Steroid-Responsive Primary T-cell Lymphoma in the Brain: Report of a Case

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A case of primary TH lymphoma involving the splenium of the corpus callosum and the parietal lobes was presented in a 64 year-old woman with symptoms of increased intracranial pressure. CT scans showed a mass in the splenium of the corpus callosum extending into both parietal lobes. Perifocal white matter edema with small central necrosis was also noted in the lesion. Malignant T-cell lymphoma was diagnosed following a stereotatic biopsy by histopathology and immunohistochemistry. Because of the marked cerebral edema and the immunohistochemical identifications of glucocorticoid receptors on the lymphoma T cells, dexamethasone was administered intravenously. A dramatic tumor regression was noted by computer-assisted tomography on the 12th day after treatment, and complete remission of the tumor was noted within three weeks. We recommend that steroid treatment should be considered as an initial regimen for intracranial T cell lymphomas positive for glucocorticoid receptors. **(Mid Taiwan J Med 2001;6:173-8)**

Key words

glucocorticoid receptor, steroid treatment, T-cell lymphoma brain

INTRODUCTION

Primary malignant lymphomas of the brain (PMLB) comprise only 0.2% to 2% of all intracranial tumors [1-5]. These lymphomas are predominately detected in the corpus callosum, cerebellum, as well as the frontal and temporal lobes of the cerebrum. Sometimes the lesion can be found extending into the periventricular white matter and the basal ganglion. The early signs and symptoms of the disease are increased intracranial pressure, various local neurological deficits, or both. Among brain lymphomas, the meningitis-type is usually associated with chronic malaise, fatigue and headache [6].

Applications such as computed tomography (CT) and magnetic resonance imaging, (MRI) have been successfully used to immediately detect abnormalities in the brain [6]. On non-contrast-enhanced images, brain lymphomas present with slightly hyperdense and occasionally isodense nodules with well-defined margins. Although prominent perifocal edema is commonly associated with PMLB, an accurate diagnosis of primary cerebral lymphomas can only be made following confirmation by histopathological and immunohistochemical studies [3,7].

In this report, we describe a case of brain lymphoma with an enhanced mass in the splenium of the corpus callosum

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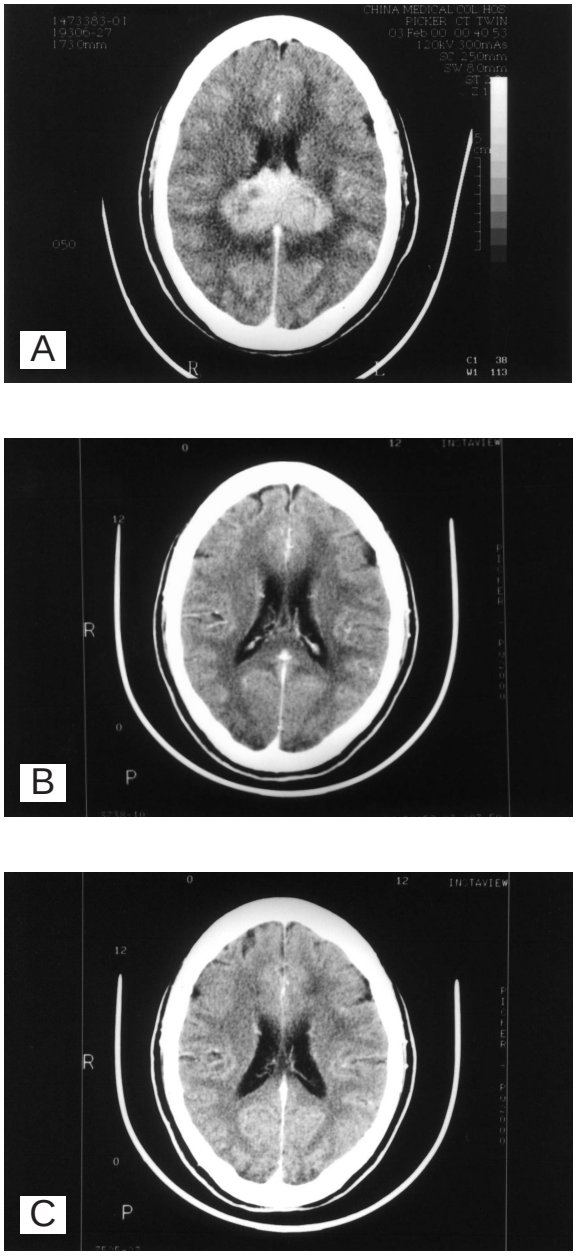

Fig. 1 A: Iodinized contrast axial computed tomography (CT) showed a marked tumor mass in the splenium of the corpus callosum extending into the parietal lobes. B: Axial CT taken at the same level 12 days after the steroid treatment showed a marked regression of the lesion and the neighboring cerebral edema. C: Axial CT taken at the same level eight months after steroid treatment showed complete remission of the tumor mass and the cerebral edema.

