CASE REPORT

Primary hypothalamic third ventricular Burkitt's lymphoma: a case report with emphasis on differential diagnosis

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ABSTRACT. A patient with primary Burkitt-type lymphoma of the central nervous system is presented. A hypothalamic–third ventricular tumour in a man 71 years of age was diagnosed histologically as Burkitt's lymphoma. Primary Burkitt's lymphoma of the hypothalamic region is extremely rare and has not been previously reported in adults.

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Despite the frequent periventricular location of many primary central nervous system lymphomas (PCNSLs) [1], the presence of a solitary primary hypothalamic and/or third ventricular lymphoma can be considered exceptional [2]. We report a case of Burkitt's lymphoma involving the third ventricle and the adjacent hypothalamic area that was difficult to differentiate from a chordoid glioma, the majority of which have been reported to occur in the same region [3].

Case report

The patient was a 71-year-old man with a medical history of pulmonary tuberculosis. He presented with complaint of general fatigue beginning 1 month before admission. Results of bacteriological examination of sputum were negative. General physical condition at the time of admission was almost normal, although he was slightly disoriented. Other than mild weakness of the right upper arm, neurological examination disclosed no abnormality. Cranial nerve examination was normal. The patient was found to be severely hypernatraemic, with a sodium level of 156 mEq l⁻¹ (normal 135–145 mEq l⁻¹). Measurements of 24 h urine output and determination of urine density confirmed the diagnosis of diabetes insipidus. Serological testing for the presence of antibodies to human immunodeficiency virus (HIV) yielded negative results. Lumbar puncture and cerebrospinal fluid (CSF) analysis revealed mild lymphocytic predominance. No bacterial growth in the CSF, including growth of *Mycobacterium tuberculosis*, was demonstrated

on staining, culture or polymerase chain reaction (PCR). CT scans revealed a hyperdense mass with irregular margins occupying the hypothalamic region and third ventricle (Figure 1). MRI disclosed a nodular lesion 2.8 cm in diameter in the same region. The tumour was isointense to slightly hypointense on T₁ weighted MR images and slightly hyperintense on T₂ weighted images; the tumour exhibited essentially uniform enhancement (Figure 2). The tumour included neither a central cystic nor a necrotic region. The bright signal seen on T₂ weighted images suggested vasogenic oedema extending into the basal ganglia, posterior limbs of the internal capsules, mid-brain and the anterior portions of the thalami. The pituitary stalk was enlarged and continuous with the mass in the hypothalamic region. Diffusion-weighted imaging, perfusion-weighted imaging and MR spectroscopy were not performed because of the patient's inability to hold still.

The lesion was partly resected to obtain a small amount of tumour tissue for diagnosis. Neuroendoscopic biopsy of the hypothalamic–third ventricular tumour yielded the histological diagnosis of Burkitt's lymphoma. The lesion was soft and bled slightly. The bleeding was quickly stopped with adequate irrigation.

On light microscopy, the mass was found to contain a monomorphic proliferation of large lymphoid cells, with a so-called “starry sky” appearance resulting from macrophages, loosely cohesive cells and frequent degeneration (Figure 3). The tumour cells were immunoreactive for the B-cell markers CD20 and CD10, but negative for bcl-2 anti-apoptotic protein. MIB-1 staining was positive in almost all neoplastic cells. These findings led to the diagnosis of Burkitt's lymphoma. The lymphocytes did not express CD3 and CD30. Other principal conditions included in the histological differential diagnosis were metastatic carcinoma and glial

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Figure 1. Non-contrast CT scan reveals a hyperdense mass in the hypothalamic–third ventricular region.

tumours, but these were excluded on the basis of negative test results for CAM5.2, glial fibrillary acidic protein and S100 protein. Chest, abdominal and pelvic CT revealed no evidence of lymphoma apart from that in the CNS.

With the diagnosis of a primary hypothalamic–third ventricular Burkitt's lymphoma, the patient received whole-brain radiotherapy of 4320 cGy fractionated into 24 sessions plus boosters of 1200 cGy fractionated into 10 sessions over the hypothalamic–third ventricular region. Post-radiotherapy brain MRI revealed marked shrinkage of the hypothalamic lesion. The patient recovered from his disorientation as well as diabetes insipidus with use of hormonal replacement therapy.

Discussion

PCNSLs are mostly seen in immunodeficient patients, especially those with AIDS; however, well-documented primary lesions have been detected in the brains of immunocompetent patients as well [4]. PCNSLs exhibit a wide range of histological types. Burkitt's lymphoma is an undifferentiated, B-cell type malignant lymphoma. Although it is the most common non-Hodgkin's lymphoma subtype in children, it accounts for <5% of all lymphomas in adults [5]. There are several forms of Burkitt's lymphoma that vary by geographical distribution, incidence and risk factors [5]. Endemic Burkitt's lymphoma is the disease originally described by Burkitt and largely found in Africa, characteristically affecting the facial skeleton in children between the ages of 2 and 9 years. Sporadic Burkitt's lymphoma, the type observed in our case, was subsequently described outside of Africa, but is morphologically similar to endemic Burkitt's lymphoma and affects mainly the abdominal viscera; it can be detected at any age, and no specific cofactor has been described for it. A third subtype of

Burkitt's lymphoma has been proposed based on its association with HIV infection.

