tıp uzmanı tarafından fikir birliğine varılarak değerlendirildi. **Bulgular:** Hastaların 82 (%73)'sinde intratorasik yayılım bulguları izlendi. Bu 82 hastanın 36'sında hiler ve mediastinal tutulum varken (lambda sign) (%44), 20 hastada sadece hiler tutulum (%24), 6 hastada sadece mediastinal tutulum (%8) ve 20 hastada (%24) difüz parankimal tutulum saptandı. Yüz on üç hastada toplam 168 alanda ekstrapulmoner tutulum gözlendi. Bu tutulumlar 59 hastada panda sign (%52), 45 hastada tükrük bezi veya lakrimal bez tutulumu (%40), 11 inguinal, 11 supraklaviküler, 7 aksiller, 4 epitroklear, 3 paraaortik ve 1 servikal bölgede olmak üzere 37 hastada lenf düğümü tutulumu (%33), 7 hastada eklem tutulumu (%6), 16 hastada meme dokusunda tutulum (%14), 2 hastada fokal karaciğer tutulumu (%2) ve 2 hastada ise kutanöz tutulum (%2) izlendi. Ga-67 sintigrafisi bulguları 4 hastada (%4) normaldi. **Sonuç:** Ga-67 sintigrafisi sarkoidozun yaygınlığının değerlendirilmesinde sıklıkla kullanılmakta olup, sadece intratorasik yayılımı değil, ekstratorasik yayılımı da saptamakta başarılı bir yöntemdir.

Anahtar Kelimeler: Sarkoidoz; galyum sitrat; sintigrafi

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Sarcoidosis is a chronic multisystem granulomatous disease of unknown origin. Noncaseous epitheloid cell granulomas are observed in the affected tissue. Although all parts of the body may be involved,

the lung is the most frequently involved organ. Involvement of the skin, eye and lymph nodes is also common.[1,2]

Ga-67 whole body scintigraphy is frequently used in the management of sarcoidosis. We usually use Ga-67 in the assessment of disease activity, response to therapy and extrapulmonary involvement.[1-5]

In this study, Ga-67 scintigraphies of 113 patients with sarcoidosis were investigated retrospectively to evaluate the sites of extrapulmonary involvement.

MATERIAL AND METHODS

One hundred and thirteen patients (49 male, 64 female; mean age 38 ± 7 years) with clinically and radiologically diagnosed sarcoidosis were retrospectively analyzed. None was taking any medical therapy (steroid, immunosuppressive, etc.) at the time of scintigraphy. Ga-67 scintigraphies were performed to assess the activity and the extent of the disease before therapy.

Whole body planar images were obtained with a single head camera (GE 3200 XRT) 48-72 hours after the intravenous administration of a mean dose of 185 MBq Ga-67. The camera had a medium-energy parallel-hole collimator using a 256x1024 word matrix with a preset time of 10 min. Acquisition was performed using the three Ga-67 photopeaks (93,184 and 296 keV) with a 20% window. The acquisition systematically included anterior and posterior views of the whole body. Spot images were taken when necessary.

Scintigrams were evaluated visually by three experienced nuclear medicine specialists, blinded to each other, reaching a final consensus.

RESULTS

Eighty-two out of 113 patients (73%) showed abnormal findings as a sign of intrathoracic involvement (Table 1). Thirty-six had hilar and mediastinal uptake (lambda sign) (44%) (Figure 1), 20 had only hilar uptake (24%) (Figure 2), 6 had only mediastinal uptake (8%) (Figure 3) and 20 had diffuse parenchymal uptake (24%) (Figure 4a-4b).

TABLE 1: The results of intrathoracic pulmonary involvements in Ga-67 scintigraphy.

