

Primary pituitary lymphoma

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Abstract

Primary CNS lymphoma (PCNSL) is now thought to constitute 3% of all intracranial neoplasms. PCNSL occurrence in the sella turcica region is an extremely rare finding. We present a 37-year-old male with primary pituitary lymphoma treated in our department. The patient, who had had no previous illnesses, was admitted to the hospital because of bilateral blurred vision. Findings on physical examination were normal except for temporal parts of field of vision deficit. No abnormalities were found in his bilateral ocular movement, facial sensory function or motor function. His blood count and biochemical profile were normal. Basic hormonal studies revealed no symptoms of panhypopituitarism. MRI demonstrated a large intrasellar mass with supra- and parasellar extension. MRS revealed decrease in NAA/tCr proportion and increase in Cho/NAA and Cho/tCr proportions. Endoscopic surgery was performed using the transsphenoidal approach. Histopathological examination demonstrated a large B-cell lymphoma. The patient received 6 cycles of CHOP chemotherapy. He was also irradiated with 6 MV photons to the whole brain to a total dose of 40 Gy and then there was a boost to the tumour to a total dose of 50 Gy. Next he was reoperated on with the fronto-temporo-sphenoidal craniotomy approach and subtotal resection of the tumour was performed. After the treatment the visual disturbances significantly decreased. Control MRI revealed a stable remnant of the tumour. Nowadays the patient has 52 months' follow-up and he has only a stable, slight visual field deficit on the upper temporal side of the right eye.

Key words: primary central nervous system lymphoma, primary pituitary lymphoma, pituitary tumours.

Introduction

Due to the progressive refinement of endocrine tests and imaging procedures, pituitary tumours are diagnosed with increasing frequency. The most common are pituitary adenomas, which account for 10-15% of all intracranial neoplasms [7]. Less frequently we can find various other pathological masses in the

suprasellar region including germ cell tumours, gliomas, meningiomas, metastatic tumours, vascular lesions, and granulomatous and infectious and inflammatory processes. Primary intracranial lymphomas are extremely rare findings in this region of the brain [5,6]. However, their incidence has grown in the United States and the United Kingdom since the early 1980s [10]. Primary CNS lymphoma (PCNSL) is now

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thought to constitute 3% of all intracranial neoplasms [6]. These tumours most commonly arise from the deep hemispheric periventricular white matter or other expected sites including the corpus callosum, cerebellum, orbits and cranial nerves [10]. Primary pituitary lymphomas (PPL) as infrequent tumours have only hypothetical risk factors such as immunodeficiency states, pituitary adenomas and lymphocytic hypophysitis [3,6,9,10]. We present a case report of a 37-year-old male patient with primary pituitary lymphoma treated in our department. This is the first case of this extremely rare disease treated in Poland presented in the available literature.

Case report

A 37-year-old man was admitted to our department in April 2001 because of headaches and worsening of visual acuity and bilateral blurred vision. The patient had had no previous illnesses. No abnormalities were found in his bilateral ocular movement, facial sensory function or motor function. Neurological examination did not reveal any other symptoms of intracranial hypertension or any other neurological deficits. The patient denied notable weight loss in the past year. There were no episodes of elevated temperature in the past. The patient

did not have known HIV infection or immunosuppression. Palpation and ultrasound examination of the abdominal cavity including liver and spleen did not show any symptoms of hepatosplenomegaly or other pathology. No palpable lymph nodes were present. Ophthalmologic examination revealed slight signs of papilloedema and bilateral defects on the temporal side of his field of vision. Blood cell count and laboratory tests revealed values within normal range. Basal hormonal studies revealed no symptoms of panhypopituitarism. The serum level of C-reactive protein was normal. MRI examination of the head revealed a large intrasellar mass (55 × 40 × 25 mm) with widening of the sella turcica, penetrating backward into the anteropontal cisterns, which were narrowed, upward enclosing the hypothalamic infundibulum and optic chiasm. Moreover the tumour was elevating the floor of the third ventricle, causing its deformation. The tumour was penetrating into both cavernous sinuses, especially on the left side, where the whole sinus was filled with the tumour. The sphenoid sinus was also partially filled with the mass. After gadolinium administration there was non-homogeneous enhancement of the tumour (Fig. 1). The first diagnosis was non-functioning pituitary macroadenoma.

