

IMAGING HIGHLIGHT

Primary hypothalamic lymphoma with extensive ventricular enhancement and hydrocephalus

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INTRODUCTION

Primary central nervous system lymphoma (PCNSL) is an aggressive malignancy arising exclusively in the central nervous system (CNS). PCNSL represents 1-5% of intracranial neoplasms and approximately 1% of all non-Hodgkin lymphomas.^{1,2} The clinical manifestation varies, depending on the location and size of the tumor. Biopsy is usually required in the diagnosis of PCNSL, and chemotherapy and/or radiotherapy were the most commonly used therapy.³ Here we report a rare case of primary hypothalamic lymphoma with extensive ventricular enhancement and hydrocephalus.

CASE REPORT

A previously healthy 59-year-old man was admitted for a 2-week history of dizziness, nausea, vomiting, hiccup, and unsteadiness in walking. Physical examination demonstrated elevated blood pressure of 200-230/100-140mmHg, temperature fluctuating between 36.5-38.5°C. He was alert, with gaze-evoked nystagmus and trunkal ataxia.

Head CT showed an isodense nodule in the sella area (Figure 1, A). Brain MRI showed a mass in hypothalamus with T1 hypointense and FLAIR isointense signals (Figure 1, B-C). Bilateral third ventricular walls (hypothalamus) showed homogeneous enhancement after gadolinium injection (Figure 1, D-E). Thickening and enhancement of pituitary stalk was seen (Figure 1, F). The walls of lateral ventricles and the fourth ventricle showed FLAIR hyperintensity (Figure 1, H, J) with linear enhancement (Figure 1, I, K). No restricted diffusion was

observed (Figure 1, G).

On day 8 of admission, he showed apathy with impairment of orientation, memory and calculation. Repeat MRI demonstrated enlarged ventricles (Figure 2, A-C), with an obstructed aqueduct of midbrain (Figure 2, D). The ventricular lesions became more obvious (Figure 2, A-C). MRI of saddle area with contrast showed homogeneous enhancement of the hypothalamic lesion extending to the anterior commissure, lamina terminalis, pituitary, mammillary bodies, and cerebral peduncles (Figure 2, E).

He had refractory hyponatremia and hyperglycemia. Hormone tests revealed hypopituitarism, with decreased levels of free thyroxine (T4), free triiodothyronine (T3), total T4 and total T3, normal thyroid stimulating hormone (TSH), decrease levels of estradiol, progesterone, testosterone and luteinizing hormone (LH), normal follicle stimulating hormone (FSH), increased prolactin, normal growth hormone, decreased insulin like growth factor 1 (IGF 1), normal adrenocorticotropic hormone (ACTH) and cortisol.

Lumbar puncture demonstrated an opening pressure of 120 mm H2O, elevated protein of 3.02g/L (normal range: 0.15-0.5g/L), elevated leukocytes of $30*10^6/L$ (polymorphonuclear 95%), glucose of 4.2mmol/L compared to the paired plasma sample of 7.7mmol/L. No tumor cells or pathogens were found in the cerebrospinal fluid (CSF).

Stereotactic biopsy of hypothalamus was performed. The tumor showed a diffuse growth pattern and angiocentricity under microscope, without a clear boundary between the tumor and

