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The evolutional stage changes in sarcoidosis on gallium-67 scintigraphy

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Gallium-67 scintigraphy has been proven as the imaging modality of choice in monitoring the presence of active disease in sarcoidosis. The purpose of this study is to analyze the patterns of evolutional stage changes of sarcoidosis while on steroid therapy by Ga-67 scintigraphy. *Methods*: Eighty-six consecutive patients with biopsy-proved sarcoidosis are evaluated by Ga-67 scintigraphy. Thirty-six of 86 patients have had a baseline and one to eight follow-up Ga-67 scintigraphs (total 136 studies). The initial follow-up scintigraphs are obtained on average about 4–12 months after the baseline study. *Results*: Seventeen of 36 patients (47.2%) are in stage IV at the time of the baseline study. Following their first course of corticosteroid therapy, 13 patients remained in the same stage and activity distribution pattern while 13 patients have shown reversion to other stages, eight patients showed complete remission while two patients became active from inactive stage. *Conclusion*: Evolutional stage changes are seen in 23 patients (63.9%), including eight patients (22.2%) who showed complete scintigraphic remission. The evolutionary stage changes remain quite variable and unpredictable. This, however, should not detract from the usefulness of Ga-67 scintigraphy in the diagnosis and prognostic evaluation of sarcoidosis, particularly when extrapulmonary involvement (Stage IV disease) is present.

Key words: sarcoidosis, classification, evolutionary stage changes, Ga-67 scintigraphy, monitor

INTRODUCTION

Gallium-67 scintigraphy has been a useful imaging modality in the diagnosis of sarcoidosis for the last two decades.[1-3] Some characteristic features or patterns of sarcoidosis on Ga-67 scintigraphy have been described.[4-6] Ga-67 uptake is proportional to the degree of inflammatory or granulomatous response and inversely proportional to the degree of fibrosis.[2,3,6] It has also been used to monitor the disease during corticosteroid therapy, along with serum angiotensin converting enzyme (ACE) levels and bronchoalveolar lavage (BAL).[7-10] Still, some investigators feel that Ga-67 scintigraphy is pivotal in the decision-making of whether corticosteroid therapy is instituted or not.[2]

In this communication, the authors detail their experience and observation on the evolutional stage changes of sarcoidosis on serial Ga-67 scintigraphy in a group of patients who were on corticosteroid therapy.

MATERIALS AND METHODS

Eighty-six consecutive patients with biopsy-proved sarcoidosis have had baseline Ga-67 scintigraphy. There were 34 men and 52 women with an age range of 21–69 years (average of 39.5). Thirty-six of the 86 patients had one to eight follow-up scintigraphs, a total of 136 scintigraphs. Initial follow-up scintigraphs were obtained on average about 4 to 12 months after the baseline scintigraphs; about 4–6 weeks following the completion of steroid treatment.

All scintigraphs were performed in the conventional way using a 5–8 mCi (185–296 MBq) of Ga-67 citrate, injected intravenously 48–72 hours before the study. WFOV cameras, GE 535 Jumbo camera, GE Maxxus dual

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head camera, Picker XP 2000 dual head camera, were used in obtaining either multiple regional static images or total body images. Each individual Ga-67 scintigraphy was compared with chest X-rays and CAT scans whenever available and careful clinical and laboratory evaluation were utilized to exclude the possible presence of other existing pathology such as pneumocystis carinii pneumonia, lymphoma, tuberculosis, etc.

