Successful Treatment of Multicentric Castleman’s Disease with Intracranial and Retroperitoneal Tumors

Key words: angiofollicular lymph node hyperplasia, meningioma, interleukin-6, irradiation therapy

Castleman’s disease (CD) is a rare lymphoproliferative disorder with benign hyperplastic lymph nodes characterized histologically by follicular hyperplasia and capillary proliferation with endothelial hyperplasia (1). CD is classified into two categories: hyaline-vascular and plasma cell (PC) types. Generalized PC-type lymphadenopathy, accompanied by generalized symptoms, has been recognized as multicentric CD (MCD) (2). To our knowledge, intracranial space-occupying CD is extremely rare. Although meningeal involvement of the central nervous system (CNS) is one of the typical manifestations of MCD, the CNS mass lesion due to MCD has not been reported. Seven cases of intracranial unicentric CD have been reported and six of them were initially misdiagnosed as meningioma (3, 4). This is the first reported case of MCD, the initial presentation of which was an intracranial tumor.

A 48-year-old man visited a neurosurgeon because of numbness around his right upper lip. A brain computerized tomography (CT) revealed a well-circumscribed mass in the left temporo-parietal area with surrounding edema (Fig. 1A). A left

Figure 1. A; enhanced CT of the head on the first admission. A well-circumscribed mass (arrows) was located in the left temporo-parietal area with surrounding edema. B; photomicrograph of the intracranial mass lesion. Numerous secondary lymphoid follicles with large and polymorphous germinal centers and wide lymphoid cuffs were noted. Plasma cells infiltrated densely among the interfollicular areas like sheets (HE stain, x400).
craniotomy revealed that the tumor was firmly attached to the dura mater and infiltrated the skull. The tumor consisted of markedly thickened dura and numerous secondary lymphoid follicles with large and polymorphous germinal centers, wide lymphoid cuffs, and dense infiltration of plasma cells in the interfollicular areas. Some of the germinal centers were penetrated with a few capillary vessels, which contained no hyaline deposits (Fig. 1B). Bone marrow of the skull overlying the tumor showed similar changes. We could not detect any clonal proliferation of the plasma/B cells using immunohistochemical stainings or polymerase chain reaction for IgH chains. Based on these findings, several pathologists agreed that the tumor should be diagnosed as PC-type CD. After surgical removal, the neurological symptom disappeared completely but a year later, a follow-up magnetic resonance imaging (MRI) showed evidence of recurrence. After a second craniotomy, the patient was referred to the hematologists of our hospital for treatment due to the presence of a residual tumor. Erythrocyte sedimentation rate was 19 mm per hour. C-reactive protein; 0.24 mg/dl (normal; ≤0.25), total protein; 7.2 g/dl, albumin; 3.9 g/dl, IgG; 2.174 mg/dl, IgA; 235 mg/dl, IgM; 126 mg/dl, interleukin-6 (IL-6); 81.1 pg/ml (normal; ≤4.0), soluble IL-6 receptor (sIL-6R); 34.4 ng/ml (normal; 14.0–46.0). An abdominal CT revealed a mass lesion in the right renal hilum, which surrounded the renal pelvis. A CT-guided needle biopsy was performed and the pathology of the specimen was compatible with PC-type CD. After the second craniotomy, he was treated with 30 Gy irradiation for residual brain and renal tumors. After the irradiation, the tumors completely disappeared and the IL-6 level decreased to 34.7 pg/ml. To date, there is no evidence of further recurrence.

We treated the first case with intracranial and retroperitoneal space-occupying MCD. We diagnosed the patient as having MCD because of intracranial and retroperitoneal tumors. It remains unsolved whether the intracranial and retroperitoneal tumors occurred simultaneously or independently because neither chest nor abdominal CTs were taken on the first admission. Since MCD usually causes generalized symptoms, it is of interest that the patient had no generalized symptoms other than the intracranial mass as well as normal sIL-6R values despite high IL-6 values. IL-6 is a pleiotropic cytokine with a wide range of biologic activities and it is thought to play a central role in the pathogenesis of CD/MCD (5). The observation that this patient had high IL-6 and normal sIL-6R suggests the possibility of the presence of aberrant IL-6 signal transduction. We did not administer corticosteroids or antineoplastic agents because he had no generalized symptoms.

Although we have treated only one patient, we feel that surgical excision followed by irradiation may cure intracranial space-occupying MCD.

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References