

LETTER TO THE EDITOR

Panhypopituitarism and diabetes insipidus in a patient with primary central nervous system lymphoma

Olivier Malaise¹, Nicolas Frusch¹, Emmanuel Beck², Sophie Servais¹, Jo Caers¹, Bernard De Prijck¹, Daniela Betea² & Yves Beguin¹

¹Department of Hematology and, ²Department of Endocrinology, CHU and University of Liège, Belgium

Primary central nervous system (CNS) lymphoma represents less than 5% of non-Hodgkin lymphomas, mainly of the B-cell type. We recently diagnosed a relapse of primary CNS lymphoma, resulting in panhypopituitarism and diabetes insipidus. This complication has rarely been described in the literature. Due to the patient's palliative situation, treatment was adapted to the context and only minimally invasive tests were performed to make the diagnosis.

A 57-year-old woman was diagnosed with a diffuse large B-cell primary cerebral lymphoma. After one course of high-dose corticosteroids and two courses of high-dose intravenous cytarabine and methotrexate, whole-brain radiotherapy (39 Gy) was successfully administered. Brain magnetic resonance imaging (MRI) confirmed a complete remission. One year after the initial diagnosis, the patient was readmitted for confusion. She had urinary incontinence with polyuria, polydipsia and a recent 2 kg weight loss, with ataxia and paresis of oculomotor nerve III. Daily medication included dexamethasone 1.5 mg.

A brain computed tomography (CT) scan identified a 2.7 cm left thalamo-peduncular lesion with a mass effect on the left lateral and third ventricles. The lesion was contrast-enhanced and surrounded by an important edema. MRI of the brain further identified hypothalamic and probably pituitary invasion (Figure 1). The history of CNS lymphoma, brain images and clinical presentation were all suggestive of brain lymphoma recurrence. Lumbar puncture showed a few lymphocytes in the cerebrospinal fluid. Disease staging excluded other lesions. Blood analysis identified hypoglycemia, a very low thyroid stimulating hormone (TSH) value at 0.02 μ IU/mL (normal [N] = 0.20–4.20) with normal-low free thyroxine (T_4) at 8.6 pg/mL (N = 7.0–17.0) and hypernatremia at 155 mmol/L (N = 135–145). Additional antepituitary hormone levels were examined. Luteinizing hormone (LH), follicle stimulating hormone (FSH) and estradiol levels were very low. Luteinizing hormone-releasing hormone (LH-RH) and thyrotropin-releasing hormone (TRH) tests confirmed central hypogonadotropic hypogonadism

and central hypothyroidism. The prolactin serum level was increased five-fold above the normal range, suggesting a defect in the pituitary stalk. Insulin-like growth factor-1 (IGF-1) levels were normal, but growth hormone (GH)-stimulating tests were not performed. Because the patient was immediately treated with methylprednisolone, the corticotrophic axis could not be investigated. Analyses exploring the post-pituitary were also performed. The 24 h urinary volume was 4800 mL with a low osmolality of 204 mOsm/kg (N = 50–1200), with the patient receiving 500 mL of parenteral fluids and drinking more than 3500 mL per day. Plasma osmolality was normal-low at 288 mOsm/kg. After administration of a nasal spray of desmopressin, the 24 h urinary volume decreased to 1800 mL. Plasma osmolality increased to 596 mOsm/kg.

A diagnosis of anterior and posterior hypopituitarism was therefore proposed. The patient was thus treated with methylprednisolone 60 mg/day to reduce cerebral edema and prevent adrenal failure, desmopressin 10 μ g/2 days, water restriction, and thyroxin 50 μ g/day. Polyuria and hypernatremia resolved. Accordingly, her neurological status and awakesness also improved. Intrathecal chemotherapy with cytarabine was initiated to try to limit tumor progression. At her request, the patient was discharged to her home, where she died a few weeks later. In the context of end-of-life care, estrogens and growth hormone were not administered due to their limited clinical interest in a palliative setting, as well as the theoretical oncogenic properties of the latter.

