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Scintigraphic Evaluation of Tumors Metastatic to the Choroid Using Technetium-99m(V)-Dimercaptosuccinic Acid

Hayyam Kıratlı,* Pınar Özgen Kıratlı† and Meral Tayan Ercan†

*Ocular Oncology Service, Department of Ophthalmology;
†Department of Nuclear Medicine, Hacettepe University School of Medicine, Ankara, Turkey

Abstract: Technetium-99m(V)-dimercaptosuccinic acid scintigraphy was used to evaluate three patients with intraocular tumors who had metastatic breast, lung, and rectal carcinomas, respectively. At the time of initial examination, two patients had no known systemic cancer, but the scintigraphy results in one patient revealed the primary site and were highly suggestive of disseminated carcinomatosis in the other patient. In the third patient, scintigraphy was successful to confirm very small bilateral intraocular tumors and also other systemic lesions. Technetium-99m(V)-dimercaptosuccinic acid scintigraphy can be reliably employed in a very select group of patients with intraocular tumors where metastatic carcinoma is a serious diagnostic possibility against a primary intraocular malignancy. This safe and promising tumor-imaging agent has the ability to demonstrate the ocular lesions and other systemic foci simultaneously, information that would prove to be crucial in both the diagnosis and the management of the patient. **Jpn J Ophthalmol 1998;42:60–65** © 1998 Japanese Ophthalmological Society

Key Words: Metastatic tumors, radionuclide, technetium-99m(V)-dimercaptosuccinic acid, uvea.

Introduction

Metastatic tumors have been widely recognized to be the most common form of intraocular malignancy, even more frequent than primary uveal melanoma.[1–4] This observation is largely derived from postmortem histopathological studies on patients with known terminal systemic cancer.[1,5] In clinical practice, however, only a few patients not in the terminal stage and presenting with a metastatic intraocular tumor that necessitates treatment could be detected. Consequently, the current belief is that clinically significant metastatic tumors are in fact much less common than primary uveal melanomas.[6]

In about 70% of patients presenting with a metastatic intraocular mass, there is a known history of prior or concurrent malignancy.[4,6] The patient may be receiving chemotherapy or may have other systemic metastases at the time of discovery of ocular involvement.[6] In a fewer number of cases, however, an intraocular tumor may be the first clinical manifestation of an otherwise occult systemic cancer.[4] In these instances, the diagnosis may still be difficult despite the currently available diagnostic modalities including ophthalmoscopy, fluorescein angiography, ocular ultrasonography (US), and magnetic resonance imaging (MRI). In this study, the ability of technetium-99m(V)-dimercaptosuccinic acid (Tc-99m[V]-DMSA) to detect intraocular metastases and also to demonstrate systemic tumors simultaneously was evaluated in three different patients.

Patients and Methods

Three patients with choroidal metastases were investigated using Tc-99m(V)-DMSA. The patients had rectal adenocarcinoma, infiltrating ductal breast carcinoma, and pulmonary epidermoid carcinoma, respectively. Three hours following intravenous administration of 740 MBq of Tc-99m-(V)-DMSA prepared by previously published methods,[7] planar and

Received: February 28, 1997
Address correspondence and reprint requests to: Hayyam KIRATLI, MD, Hacettepe Universitesi Tıp Fakültesi, Göz Anabilim Dalı, Sıhhiye 06100, Ankara, Turkey

Jpn J Ophthalmol 42, 60–65 (1998)
© 1998 Japanese Ophthalmological Society
Published by Elsevier Science Inc.

0021-5155/98/$19.00
PII S0021-5155(97)00110-X

SPECT imaging were performed with a low-energy all-purpose collimator and a dual-head gamma camera (Genesys, ADAC Lab, CA, USA).

