Primary intracranial Hodgkin's lymphoma without dural attachment

Case report

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A very rare case of primary intracranial Hodgkin's lymphoma without dural attachment is reported. Based on a review of the literature and the clinical results in the present case, recommended therapy consists of surgical excision whenever possible, followed by radiotherapy.

Key Words • Hodgkin's disease • lymphoma • craniotomy • radiotherapy

CENTRAL NERVOUS SYSTEM (CNS) involvement in Hodgkin's disease is found relatively infrequently.5,8,11,20 Whisnant, et al.,19 estimated that the ratio of intraspinal to intracranial involvement ranged from 2:1 to 3:1; the incidence of intracranial involvement is most often estimated to range from about 12% to 25% of cases.5,6,30 A review of the literature indicates that Hodgkin's disease most often involved the brain either as a mass or as a diffuse infiltrate of the meninges,4 with dural involvement much more common than parenchymal lesions.1,8,13 Intracranial involvement is usually the result of hematogenous metastasis or meningeal infiltration from systemic Hodgkin's disease.12,13 Primary Hodgkin's disease has been found both in the brain as a parenchymal lesion,1,5,7,15,17,21 and in the dura mater,12 but this is an extremely rare event.

In this paper, we report only the ninth known occurrence of primary Hodgkin's disease presenting as a parenchymal brain neoplasm without dural attachment or evidence of systemic involvement, and review the clinical presentation, diagnostic criteria, and management strategy of this exceedingly rare entity.

Case Report

This 53-year-old woman was initially evaluated as an outpatient with a 2-month history of severe diffuse headaches. She had previously been evaluated by a neurologist; an electroencephalogram was within normal limits and a computerized tomography (CT) scan without contrast enhancement was suggestive only of mild diffuse ventriculomegaly. The patient was diagnosed as having vascular headaches and was given a routine follow-up appointment. The headaches increased in both severity and duration and she began noticing subtle weakness in her right arm and leg, manifest as "dropping things" and gait difficulties; she therefore presented for further evaluation.

Examination. Physical examination revealed pronounced cerebellar dysfunction manifest as right upper-extremity past-pointing with intention tremor, impaired finger-to-nose coordination, dysdiadochokinesis, and inability to tandem gait. Funduscopic examination showed a mild loss of the physiological cup, but the disc margins remained sharp and there was no evidence of papilledema. That evening, a magnetic resonance (MR) image was obtained, with gadolinium diethylenetriamine penta-acetic acid contrast enhancement and with attention to the posterior fossa. Following this test, the patient experienced a subjective worsening in her gait and presented to the Emergency Department with the MR image in hand. The MR image clearly showed a 4 × 2-cm mass in the medial aspect of the right cerebellar hemisphere with no evidence of acute hydrocephalus (Fig. 1).
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Fig. 1. Magnetic resonance T1-weighted image with gadolinium diethylenetriamine penta-acetic acid of the posterior fossa demonstrating a approximately 4 × 2-cm lesion.

ministration was begun. She was scheduled for an elective excisional biopsy the following morning. Routine laboratory studies were normal. Neurological examination was essentially unchanged from that noted at her original presentation.

Operation. A posterior fossa craniectomy was performed. Along the midline of the cerebellar hemisphere at the level of the tentorium, a very hard, rubbery, tan mass lesion was encountered. Careful exploration with the operating microscope revealed this to be a well-encapsulated mass with no dural attachment. Because of the size of the mass, it was purposely removed en bloc in two separate pieces in order to minimize cerebellar retraction. Surgical removal of the mass proceeded without incident and the wound was closed in the customary fashion. Frozen-section diagnosis indicated lymphoma.

Pathological Examination. The excised specimen consisted of multiple fragments of firm gray-and-tan tissue, measuring 3 × 2.5 × 2 cm. The tissue was embedded in optimal cutting temperature medium and snap frozen in liquid nitrogen, as well as fixed in neutral buffered formalin and B5. Light microscopic examination revealed a variably cellular neoplasm, infiltrating the residual cerebellum (Fig. 2 left) and inciting a fibroblastic reaction. Vaguely nodular, densely cellular foci alternated with irregular, hypocellular fibrotic and necrotic areas. The cellular infiltrate was polymorphous, with a background of normal small lymphocytes, eosinophils, and a few plasma cells within which large, atypical, often multinucleated cells were identified. These large cells, which had a tendency to cluster, were interpreted as Reed-Sternberg cells and their variants (particularly lacunar cells) (Fig. 2 right). No dura was identified. Immunohistochemical staining for the leukocyte common antigen (CD 45) and Leu-M1 (CD 15) were performed using the avidin-biotin-peroxidase conjugate technique. The primary antisera were unlabeled monoclonal antibodies (lymphocytotoxic antibody (LCA) and Ber-H2 antibody). The small lymphocytes were positive for LCA and negative for Leu-M1 (B5 fixed tissue) and Ber-H2. The Reed-Sternberg cells and their variants were negative for LCA and positive for Ber-H2 and Leu-M1. The morphology, architectural features, and immunohistochemical reactions supported a diagnosis of Hodgkin's disease, the nodular sclerosis type. A bone marrow biopsy was negative for Hodgkin's disease; cerebrospinal fluid cytological examination, using filters and cytocentrifuge preparations, revealed no neoplastic cells.

