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Gallium-67 and Technetium-99m-MDP Scintigraphy for Osseous Involvement in Lymphoma

TO THE EDITOR: We read with interest the article by Bar Shalom et al. (*1*). The authors used high-dose ^{67}Ga and concluded that ^{67}Ga uptake by ^{67}Ga-avid lymphoma involving bone may be used to monitor osseous response to treatment (*1*). Moreover, they hypothesized that after effective treatment, ^{67}Ga scintigraphy will normalize earlier when compared to bone scintigraphy.

We wish to add our experience using low dose ^{67}Ga, discuss occasional discrepancies using both tracers and present previously unreported false-positive studies.

In a retrospective study of data collected over the last 5 yr, we studied 12 of 87 patients suffering from Hodgkin's (n = 7) or non-Hodgkin's lymphoma (n = 5): 6 men and 6 women; mean age 37 yr; range: 16–66 yr. Inclusion criteria consisted of: (a) ^{67}Ga avidity of involved lymph nodes, (b) bone involvement confirmed by x-ray and/or CT, (c) availability of ^{67}Ga and ^{99m}Tc-MDP bone scintigraphies (mean time interval 7 ± 6 days) before and after treatment with a mean of 4.5 mo follow-up intervals. Gallium whole-body scintigrams were obtained after intravenous injection of 2–4 mCi ^{67}Ga using a single-headed gamma camera equipped with a medium-energy collimator. For both anterior as well as posterior views, images of 600–800 kcts were collected.

Of the 12 patients, bone involvement was found in one (n = 5), two (n = 4), three (n = 2) and four (n = 1) skeletal sites, respectively. In two patients (A and B), ^{67}Ga uptake was more intense at one site compared to ^{99m}Tc-MDP uptake, while in two other patients (C, D) ^{67}Ga scintigraphy failed to show one site of involvement. In all 12 patients, control ^{67}Ga scintigraphs were normal, which corresponded with a complete remission as judged by oncological criteria and/or follow-up; however, control bone scintigraphy remained positive.

Contrary to the findings of Orzel et al. (*2*), our data obtained using low-dose ^{67}Ga confirmed the findings by Bar Shalom et al. (*1*) and their hypothesis that ^{67}Ga scintigraphy will normalize earlier after effective treatment compared to bone scintigraphy. We suggest that the lower detection rate of ^{67}Ga scintigraphy compared to ^{99m}Tc-MDP bone scintigraphy in the series presented by Orzel et al. (*2*) may be due to the use of the bone scan as the gold standard for the detection of lymphomateous osseous involvement rather than to the low dose of ^{67}Ga injected.

In the article by Bar Shalom et al. (*1*), possible explanations for the occasional discrepancies between ^{67}Ga and bone scintigraphy were not discussed. In the intermediate and high-grade subgroups of non-Hodgkin's lymphoma patients in whom the sensitivity of ^{67}Ga scintigraphy for disease detection is high, ^{99m}Tc-MDP uptake reflecting osteoblastic activity may be low since 77% of bone lesions are lytic. This is illustrated by Patient A in our series and the two patients with bone scintigrams and CT scans in the series by Bar Shalom et al. (*1*). This discrepancy is less likely to occur in Hodgkin's lymphoma since only 14% of bone lesions are lytic (*3*). Gallium-67 scintigraphy may also perform better than ^{99m}Tc-MDP bone scintigraphy when involvement is limited to bone marrow without osseous invasion. Tumoral heterogeneity (*4*) and overlap between sites of normal ^{67}Ga uptake, and osseous lymphoma localizations may account for ^{67}Ga false-negative and ^{99m}Tc-MDP-positive sites. In our Patient D, involvement of the left maxillary region was not detected on ^{67}Ga scintigraphy because of overlap of normal ^{67}Ga uptake in the nasopharyngeal region. This interference could be important in endemic Burkitt's lymphoma in which the most common sites involved are the mandible and maxilla (*5*). Because of the retrospective character of this study, SPECT, which could enable detection of lesions overlapping with sites of normal, uptake was not performed.

In addition to osseous involvement in ^{67}Ga-avid lymphoma, noninflammatory conditions (*6*), including trauma (*6,7*), untreated Paget's disease (*8*) and osteomyelitis (*9*), may also present as both ^{67}Ga-and ^{99m}Tc-MDP-positive bone lesions. In our series, both bone marrow expansion and bone infarction presented as previously unreported scintigraphic imitators of osseous involvement (*10*).

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REPLY: We thank Dr. Van de Wiele and his colleagues for their interest in our paper on ^{67}Ga in lymphoma of the bone (*1*) and appreciate the fact that they had essentially the same results.

We did not hypothesize that ^{67}Ga will show response to treatment. Rather, we described our findings such that "scintigraphy also correctly monitored bone response to treatment in all but one of the 16 patients." It has been clearly established before that bone scintigraphy is not useful for monitoring response in cancer patients (*2*). Van de Wiele et al. found that ^{67}Ga scintigraphy correctly monitored response in all 12 patients while bone scintigraphy did not. This is similar to our results.

It is indeed a common, but not a properly studied, belief that ^{67}Ga is taken up only by high- and intermediate grade-lymphoma. When using high doses of ^{67}Ga and dual-head high sensitivity cameras with ^{67}Ga dedicated collimators, however, the sensitivity in most types of low-grade lymphoma is quite similar to that of high- and intermediate-grades. Moreover, SPECT helps in separating normal tissue overlapping lesions and in determining accurate localization of lesion.

None of our patients had bone trauma, Paget's disease or osteomyelitis which, as Van de Wiele et al. correctly state, may take up ^{67}Ga. In practice, however, the specificity of ^{67}Ga scintigraphy in lymphoma is high. This is not because ^{67}Ga is taken up only by lymphoma but because scintigraphy is done only when there is histological proof for lymphoma. The population bias therefore is high.

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