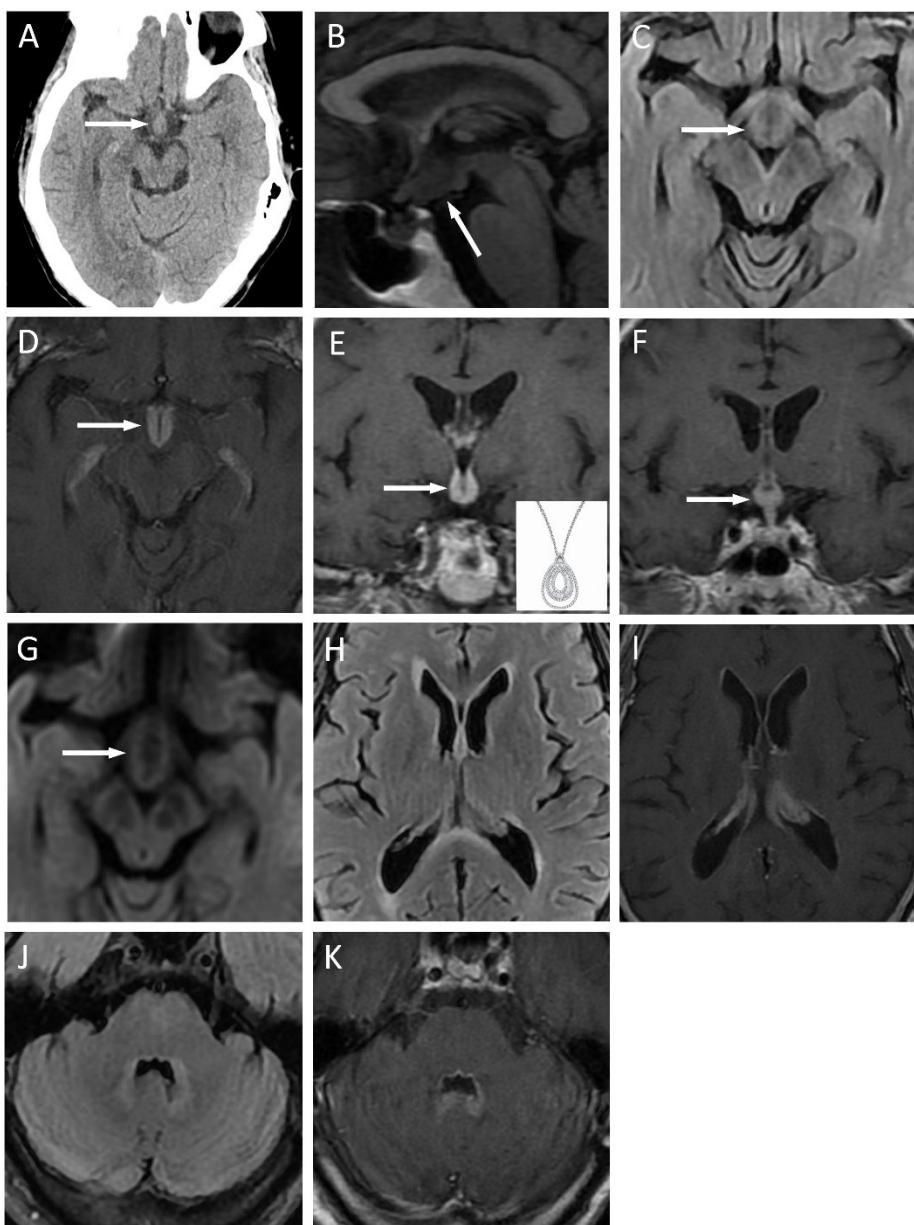


Figure 1. Initial CT and MRI on admission.

Head CT showed an isodense nodule in the sella area (A). Brain MRI showed a mass in hypothalamus with T1 hypointense (B) and FLAIR iso-intense (C) signals, extending to cerebral peduncles. The bilateral third ventricular walls (hypothalamus) showed homogeneous enhancement after gadolinium injection (Figure 1 D-E). The enhanced lesion looks like a pendant in coronal view (E). Thickening and enhancement of pituitary stalk was shown (F). The walls of bilateral lateral ventricles and the fourth ventricle showed FLAIR hyperintensity (H, J) with linear enhancement (I, K). No restricted diffusion was observed in these lesions (G).

normal brain tissue (Figure 3, A). The tumor cells had a medium size and round or oval shapes. Large nuclei with prominent nucleoli and high mitotic activity were noted (Figure 3, B). Immunohistochemistry showed that tumor cells

were positive for LCA, CD20, MUM-1, Bcl-6, Bcl-2 and Vim (Figure 3, C), and negative for CD10, CD3, CD138, CD38, MPO, GFAP, CK and Neu-N (Figure 3, D). The Ki-67 labeling index of the tumor was 60%. The diagnosis was