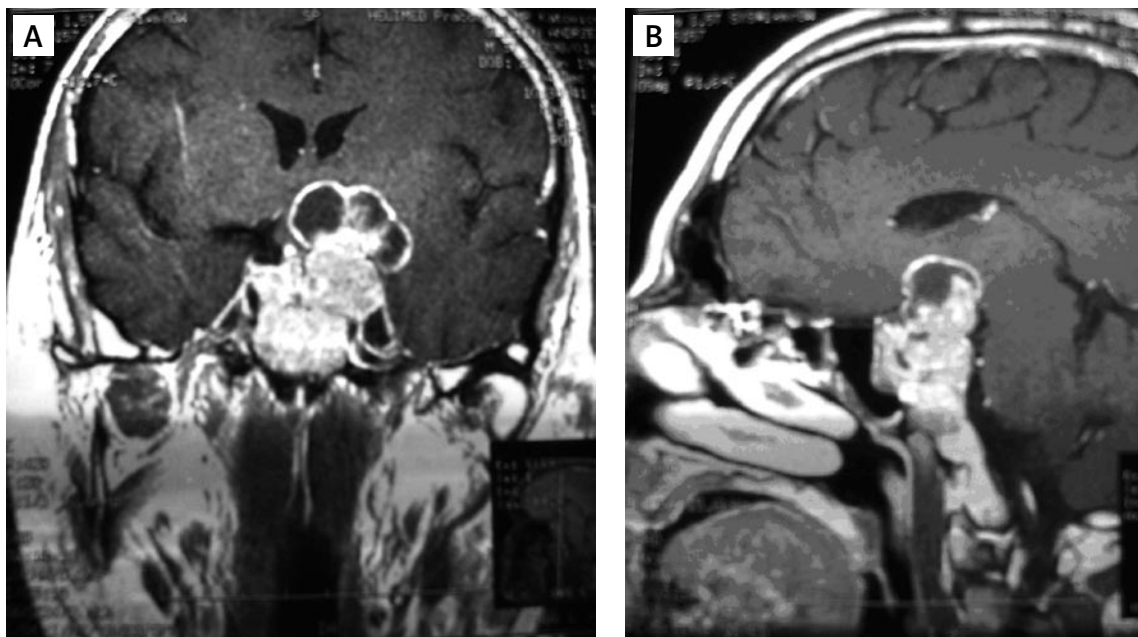


Fig. 1A-B. MRI T1-weighted scans on admission: A) frontal section, B) sagittal sections

The patient underwent endoscopic transsphenoidal pituitary tumour partial resection without any intraoperative or postsurgical complications. During surgery we found that the tumour filled a large part of the intrasellar and parasellar regions. It also penetrated into the normal pituitary tissue without any capsule. Histopathological examination of the surgical specimen demonstrated a mass containing loosely cohesive cells with numerous mitotic figures. Routine examination revealed pituitary gland tissue with prevalent diffuse, extensive infiltrate of small, uniform cells, with foci of cellular aggregates, perivascular localization of the infiltrate and trace tendency to form lymph follicles with germinal centres. The tumour showed positive immunocytochemical responses against leukocyte common antigen (LCA), B-cell marker CD 20 (L26), CD79 alpha and negative responses against CD3 and CD30. MR spectroscopy revealed decrease in NAA/tCr proportion, which indicated diminished level of N-acetylaspartate within the tumour and increase in Cho/NAA and Cho/tCr proportion. Moreover there were intense MRS signals derived from lactates and free lipids. Based on this profile, diagnosis was established as: large B-cell malignant lymphoma. CD20(+), CD79alpha(+), CD30(-). Relevant histopathological pictures after immunostaining are shown in Figures 2, 3 and 4.

After the surgery, in May and June 2001, the patient received 6 cycles of chemotherapy with the CHOP protocol which includes cyclophosphamide,

vincristine, adriamycin and prednisone. He was also irradiated with 6 MV photons to the whole brain to a total dose of 40 Gy (fraction dose 2 Gy/tumour) and then there was a boost to the tumour with 20 MV photons (with fraction dose 2 Gy/tumour) to a total dose of 50 Gy.

Ophthalmologic control examination (February 2002) did not reveal any defects of field of vision. There was regression of the parasellar mass volume

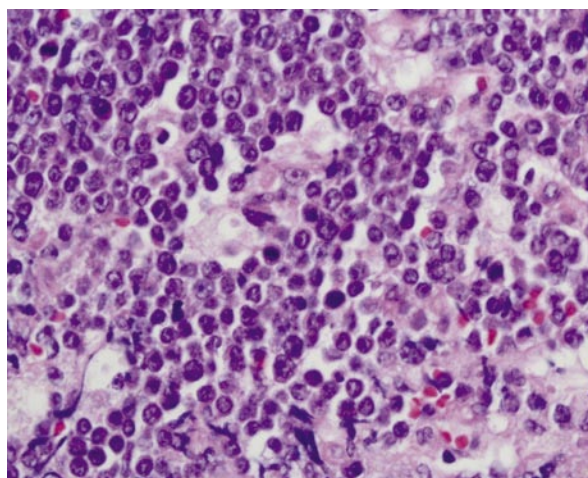


Fig. 2. Tissue of pituitary gland with monotonous, cell-rich infiltrate of lymphoma. Numerous abnormal mitotic figures in neoplastic nuclei are visible. HE staining. Magnification 400 ×

