

Case Report

Primary central nervous system lymphoma presenting with panhypopituitarism and diabetes insipidus

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ABSTRACT

Lymphoma involving the hypothalamus is very rare. We present a case of a 48-year-old man with primary central nervous system lymphoma (PCNSL) presenting with hypothalamic and pituitary stalk lesions with frontal masses, causing diabetes insipidus and panhypopituitarism. Brain MRI with gadolinium enhancement demonstrated vivid enhancing hypothalamic and pituitary stalk lesions with frontal masses. Brain biopsy and subsequent histopathological examination were compatible with diffuse large B-cell non-Hodgkin's lymphoma. After treatment with six cycles of intravenous high dose methotrexate-based chemotherapy, there was complete resolution of MRI finding. Steroid replacement was withdrawn but diabetes insipidus, hypothyroidism and hypogonadotropic hypogonadism persisted. Regular follow up with adequate hormone replacement is crucial even there is apparent resolution of the tumor.

INTRODUCTION

Primary central nervous system lymphoma (PCNSL) is an uncommon form of non-Hodgkin's lymphoma, comprising about 3% of all brain primary tumors that can affect any part of the brain or spinal cord¹. Currently, PCNSL represents less

than 1% of non-Hodgkin lymphoma² mainly of the B-cell type and are most commonly associated with immunodeficiency. The incidence of PCNSL has increased only slightly in the past 10 years in individuals above the age of 60, and now stands at 0.5 per 100,000 patient-years.¹

Isolated lesions are commonly seen in the frontal lobes, periventricular white matter, or the corpus callosum. PCNSL involving the hypothalamus, pituitary stalk, or pituitary gland with hypopituitarism in adult immunocompetent patients is very rare and only sporadic cases have been reported.³⁻⁶ In this article, we report a case of an immunocompetent PCNSL patient with frontal and hypothalamic lesions who presented with diabetes insipidus and anterior pituitary hormone deficiencies from lesions in the hypothalamus and pituitary stalk.

CASE HISTORY

A 48 –year-old man presented with a 2-month history of progressive headache and polyuria. He reported decreasing libido and decreased shaving for 4 months.

On physical examination, the patient was alert and cooperative. He had 20/70 and 20/50 visual acuity in the right and left eye respectively and his visual field was normal. Only a soft consistency of the bilateral testes was noted. His past medical history was unremarkable. He was found to have a serum sodium of 147 mmol/L, urine osmolality

of 95 mosmol/kg. While serum osmolality was not collected, after dDAVP treatment, urine osmolality increased to 809 mosmol/kg. These findings were consistent with diabetes insipidus. Initial hormonal work up confirmed multiple anterior pituitary hormone deficiencies. The anterior pituitary axis hormones were decreased, except for prolactin (PRL) which was increased slightly at 48.29 ng/mL. Gonadotropin levels (FSH and LH) were low, while TSH level was normal. The morning cortisol level was low (Table 1). Magnetic resonance imaging (MRI) of the brain revealed an isointense T1 and hyperintense T2 mass involving the hypothalamus with homogeneous and vivid enhancement, exerting pressure effect to the optic chiasm. The pituitary stalk was displaced downward with some thickening at the proximal part of the pituitary stalk. There were also two masses in the right frontal region with massive vasogenic edema. The lesions were isointense on T1-weighted images with homogenously vivid enhancement after gadolinium administration. The pituitary gland architecture was well preserved (Figure 1).

Table 1 Initial laboratory testing values of the pituitary gland axis hormone

Pituitary hormones	Value	Reference range
Cortisol	1.5	3.7 - 19.4 ug/dL
FSH	0.22	0.95 - 11.95mIU/mL
Free T4	0.63	0.7 - 1.48 ng/mL
LH	0.06	0.57 - 12.07 mIU/mL
Prolactin	48.29	3.48 – 19.4 ng/mL
Testosterone	0.11	1.95 - 11.38 ng/mL
TSH	0.525	0.35 - 4.94 uIU/mL

