Splenic Uptake of Tc-99m Sulfur Colloid in Malignant Melanoma

In a recent letter in this journal, Nathanson and Kahn (*1*) reported on a review of Tc-99m sulfur colloid (Tc-SC) scans in 24 patients with malignant melanoma. They found no case of augmented splenic activity that could not be explained by associated liver or splenic disease.

Their findings are not only in conflict with a number of other studies (*2–4*), but they suggested that the excess splenic uptake in a significant proportion of patients with malignant melanoma, reported by Goldman et al. (*2*), might be related either to unappreciated and incidental hepatic disorders or to technical problems related to "estimating absolute count rates."

Goldman et al. specifically excluded patients who had *any* biochemical, clinical, or scan evidence of hepatic abnormality, and it is therefore highly unlikely that the ten patients (34%) with malignant melanoma who showed augmented splenic activity had diffuse liver disease without biochemical, clinical, or scan evidence of abnormality. With regard to the possible technical problems, it is clearly difficult to assess absolute activity from clinical images, however, they are obtained. There was no attempt in the study by Goldman et al. to use "absolute count rates" per se. The clear, albeit arbitrary, criteria used were applied identically to a control group of 60 patients, and this group showed an incidence of augmented activity in 1.8% of the cases. It is not likely that incidental causes for augmented splenic uptake (e.g., infection) were present in a high proportion only of the melanoma group and not in the control group, and we therefore feel the observations of Goldman et al. were valid.

Nathanson and Kahn, on the other hand, do appear to be using some absolute criteria of relative activity, which are not detailed in their letter. Since they do not apply these criteria equally to a control group, we wonder about the validity of judgments regarding splenic activity, such as "upper limits of normal" or "small normal"—or if, indeed, such absolute judgments could have any meaning.

Because of the difficulties inherent in making such judgments precisely in a clinical setting, a recent report by Chandra et al. (*5*) is of particular interest. This report bears out the findings of the clinical studies showing that malignant melanoma in itself was more often associated with augmented splenic activity. In the Chandra report, 72 mice were divided into three groups. Group 1 received implants of malignant melanoma; Group 2 received implants of mammary adenocarcinoma; and Group 3, the control, received no implants. From 14 to 17 days after implantation, the mice were given i.v. Tc-SC, then killed, and distribution studies performed. This study found that, even though the mice with malignant melanoma and mammary adenocarcinoma both had heavier spleens (statistically significant) than the control group, the specific activity—i.e., activity per gram—of the spleen was significantly higher only in the group of mice bearing malignant melanoma (with no evidence of visceral metastases).

Nathanson and Kahn concluded that a finding of augmented splenic uptake on Tc-SC liver-spleen scans in patients with melanoma is "probably not useful for diagnostic or prognostic purposes." This is unlikely to be a valid conclusion in view of a recent combined study at New York University and Harvard (*6*). In this study, Sober and coworkers reviewed the Tc-SC scans of 150 patients with malignant melanoma with no evidence of visceral involvement. They found that the prognoses of certain patients, who initially showed augmented splenic activity as the only abnormal finding, were significantly worse than those of patients who did not demonstrate this finding.

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Reply

This disease is well known for its propensity for widespread metastatic dissemination. In a series of patients studied between 1952 and 1966, before the common use of the most sensitive methods of radionuclide imaging of the spleen, 4% of a large series of melanoma patients had clinically diagnosed splenic metastases, and 36% of a smaller group were observed to have such metastases at autopsy (*1*). In a more recent study, 50% of patients with abnormal splenic uptake had splenic metastases at autopsy (*2*). Therefore, the hypothesis that increased splenic uptake of Tc-99m sulfur colloid in melanoma was associated with poor prognosis (*3*) necessitated exclusion of the possibility that such increased uptake might be related to metastatic disease in the spleen. The series of 24 melanoma patients mentioned in a previous letter (*4*) was, in fact, reported because of my somewhat surprising failure to confirm the findings of Goldman et al. (*5*) that 45% (10/22) of patients with melanoma and normal hepatic scans and function tests had unexplained increased uptake of isotope in the spleen. Since the publication of that letter, we have reviewed a larger series of approximately 55 patients who are clinically staged in categories of primary, local, or regional recurrent melanoma without evidence of visceral metastases. In this group, five patients have now been found with a distinct suggestion of increased splenic uptake. These patients are all male, but otherwise do not appear to have unique characteristics regarding age, type of primary, site of primary, etc. In addition to routine clinical studies, quantitative immunoglobulins (including IgE), PHA stimulation of peripheral blood lymphocytes, monocyte function, T and B cell markers in peripheral blood, and complement levels (including C_{1q}), have all been carried out and are within normal limits. In the followup of these pa-

tients (mean approximately 6 mo), one has already relapsed with intraabdominal (and probably splenic) metastases. Another has been found to have abnormal gallium scan findings in the mediastinum, suggesting the possibility of relapse. Berjian et al. (*2*) have suggested that for those patients in whom resolution of increased splenic size to normal size occurs, a good prognosis will ensue. The reverse is true for patients with persistent increased uptake. This suggestion might reconcile our findings with those of Sober et al. (*3*).

The clearcut answer to the question of whether increased splenic uptake of Tc-99m sulfur colloid represents a remote effect of melanoma, presumably mediated by some humoral mechanism, or whether it simply indicates diffuse micrometastases in the spleen, however, will be resolved only when it is possible to carry out histopathologic examination on a significant number of spleens in these patients.

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