Table 1 Chest radiography classification of sarcoidosis

Stage 0	Normal
Stage I	Bilateral hilar adenopathy
Stage II	Bilateral hilar adenopathy and diffuse parenchymal infiltrates
Stage III	Diffuse parenchymal infiltrates without hilar adenopathy

Table 2 Gallium-67 scintigraphy classification of sarcoidosis (1986, Goslar, FRG)

Stage 0		Normal
Stage I		Bilateral hilar adenopathy
Stage II		Bilateral hilar adenopathy and parenchymal infiltrates
Stage III		Parenchymal infiltrates without hilar adenopathy
Stage IV	(A)	Extrapulmonary adenopathy
	(B)	Liver, spleen, skin or bone

Table 3 Baseline scintigraphy of all 86 patients

Stage 0	: 5			
Stage I	: 26			
Stage II	: 6			
Stage III	: 6	Intrathoracic findings		
Stage IV	: 43	hilar	:	28
		hilar & parenchymal	:	7
		parenchymal	:	8

Classification Based on Chest Radiograph and Ga-67 Scintigraphy:

Current general medical literature classifies the various stages of sarcoidosis on the basis of chest radiographic findings[11–14] (See Table 1). This radiographic classification is inadequate since it is limited only to the chest and does not address the presence of extrapulmonary pathology. Other organs and parts of the body such as lymph nodes, eyes, salivary glands, liver, spleen, central nervous system, myocardium, muscles, and cutaneous tissue are

Table 4 Baseline scintigraphy among 36 patients with follow-up studies

Stage 0	4 of 36 (11.1%)
Stage I to III	15 of 36 (41.7%)
Stage IV	17 of 36 (47.2%)

Table 5 Evolutional changes of staging of sarcoidosis

Follow-up	Baseline Staging →				
	0	I	II	III	IV
0	**2**	2	1	1	4
I		**2**	1		3
II			**1**		1
III	1			**4**	1
IV	1	3			**4 + 4***

4*: While the extrapulmonary component remains unchanged, the intrathoracic distribution pattern changed from I *to* II (1); I *to* III (2); II *to* I (1). Hence, these "4*" patients are included in the group with evolutional stage changes.

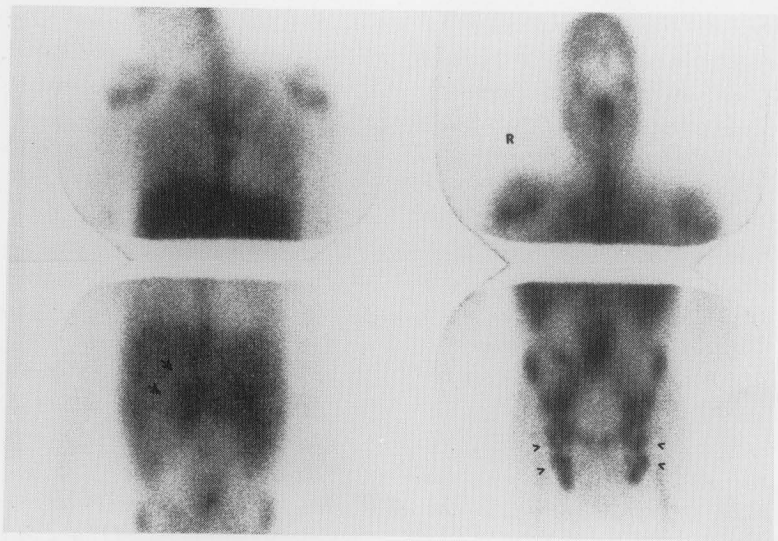


Fig. 1 A patient with Stage IV (B) sarcoidosis. Note lymphadenopathy in the inguinal (arrowheads) and paracaval (arrows) areas and hepatosplenomegaly in addition to the lung parenchymal uptake.

Table 6 Stage changes during therapy

Baseline study		Follow-up study
2 in Stage 0	→	Stage III & IV
8 in Stage I–IV	→	Stage 0
13 in Stage I–IV	→	Variable Stages* (See Table 7)
13 in Stage I–IV	:	No change in stage & pattern

Table 7 13* in Stage I–IV → variable stages

Baseline	Follow-up	Case
Stage I	Stage IV	3
Stage II	Stage I	1
Stage IV	Stage I	3
	Stage II	1
	Stage III	1
	Stage IV**	4

4**: While the extrapulmonary component remains unchanged, the intrathoracic distribution pattern changed from I *to* II (1); I *to* III (2); II *to* I (1). Hence, these "4**" patients are included in the group with evolutional stage changes.