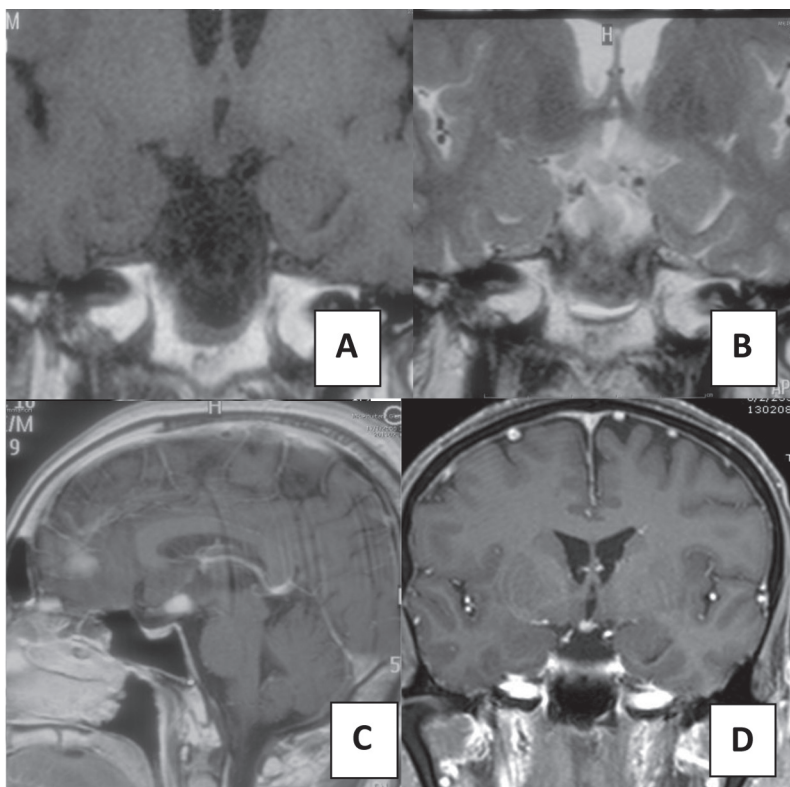


Figure 1 A, B: There is an isointense T1 and hyperintense T2 mass involving the hypothalamus with pressure effect to the optic chiasm. C,D: On post Gadolinium T1 weighted images, the lesions show homogeneous and vivid enhancement

Due to massive vasogenic edema and adrenal insufficiency, high dose dexamethasone was given. Then the patient underwent an endoscopic tumor biopsy and a craniotomy with tumor removal from frontal lobe lesion. Desmopressin (dDAVP) and pituitary hormone replacement with glucocorticoids and levothyroxine were given. His general condition, polyuria and electrolytes abnormalities improved markedly postoperatively.

Histopathological examination of the surgical specimen showed neoplastic cells with abundant cytoplasm and pleomorphic nuclei with considerable mitotic activity (Figure 2). These atypical large cells were positive for the leukocyte common antigen (LCA). Malignant lymphoma was diagnosed and these cells were diffusely positive for CD20

which indicated B-cell origin. In primary CNS lymphoma, more than 95% are diffuse large B-cell lymphoma, the others are low-grade B-cell lymphoma, other types of B-cell lymphoma such as Burkitt lymphoma, T-cell lymphoma and Hodgkin lymphoma⁷. Beside CD20. The tumor cells were positive for Bcl-6, MUM1, focally positive 20% for Bcl-2 and Ki67 positive 90% of tumor nuclei. While the specific T-lymphocyte marker, CD3 was negative and CD5, CD10 CyclinD1 and EBER were negative all⁷. The histopathological and immunohistochemistry results were compatible with the diagnosis of a diffuse large B-cell non-Hodgkin's lymphoma. Computed tomography (CT) of chest and abdomen (including bone marrow examination) excluded other neoplastic foci. HIV testing was negative. The