Case Reports

Case 1

A 28-year-old, pregnant woman in her third trimester presented with the complaint of gradually decreasing visual acuity in her left eye for 1 month. Her best corrected visual acuity was 20/20 in her right eye and counting fingers in the left eye. Anterior segments of both eyes and right fundus were within normal limits. Fundoscopy of the left eye showed a creamy-yellowish solid mass 3 mm temporal to the disc, measuring 10 × 10 × 3.5 mm (Figure 1). There was minimal subretinal fluid over the tumor but there were no cells in the vitreous. A-mode US revealed medium internal reflectivity, and B-mode US showed an irregular, homogeneously solid choroidal mass. T1-weighted (T1W) MRI without contrast demonstrated that the mass was hyperintense compared to the vitreous; T2W images showed the tumor to be isointense compared to the vitreous. The results of systemic evaluations including a thorough obstetric examination were all unremarkable. With the presumptive diagnosis of possible amelanotic choroidal melanoma, it was decided to follow the patient very closely until the baby could be delivered safely, and iodine-125 plaque brachytherapy was scheduled thereafter. One month later, there was no change in the ocular tumor, but the patient was hospitalized because of intrauterine death of the fetus. However, the left choroidal mass suddenly started to grow rapidly after the removal of the dead fetus. The results of all systemic examinations were again negative, but Tc-99m(V)-DMSA scintigraphy revealed marked uptake in the left eye (Figure 2) and questionable multiple uptakes in the vertebral bodies and several other bones. Meanwhile, the tumor almost filled the left eye in 1 week, resulting in total exudative retinal detachment and elevated intraocular pressure. The eye was enucleated, and histopathologic examination revealed a metastatic adenocarcinoma possibly arising from the gastrointestinal system. The tumor was composed of adenoid structures in a fibrous stroma, and there were abundant signet-ring-type mucin-secreting cells (Figure 3). A meticulous survey of the gastrointestinal system showed a minute lesion in the rectum that ultimately proved to be the primary malignancy. Despite intensive chemotherapy, the patient expired a few months later.

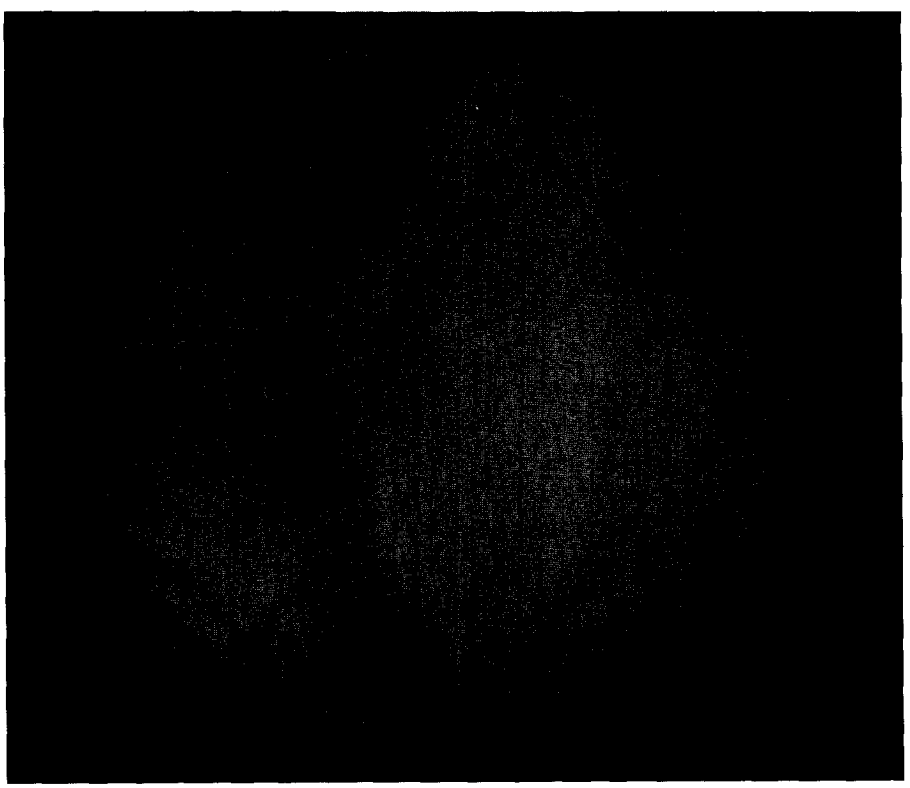

Figure 1. Left fundus of patient 1, showing amelanotic, well-circumscribed solitary choroidal mass that later proved to have metastasized from rectal adenocarcinoma.

