Secondary malignant lymphoma of the central nervous system with delayed high uptake on $^{123}$I-IMP single-photon emission computerized tomography

Case report

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A case of secondary central nervous system (CNS) lymphoma with high uptake in the delayed image of N-isopropyl-$^{123}$I-p-iodoamphetamine ($^{123}$I-IMP) single-photon emission computerized tomography (SPECT) is presented. Previous to this report, only six cases of brain tumor with high uptake on the delayed $^{123}$I-IMP SPECT scan have been reported, two of which were CNS malignant lymphomas. Of 19 brain tumors examined with $^{123}$I-IMP SPECT at Kameda General Hospital, this case was the only one that showed high uptake in the delayed image. These data imply that $^{123}$I-IMP SPECT, which has now become rather obsolete as a tumor-imaging method, can be useful in diagnosing CNS malignant lymphoma.

Key Words • lymphoma • brain neoplasm • single-photon emission tomography • isotope uptake

A central nervous system (CNS) malignant lymphoma was once regarded as a rare brain tumor. However, the incidence of this tumor is now rising markedly, due in part to an increase in the number of immunocompromised patients, including those with acquired immunodeficiency syndrome (AIDS) and those undergoing chemotherapy and organ transplants. A correct diagnosis is essential for optimum treatment, but the diagnosis of malignant lymphoma without a specimen for histological examination is still difficult, despite the use of advanced diagnostic modalities.

N-isopropyl-$^{123}$I-p-iodoamphetamine ($^{123}$I-IMP) single-photon emission computerized tomography (SPECT) is a common diagnostic tool for measuring cerebral blood flow (CBF). Its potential use in diagnosing brain tumors is generally believed to be limited because brain tumors are usually shown as a defect on $^{123}$I-IMP SPECT images and the sensitivity does not surpass that of computerized tomography or magnetic resonance imaging. However, there have been reports of some exceptional cases with $^{123}$I-IMP SPECT scans demonstrating an accumulation of IMP in brain tumors. Most of these tumors have exhibited a high uptake only in the early study, but a very limited number of cases also exhibited a high uptake in the delayed scan. We have found an unexpectedly high frequency of CNS malignant lymphoma among these cases, which stimulated us to perform $^{123}$I-IMP SPECT on a patient with a known secondary CNS malignant lymphoma.

We describe a case of secondary malignant lymphoma showing a high uptake in both the early and delayed images. These findings imply that $^{123}$I-IMP SPECT could play a role in diagnosing malignant lymphoma of the brain.

Case Report

This 42-year-old woman presented to our clinic with a 1-month history of altered personality and increased somnolence. Eight and 2 months previously, she had undergone repeated biopsies of a left breast tumor at another hospital, but the results of these biopsies could not be obtained.

Examination. On admission, she had a small and rather hard tumor in the left breast. Neurological examination revealed somnolence, slowness of mental activity, anomic aphasia, and very mild right hemiparesis. Serological examination for the adult T-cell lymphoma virus and the AIDS virus was negative.
Computerized tomography with and without contrast enhancement revealed a mass with slightly increased density and homogeneous enhancement located deep in the left frontal lobe; several other small enhancing masses were also noted (Fig. 1). The patient underwent SPECT, using a gamma camera (fitted with a high-resolution slant-type collimator) and an image processor,\(^*\) at 15 minutes and at 4 hours after intravenous administration of \(^{123}\text{I-IMP} (6 \times 37 \text{ mBq}).\) The left frontal mass showed very high IMP uptake on both the early and delayed scans (Fig. 2). Increased CBF within the frontal mass was revealed on \(^{133}\text{Xe} \text{inhalation SPECT.}\) Gallium-67 scintigraphy showed high uptake in the left frontal lobe, but in no other location (including the left breast). Metastasis from the left breast tumor was suspected, so the patient underwent biopsy of the breast lesion. The diagnosis was malignant lymphoma.