Primary Burkitt's lymphomas of the brain are extremely rare, with fewer than 10 such cases reported in the literature [6–9]. The diagnosis of a primary Burkitt's lymphoma presenting as a unique, solitary mass located in the hypothalamic and/or third ventricular region is very unusual. An extensive search among a series of PCNSLs [1, 10–14] and third ventricular tumours [15–17], as well as isolated case reports, indicated that this is the first reported case of primary Burkitt's lymphoma occurring in the hypothalamic third ventricular region in an adult.

Unfortunately, the MRI findings in this case were not specific for Burkitt's lymphoma. Pituitary macroadenomas, craniopharyngiomas, meningiomas, metastases, optic and hypothalamic pilocytic astrocytomas, and aneurysms account for more than 75% of hypothalamic third ventricular lesions. Other less common entities include Rathke cleft cysts, hamartomas of the tuber cinereum, and granulomatous diseases such as sarcoid, tuberculosis and eosinophilic granuloma. Chordoid glioma expands the differential diagnosis of third-ventricular masses further.

A chordoid glioma was suspected in light of the patient's age and the imaging appearance of a solid lesion with nodal margins. Chordoid glioma has recently been added to the World Health Organization glioma classification scheme [18]. Pomper et al [3] reported that chordoid gliomas were located in the region of the hypothalamus and anterior third ventricle, were ovoid in shape and were well circumscribed. They noted that tumours were isointense on T_1 weighted MR images and isointense to slightly hyperintense on long repetition time MR images; the tumours exhibited essentially uniform enhancement. In two of their patients, T_2 bright signal due to vasogenic oedema extended into the optic tracts, the basal ganglia, posterior limbs of the internal capsules, and lateral geniculate nuclei of the thalami. These imaging characteristics were almost the same as in our patient, except that posterior displacement of the pituitary infundibulum was demonstrated in one of their patients; the infundibulum could not clearly be considered normal in our case, probably owing to tumour involvement of its superior aspect. This difference may be explained, at least in some cases, by difference in tumour spread. Because chordoid gliomas are pathologically low-grade tumours, they may tend to displace adjacent structures instead of infiltrating them. Although Pomper and colleagues reported that vasogenic oedema might help to distinguish chordoid glioma from lymphoma or meningioma, in our case differential diagnosis between Burkitt's lymphoma and chordoid glioma might have been impossible based on this finding alone. Radiological findings for chordoid gliomas on advanced types of imaging, such as diffusion-weighted imaging, perfusion-weighted imaging and MR spectroscopy, have not been reported in the literature.

Differentiation of Burkitt's lymphoma from optic/hypothalamic glioma may be difficult using imaging alone. That the latter is a tumour of childhood enables differentiation on clinical grounds.

Tuberculosis in the CNS appears as various conditions, including tuberculoma, vasculitis, cerebral infarction,

Figure 2. MRI. (a) Axial T_1 weighted image shows a Burkitt's lymphoma that is isointense to slightly hypointense located in the hypothalamic-third ventricular region. (b) Corresponding T_2 weighted image shows the lesion to be slightly hyperintense relative to white matter. Note vasogenic oedema within the basal ganglia (arrows), posterior limbs of the internal capsules and mid-brain. (c) Contrast-enhanced coronal T_1 weighted gradient-echo MR image reveals a densely enhancing hypothalamic third ventricular mass. (d) Contrast-enhanced sagittal T_1 weighted spin-echo MR image shows that the tumour is separate from the pituitary gland. No displacement of the pituitary stalk is seen.

meningitis and cranial neuritis, as well as hydrocephalus. Among them, tuberculous meningitis tends to exhibit intense enhancement of the leptomeninges covering the basilar cisterns. However, we did not consider tuberculous

meningitis likely in our patient, despite his history of pulmonary tuberculosis, as the mass lesion was clearly demonstrated in the hypothalamic third ventricular region and no concomitant involvement of the meninges was

Figure 3. Photomicrographs. (a) The mass contains loosely cohesive cells with frequent cell degeneration (hematoxylin and eosin staining). The lymphocytes are positive for (b) the B-cell antigen CD20, (c) CD10 with dark membrane staining, and (d) MIB-1.

demonstrated. Furthermore, the negative results on bacteriological examinations, such as CSF staining, culture and PCR, indicated that the patient's tuberculosis was inactive.

Neurosarcoidosis most commonly involves the meninges, cranial nerves, hypothalamus and infundibular stalk. It occasionally results in a focal extra-axial or parenchymal mass and can mimic meningioma or glioma [19]. The lack of signs of systemic involvement in our patient aided differentiation from other neurological disorders.

Tuberculum sellae meningiomas account for 3–10% of all meningiomas [20], and their typical signal intensity on MRI is similar to that in our patient. Furthermore, Sklar et al [21] reported a case of tuberculum sellae meningioma with optic tract oedema and concluded that meningioma cannot be excluded on the basis of the presence of oedema. Lack of direct continuity with the adjacent dura-covered structures ruled out this possibility in our patient.