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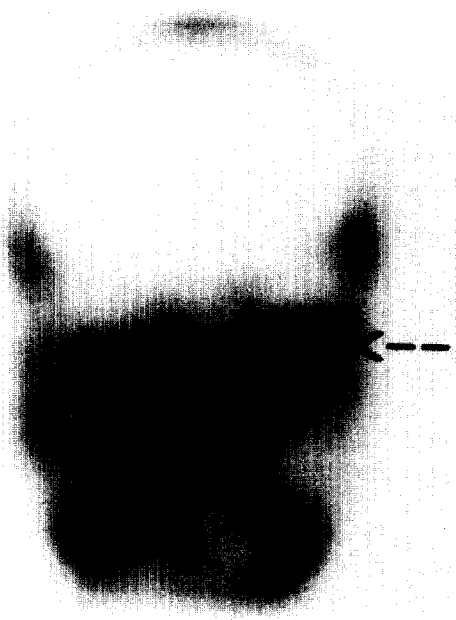

Figure 2. Technetium-99m(V)-dimercaptosuccinic acid scintigraphy of patient 1 demonstrating accumulation of agent in left eye (arrow), which contained the tumor.

Case 2

A 37-year-old otherwise healthy man was referred to our center because of an intraocular mass in his left eye, found incidentally on a routine eye examination. He had been told it was a choroidal melanoma. His best corrected visual acuity was 20/20 in the right eye and 20/60 in the left eye. The only ocular abnormality was a moderately pigmented choroidal mass measuring 10 × 10 × 4.5 mm in the temporal aspect of the left eye. There was no subretinal fluid. A-mode US showed a very low internal reflectivity, and B-mode US displayed an acoustically hollow, dome-shaped choroidal tumor. Fluorescein angiography showed late diffuse hyperfluorescence of the mass. The tumor was hyperintense compared to the vitreous on T1W MRI scans (Figure 4) and hypointense of T2W images. A Tc-99m(V)-DMSA scintigraphy performed at this stage showed two distinct foci of uptake—one in the left eye and the other in the right lung (Figures 5A, 5B). Computed tomography of the thorax also confirmed the presence of the second mass. Incisional biopsy under bronchoscopy revealed nonsmall cell epidermoid carcinoma. At the histopathological level, there were nests of mixed spindle-shaped cells and round pleomorphic malignant cells within the stroma underlying the ciliated respiratory epithelia. There was poor epithelial differentiation. Staining with HMB-45, a monoclonal mouse anti-human melanoma antibody clone (DAKO, Glostrup, Denmark), was negative. The patient was then subjected to a chemotherapy protocol, and 5 months later both pulmonary and ocular tumors had regressed considerably.

Case 3

A 38-year-old woman with a known infiltrating ductal-type breast carcinoma for the past 11 years

Figure 3. Photomicrograph of section from enucleated eye of patient 1 demonstrating many adenoid structures of varying size and signet-ring cells (arrows) with nuclei pushed toward the cell periphery as a result of excessive amounts of intracytoplasmic mucin (hematoxylin and eosin; bar = 10 μm).

Figure 4. T1-weighted magnetic resonance imaging scan of patient 2 after contrast agent administration showing left intraocular tumor which is hyperintense compared to vitreous.

