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Multicentric Involvement of Non-Hodgkin's Lymphoma in the Central Nervous System and Testis

—Case Report—

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Abstract

A 73-year-old male presented with diffuse mixed B cell lymphoma with involvement of the central nervous system (CNS) and testis manifesting as mild disorientation and aphasia. A left frontal cerebral mass and a right testicular tumor were found, and both lesions were surgically resected. Histological examination revealed diffuse mixed B cell type malignant lymphoma in the CNS and testis. The patient received irradiation to the head, and his initial symptoms improved. Pelvic computed tomography revealed enlargement of the contralateral testis and prostate. Needle biopsy confirmed lymphoma. The patient died 5 months after the initial diagnosis of septic shock. Autopsy examination revealed lymphoma cell invasion of the lung, bone marrow, prostate gland, and thalamus, but without involvement of the systemic lymph nodes. In a patient with an intracranial lymphoma, it is important to determine if the lesion is primary or metastatic and to plan medical treatment including systemic chemotherapy as soon as possible. Improvement of the prognosis of systemic non-Hodgkin's lymphoma with CNS involvement requires the detection and effective treatment of systemic lesions as well as the control of the CNS lesions.

Key words: non-Hodgkin's lymphoma, central nervous system lymphoma, testis, extra-nodal lymphoma

Introduction

Central nervous system (CNS) lymphoma initially presenting as an intraparenchymal mass and manifesting as CNS symptoms is likely to be the primary lesion.[5,9,10] Nevertheless, careful examination may reveal systemic non-Hodgkin's lymphoma (NHL). In recent years, CNS involvement has been found at the initial medical examination in 1.2% to 2.1% of patients with systemic NHL.[1,11] We report a case of diffuse mixed B cell lymphoma associated with multicentric involvement of the CNS and testis.

Case Report

A 73-year-old man developed appetite loss and decreased verbal response. He had no past medical history except for hypertension since his fifties. On admission, neurological examination revealed mild disorientation and aphasia. Magnetic resonance (MR) imaging demonstrated a left frontal mass lesion which had invaded the opposite hemisphere through the corpus callosum, with diffuse enhancement by contrast medium (Fig. 1). Angiography showed a faint stain corresponding to the tumor location. Chest and abdominal computed tomography (CT) revealed no abnormalities. Complete blood count and laboratory examination found no abnormalities except for an increased level of soluble interleukin-2 receptor (4000 U/ml, normal range 220–530 U/ml). There was no evidence of human immunodeficiency virus or Epstein-Barr virus infection. A painless, right testicular enlargement about the size of a chicken egg was noticed 2 days before the operation. Ultrasonography indicated a lymphoma.

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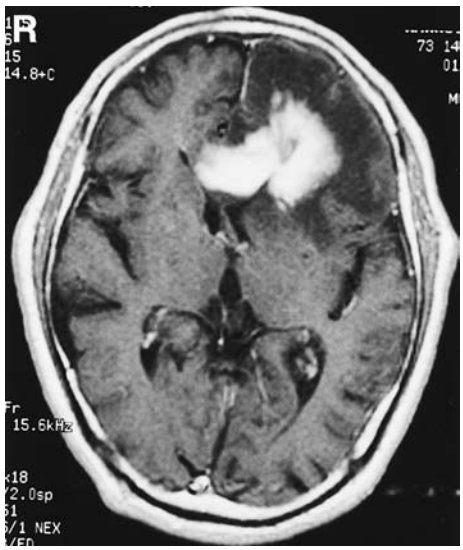

Fig. 1 T_1**-weighted magnetic resonance image with contrast medium showing an abnormal enhanced lesion in the left frontal lobe and corpus callosum.**

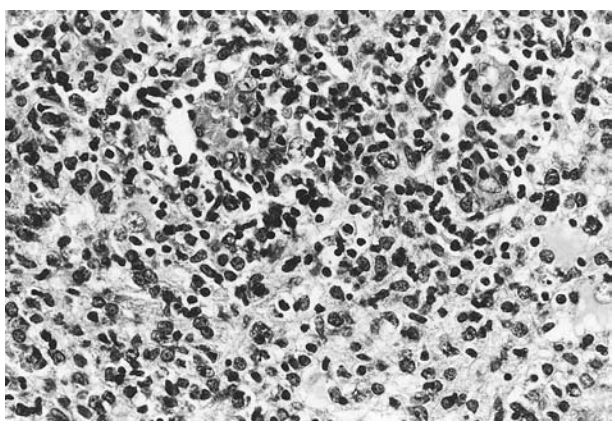

Fig. 2 Photomicrograph of the cerebral tumor specimen demonstrating invasion of the brain and perivascular spaces by small lymphocytes. HE stain, ×200.