Table 8 Extrapulmonary sites in 17 patients in Stage IV sarcoidosis

Anatomic sites	n	Prevalence/17 patients (%)
Inguinal (ING)	8	47.1
Paracaval (CAVA)	7	41.2
Supraclavicular	2	11.8
Spleen	2	11.8
Axillary	2	11.8
Scrotal	1	5.9
Pericardial	1	5.9
Skin/Others	2	11.8

involved with varying frequency in this disease.[13] Moreover, the radiographic classification is based on descriptive changes and does not correlate with the clinical activity of the disease. There is a dichotomy between the radiographic stages that are currently used and the actual clinical symptoms and the course of disease itself.[12]

It is for the preceding reasons that a classification based on Ga-67 scintigraphic features was introduced in 1986 in Goslar, F.R.G.[15] (See Table 2). This Ga-67 scintigraphic classification had been expanded to include stages IV (A) and (B) which take into account the presence of any extrapulmonary adenopathy or other organ or site involvement (Fig. 1).

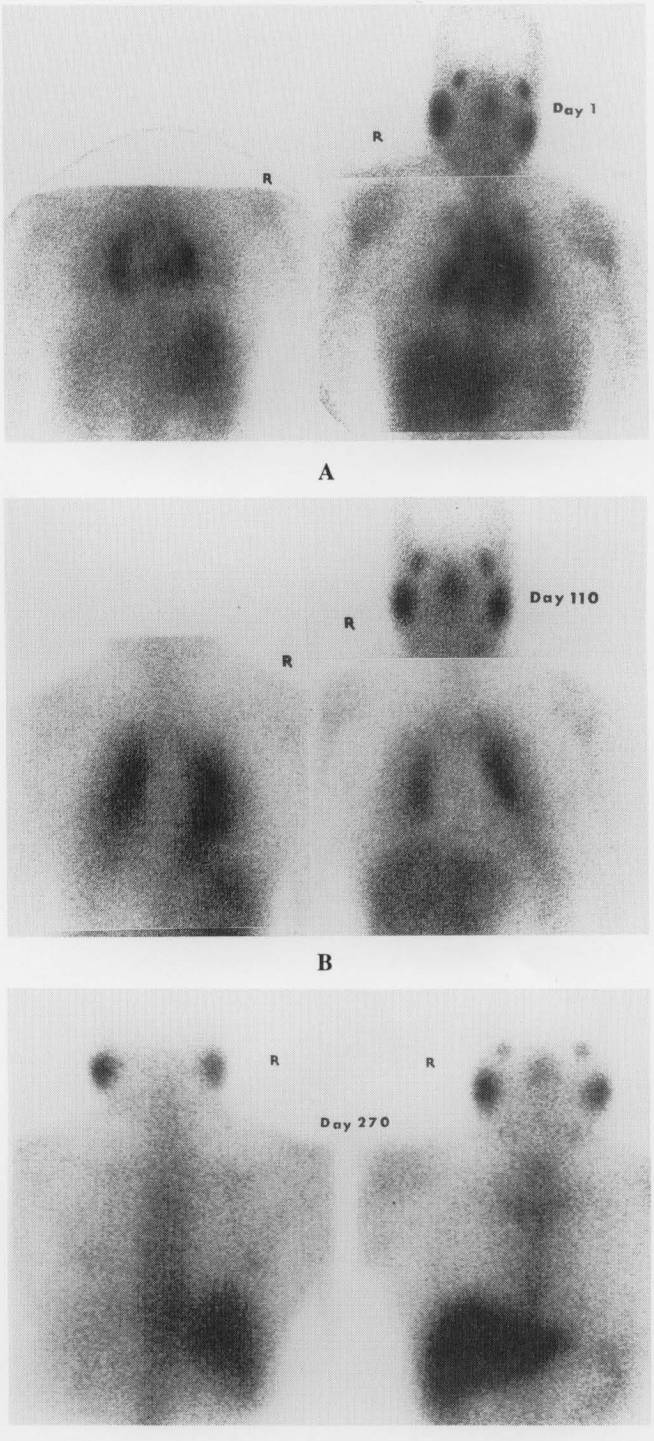
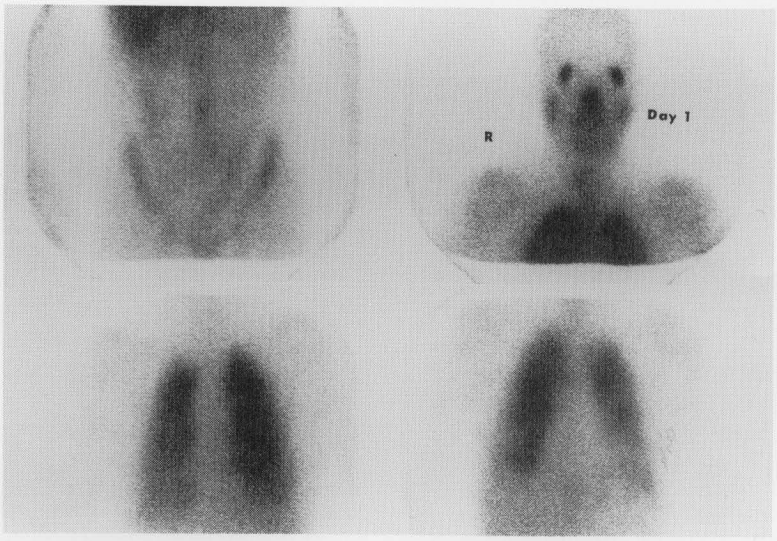


