PRIMARY LYMPHOMA OF THE CENTRAL NERVOUS SYSTEM: A DIAGNOSTIC PROBLEM

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Primary lymphoma of the central nervous system (CNS) is difficult to diagnose because of the difficulty in differentiating it from multiple sclerosis, sarcoidosis, metastatic disease, chronic granulomatous disease, and cerebral cysticercosis. With the patient presented in this report, no abnormalities were found after performing laboratory tests, using radiographic modalities, and taking biopsies. Dexamethasone treatment was initiated, and patient's symptoms improved.

Primary CNS lymphoma was not diagnosed until a year after presentation, due to lack of tissue diagnosis. CNS must be suspected when a diagnosed tumor treated with steroid is not found at surgery. It is suggested that a computerized tomographic scan be requested before the start of steroid therapy, as the lesion can disappear with steroid treatment.

Primary lymphoma of the central nervous system (CNS), without any evidence of nodal, marrow, or systemic involvement, is rare. Its incidence has been 1.83 per million per year.[1] It is difficult to diagnose, especially when the lesions disappear with steroid therapy.[2,3] The following case report of primary lymphoma of CNS demonstrates one approach to the problems of management and treatment.

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CASE REPORT

A 55-year-old black man was admitted to the medical center in March 1983, because of progressive headache and personality changes, loss of memory, and disorientation. The neurological examination was otherwise normal. A computerized tomographic (CT) scan of the brain showed multiple enhancing lesions surrounded with edema of the left frontal parietal and the right frontal parietal temporal regions (Figure 1, A). Dexamethasone was given intravenously at a dose of 4 mg every six hours. The patient's symptoms improved on the following day.

A thorough investigation was done to determine metastasis, including chest and abdomen films; stool for occult blood; urinalysis; chemical determinations; carcinoembryonic antigen; bone marrow biopsy and aspiration; CT scan of the abdomen, liver, spleen, and kidneys; renal sonography; and bone scan. Neither laboratory investigations nor radiographic modalities revealed any abnormalities.

Two weeks after admission, a craniotomy was performed in the right frontal region. Multiple biopsies were taken but did not show any abnormality. A repeat CT scan of the brain was taken after the brain biopsy, and complete disappearance of the lesions was demonstrated. The diagnosis of primary lymphoma of the brain was suspected. Dexamethasone was continued for three months and tapered off. Another CT scan was done in August 1983, and normal features were seen (Figure 1, B).

The patient was well until March 1984; then he developed progressive, nonfluent aphasia. On repeat CT scan, an enhancing mass lesion was seen with surrounding edema in the left temporal area exerting a mass effect, shifting the midline structure to the opposite side (Figure 1, C). The patient was again

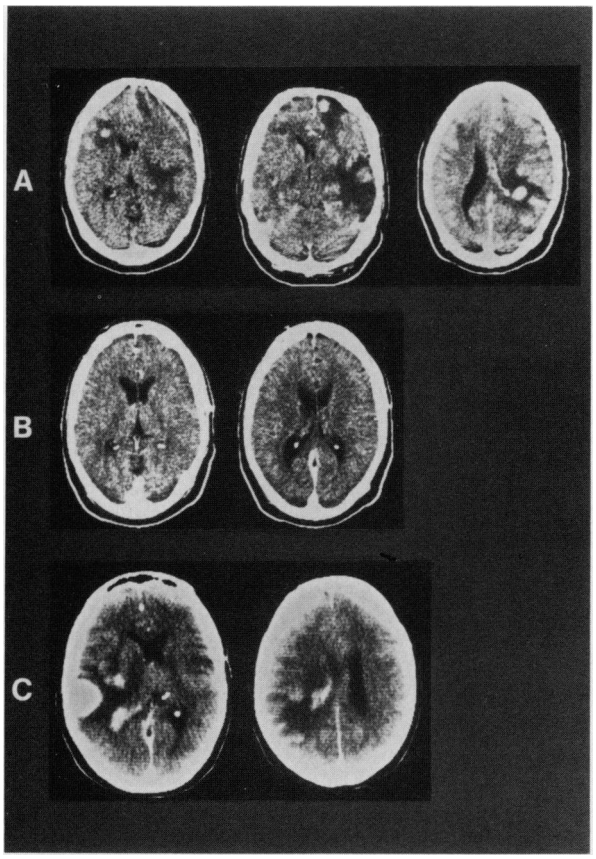

Figure 1. On computerized tomographic scan with contrast, multiple enhancing lesions surrounded by edema of the left frontal parietal and right frontal parietal temporal regions (A). Normal CT scan after treatment with steroids (B). Appearance of an enhancing mass lesion with surrounding edema in the left temporal area (C)

given dexamethasone, 4 mg every six hours. His language disorder improved; however, he had intermittent confusion with mild right-sided weakness in spite of continuous high doses of dexamethasone. The patient was readmitted, and a thorough investigation for metastasis was again carried out but no abnormality was detected. A cerebral angiogram was done; an avascular mass was demonstrated in the temporal region. A brain biopsy was carried out for the second time and a pathologic diagnosis of malignant lymphoma was confirmed.

The patient was treated with radiation therapy. The clinical symptoms gradually improved; however, the patient died suddenly. A massive myocardial infarction was suspected. Consent for autopsy was denied.

DISCUSSION

Although the diagnosis of primary CNS lymphoma can be confirmed by biopsy, autopsy, or therapeutic trial, most primary CNS lymphoma is still diagnosed at autopsy because of the difficulty in differentiating it from multiple sclerosis, sarcoidosis, metastatic disease, chronic granulomatous disease, and cerebral cysticercosis. The patient in this report was diagnosed after the second biopsy, which occurred about one year later. The treatment was delayed due to the lack of tissue diagnosis. Retrospectively, primary CNS lymphoma must be suspected when a diagnosed tumor treated with steroid is not found at surgery.[3]

Early diagnosis of primary CNS lymphoma is critical because the combination of chemotherapy and radiotherapy has changed the prognosis of malignant lymphoma of the CNS in a favorable direction, leading to long-term survival of patients and sometimes permanent cure.[1,4–6] It is important to make a correct diagnosis of this potentially curable disease as early as possible before brain surgery is done, so that resection can be avoided and chemotherapy and radiation started without delay.

The tumor tissue may also cause some diagnostic problems; it may be interpreted as a malignant glioma because gemistocytic astrocytes seen in pathologic section are reactive, not neoplastic. In case of doubt the use of immunohistochemical stains can distinguish many of these malignant neoplastic cells by their specific markers. The diagnosis of primary CNS lymphoma may also be made based on documentation of a monoclonal population of malignant B cells in the cerebrospinal fluid.[7]

There is a wide variation in the CT scan appearance of brain lymphoma. Computerized tomography is a reasonably sensitive modality in the detection of small CNS lesion; unfortunately, it is not very specific. There are, almost always, a few "differential diagnoses" attached to every suspected neoplastic lesion of the brain. Recently, Holtis et al[8] studied a CT scan appearance of malignant lymphoma of the brain. The typical appearance of primary brain lymphoma is of a relatively large tumor with sharp demarcation and mild edema. There is a moderate to marked contrast enhancement and the tissue is usually homogenous; often multiple tumors tend to situate near the walls of the ventricles in the basal ganglia, corpus callosum, and cerebellum. These characteristics, in combination with a thorough history, might lead to the diagnosis.

However, in the case of steroid response in primary CNS lymphoma, it is suggested that a CT scan be requested before the start of steroid therapy, as the lesion can disappear with steroid treatment.

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