Although metastatic tumour could not be ruled out in the present case, absence of any primary malignancy on chest, abdominal and pelvic CT made it unlikely.

In conclusion, primary Burkitt's lymphoma should be included in the differential diagnosis of a mass arising from the hypothalamic third ventricular region. Although it may be difficult to differentiate from chordoid gliomas, it appears possible that the infiltrative nature of the lesion may be predictive of higher grade tumours.

References

1. Yasargil MG. Primary CNS non-Hodgkin lymphoma and primary intracranial sarcoma. In: *Microneurosurgery*. Stuttgart, New York: Georg Thieme Verlag; 1996:375–8.
2. Lanzieri CF, Sabato U, Sacher M. Third ventricular lymphoma: CT findings. *J Comput Assist Tomogr* 1984;8: 645–7.
3. Pomper MG, Passe TJ, Burger TC, Scheithauer BW, Brat DJ. Chordoid glioma: a neoplasm unique to the hypothalamus and anterior third ventricle. *Am J Neuroradiol* 2001;22: 464–9.
4. Eby NL, Grufferman S, Flannelly CM, Schold SC Jr, Vogel FS, Burger PC. Increasing incidence of primary brain lymphoma in the US. *Cancer* 1988;62:2461–5.
5. Orem J, Mbidde EK, Lambert B, Sanjose S, Weiderpass E. Burkitt's lymphoma in Africa, a review of the epidemiology and etiology. *Afr Health Sci* 2007;7:166–75.

6. Valsamis MP, Levine PH, Rapin I, Santorineou M, Shulman K. Primary intracranial Burkitt's lymphoma in an infant. *Cancer* 1976;37:1500-7.
7. Kobayashi H, Sano T, Li K, Hisawa K. Primary Burkitt-type lymphoma of the central nervous system. *Acta Neuropathol* 1984;64:12-14.
8. Hegedus K. Burkitt-type lymphoma and reticulum-cell sarcoma. An usual mixed form of two intracranial primary malignant lymphomas. *Surg Neurol* 1984;21:23-9.
9. Monabati A, Rakei SM, Kumar P, Taghipoor M, Rahimi A. Primary Burkitt lymphoma of the brain in an immunocompetent patient. *J Neurosurg* 2002;96:1127-9.
10. Bataille B, Delwail V, Menet E, Vandermarcq P, Inghand P, Wager M, et al. Primary intracerebral malignant lymphoma: report of 248 cases. *J Neurosurg* 2000;92:261-6.
11. Jahnke K, Schilling A, Heidenreich J, Stein H, Brock M, Thiel E, Korfel A. Radiologic morphology of low-grade primary central nervous system lymphoma in immunocompetent patients. *Am J Neuroradiol* 2005;26:2446-54.
12. Kaufmann TJ, Lopes MB, Laws ER Jr, Lipper MH. Primary sellar lymphoma: radiologic and pathologic findings in two patients. *Am J Neuroradiol* 2002;23:364-7.
13. Silfen ME, Garvin JH Jr, Hays AP, Starkman HS, Aranoff GS, Levine LS, et al. Primary central nervous system lymphoma in childhood presenting as progressive panhypopituitarism. *J Pediatr Hematol Oncol* 2001;23:130-3.
14. Kozáková D, Machálek K, Brtko P, Szépe P, Vanuga P, Pura M. Primary B-cell pituitary lymphoma of the Burkitt type: case report of the rare clinic entity with typical clinical presentation. *Cas Lek Cesk* 2008;147:569-73.
15. Slone HW, Blake JJ, Shah R, Guttikonda S, Bourekas EC. CT and MR findings of intracranial lymphoma. *AJR Am J Roentgenol* 2005;184:1679-85.
16. Pascual JM, Gonzalez-Llanos F, Roda JM. Primary hypothalamic-third ventricle lymphoma. Case report and review of the literature. *Neurocirugia* 2002;13:305-10.
17. Erdag N, Bhorade RM, Alberico RA, Yousuf N, Patel MR. Primary lymphoma of the central nervous system. *AJR Am J Roentgenol* 2001;176:1319-26.
18. Brat DJ, Scheithauer BW, Cortez SC, Reifenberger G, Burger PC. Chordoid glioma of the third ventricle. In: Kleihuis P, Cavenee WK, editors. *Pathology and genetics of tumours of the nervous system*. 2nd edition. Lyon: International Agency for Research on Cancer; 90-91.
19. Katzman GL. Nonneoplastic and tumorlike disorders. In: Osborn AG, editor. *Diagnostic imaging: brain*. Salt Lake City: Amirsys; 2004: II/4-52-55.
20. Miller NR. Walsh and Hoyt's clinical neuro-ophthalmology. Baltimore: Williams & Wilkins, 1991.
21. Sklar EML, Schatz NJ, Glaser JS, Sternau L, Seffo F. Optic tract edema in a meningioma of the tuberculum sellae. *Am J Neuroradiol* 2000;21:1661-3.