extending into both parietal lobes. We used immunohistochemical methods to study the expressions of CD3, CD4, CD8, CD10, CD14, CD20, CD25, CD27, CD30, CD45RO, CD56, CD68, CD80, CD86, HLA-DR, T cell receptors (TCR) and glucocorticoid receptors (GR) in brain lymphoma cells. Expressions of CD3, CD4, CD25, CD30, CD45RO, HLA-DR, GR and monoclonal TCR of Vα1 and Vβ5.2 were identified. Based on the findings of GR expression, dexamethasone was administered. The patient responded well to the treatment and the lesion reached complete remission within three weeks.

CASE REPORT

A 64-year-old woman was admitted to the hospital following a weeklong complaint of progressively worsening headaches, dizziness and gradual loss of vision in the left eye. Optical examination showed a slight hemorrhage in the left vitreous body. Neurological examination did not detect any motor or sensory abnormalities. However, CT scans revealed a mass in the splenium of the corpus callosum extending into both parietal lobes. Perifocal white matter edema with small central necrosis was also noted in the lesion (Fig. 1A). A small biopsy was therefore taken by a stereotatical procedure in order to determine the diagnosis of the mass.

Histopathologically, the specimen consisted of a population of mixed small and large lymphoid cells with evident invasion of the neighboring vessels. Immunohistochemical studies of a panel of lymphocyte markers (Dako, Carpenteria, California), TCR α/β (Serotec, Oxford, United Kingdom) and GR (Santa Cruz Biotechnology, Santa Cruz, California) were performed on tumor specimens using the LSAB method (Dako, Carpenteria, California) [8]. Briefly, a paraffin block was cut into 4 μm sections. The wax was melted in a 65 ℃ oven overnight. The slides were deparaffinized in xylene, and the xylene was removed subsequently with absolute alcohol before immunostaining. The slides were incubated with the respective antibodies, and then with linker-conjugated anti-mouse/anti-rabbit immunoglobulin. The chromogenic reaction was visualized by

peroxidase-conjugated streptavidin and aminoethyl carbazole (Sigma, St. Louis, Missouri). The slides were counter-stained with hematoxylin. Positive staining was recognized under the microscope as crimson granules. Immunohistochemical study of the tumor cells showed the following results: $CD3^+$, $CD4^+$, $CD8^-$, $CD10^-$, $CD14^-$, $CD19^-$, $CD20^-$, $CD25^+$, $CD27^-$, $CD30^+$, $CD45RO^+$, $CD56^-$, $CD68^-$, $CD80^-$, $CD86^-$, HLA-DR^+, and GR^+ (Fig. 2). Results of the TCR α/β panel showed monoclonal TCR of Vα1 and Vβ5.2, indicating that the tumor was a T helper-type of primary T-cell lymphoma.

Results of the hematology, urinalysis and blood chemistry work-ups, however, were normal: hemoglobin, 13.9 g/dL; white blood cell count, 8,130/μl (43.7% neutrophils, 47.9% lymphocytes, 4.8% monocytes, and 0.1% eosinophils). HIV test was negative. Distant involvement was not detected following examinations of bone marrow, chest X-ray and abdominal ultrasonography.

Because of the marked cerebral edema, and due to the identification of T cell lymphoma by immunohistochemical analysis, dexamethasone (8 mg/day) was administered intravenously. The brain edema and the disease-associated symptoms subsided within a few days following the initial treatment, and on the 12th day a marked regression of the lesion as well as the surrounding edema was evident (Fig. 1B). The patient's vision also improved markedly. Therapy with dexamethasone was continued for an additional week, and the patient was discharged. The follow-up examinations at the third and the eighth month showed complete remission of the lesion (Fig. 1C). No neurological symptoms have been detected since.

DISCUSSION

The results presented above show that the lymphoma cells from this patient expressed CD3, CD4, CD25, CD30, CD45RO, HLA-DR, GR and monoclonal TCR of Vα1 and Vβ5.2. Expressions of these markers were detected by immunohistochemistry.

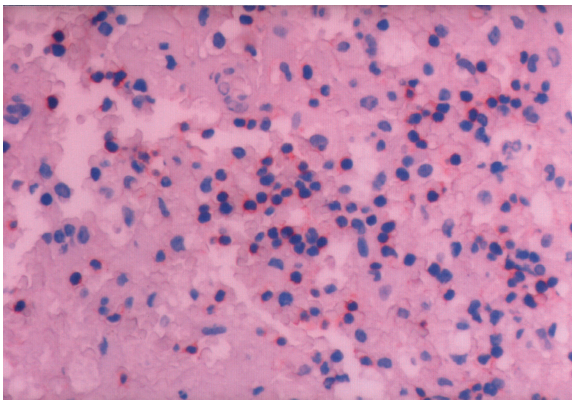

Fig. 2 Representative example of GR-positive lymphoma cells of the brain identified by immunohistochemistry (original magnification ×250).