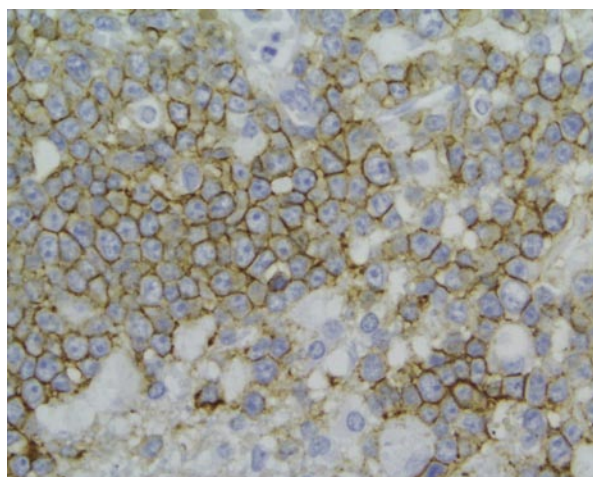


Fig. 3. Strong immunoreaction of CD20 antigen in the membranes. Immunocytochemical response against CD20. Magnification 400 ×

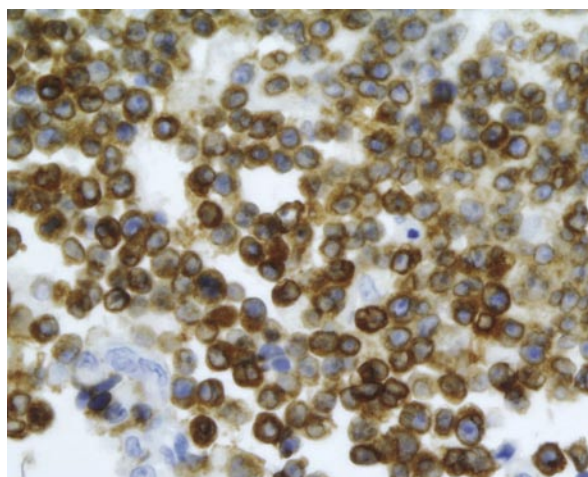


Fig. 4. Monoclonal character of the infiltrate confirmed by strong positive membranous and cytoplasmic response against CD79alpha. Immunocytochemical response against CD79alpha. Magnification 400 ×

in control MRI, but part of the tumour penetrating into the left cavernous sinus was still present. In the next two months the patient presented progressive clinical deterioration, mainly in the field of psychosocial activities. He also suffered bilateral blurred vision. The examination again revealed bilateral visual field defects and bilateral optic nerve atrophy. Next control MRI revealed progression of the tumour. Therefore in the next step of treatment we decided to reoperate on the patient. Fronto-temporo-sphenoidal craniotomy and subtotal tumour resection were performed in May 2002. During surgery we found some masses with radiation necrosis but also parts of the still viable tumour. Once again the tumour penetrated into normal pituitary tissue. The postoperative course was uneventful. After the surgery we observed a gradual improvement in clinical status of the patient. The patient's neurocognitive problems improved shortly after surgery. Histopathological analysis of the tumour specimens confirmed the diagnosis of large B-cell lymphoma. Control MRI revealed significant decrease of tumour volume. Visual disturbances significantly decreased just after the treatment. The next control MRI examinations revealed a stable remnant of the tumour (Fig. 5). Nowadays the patient has 52 months' follow-up and he has

only a stable, slight visual-field defect on the upper temporal side of the right eye. Interestingly, despite the fact that a large part of the tumour mass is located inside the sella turcica and is evidently exerting pressure and infiltrating into the pituitary gland and hypothalamic infundibulum, in the whole period of treatment hormonal disturbances as well as diabetes insipidus symptoms were absent.

Discussion

Primary pituitary lymphoma (PPL) is an exceedingly rare entity in immunocompetent patients [5,6,10]. The origin of PCNSL, especially PPL, still remains unknown. Probably the tumour may arise from resident lymphoid tissue in the CNS. Another theory implies that normal lymphocytes could enter the CNS with inflammatory processes and then undergo neoplastic transformation [2]. Most PCNSLs in immunocompetent patients are diffuse large B-cell lymphomas, characterized by poor prognosis compared with systemic forms. Neurological symptoms of PPL, except headaches, strictly reflect tumour location. Intra- and suprasellar location is associated mainly with hypopituitarism and visual disturbances such as blurred vision and visual field deficits. On the other hand