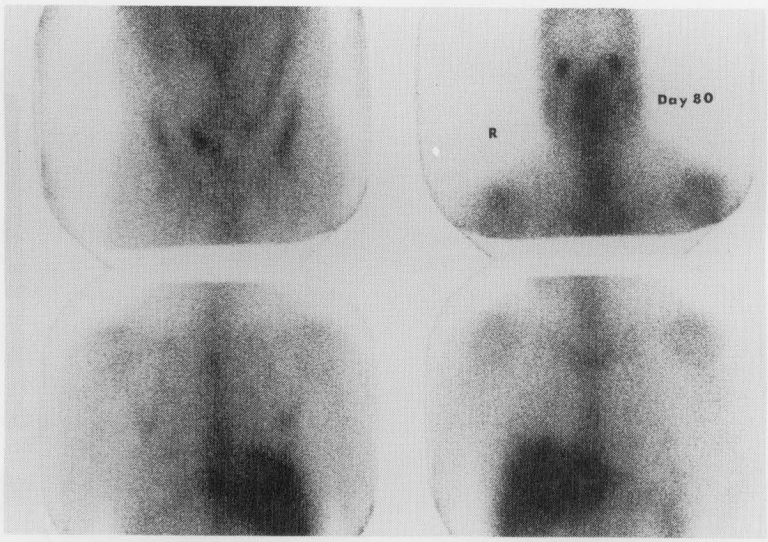
Fig. 2 A, B & C: A baseline Ga-67 scintigraph with Stage I has progressed to Stage II (day 110) and undergone complete remission on day 270 (I *to* II *to* 0).