Previous reports have described patterns of CD2, CD3, CD5, CD25, CD45RO and HLA-DR expression in PMLB specimens [3,7]. By using immunocytochemical methods, Nitta et al [3], and Kanavaros et al [7], further demonstrated that PMLB is a clonal lymphocytic disorder of T helper/inducer cells, which is similar to our findings. Usually, the prognosis of PMLB is poor when the patient is not properly treated with a survival rate of 1.8 to 3.3 months after diagnosis [9]. With radiotherapy alone, the median survival rate could reach 10 months. When radiotherapy is combined with intraventricular administration of methotrexate, the average time of recurrence can be postponed to 41 months [9].

Interestingly, patients with primary CNS lymphomas have been successfully treated simply with corticosteroids [7,9]. Steroid-sensitivity of tumor cells could be mediated by the direct oncolytic effects of corticosteroids on the lymphoreticular cells, and the decrease of brain edemas could be caused by interfering adjacent cerebral parenchyma cells [6]. Studies have shown that the action of steroids might be caused by interfering with the presence of GR as well as the immunological criteria of the cell types, although the results are debatable [1], It is

worth noting that although the reduction of the tumor burden and brain edema might be visible within a few days of treatment, the effects of steroids could decline overtime, and in most cases, tumor recurrence can be identified shortly after the steroids are withdrawn from the regimen [2].

Fortunately, there was no tumor recurrence in our case, and the patient was fine and healthy seventeen months after the initial treatment. Although immunophenotyping is available for identifying the clonality of the tumor cells, it does not predict the progression of the disease or drug responsiveness [2,10-12]. Immunohistochemical characterization of tumor cells is equally important, and the present study should shed light on the status of glucocorticoid receptors and their influence on steroid sensitivity. Expressions of GR in the cytoplasm of lymphoma cells seem to indicate an association between steroid responsiveness and the regression of brain tumors [1,5,6,9]. However, the mechanism of how steroids cause tumor regression remains to be determined. Our observations provide a focus for future studies hoping to elucidate the action and the order by which expression of glucocorticoid receptors, chemotherapies, and cerebral edemas interact with each other.

In conclusion, T-cell PMLB is a rare entity [1-5]. In this report, we diagnosed primary brain lymphoma in a patient by radiological evaluation, and immunohistochemical characterizations. Identification of GR expression in the cytoplasm of lymphoma cells was correlated with steroid responsiveness and regression of the brain tumor. These results indicate that steroid treatment should be considered for an intracranial T cell lymphoma positive for glucocorticoid receptors in the cytoplasm. Nevertheless, glucocorticoids are not recommended as the sole initial treatment of PMLB. Standard therapies should be supplemented whenever the physician decides radiotherapy and/or chemotherapy are necessary. Otherwise, both radiotherapy and chemotherapy should be postponed in patients who were responding completely [11-13].

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對類固醇治療有反應的腦內 T 細胞淋巴瘤：病例報告

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腦內T細胞淋巴瘤是一種很少見的腦內惡性腫瘤，它的病灶主要在胼胝體、小腦以及大腦的前葉或顳葉；有時候，病灶可延伸到腦室周圍的白質與基底核。電腦斷層掃描通常能立即找出腦內之異常，尤其是一些具有高密度或同密度的腦內小結；有時，腦內水腫是腦內腫瘤的徵兆，但是確實的診斷仍有待組織病理與免疫組織化學的結果顯示。此次，我們報告一位64歲女性腦內 T 細胞淋巴瘤病例。此女性病患的胼胝體壓部腫塊是以電腦斷層掃描檢測出來，腫塊已延伸到大腦顳葉的兩旁；神經外科以立體定位的小針採樣法取生檢體，腫瘤切片則以HE染色和免疫組織化學染色法染色輔助診斷。組織病理及免疫組織化學染色法顯示爲腦內 T 細胞淋巴瘤；因爲淋巴瘤的細胞質富含糖皮質激素受體，因此，病人以靜脈注射腎上腺皮質類固醇治療三週，並繼續以電腦斷層掃描檢追蹤，病人在治療的第十二天有顯著的改善，第三週則達完全緩解。因此，我們建議，如果腦內 T 細胞淋巴瘤的細胞質富含糖皮質激素受體，病人應該考慮以靜脈注射腎上腺皮質類固醇作爲初步治療。（中台灣醫誌 2001;6:173-8）

關鍵詞

糖皮質激素受體，類固醇治療，腦內 T 細胞淋巴瘤

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