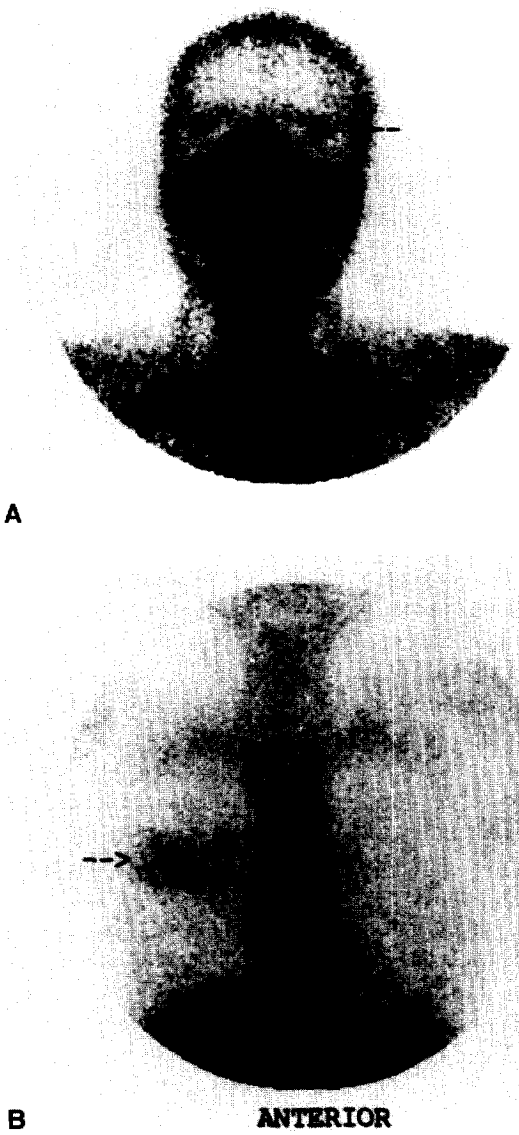

Figure 5. (**A**) Scintigraphic scan using technetium-99m(V)-dimercaptosuccinic acid shows increased uptake in the left eye (arrow) of patient 2. (**B**) Simultaneous imaging of the chest and abdomen revealed significant uptake in the right lung (arrow), which proved to be the primary malignant tumor.

presented with gradual bilateral visual loss. Her best corrected visual acuity was counting fingers in both eyes. The anterior segments were normal. However, there was massive exudation, so that the retinas were visible behind the lens in both eyes (Figure 6). Multiple small, pale, cream-colored lesions were visible at the choroidal level bilaterally. The largest of these tumors measured 4.5 × 4.5 × 2.5 mm. Systemic evaluation revealed several enlarged right axial lymph nodes, and an incisional biopsy from these confirmed the presence of metastatic carcinoma. Histopathologic examination of the excised specimens showed anaplastic cells with large, irregular hyperchromic nuclei dispersed in solid cell nests that disrupted and replaced the architecture of the lymph node. A Tc-99m(V)-DMSA scintigraphy was done to screen other possible locations of metastases, and it clearly demonstrated the ocular lesions (Figure 7) and the axial nodal tumors simultaneously. The patient then received chemotherapy and external beam radiotherapy to both eyes. Six months later, there was partial regression of the ocular tumors, and her visual acuity was 20/80 in both eyes.

Results

In all three patients, Tc-99m(V)-DMSA accumulated sufficiently in those eyes that contained metastatic carcinomas to allow clear detection by scintigraphy. Even tumors that were less than 5 mm in diameter could be demonstrated. In patients 1 and 2, in whom metastatic disease was not primarily suspected initially, Tc-99m(V)-DMSA revealed other foci of accumulation and greatly contributed to the final diagnoses. In patents 2 and 3, this agent confirmed and documented the regression of ocular and systemic tumors after treatment.

Discussion

Scintigraphic visualization of ocular tumors has been previously attempted by using several other ra-

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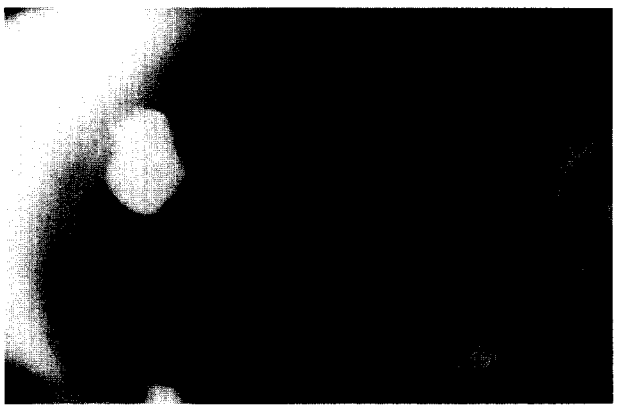

Figure 6. Massive total exudative retinal detachment visible behind the lens, in the right eye of patient 3, due to multiple small choroidal metastases.