The brain tumor was resected and an orchiectomy was performed. The boundary between the cerebral tumor and normal brain tissue was extremely unclear, both macroscopically and by ultrasonography. Examination of the frozen section indicated a high-grade glioma, so a frontal lobectomy including the tumor was performed. Histological examination revealed a diffuse mixed B cell type malignant lymphoma in both the brain and the testicular lesions (Fig. 2). After the operation, bone marrow aspiration biopsy showed hypercellularity and lymphoid cell infiltration. Pelvic CT revealed swelling of the left testicle and prostate gland, with gallium accumulation in both lesions. Needle biopsy of the prostate confirmed lymphoma.

The patient received 30 Gy whole brain irradiation with 10 Gy booster irradiation. His clinical symptoms improved. Repeat brain MR imaging found no recurrence. Chemotherapy was planned after the radiotherapy, but he developed pneumonia just before. After the pneumonia had improved, a small nodular density in the lung and increased interleukin-2 receptor level were detected, both of which were probably due to progression of the underlying disease. The patient underwent one session of CHOP therapy (cyclophosphamide, doxorubicin, vincristine, and prednisone) 5 months after the initial diagnosis. Unfortunately he died of septic shock. Autopsy examination revealed that lymphoma cells had invaded the lung tissue, bone marrow, prostate gland, and thalamus, but no involvement of the systemic lymph nodes.

Discussion

Initial examination of this patient revealed both CNS and testicular lymphoma. Testicular lymphoma tends to invade the CNS, with the incidence increasing to 18.7% (36/192) during the clinical course.[3,4,7,14,17,20,22,24,26] Furthermore, testicular involvement and bone marrow involvement are statistically significant risk factors for CNS involvement.[1,12] On the other hand, extracranial invasion of CNS lymphoma occurs in various organs of the body,[16] but testicular infiltration was confirmed in four of 14[2] and three of six[24] cases, so CNS NHL also tends to invade the testis. Even considering the prostate lesion, we cannot conclude which was the primary lesion.

A series of autopsy findings in seven patients with testicular lymphoma detected a high incidence (41%) of vascular invasion, and six of the seven patients (86%) had lung metastasis, which suggests that testicular lymphoma may metastasize to the CNS through the blood.[19] However, the actual mechanism of involvement is imperfectly understood. The incidence of testicular lymphoma is higher in patients aged 60 years and above,[6] but both conditions are rare, as testicular lesion was found in only 1.4% to 2.3% of patients with systemic NHL,[4,17] and primary CNS lymphoma in only 1.2% to 3.8% of all patients with NHL.[1,11] Both organs are recognized as immunologically privileged sites protected by the blood-brain barrier and blood-testis barrier. One theory of the etiology of CNS lymphoma suggests that the immune reaction or chemical

agent cannot destroy the lymphoma after invasion of the CNS or testis for this reason, whereas lymphoma is easily destroyed in other organs.[15] This may explain why CNS and testicular lymphoma tend to show mutual invasion.

In our case, the cerebral lesion at initial diagnosis could be categorized as an intracranial mass type according to Hochberg's classification.[10] CNS involvement in systemic lymphoma often shows meningeal spread, but the incidence of intracerebral mass is low, at approximately 13–20%.[9,13] Recently, 61% of cases have shown parenchymatous involvement, possibly due to the wider use of MR imaging.[1] The radiological, histological, and therapeutic characteristics of lymphoma presenting with an intracerebral mass cannot distinguish a primary from a secondary lesion,[13,23] which requires systemic examination. Of 128 cases initially thought to be primary CNS lymphoma, careful systemic examination revealed five (3.9%) occult systemic NHL cases: one of the bone marrow, two of the abdominal lymph nodes, one of the intraabdominal organ, and one of the intrapelvic organ.[18] Two of 16 cases initially considered to be primary CNS lymphoma had involvement of the retroperitoneal lymph node and the bone marrow.[8] Therefore, patients presenting with mass type CNS lymphoma require careful systemic examination, including bone marrow aspiration biopsy, and chest, abdominal, and pelvic CT to identify systemic lymphoma. The testes should also be investigated in males.

The survival period for patients with primary CNS NHL has been prolonged from 10–18 months[5] to 20.9 months[25] in recent years. On the other hand, patients with CNS involvement in systemic NHL have an extremely poor average survival of 2 to 6 months.[9,13,21] Systemic disease determines the prognosis in these patients. In fact, the autopsy of the present patient revealed that the brain lesion was minute and not the cause of death, which probably followed from the surgical resection plus radiation and invasion of lymphoma cells into the lung and bone marrow.

In patients with intracranial lymphoma, it is important to determine if the lesion is primary or metastatic and to plan medical treatment including systemic chemotherapy as soon as possible. Improvement of the prognosis of systemic NHL with CNS involvement requires the detection and effective treatment of systemic lesions as well as the control of the CNS lesions.

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