**Operation.** The patient's condition deteriorated further. Removal of the left frontal mass was performed for decompression. The histological diagnosis was diffuse, large-cell malignant lymphoma (Fig. 3). Examination of the surface marker revealed that this lymphoma was of the B-cell type.

**Postoperative Course.** The patient recovered well from the operation, and then underwent whole-brain radiotherapy (32.4 Gy) and systemic chemotherapy. She remained well for 4 months after the operation, but then local recurrence with cerebrospinal fluid dissemination occurred. An Ommaya reservoir was placed in order to administer intrathecal as well as systemic chemotherapy. The patient's clinical course deteriorated thereafter due to agranulocytosis, and she died of respiratory complications.

**Discussion**

The \(^{123}\text{I-IMP} \text{radionuclide is mainly utilized to measure CBF. Measurement of CBF via} \ ^{123}\text{I-IMP SPECT is based on the following hypothesis. After intravenous injection of} \ ^{123}\text{I-IMP, this agent easily penetrates the blood-brain barrier owing to its lipophilicity. Subsequently, IMP binds to the nonspecific amine receptors within brain tissue, and long-lasting retention is observed.}\(^6\) Thus, the SPECT image visualized depends on the regional CBF, the number of amine receptors, and the elapsed time after injection. Early images mainly reflect the regional CBF, while delayed images indicate the number of amine receptors. Brain tumors are thought to be lacking in these receptors\(^7\) so they are visualized as a focus of decreased uptake, at least in the delayed images.

A few brain tumors with high IMP accumulation have been reported, but most showed high accumulation only in the early image. Very few tumors reported in the literature showed increased uptake in delayed \(^{123}\text{I-IMP SPECT images.}\)\(^4\) To our knowledge, only six such cases have been reported to date; these included two malignant lymphomas, one malignant astrocytoma, two metastatic brain tumors (one bronchial carcinoid and the other was not specified), and one cellular blue nevus. Our case is the third CNS malignant lymphoma to be reported. These tumors showed retention of \(^{123}\text{I-IMP on the delayed SPECT scans and thus could be interpreted as having amine receptors. The reason why they possess amine receptors is not yet well understood. However, cellular blue nevus tumors take up amine precursors for melanin production and carcinoid tumors can take up amine precursors and decarbboxylate.}\)

To date, 19 brain tumors have been examined via \(^{123}\text{I-IMP SPECT at our hospital. Five were metastatic tumors, four meningiomas, three astrocytomas, three malignant astrocytomas, one craniopharyngioma, one ependymoma, one germinoma, and one malignant lymphoma. Among these tumors, the malignant lymphoma was the only one to show high uptake of} \ ^{123}\text{I-IMP on the delayed image.}\)

Considering the relative rarity of malignant lymphoma, the unusually high incidence of these tumors showing increased uptake in delayed \(^{123}\text{I-IMP SPECT images seems to imply that malignant lymphomas may express amine receptors as a characteristic feature. Of course, we cannot tell from currently available data how many malignant lymphomas show increased uptake or how many of these tumors showing increased uptake...**
Secondary CNS lymphoma with high $^{123}$I-IMP uptake

**Fig. 2.** Early (left) and delayed (right) $^{123}$I-IMP single-photon emission computed tomography images. Left: An area of high uptake is seen surrounded by an area of low uptake in the frontal lobe (images 3 and 4). These correspond to the tumor mass and the surrounding edema, respectively. Right: The tumor continues to be demonstrated as an area of high uptake on the delayed scan (images 3 and 4).

uptake are malignant lymphomas. However, $^{123}$I-IMP SPECT is a safe and easily performed examination that creates little burden for the patient. We therefore recommend this diagnostic tool when malignant lymphoma is suspected. If the test result is positive, the possibility of a malignant lymphoma diagnosis increases greatly. The specificity and sensitivity of this examination in diagnosing malignant lymphoma should be determined more precisely in the future; for this purpose, it is necessary to collect more cases.

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**References**


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**Fig. 3.** Photomicrograph of a section of the left frontal tumor showing a diffuse distribution of large lymphocytes. H & E, x 400.