Findings	Number of patients (n=)	%
Hilar and mediastinal uptake	36	44
Hilar uptake	20	24
Mediastinal uptake	6	8
Diffuse parenchymal uptake	20	24

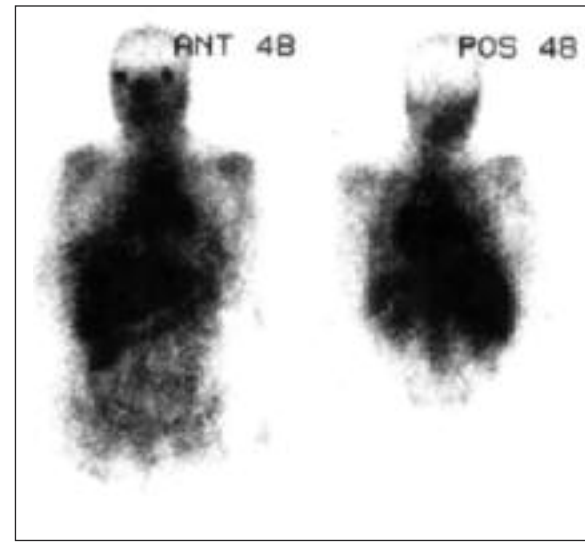

FIGURE 1: Hilar and mediastinal uptake.

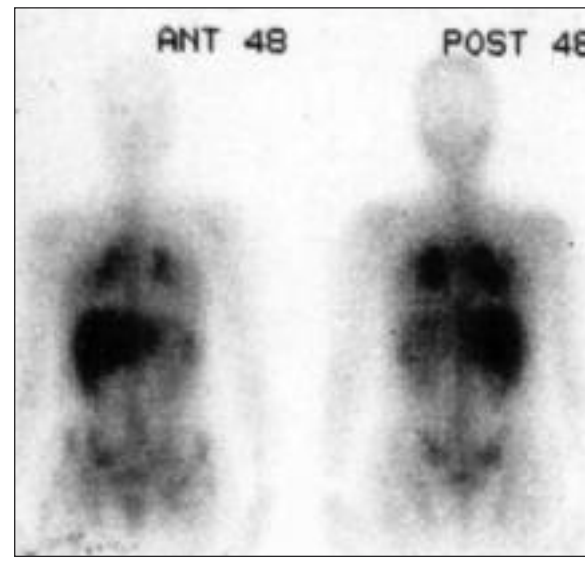

FIGURE 2: Hilar uptake.

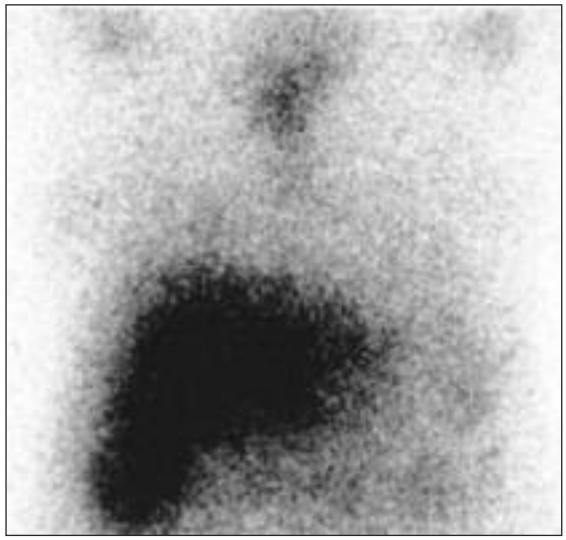

FIGURE 3: Mediastinal uptake.

FIGURE 4A: Diffuse parenchymal uptake.

FIGURE 4B: Computed tomography findings confirmed "sarcoidosis" in the same patient.

In 113 patients, 168 sites of extrapulmonary involvement were observed. Fifty-nine had panda sign (52%) (Figure 5), 45 had salivary or lacrimal gland uptake (40%) (Figure 6), 37 had lymph node uptake (33%) (Figure 7)-11 inguinal, 11 supraclavicular, 7 axillary, 4 epitrochlear, 3 paraaortic and 1 cervical region-and 7 had articular uptake (6%) (Figure 8). Sixteen patients had breast uptake (14%) (Figure 9), 2 patients had focal liver uptake (2%) (Figure 10A-10B) and two had cutaneous uptake (2%) (Figure 6). Table 2 summarizes these results.

