Signet-ring cell lymphoma of the central nervous system

Case report

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Signet-ring cell lymphoma is a rare tumor described in the lymph nodes, skin, tonsils, thyroid, salivary gland, and ocular orbit. This is the first case report of a B-cell signet-ring cell lymphoma in the central nervous system with Dutcher and Russell bodies, signet-ring nuclei, intracisternal crystalline inclusions, and immunoglobulin M positivity. The patient is doing well 2 years after surgery and postoperative radiation therapy. No definitive prognostic characteristics have been elucidated. This disease entity can only be suspected on histological grounds and confirmed by immunocytochemical and ultrastructural studies.

KEY WORDS • brain neoplasm • lymphoma • signet-ring cell lymphoma

LYMPHOMAS, both primary and metastatic, account for 1% to 3% of the tumors in the central nervous system (CNS). However, this incidence will probably increase due to longer survival rates from better chemotherapeutic and radiation techniques and to the increasing number of transplant recipients and patients with acquired immunodeficiency syndrome (AIDS). The term “signet-ring cell lymphoma” has been used to designate a rare morphological variant of non-Hodgkin’s lymphoma first described in 1978 by Kim, et al.,13 in the lymph nodes or in the mesentery of seven patients. The signet-ring cell is due to the presence of eosinophilic cytoplasmic inclusions, with a clear, vacuolated, or Russell body-like appearance, displacing the nucleus to the periphery. Markers for light and heavy immunoglobulin (Ig) chains indicate that most of the reported cases were B-cell derivations, whereas three cases expressed T-cell phenotypes. Since 1978, authors have reported this disease entity in peripheral,9,11,12,14,21 retroperitoneal,16,18,20 and mesenteric lymph nodes,13,16 skin,7,8,21 tonsils,3 thyroid,1 salivary gland,19 and orbit.4 This is the first reported case of signet-ring cell lymphoma in the CNS.

Case Report

This 64-year-old white retired salesman with a history of myocardial infarction presented for evaluation of two tonic/clonic seizures involving all extremities. He apparently lost consciousness and was amnesic with his last seizure.

Examination. Physical examination demonstrated no focal neurological deficits. A computed tomography (CT) scan revealed a contrast-enhanced lobulated right frontal lobe mass with a large amount of surrounding edema, possibly invading the corpus callosum and right caudate nucleus (Fig. 1). Selective right internal carotid arteriograms demonstrated a shift of the anterior cerebral artery to the left and caudally. The sylvian triangle was displaced inferiorly with tumor vessels visualized with some puddling and early medullary draining veins.

Operation. The patient underwent right frontal craniotomy for subtotal removal. The gray-tan tumor was firm but suetable.

Pathological Examination. Light microscopy demonstrated a diffuse tumor growth pattern and a moderate perivascular desmoplastic response induced by the tumor. The tumor cells tended to grow in an angiocentric fashion, and this pattern was particularly evident at the edges of the lesion where perivascular infiltrates permeated the adjacent gliotic and edematous brain. The infiltrating noncohesive cells were characterized by variably conspicuous amphophilic to eosinophilic...
FIG. 1. Contrast-enhanced computerized tomography (CT) scan of the head showing a right frontal enhanced lesion with a hypodense center. There is effacement of the right frontal horn and a right-to-left shift of approximately 5 mm.

pseudoinclusions present in nearly every cell (Fig. 2). Immunohistochemical reaction for IgM showed this intranuclear material to be faintly positive in the minority of cells. The IgM and IgA preparations were negative.

Electron microscopy studies confirmed the presence of prominent intranuclear pseudoinclusions (Dutcher bodies). A minority of cells had distended cisternae of rough endoplasmic reticulum containing the same kind of finely granular stored proteinaceous material in the cytoplasm (Russell bodies). Figure 3 illustrates a representative tumor cell with abundant cytoplasmic stacks of rough endoplasmic reticulum representing the most conspicuous feature (after the intranuclear pseudoinclusion) of the tumor cell.

Postoperative Course. A search for lymphoma throughout the patient's body was performed, including bone marrow biopsy and aspiration and abdominal CT. The findings were negative, indicating an apparent primary CNS lymphoma. The patient was treated with phenobarbital and received 4140 external rads to the whole brain via 23 treatments of 180 rads each, over a total duration of 31 days, with a 1980-rad boost to the tumor area. His total dose was given via 34 treatments of 180 rads each, over a total duration of 46 days. Postoperatively, the patient's neurological examination demonstrated hesitant speech. A postradiation CT scan revealed excellent shrinkage of the tumor 12 months postsurgery. An area of decreased density was present within the right frontal lobe, consistent with an area of resection and/or encephalomalacia. Presently, the patient is neurologically stable. His speech is still hesitant and at times he has difficulty in walking, although he has no focal weaknesses.

Discussion

Central nervous system lymphomas are recently drawing more attention because of an increase in the number of patients with immunosuppression from organ transplantations and immunodeficiency such as in AIDS, and the extended longevity of patients with lymphoma. With improved diagnostic methods in neuroradiology and immunocytochemistry, this disease is being studied further.

Primary lymphomas in the CNS comprise 0.7% to 1.6% of the total lymphomas reported. Lymphoma presently represents 1% of all primary intracranial neoplasms. The peak age incidence is 55 to 65 years old, and there is a male predominance of 2:1. Half of the patients with lymphomas of the brain have systemic lymphoma. Intracranial lymphoma occurs in approximately 60% of patients with acute lymphocytic leukemia, 25% of patients with non-Hodgkin's lymphoma, and in only 1% to 3% of patients with Hodgkin's disease. Some of the patients harboring lymphoma...
CNS signet-ring cell lymphoma

This tumor has small indented follicular cells in a nodular and diffuse pattern. The Russell body inclusions found to be displacing the nuclei peripherally can contain IgM, indicating apparent B-cell derivation. These inclusions show homogeneous, slightly electron-dense material within distended rough endoplasmic reticulum. It can be postulated that the vacuoles are either a collection of abnormal proteins or the result of a basic defect in Ig transport and secretion from the cell. Immunocytochemical staining of the vacuoles gives evidence that many of the vacuoles are formed by the accumulation of cytoplasmic Ig without Ig transport or secretion.

Navas-Palacios, et al., \(^6\) have classified signet-ring cell lymphomas into three subtypes: Type I has Russell bodies, distended loops of endoplasmic reticulum, and is positive for IgM; Type II has clear cytoplasmic vacuoles and is positive for IgG; and the third type is ill-defined and corresponds to nonmembrane-bound cytoplasmic accumulation of granular, fibrillary, and crystalline material. Variations and combinations of the subtypes of this classification have been reported. Our case fits into the first subtype.

In summary, signet-ring cell lymphoma is a rare variant of lymphoma that can be either B cell or T cell. This is the first described CNS case of B-cell signet-ring cell lymphoma with Dutcher and Russell bodies, signet-ring cell nuclei, inclusions, and IgM positivity. No definitive prognostic characteristics have been elucidated as yet. Since a negative work-up was performed to rule out metastasis in this case, the tumor was apparently a primary CNS lymphoma rather than a lymphoma of nodal tissue. This would be similar to the primary signet-ring cell lymphoma of the thyroid gland reported by Allevato, et al.\(^1\)

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