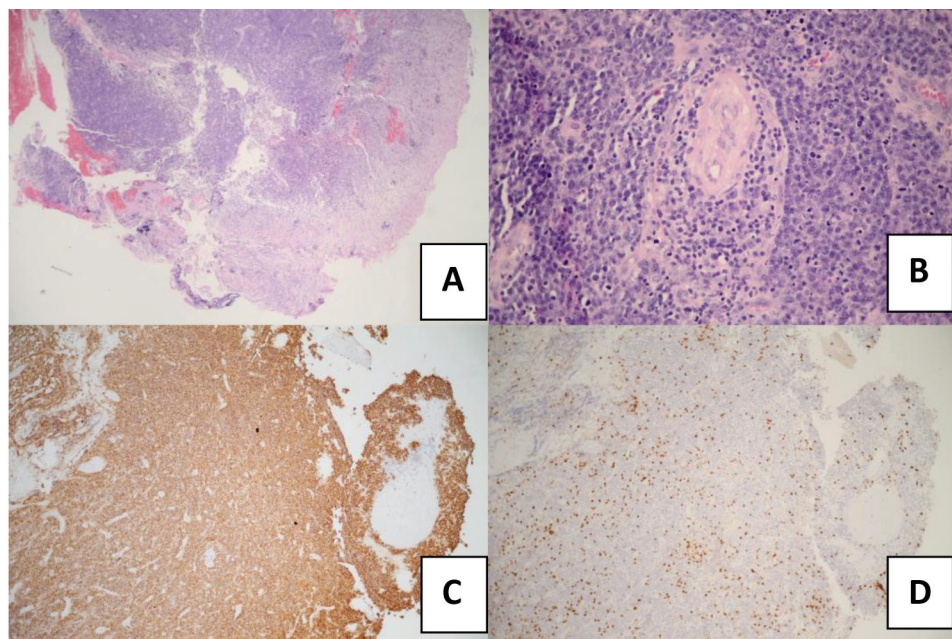


Figure 2 Tumor histopathology. A : Tumor cell in infiltration pattern (40X), B : Atypical large tumor cells infiltration in angiocentric pattern (400X), C: Membrane staining of the tumor cells with an antibody to CD20, indicating a B-cell origin(100X) D: Negative membrane staining for CD3(100X)

patient was treated with 6 cycles of high dose intravenous methotrexate ($3.5 \text{ mg}/1.73 \text{ m}^2$) and Ara-C.

At his 6-month follow-up, complete radiological remission of the lesions was achieved with recovery of secondary adrenal insufficiency. Steroid replacement was then withdrawn. However, his diabetes insipidus and secondary hypothyroidism persisted, necessitating thyroid hormone, testosterone and desmopressin therapy.

DISCUSSION

Primary central nervous system lymphoma (PCNSL) with hypothalamic involvement presenting with DI and hypopituitarism has been reported in few patients. Although CNS lymphoma occurs more frequently in immunocompromised patients, incidence peaked in the mid-1990s and has now declined. This might be related to changes in HIV incidence and management^{2,8}. In contrast, the incidence remains high among older patients (>60

years) who are mostly immunocompetent⁹. The reason for this increasing incidence is unknown.

Unlike our case, most of the previously cases had isolated hypothalamic or pituitary involvement, making the diagnosis of lymphoma more difficult. Our patient was an immunocompetent patient presenting with frontal lesions together with diabetes insipidus, hypopituitarism and hyperprolactinemia resulting from hypothalamic involvement. The MRI findings included homogenously enhancing masses in the hypothalamus and frontal area, which are typical for PCNSL. Histopathological examination confirmed the diagnosis of PCNSL at both lesions.

Although the prognosis remains poor for the majority of patients, approximately 20-30% of cases can be cured². The best treatment strategy has yet to be defined^{10, 11}. However, biopsy followed by corticosteroids, high dose methotrexate (MTX)-based chemotherapy and/or radiotherapy are the current treatment options. PCNSL is a highly

radiosensitive and chemosensitive tumor² which can result in a resolution of the tumors, however anterior pituitary hormone deficiency and diabetes insipidus generally persist. Due to irreversible damage of the hypothalamus, regular follow up and adequate hormone replacement therapy are crucial even there is apparent resolution of the tumor.

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