Four patients had normal Ga-67 scintigraphy (4%).

Eighty patients had both extrapulmonary and intrapulmonary uptake (72%).

DISCUSSION

Ga-67 whole body scintigraphy is an important method to evaluate the disease activity, response to therapy and the extent of sarcoidosis particularly when extrapulmonary involvement (stage IV disease) is present.[3-6] In this study, our aim was to investigate the frequency and localization of extrapulmonary involvement in sarcoidosis with Ga-67 scintigraphy.

Normal biodistribution of Ga-67 is in the bony skeleton, the liver, the spleen, the nasolacrimal glands and the colon. The normal uptake of Ga-67 by the liver and spleen makes it difficult to detect the involvement of these organs in sarcoidosis.

Up to 30% of patients with sarcoidosis present with extrapulmonary disease. Sarcoidosis often affects skin, eyes and liver; less often spleen, nerves, salivary glands, bones and joints; rarely affects breast and kidneys. Karalezli et al studied 50 cases with histopathologic diagnosis of sarcoidosis and reported 40% etrapulmonary involvement.[7]

Ga-67 has been used to detect extrapulmonary involvement in sarcoidosis for years. In 1987, Prashant et al investigated the extrapulmonary involvement in sarcoidosis and reported that the most common site of radiogallium accumulation was the

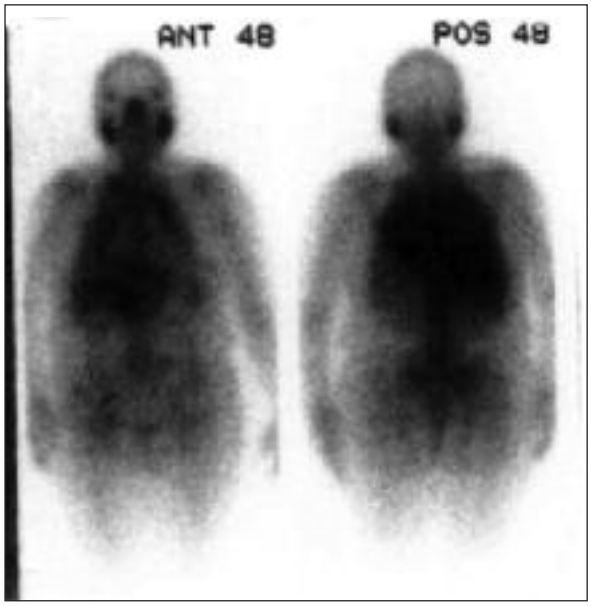

FIGURE 5: Panda sign.

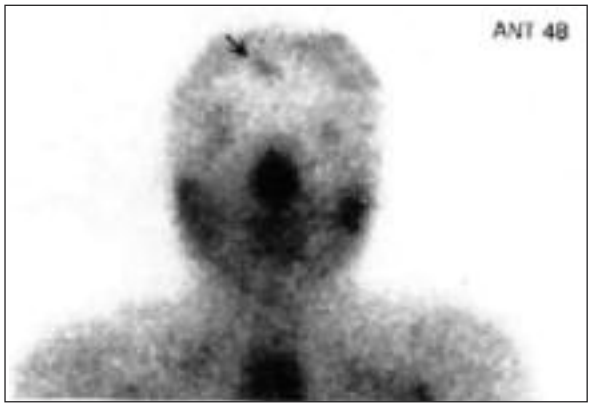

FIGURE 6: Salivary-lacrimal glands uptake and cutaneous uptake shown with arrow.

salivary glands (50-60%) followed by the lymph nodes (20-30%), spleen (50-60%), liver (60-70%), cutaneous tissue (10-35%), bone (1-13%), skeletal muscle (5-80%) and myocardium (25%).[8] On the other hand, Weinreb et al showed that in 87% of cases, symptomatic or asymptomatic lacrimal gland involvement was present.[9]

Sulavik et al also studied the etrapulmonary involvement in sarcoidosis and observed that lacrimal glands were the most common sites of Ga-67 uptake (88%). Other extrapulmonary findings were panda sign (41%), lymph nodes (17%), nasal uptake (8%), breast uptake (8%), periportal accumulation (6%), cutaneous (4%) and myocardium (1%). In this study, the panda sign was the most common site of extrapulmonary involvement, followed by the salivary or the lacrimal glands, lymph nodes, joints, breast, cranium and liver. Our results were in agreement with the data of Sulavik et al except for the frequency of lacrimal gland uptake.