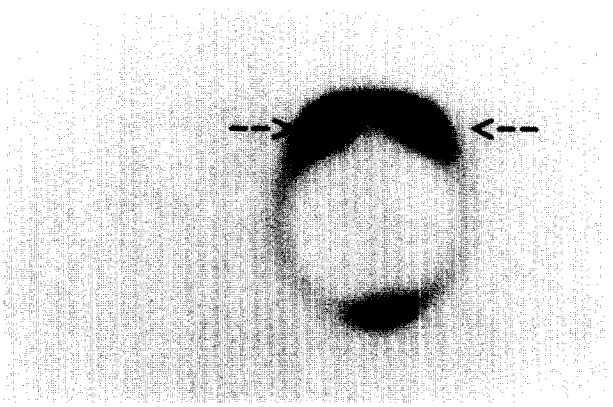

Figure 7. Technetium-99m(V)-dimercaptosuccinic acid scintigraphy of patient 3 showing bilateral significant ocular uptake (arrows).

dio pharmaceuticals.[8,9] However, all these agents tested so far have various shortcomings, and at present there is no agent available commercially for routine application. A simple-to-prepare, inexpensive agent, preferably in kit form, labeled with this ideal radionuclide, Tc-99m, would be very useful.

Technetium-99m(V)-dimercaptosuccinic acid, first developed by Yokoyama et al,[10,11] recently emerged as an excellent tumor-detecting agent in nuclear oncology. This substance has been shown to accumulate in a vast variety of malignant and benign soft tissue tumors including medullary thyroid carcinoma,[12] rhabdomyosarcoma, hemangiosarcoma, malignant fibrous histiocytoma,[13] aggressive fibromatosis,[7] plasmacytoma,[14] multiple myeloma,[15] head and neck squamous carcinomas,[16] schwannoma of the extremities,[17] and tenosynovial giant cell tumor.[18] Some rare tumors like renal cell, adrenal, and pharyngeal carcinomas were also documented by this technique.[19] Furthermore, skeletal, soft tissue, and central nervous system metastases in patients with breast carcinoma have been unequivocally demonstrated with Tc-99m(V)-DMSA.[20,21]

The proposed mechanism for the avid accumulation of Tc-99m(V)-DMSA in these tumors is linked to the phosphate metabolism or pH of the tumor and the blood flow through the lesion.[22] In fact, Tc-99m(V)-DMSA was originally designed as a metabolic mimic of the phosphate ion in its distribution pattern, which would be taken up by the cancer cells and supposedly be hydrolyzed within the cell.[16] In one study, Tc-99m(V)-DMSA was found to be 100% sensitive for malignant soft tissue tumors; all tumors in which this agent accumulated were malignant and necessitated biopsy or surgery.[22] The authors concluded that the absence of Tc-99m(V)-DMSA uptake could indicate that the tumor was not malignant.[22]

The applications of Tc-99m(V)-DMSA scintigraphy in intraocular neoplastic lesions have not been extensively studied, partly because of the fact that most of these tumors can be recognized easily by the currently available diagnostic techniques. Recently, we reported that Tc-99m(V)-DMSA was of value in a case of an amelanotic uveal melanoma.[23] In that particular case, the lack of any uptake other than by the eye contributed to the authors' final impression that the amelanotic mass they were to treat would most likely be a primary intraocular tumor rather than a metastasis of some systemic malignancy.[23] Our clinical experience suggests that, in a very limited number of patients where diagnostic uncertainty still persists despite the commonly available diagnostic tools, Tc-99m(V)-DMSA can provide much vital information to the clinician. In the first place, this test may simultaneously reveal another location of significant uptake, a finding that will certainly warrant extensive search for a possible primary site. Also, the disclosure of multiple systemic uptakes could strengthen the impression that the tumor that one is dealing with may be part of a disseminated carcinomatosis. However, out data lend support to the fact that Tc-99m(V)-DMSA is far from being specific for any particular type of intraocular malignant tumor; therefore, the results should be interpreted cautiously.

We conclude that, on rare occasions, Tc-99m(V)-DMSA scintigraphy, which is a safe and noninvasive test, may have a complementary role in the diagnosis, investigation, and decision-making process of some atypical malignant intraocular tumors. Although time

consuming, whole-body scanning should be done for these patients in an effort to detect any abnormal extraocular uptake.

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