A limitation to our observation lies in the difficulty of performing endocrine tests to study the corticotrophic axis because of the administration of corticosteroids. The IGF-1 serum level was normal, but dynamic tests were not used to study the somatotrophic axis in this context of palliative care. Panhypopituitarism has also been described after brain irradiation, but usually after a cumulative dose of 50–60 Gy with symptoms occurring several years after irradiation, and growth hormone is usually the first to be deficient, which was not the situation in our case.

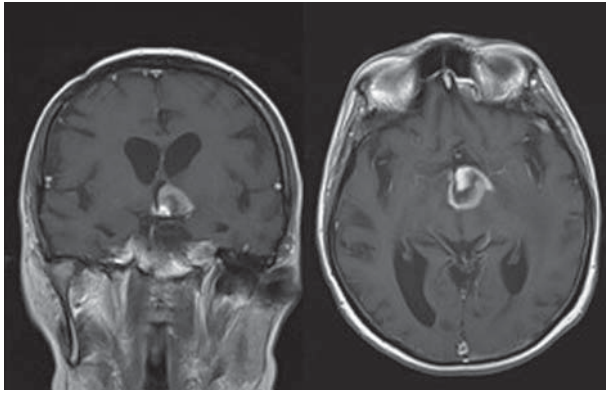


Figure 1. Frontal and transverse T1-weighted brain MRI, after gadolinium injection.

To the best of our knowledge, excluding all other hypothalamic or pituitary concomitant causes that could also explain the symptoms, there are about a dozen reported cases of primary cerebral lymphoma with hypothalamic or pituitary involvement leading to panhypopituitarism or diabetes insipidus [1–10]. The association of ante-pituitary deficiency, hyperprolactinemia and diabetes insipidus, secondary to lymphoma infiltration, has only been reported a couple of times in the literature [5,8,9]. We introduced adequate hormonal supplementation to increase the patient's comfort, with rapid clinical improvement, in an otherwise compromised situation due to progression of the lymphoma. Diagnostic tests and treatment were adapted, taking into account the patient's palliative situation.

Potential conflict of interest: Disclosure forms provided by the authors are available with the full text of this article at www.informahealthcare.com/lal.

References

- [1] Capra M, Wherrett D, Weitzman S, et al. Pituitary stalk thickening and primary central nervous system lymphoma. *J Neurooncol* 2004;67:227–231.
- [2] Katz BJ, Jones RE, Digre KB, et al. Panhypopituitarism as an initial manifestation of primary central nervous system non-Hodgkin's lymphoma. *Endocr Pract* 2003;9:296–300.
- [3] Kaufmann TJ, Lopes MB, Laws ER, et al. Primary sellar lymphoma: radiologic and pathologic findings in two patients. *Am J Neuroradiol* 2002;23:364–367.
- [4] Landman RE, Wardlaw SL, McConnell RJ, et al. Pituitary lymphoma presenting as fever of unknown origin. *J Clin Endocrinol Metab* 2001;86:1470–1476.
- [5] Layden BT, Dubner S, Toft DJ, et al. Primary CNS lymphoma with bilateral symmetric hypothalamic lesions presenting with panhypopituitarism and diabetes insipidus. *Pituitary* 2011;14:194–197.
- [6] Liu JK, Sayama C, Chin SS, et al. Extranodal NK/T-cell lymphoma presenting as a pituitary mass. Case report and review of the literature. *J Neurosurg* 2007;107:660–665.
- [7] Quintero Wolfe S, Hood B, Barker J, et al. Primary central nervous system lymphoma mimicking pituitary apoplexy: case report. *Pituitary* 2009;12:76–79.
- [8] Samuels MA, De la Monte S. Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 36–1994. A 49-year-old man with hypopituitarism, multifocal neurologic defects, and an intracranial mass. *N Engl J Med* 1994;331:861–868.
- [9] Shaw JA, Strachan FM, Sawers HA, et al. Non-Hodgkin lymphoma with panhypopituitarism, hyperprolactinaemia and sixth nerve palsy. *J R Soc Med* 1997;90:274–275.
- [10] Silfen ME, Garvin JH Jr, Hays AP, et al. Primary central nervous system lymphoma in childhood presenting as progressive panhypopituitarism. *J Pediatr Hematol Oncol* 2001;23:130–133.