RESULTS

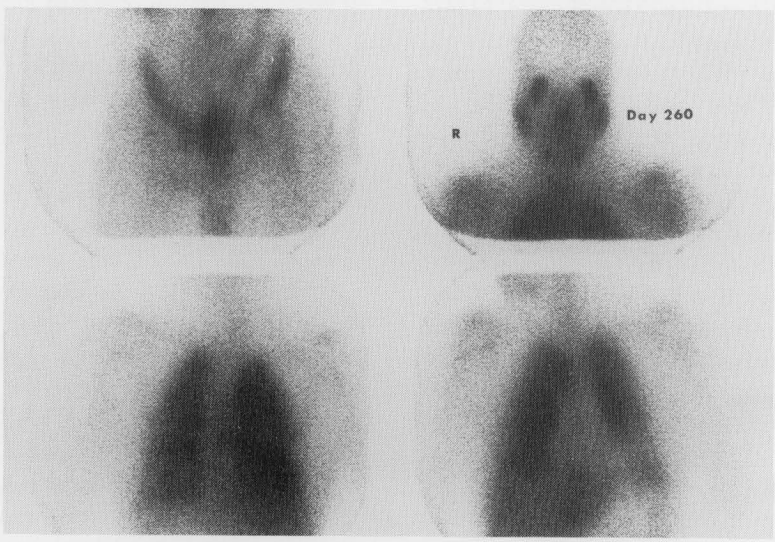
Table 3 shows the number of patients of each stage of all 86 patients. Table 4 outlines the baseline stage findings in 36 patients with follow-up studies. Following their first course of corticosteroid therapy (Tables 5, 6 & 7), two patients in Stage 0 remained inactive (0 *to* 0) while two others progressed to Stage III and IV (0 *to* III/IV). Of 15 patients in Stage I to III, four have undergone complete remission (I–III *to* 0) and seven remained in the same stage (I–III *to* I–III) while three in Stage I progressed to



A

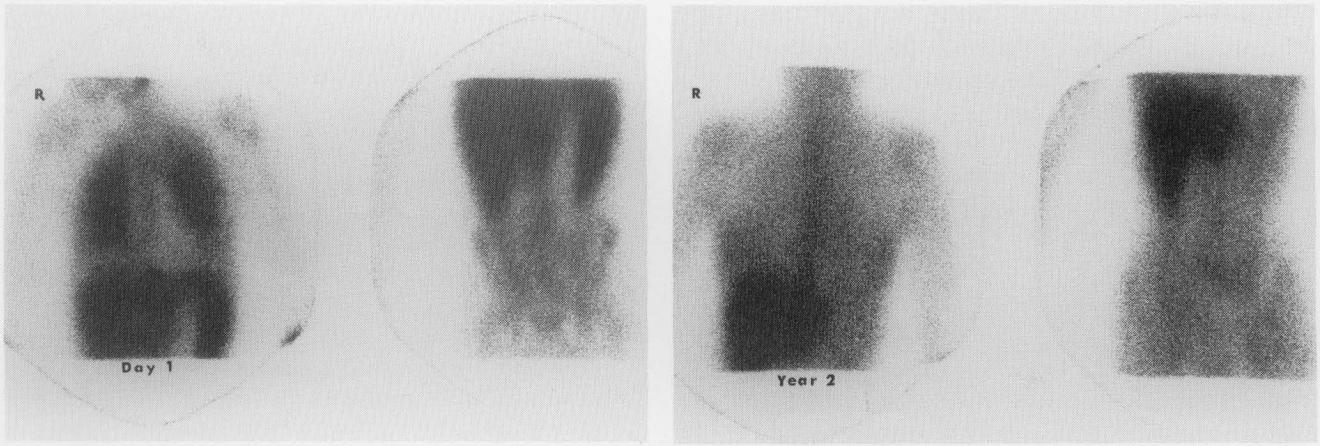


B



C

Fig. 3 A, B & C: A patient with Stage III sarcoidosis on day 1 has undergone complete remission in 80 days, only to revert back to Stage III again on day 260 (III *to* 0 *to* III).



A B

Fig. 4 A & B: A baseline Ga-67 scintigraph shows diffuse lung parenchymal activity and hepatosplenomegaly with diffuse intense splenic activity (Stage IV (B)). The scintigraph obtained 2 years later shows complete resolution of lung activity and normal sized liver and spleen.

