Nonantigen-Specific Tissue Localization of Monoclonal Antibodies

TO THE EDITOR: With great interest we read the recent editorial by A. J. Fischman in The Journal of Nuclear Medicine (1). In his contribution, Fischman stresses the importance of considering nonantigen-specific tissue localization when specific antibody targeting is evaluated. While conducting radioimmunomaging studies of patients with ovarian carcinoma, we recently encountered a case which may provide complementary information, supporting his editorial message.

We studied 31 patients suspected to have primary or recurrent ovarian carcinoma by using indium-111-labeled-OV-TL 3 F(ab')2. OV-TL 3, a murine monoclonal antibody (MoAb), recognizes a cell-surface antigenic determinant (OA3) present on more than 90% of human ovarian carcinomas of various histologic types (2). Twenty-two out of the 31 patients underwent surgery within 5–7 days following intravenous administration of 140 MBq 111In-OV-TL 3 F(ab')2. In these 22 patients, imaging results were compared with histopathologically confirmed findings at operation (3). In only 1 out of 22 patients was a false-positive result obtained at immunoscintigraphy. The tumor-to-background ratio using a region of interest technique with measurement in lesion and contralateral site was 1.3 throughout the 96-hr study period. In this patient, a large colon carcinoma was removed at operation. Extensive immunohistochemical analysis, using standard indirect immunoperoxidase techniques, indicated that this carcinoma was negative for the OV-TL 3 associated antigenic determinant OA3.

This result clearly demonstrates that in this case localized 111In uptake was the result of one or more nonspecific mechanisms. Enhanced vascular permeability in tumor tissue, as suggested to explain accumulation of 111In-labeled human polyclonal nonspecific IgG in inflammatory processes in rats, is one possible mechanism (4). Secondly, trapping of 111In in tumors similar to that in the reticuloendothelial system could provide an additional explanation. These and other nonspecific mechanisms probably play a role in cases where the presence of specific antigens is clearly demonstrated.

We agree with Fischman that demonstration of the specific antigen in a tumor does not necessarily mean that positive immunoscintigraphy is primarily due to antigen-antibody interaction. Further studies on the mechanism of nonspecific localization of MoAbs in tumors and other lesions are needed to clarify the impact of the hybridoma technology on daily clinical nuclear medicine.

REFERENCES


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Nonspecific Uptake in Radioimmunoscintigraphy

TO THE EDITOR We found the article of Kairemo et al. (1) and the editorial by Fischman (2) very interesting in understanding aspecific uptake in radioimmunoscintigraphy (RIS). Since 1984, we demonstrated the possible effect of pathophysiologic conditions, such as changes in permeability or “biologic barriers,” on the in vivo distribution of radiolabeled monoclonal antibodies (MoAbs) (3,4). In fact, in one of our melanoma patients, analyzed two days after the complete removal of the neoplastic lesion, a slight activity was demonstrated at the level of the surgical area (3). In this case, a F(ab')2, labeled with technetium-99m, reacting against a high molecular weight melanoma-associated antigen was utilized (Tecnemab, Sorin, Saluggia).

Similar results were obtained in other fields of our experience, mainly related to the evaluation of colon and ovarian cancer (5–7). For example, an intense uptake of MoAb B72.3 labeled with iodine-131 (131I) was observed at the level of surgical scar in a patient with ovarian cancer, disease free at the moment of the study, 20 days after second-look surgery. The increased activity was apparent in scans performed at different times, between 24 and 72 hr after i.v. injection of 111MBq of 131I-B72.3 (Sorin, Saluggia). No significant amount of free iodine was present. Serum levels of CA 125 were increased at the moment of the study (184 U/ml). At present, this patient is disease-free and shows normal levels of CA 125.

Possibility of nonspecific uptake has been also found in brain lesions, in the absence of neoplastic localization, because of brain-blood barrier rupture. In these cases, as demonstrated...