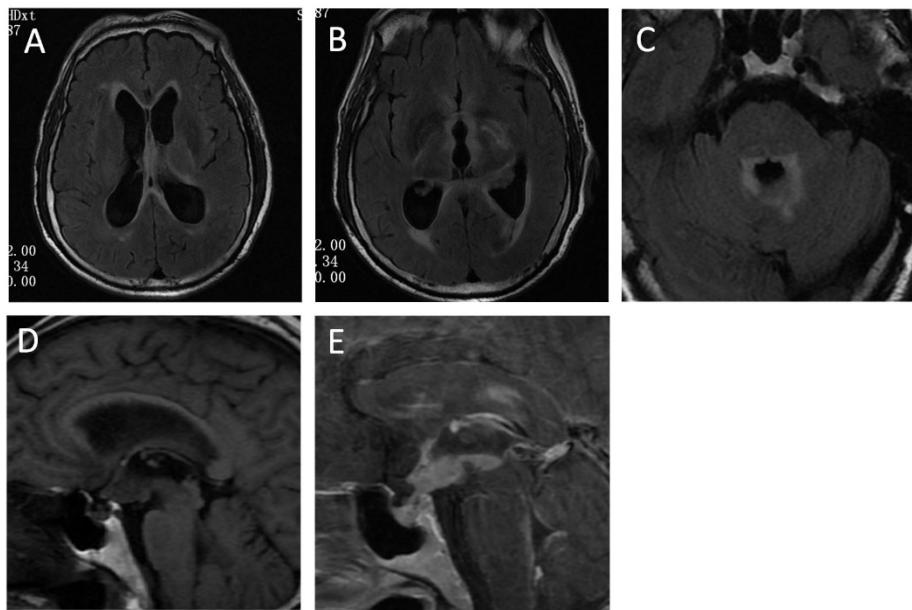


Figure 2. MRI on day 8 of admission.

MRI demonstrated enlarged ventricles (A, B, C), with an obstructed aqueduct of midbrain (D) (compared to Figure 1, B). The lesions surrounding the ventricles became more obvious on FLAIR weighted imaging (A, B, C). MRI of saddle area with contrast showed homogeneous enhancement of the hypothalamic lesion extending to the anterior commissure, lamina terminalis, pituitary, mammillary bodies, and cerebral peduncles (E).

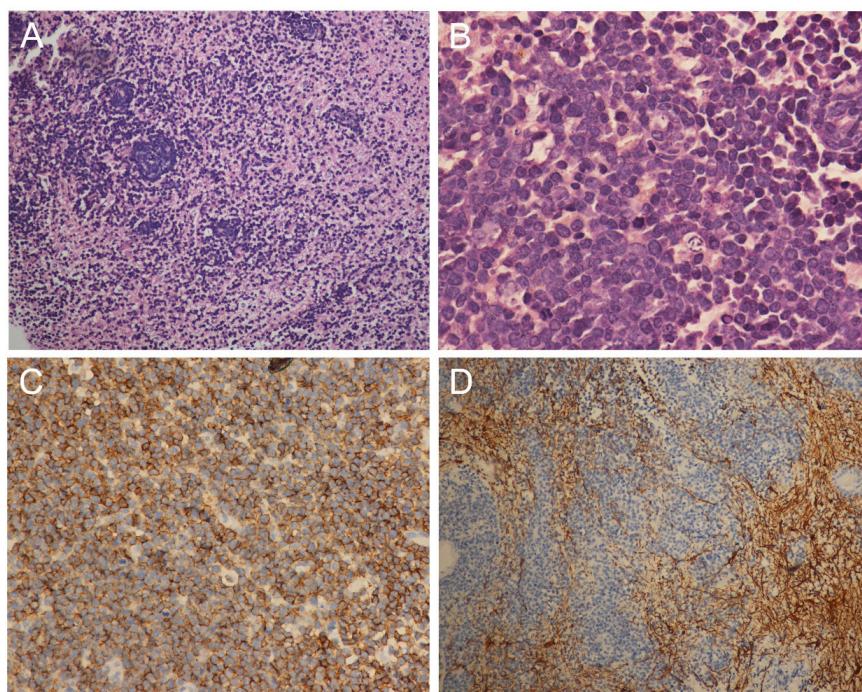


Figure 3. Pathological findings.

(A) The tumor showed a diffuse growth pattern and angiocentricity. (H&E stain; $\times 100$). (B) The tumor cells had a medium size and round or oval shapes. Large nuclei with prominent nucleoli and high mitotic activity were noted. (H&E stain; $\times 400$). (C) The tumor cells expressed CD20, a pan-B cell marker. (En Vision; $\times 200$). (D) The tumor cells were negative for GFAP. (En Vision; $\times 100$)

