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Visualization of orbital retinoblastoma with technetium-99m (V) dimercaptosuccinic acid

Pınar Özgen KIRATLI,* Hayyam KIRATLI** and Meral T. ERCAN*

*Departments of *Nuclear Medicine and **Ophthalmology, Ocular Oncology Unit, Hacettepe University Faculty of Medicine, Ankara, Turkey*

The potential contributions of technetium-99m (V) dimercaptosuccinic acid scintigraphy in the evaluation of orbital retinoblastoma, its local extensions and metastases were assessed in this study. Both planar and SPECT images clearly demonstrated the primary tumor and metastatic sites. Following confirmation of our results by contemporaneous ultrasonography, MRI and a subsequent incisional biopsy, the patient was treated with external beam radiotherapy and chemotherapy. This preliminary study showed that in combination with other diagnostic tests, Tc-99m (V) DMSA scintigraphy may play a role in the detection and follow-up of the local tumor extensions and metastases in patients with retinoblastoma.

Key words: retinoblastoma, orbit, technetium-99m (V) DMSA, magnetic resonance imaging

INTRODUCTION

RETINOBLASTOMA is the most common, malignant intraocular tumor of childhood and requires accurate diagnosis and prompt treatment.[1] Massive orbital extension or orbital recurrence following enucleation of eyes containing retinoblastoma is fortunately rare but may still be encountered in patients with late diagnosis or in areas with underprivileged medical facilities.[2] In one large series, orbital retinoblastoma constituted up to 12% of all cases of retinoblastoma.[3] Initial presentation with a massive orbital mass without a documented history of intraocular retinoblastoma may pose diagnostic and therapeutic challenges to the clinician. A child with massive orbital and metastatic retinoblastoma is presented and the contribution of imaging with technetium-99m (V) dimercaptosuccinic acid (Tc-99m DMSA) to the confirmation of other metastatic foci is discussed in this report.

CASE REPORT

A 6-year-old boy with a history of "intractable left iridocyclitis" for a year underwent diagnostic and therapeutic vitrectomy elsewhere. The aspiration material did not suggest malignancy on histopathologic examination. Following the operation, his "uveitis" became more severe and the eye was eviscerated. Histopathologic examination of the surgical material was inconclusive as the tissues were found to be necrotic. The patient was then referred to us for a rapidly enlarging left orbital mass that took place in two months.

There were marked left proptosis and two distinct subcutaneous masses under his scalp. There was severe chemosis of the left conjunctiva with protrusion of the previously inserted hydroxyapatite implant. There was a huge, non-tender, highly vascular and palpable mass that completely filled the left orbit. Over his left parietal bone was a subcutaneous rubbery mass which measured $10 \times 10 \times 8$ cm, and over his right frontal bone was a similar lesion that measured $5 \times 4 \times 2$ cm. His blood chemistry was normal, but bone marrow aspiration biopsy showed polymorphic cells with deeply basophilic nuclei with a partial rosette formation.

Orbital B mode ultrasonography showed an irregular, solid mass that had medium to high internal reflectivity on A mode. T1-weighted (T1W) magnetic resonance imaging (MRI) studies at initial presentation disclosed massive involvement of the left orbit by the tumor which was homogeneously hypointense compared to the orbital fat (Figure 1). Necrotic and hemorrhagic portions of the tumor located inferior to the implant were hyperintense

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For reprint contact: Hayyam Kıratlı, M.D., Assistant Professor, Hacettepe Hastanesi Göz Anabilim Dalı, 06100 Sıhhıye, Ankara, TURKEY.