Stage IV (I *to* IV) and one in Stage II changed to Stage I (II *to* I). In one patient, baseline Stage I disease has progressed to Stage II on day 110 but has undergone complete remission on day 270 (I *to* II *to* 0; Figs. 2A, B & C). Another patient with baseline Stage III disease has undergone complete remission on day 80, only to revert to Stage III on day 260 (III *to* 0 *to* III; Figs. 3A, B & C). Table 8 shows extrapulmonary sites in 17 patients in Stage IV, inguinal lymph node involvement being most frequent (47.1%). Of these 17 patients, four underwent complete remission (IV *to* 0) and four remained unchanged (IV *to* IV) while five changed to other stages (IV *to* I–III) and four others showed interval changes of the intrathoracic distribution pattern but remained within the same staging category (IV *to* IV*). Figures 4A & B show complete disappearance of diffuse lung parenchymal activity as well as decrease in size and activity of both liver and spleen in two years.

DISCUSSION

In reviewing our data, somewhat unexpected was that 47.2% of our patients (17 of 36) had stage IV disease at the time of the baseline study (See Table 4). This means that 47.2% of the patients at the time of scintigraphic diagnosis already had disease involvement outside the thoracic cavity. These data are probably in keeping with the variable yet insidious onset and presentation of clinical findings of this disease.[14] The presence of already extensive disease in newly diagnosed patients suggests that pathology may be already far reaching at the outset and was not merely confined to the thorax. This implies that patients who have disease apparently confined to the chest only as seen on chest radiograph should in fact undergo further more extensive evaluation of other systems. This observation is not apparent in the pre-Ga-67 literature based on already published reports probably because imaging diagnosis of the disease was based solely on chest radiographic findings and diagnostic exploration for extrapulmonary involvement may have been more limited.

With the exception of the eight patients (22.2%) who went into complete remission on Ga-67 scintigraphy, it is clear that the foregoing changes observed in these series of patients during therapy have a variable and no clear predictable pattern of change. The Ga-67 activity patterns and the evolutional stage changes that have occurred in 63.9% of the cases are distributed all over the board. No explanation for this variability of pattern change was evident from our data. These unpredictable and variable scintigraphic patterns, however, should not detract from the overall role of Ga-67 scintigraphy in the documentation and clinical follow-up of the disease itself while the patients are on therapy. In our series, altogether 23 of 36 (63.9%) patients with abnormal gallium activity showed either regression or progression of uptake. These evolutional changes, particularly in patients with stage IV disease, were best captured by Ga-67 scintigraphy because of the whole body capability that can only be offered by this modality. Many authors[8,16–18] agree that the Ga-67 scintigraphy is and remains the imaging modality of choice not only in documenting the presence or extent of the disease process itself but also in monitoring the progression or regression of the disease.

The concurrent determination of serum ACE level and/or performance of BAL along with Ga-67 scintigraphy have their own proponents and detractors.[8,18,19] Schoenberger and colleagues found serum ACE to be a poor predictor of the severity of alveolitis in sarcoidosis.[18] Beaumont and co-workers also found Ga-67 scintigraphy to be more sensitive in identifying active disease than any other traditional methods of investigation, including se-

rum ACE and BAL levels.[8] On the other hand, Okada and associates advocate that chest radiograph and serum ACE level are sufficient to reflect any disease activity.[20]

The use of CT scan has been explored recently.[21] Its cost and radiation exposure are probably inhibiting factors for its routine use, specially when there exists an easy to perform and effective imaging modality such as Ga-67 scintigraphy.

CONCLUSION

Clearly dramatic evolutional stage changes, both regression and progression were observed in 63.9% (23 cases) of patients with biopsy-proved sarcoidosis on Ga-67 scintigraphy following corticosteroid therapy. Albeit, the evolutional stage changes are variable and unpredictable, except for the 22.2% (8 cases) that have undergone complete remission, Ga-67 scintigraphy remains the imaging modality of choice. Based on our data we were unable to come up with an apparent explanation for these variability and unpredictability of the scintigraphic changes. This was not only in the diagnosis and documentation of the extent of the disease but also in the monitor of the clinical activity of the disease. This was particularly true when there is extra-pulmonary involvement.

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