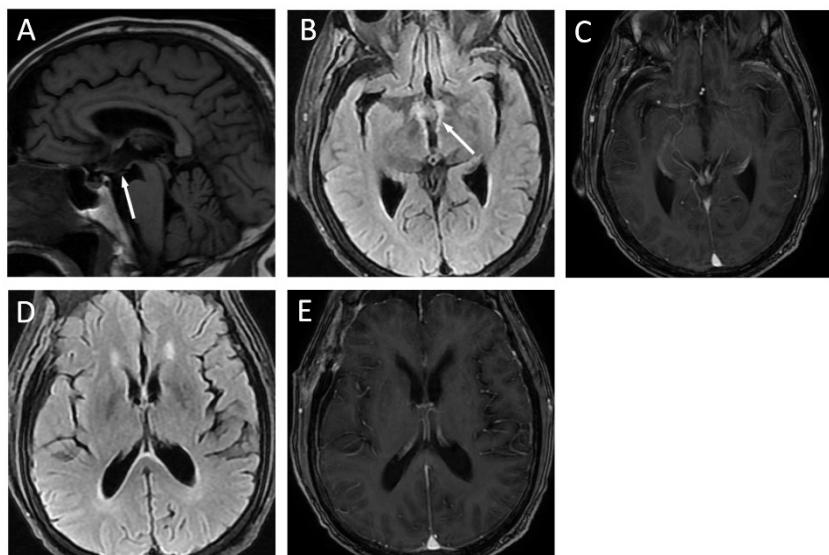


Figure 4. Post-treatment MRI

After treatment MRI showed a marked regression of tumor lesions (arrow) (A, B). The ventricular walls still had FLAIR hyperintensity (B, D), however without any enhancement (C, E). Ventricular enlargement disappeared and the aqueduct of midbrain was open again (A).

diffuse large B-cell lymphoma, non-germinal cell phenotype. Contrast total body CT scan had not showed other lesions, and final diagnosis of primary diffuse large B-cell lymphoma of the CNS was made.

A week after the completion of the first phase of treatment with temozolomide, he showed marked improvement in dizziness, nausea, hiccup, apathy and cognition, and normalization of hypertension, hyperthermia, hyperglycemia and hyponatremia. MRI showed a marked regression of tumor lesions (Figure 4, A-B). The ventricular walls still had FLAIR hyperintensity (Figure 4, B, D), however without any enhancement (Figure 4, C, E). Ventricular enlargement disappeared, with the aqueduct being open again (Figure 4, A).

DISCUSSION

Our patient with PCNSL has three notable features: hypothalamic location, extensive ventricular enhancement, and hydrocephalus.

According to review of literature, PCNSL presents as a solitary intracranial mass lesion in 60%-70% of patients, mostly located in the cerebral hemispheres (38%), thalamus/basal ganglia (16%), corpus callosum (14%), periventricular regions (12%), and cerebellum (9%).³ Hypothalamus is an unusual location of PCNSL rarely reported.⁴⁻¹⁰ The hypothalamic involvement in our case was symmetrical. Thick

enhancement of bilateral third ventricular walls on post-gadolinium MRI scan made the tumor look like a pendant in coronal view (Figure 1, E). The lymphoma extended into surrounding structures including anterior commissure, lamina terminalis, pituitary, mammillary bodies, and cerebral peduncles. Our patient had manifestations of hypothalamic dysfunction (hyperthermia, hypertension, hyponatremia, hyperglycemia, and hypopituitarism) and impaired cognition, which reflected the neuroanatomical location of these lesions.

Another unusual feature of our patient was ventricular linear enhancement on post-gadolinium MRI. The radiological sign had been rarely reported in PCNSL.^{7,11} The thin ventricular lesion probably resulted from implantation metastasis by CSF seeding, in spite of a negative CSF cytological study. Ependymal enhancement can be also seen in ventriculitis from various infectious pathogens. The most common pathogens include bacteria¹² and virus (especially cytomegalovirus).¹³ Ventriculitis associated with tuberculosis¹⁴, candidiasis¹⁵ or toxoplasmosis¹⁶ have also been rarely reported. Pencil-thin ependymal enhancement has been recently recognized in neuromyelitis optica spectrum disorders (NMOSD).¹⁷ Isolated ependymal metastatic involvement has been described for extracranial tumors.¹⁸ Thus, differential diagnosis of linear ventricular enhancement is wide.

The third unusual feature was hydrocephalus. Kim reported a case of PCNSL presenting with normal pressure hydrocephalus (NPH), and assumed that leptomeningeal involvement that was not evident on MRI may be responsible for the development of communicating hydrocephalus.⁷ Ishizaki reported a case of primary leptomeningeal B-cell lymphoma with NPH.¹⁹ Our case did not show leptomeningeal involvement on MRI. An intriguing finding was that aqueduct of midbrain was obliterated on MRI when hydrocephalus presented, and was open when hydrocephalus disappeared after chemotherapy. We assume that obstructed or narrowed aqueduct might be partly responsible for hydrocephalus in our case.

These unusual manifestations made the diagnosis challenging. Stereotactic biopsy of hypothalamus finally confirmed the diagnosis of PCNSL with early initiation of chemotherapy followed by marked improvement.

In conclusion, PCNSL should be considered when patients presented with hypothalamic lesion/dysfunction, linear ventricular enhancement, or hydrocephalus. Although invasive, stereotactic biopsy may be necessary to confirm the diagnosis.

DISCLOSURE

Conflict of interest: None

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