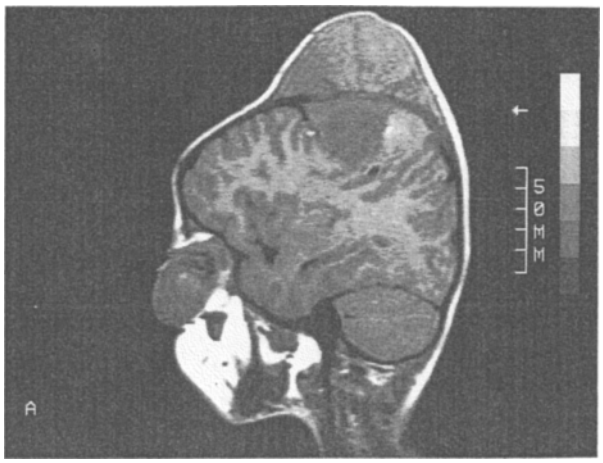

Fig. 1 Sagittal T1-weighted MRI scan demonstrate massive involvement of the left orbit by the tumor which was homogeneously hypointense compared to the orbital fat. Necrotic and hemorrhagic components of the tumor located inferior to the implant was hyperintense (open arrow) with respect to the rest of the mass. There were also other tumor foci under the scalp with extension to the superior cerebral hemispheres (arrow).

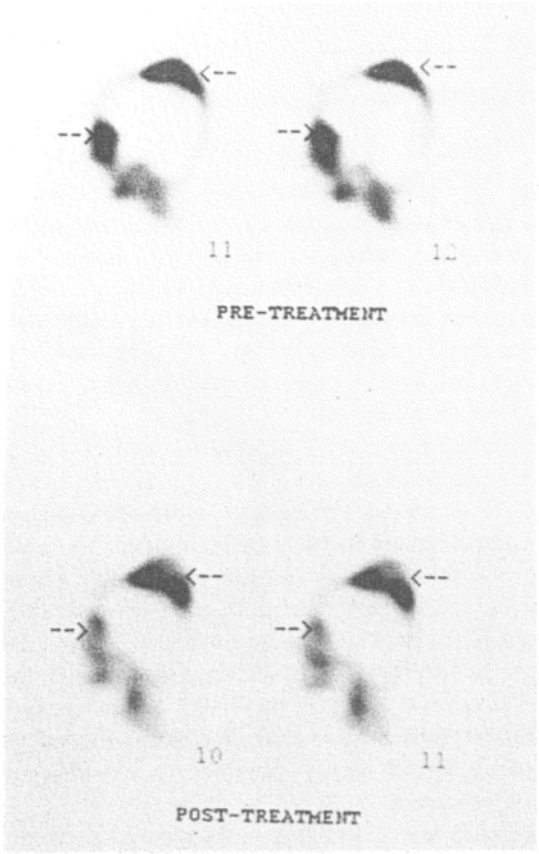

Fig. 2 Sagittal slices of the SPECT study with Tc-99m (V) DMSA show intense uptake in the left eye and orbit and left parietotemporal region of the calvarium (upper row). Repeat study six months following chemotherapy and radiotherapy demonstrates decreased uptake around the left eye, but there was increased radiotracer accumulation in the calvarial bones over the interval (bottom row).

compared to the rest of the mass. There were other tumor foci under the scalp that also involved the superior cerebral hemispheres.

Following administration of 350 MBq of Tc-99m (V) DMSA prepared according to previously published methods,[4] planar and SPECT imaging were performed at 3 hours with a LEHR collimator and a dual head gamma camera (ADAC-Genesys, CA, USA). SPECT images showed significant uptake in the left eye and orbit and in the left parietotemporal bone (Figure 2). The less intense activity of the cerebral mass was thought to be due to the presence of non-viable necrotic areas within the tumor.

Histopathologic examination of the incisional biopsies from the left orbit and scalp showed a neuroectodermal tumor suggestive of retinoblastoma. There were also extensive areas of tumor necrosis within the lesion. The patient then underwent intensive chemotherapy and fractionated radiotherapy.