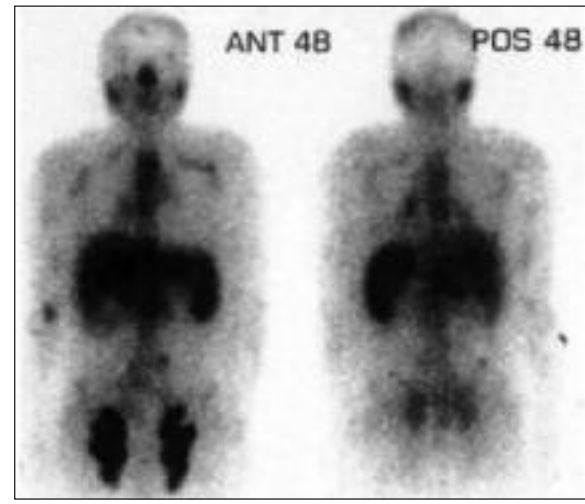

FIGURE 7: Axillary, supraclavicular, epitrochlear, inguinal and paraaortic lymph nodes uptake.

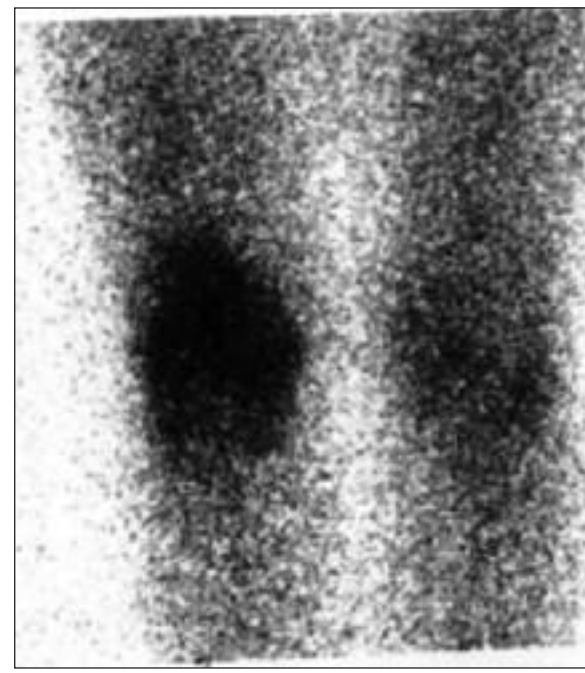

FIGURE 8: Ga-67 accumulation in the right knee.

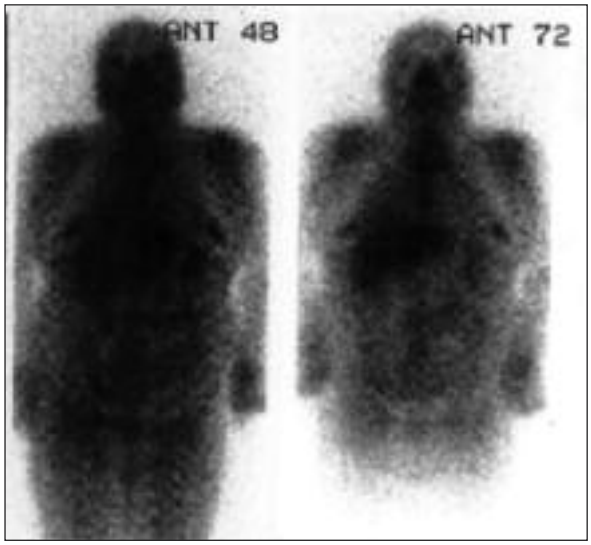

FIGURE 9: Bilateral breast uptake.