Postoperative Course. Two days following surgery, the patient's neurological examination had returned to normal. A complete survey examination, including CT of the chest, abdomen, and pelvis, and a bone marrow biopsy, were all within normal limits. The patient subsequently received craniospinal irradiation to a total of 3600 cGy in 180 cGy fractions, with a boost to the posterior fossa to a total of 4500 cGy. At her 6-month follow-up examination, she remained neurologically intact with no evidence of recurrent tumor (Fig. 3).

Discussion

Although intracranial Hodgkin's disease is uncommon, the recently predicted threefold increase in the incidence of primary CNS lymphoma may result in the identification of increased numbers of cases of Hodgkin's disease with CNS involvement.

Diagnosis of Intracranial Hodgkin's Disease

There was skepticism when a diagnosis of intracranial Hodgkin's disease was made in this patient, particularly since it was the initial or the only site of involvement. However, both the morphological features of the tumor (namely, Reed-Sternberg cells and their variants in an appropriate background of normal immunoreactive cells) and the immunohistochemical reactions (Leu-M1-positive, Ber-H2-positive, LCA-negative) support a diagnosis of Hodgkin's disease. The presence of lacunar cells and a few fibrous bands supports the nodular sclerosis subtype.

Although the diagnosis of Hodgkin's disease is based on characteristic morphological findings, immunohistochemical studies, such as those demonstrated in this case, may be supportive of the diagnosis. The most useful markers are CD 30 (Ber-H2 or Ki-1), CD 15

* Leu-M1 supplied by Becton-Dickinson, Mountain View, California, and avidin-biotin-peroxidase conjugate supplied by Vector Laboratories, Burlingame, California.

† Lymphocytotoxic and Ber-H2 antibodies supplied by Dako, Inc., Santa Barbara, California.

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(Leu-M1), epithelial membrane antigen, and CD 45 (leukocyte common antigen). Other authors have applied immunohistochemical techniques in their reported cases of Hodgkin's disease. In the case reported by Sickler, et al., Reed-Sternberg cells were CD 30-positive and positive for IRac; staining for the Leu-M1 antigen was unsatisfactory due to improper fixation. The case reported by Ashby and others exhibited positive staining for Leu-M1 and LN2. Using formalin-fixed tissue, the case of Bender and Mayernik showed no staining for Leu-M1 and LCA.

The subtype of the present case (nodular sclerosis) does not affect the prognosis of this patient. However, it is in contrast to the observations of Sanchez et al., made prior to the availability of monoclonal antibody typing, that all cases of intracranial Hodgkin's lymphoma are equally divided between the mixed cellularity and lymphocyte-depleted types. Our case is similar to one reported by Doorly, et al., in that an isolated cerebellar mass without dural attachment was identified. Most of the cases in which monoclonal antibody typing has been carried out resulted in a nodular sclerosis subtype diagnosis.

**Treatment of Intracranial Hodgkin's Disease**

Dujovny, et al., recognized the value of surgical intervention in treating intracranial Hodgkin's disease. Their review showed that the average postoperative survival time was measured in years, as compared to months for all other treatments. It is well known that Hodgkin's disease, as well as other malignant lymphomas, are radiosensitive tumors. However, the longest duration of survival in the series of Dujovny, et al., was obtained when surgical removal was combined with radiation therapy.

Based on the increased survival time seen with surgery combined with radiotherapy and the excellent result achieved to date in the present case, the authors recommend the removal of solitary intracranial masses followed by irradiation consisting of 4500 cGy to the primary site and 3600 cGy to the remainder of the CNS. In cases where there are multiple intracranial masses or the mass is inaccessible for resection, a CT-guided stereotactic brain biopsy can provide a tissue diagnosis that would allow institution of appropriate radiotherapy and/or chemotherapy. Based on the radiosensitive nature of these lesions, stereotactic radiosurgery may also prove to be an excellent alternative therapy; however, this therapy might be reserved for multiple or surgically inaccessible lesions.

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References

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