Four months later, despite vigorous chemotherapy and radiotherapy, metastatic foci under the scalp and cerebrum did not regress but continued to enlarge. The orbital tumor however did improve slightly to the degree that the child had a more acceptable cosmesis. A repeat Tc-99m (V) DMSA scintigraphy was performed on that occasion. Although the uptake of the radioactivity in and around the left the eye decreased, the metastatic areas clinically unresponsive to treatment demonstrated even more uptake in the calvarium. The child did well for more than a year, until he died in a car crash. Autopsy was not performed.

DISCUSSION

Retinoblastoma in older patients (older than 5 years of age) may present with atypical symptoms and signs and may occasionally be misdiagnosed as panophthalmitis, endopthalmitis or uveitis.[5] Delay in the diagnosis and appropriate treatment may lead to orbital recurrence and distant metastases as evidenced by our patient. In such rare cases, some selected studies including orbital ultrasonography, computed tomography and/or MRI scans may provide important information about the extent and dissemination of the tumor.

Scintigraphic demonstration of retinoblastoma with monoclonal antibodies (MAb) have provided highly specific molecular recognition that could characterize and selectively localize tumor cells.[6] These antibodies can be labeled with various ligands such as; iodine-125, iodine-131, technetium-99m and indium-111m. Nevertheless, lack of tumor specific target antigens, heterogeneity and swift antigenic modification of tumors, low antigen densities and immunoconjugate localizations, poor penetration of high molecular weight reagents, rapid clearance of conjugates, non-specific retention and interactions of the components and the patients' own reaction to foreign immunoglobulins limit the applicability of these tech-

niques.[6] In addition, high cost, and high radiation dose absorbed by the liver, spleen and bone marrow are still obstacles to the routine use of MAb imaging.

Conventional tumor imaging agents can also occasionally be used in patients with disseminated metastatic retinoblastoma. A recent study compared Tc-99m sestamibi and Tl-201 and found that the former agent was superior to Tl-201 in the detection of soft tissue and bone metastases in retinoblastoma.[7] A new tumor detecting agent pentavalant Tc-99m dimercaptosuccinic acid has been developed by Yokoyama et al.[8] Many studies have reported Tc-99m (V) DMSA accumulation in a variety of soft tissue and bone tumors, head and neck tumors, medullary carcinoma of the thyroid and lung cancer.[8,9] Tc-99m (V) DMSA appears to be a promising imaging agent in ocular oncology. Recently, a choroidal melanoma was satisfactorily demonstrated with Tc-99m (V) DMSA scintigraphy.[10] Later, in a series of twelve patients with posterior uveal melanoma, this imaging agent was found to be reliable both in the diagnosis and documenting the response to treatment after iodine-125 plaque brachytherapy.[11] Tc-99m (V) DMSA scintigraphy proved to be of significant value also in patients with atypical choroidal masses and choroidal metastases who were initially suspected of harboring uveal melanoma.[12] In these patients, the simultaneous demonstration of multiple systemic uptakes led to the discovery of occult visceral carcinomas.[12] These studies imply that the accumulation of Tc-99m (V) DMSA is not specific to any single type of intraocular malignancy. On the other hand, there is no information about the specificity and sensitivity of this agent in the detection of intraocular retinoblastoma because of lack of experience with a larger number of patients with this tumor and with other conditions.

The diagnosis of intraocular retinoblastoma and differentiation from several simulating lesions can easily be made by clinical examination and current ancillary tests in the majority of patients. The high accuracy and reliability of these tests limit the need for scintigraphic evaluation but our experience with this single patient suggests that Tc-99m (V) DMSA scintigraphy can provide useful information in advanced cases of orbital retinoblastoma by demonstrating the extent of the extraocular disease and unsuspected metastatic sites. Also, increased uptake of some parts of the tumor after treatment correlated well with the clinical lack of response and enlargement of the foci of these tumors. In the final account, retinoblastoma should be added to the list of tumors where there is avid accumulation of Tc-99m (V) DMSA.

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