FIGURE 10A: Focal liver uptake shown with the arrow.

Weinreb described lacrimal glands as a normal localization of Ga-67 and reported lacrimal gland uptake in 87% of patients with proven sarcoidosis and in 31% of patients without sarcoidosis but with other ocular or pulmonary disease.[9] In this study, we found lacrimal gland uptake in forty five out of one hundred thirteen patients but we could not distinguish pathological uptake from physiological uptake on the images. This was one limitations of this study.

Panda sign was present in 59/113 patients in our study. It is not specific to patients with sarcoidosis and it appears in other conditions. On the other hand, the presence of lambda and panda signs concurrently is specific to sarcoidosis. [10] In this study, 26 out of 113 patients had both the lambda and the panda signs.

Lymph node uptake was 33% in our study. The involvement of superficial lymph nodes was proved with biopsy and paraaortic lymph nodes were confirmed with other diagnostic imaging methods (USG, CT). In other studies, the rate of lymph node involvement was almost identical.

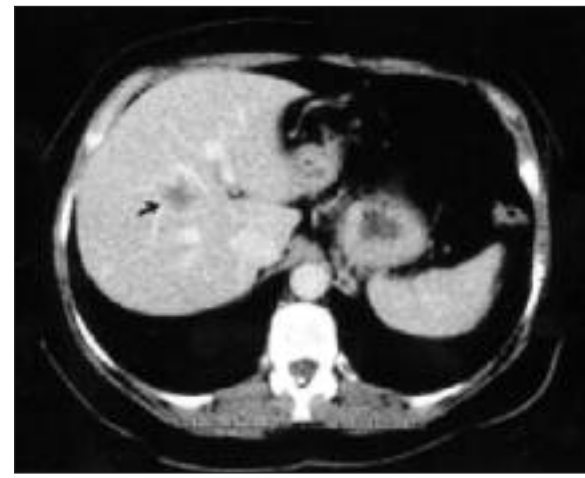

FIGURE 10B: The mass was detected also with abdominal CT.

TABLE 2: The results of extrapulmonary involvements in Ga-67 scintigraphy.

Findings	n	%
Panda sign	59	52
Increased salivary or lacrimal gland uptake	45	40
Lymph nodes uptake	37	33
Articular uptake	7	6
Breast uptake	16	14
Focal liver uptake	2	2
Cutaneous uptake	2	2

Diffuse and bilateral Ga-67 breast uptake was detected in 14% in our study. In another study, it was reported as 8%.[11] The Ga-67 uptake of the breast is frequently seen in the patients who are lactating, at menarche or taking birth control pills.[12] The retrospective analysis of the history of such patients revealed that the uptakes were due to menarche or birth control pills.

The articular uptake in this study was 6%. The articular uptake of Ga-67 may be observed in other pathologies like osteoarthritis and degenerative bone disease.

Cutaneous uptake was detected in 2/113 (2%) patients in our study. In one patient, histopathologic examination showed erythema nodosum in the frontal region.

Although 60-70% of patients with sarcoidosis have hepatic granulomas, clinical findings (i.e. hepatomegaly, intrahepatic cholestasis, portal hypertension) and abnormalities in laboratory findings are present in only 20-25%.[8] It is difficult to detect hepatic granulomas because liver is a site of physiologic uptake of Ga-67. The assessment of focal Ga-67 uptake in the liver of two patients proved to be hepatic granulomas by other diagnostic methods (ultrasonography and computed tomography).

Hyung-Sun Sahn et al described muscular involvement in sarcoidosis detected by Ga-67 imaging and MRI.[13] They determined that muscular involvement was frequently asymptomatic (50-80%) and might present with various clinical symptoms. Similar studies showed that Ga-67 imaging was a useful method in evaluating muscular involvement.[14-16] We did not observe any muscular uptake in Ga-67 images.

In conclusion, Ga-67 scintigraphy has been used to evaluate the extent of sarcoidosis. It demonstrates intrathoracic as well as extrathoracic involvement. It is useful in evaluating lesions that are not detected on clinical examination.

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