Fig. 5A-B. Actual MRI T1-weighted scans: A) axial section, B) sagittal sections

infiltration of hypothalamus is associated with water imbalance syndromes such as diabetes insipidus and syndrome of inappropriate antidiuretic hormone secretion. Less common symptoms are altered sexual behavior and eating disorders (hyperphagia) [2]. Tumours penetrating into the cavernous sinuses can press adjacent cranial nerves. Our patient presented only optic disturbances and headaches. Despite the huge mass of the tumour the hormonal tests remain normal. Also there were no symptoms of water imbalance syndromes. Moreover, the parenchymal origin of this tumour appears unlikely considering the absence of corresponding clinical syndromes. Symptoms and signs of systemic lymphoma are typically absent at the time of first presentation [8]. In MRI examination PPL are mass lesions, iso- or hypointense on T1- and T2-weighted images [4]. The lack of T2 hyperintensity can be explained by dense cellularity and high nucleus-to-cytoplasm ratio of these tumours. This MRI feature can be useful in differential diagnosis of these tumours. On the other hand PCNSLs are significantly hyperintense after contrast administration in MRI. [10] PCNSLs are aggressive malignant tumours with very poor prognosis without treatment. In a group of 32 PCNSL patients Yi et al. observed 26 months median overall survival time [11]. Because most of these tumours are diffusely infiltrative in white matter the extension of surgery should be limited to biopsy or slight cytoreduction if intracranial hypertension syndrome occurs [2]. However, Alecio-Mattei et al. recently published the data of nine patients with PCNSL with the conclusion that complete surgical resection followed by radiotherapy have shown good results. In contrast to the literature, the authors regard chemotherapy as a secondary line treatment and recommend its use only in some selected cases [1]. The most frequent type of intrasellar tumours are pituitary adenomas. Except for the cases of prolactinoma, the best method of treatment of these tumours is, if possible, complete surgical resection. The above-presented PPL can mimic large non-functioning pituitary adenoma. In our opinion combination of adjuvant therapies, after surgery, including radiotherapy and chemothera-

py, is the most rational method of management of PCNSL, especially in cases of PPL. In these specific types of tumours total resection is in most cases impossible because of its penetrating character into adjacent structures. That is why the team of specialists including neurologists, ophthalmologists, endocrinologists and neurosurgeons should take into consideration the possibility of occurrence of such rare tumours in planning the range of resection and future adjuvant treatment.

References

1. Alecio-Mattei T, Alecio-Mattei J, Aguiar PH, Ramina R. Primary central nervous system lymphomas in immunocompetent patients. *Neurocirugia (Astur)* 2006; 17: 46-53.
2. Baehring JM, Hochberg FH. Central nervous system lymphoma in AIDS and non-AIDS patients. In: Black PM, Loeffler JS (eds.). *Cancer of the nervous system*. Lippincott Williams and Wilkins 2005; pp. 589-603.
3. Baumgartner JE, Rachlin JR, Beckstead JH, Meeker TC, Levy RM, Wara WM, Rosenblum ML. Primary central nervous system lymphomas: natural history and response to radiation therapy in 55 patients with acquired immunodeficiency syndrome. *J Neurosurg* 1990; 73: 206-211.
4. Erdag N, Borade RM, Alberico RA, Yousuf N, Patel MR. Primary lymphoma of the central nervous system: typical and atypical CT and MR imaging appearances. *AJR Am J Roentgenol* 2001; 176: 1319-1326.
5. Freda PU, Post KD. Differential diagnosis of sellar masses. *Endocrinol Metab Clin North Am* 1999; 28: 81-117.
6. Giustina A, Gola M, Doga M, Rosei EA. Clinical review 136: Primary lymphoma of the pituitary: an emerging clinical entity. *J Clin Endocrinol Metab* 2001; 86: 4567-4575.
7. Gsponer J, De Tribolet N, Deruaz JP, Janzer R, Uske A, Mirimanoff RO, Raymond MJ, Rey F, Temler E, Gaillard RC, Gomez F. Diagnosis, treatment, and outcome of pituitary tumors and other abnormal intrasellar masses. Retrospective analysis of 353 patients. *Medicine (Baltimore)* 1999; 78: 236-269.
8. Herrlinger U, Schabet M, Bitzer M, Petersen D, Krauseneck P. Primary central nervous system lymphoma: from clinical presentation to diagnosis. *J Neurooncol* 1999; 43: 219-226.
9. Huang YY, Lin SF, Dunn P. Primary pituitary lymphoma presenting as hypophysitis. *Endocr J* 2005; 52: 543-549.
10. Kaufmann TJ, Lopes MB, Laws ER, Lipper MH. Primary sellar lymphoma: radiologic and pathologic findings in two patients. *AJNR Am J Neuroradiol* 2002; 23: 364-367.
11. Yi JQ, Lin TY, He YJ, Huang HQ, Xia ZJ, Xia YF, Xu RH, Guo Y, Guan ZZ. [Primary central nervous system lymphoma - a report of 32 cases with literature review]. *Ai Zhong* 2006; 25: 476-480.