Brain Tumor Pathol (2012) 29:216–220
DOI 10.1007/s10014-012-0086-0

CASE REPORT

Rare suprasellar glioblastoma: report of two cases and review of the literature

Doreen Lemm · Francine Hehn de Oliveira · René-Ludwig Bernays · Ralf Alfons Kockro · Spyros Kollias · Ingeborg Fischer · Elisabeth J. Rushing

Received: 13 September 2011 / Accepted: 31 January 2012 / Published online: 19 February 2012

Abstract
Background and importance The suprasellar and hypothalamic/chiasmatic regions can harbor a broad range of pathologic conditions, both neoplastic and nonneoplastic; however, malignant gliomas are extremely rare in those regions.
Clinical presentations Patient 1 was a 70 year-old man with weight loss and rapidly progressive visual impairment. A mass centered in the hypothalamus was detected on magnetic resonance (MR) imaging. The second patient, a 45 year-old woman, complained of visual symptoms and headaches. MR imaging revealed a combined intra- and suprasellar mass. In both instances, the preoperative differential diagnosis favored craniopharyngioma. Histological examination confirmed the diagnosis of glioblastoma.
Conclusion We report two rare adult cases of hypothalamic/chiasmatic glioblastoma. The authors review the literature, highlighting the importance of considering this rare entity in the differential diagnosis of suprasellar and hypothalamic lesions.

Keywords Chiasm · Glioblastoma · Hypothalamus · MR · Suprasellar

D. Lemm (✉) · F. H. de Oliveira · I. Fischer · E. J. Rushing
Institute of Neuropathology, University Hospital Zurich, Schmelzbergstrasse 12, 8091 Zurich, Switzerland
e-mail: doreen.lemm@gmx.ch

R.-L. Bernays · R. A. Kockro
Department of Neurosurgery, University Hospital Zurich, 8091 Zurich, Switzerland

S. Kollias
Institute of Neuroradiology, University Hospital Zurich, 8091 Zurich, Switzerland

Introduction

Glioblastoma (GBM) constitutes the most common adult brain tumor, with most cases arising in the subcortical white matter of the cerebral hemispheres. Examples of GBM in the hypothalamic/chiasmatic or suprasellar region have been seldom reported. We report two rare cases of suprasellar or hypothalamic/chiasmatic region GBM that were radiographically interpreted as being consistent with craniopharyngioma. Our report emphasizes the challenges of preoperative diagnosis and the important role of pathologic examination in establishing the diagnosis.

Case reports

Clinical presentation case 1

This 70 year-old man reported a 3-month history of appetite loss with accompanying weight loss and rapidly progressive visual loss and fatigue for 4 weeks. In addition, gait difficulties and left hemiparesis emerged 4 days prior to admission to the hospital. Endocrinologically, there was a hypopituitarism identified with low blood level of thyroid-stimulating hormone (0.03 mU/l, reference 0.30–3.18 mU/l), normal level of adrenocorticotropic hormone (ACTH) and higher level of prolactin (29.2 µg/l, reference 4.0–15.2 µg/l). Blood levels were also decreased for testosterone (<0.09 nmol/l, reference 4.59–31.1 nmol/l) and cortisol (13 mmol/l, reference 171–536 mmol/l). Past medical history was significant for hypertensive cardiomyopathy; normochromic, normocytic anemia; and pulmonary emphysema. There was no known history of inherited tumor syndromes. The patient reported a 17-pack-year smoking history 29 years prior to admission.

Medications included prednisone 5 mg, vitamin D_3, and calcium. As part of the workup, he underwent magnetic resonance (MR) imaging. A contrast-enhancing mass lesion centered on the hypothalamus measuring 2.3 × 2.8 × 2.1 cm was identified (Fig. 1a, b). Anteriorly, the lamina terminalis appeared distorted. The findings were reported to be most consistent with craniopharyngioma, with less likely considerations including germinoma, glioma, metastasis, lymphoma, or sarcoidosis.

Operation and postoperative course

As the tumor involved nearly the complete hypothalamus, the aim of surgery was biopsy or partial resection by transsphenoidal approach rather than total tumor removal. Intraoperatively, the tumor was identified above the pituitary gland, appeared greyish yellow, and was soft and amenable to partial removal by suctioning. Intraoperative histopathologic consultation revealed the diagnosis of a malignant glioma. The patient recovered well from the operation; however, 1 month after discharge, he was seen in another hospital after experiencing what was described as a collapse. Further details of the episode are not available; however, records indicate that he rejected radiation and adjuvant chemotherapy, because the family elected to pursue alternative medicine options.

Histological examination

Pathological evaluation revealed a moderately cellular neoplasm comprising cells with irregular-shaped nuclei and eosinophilic cytoplasm and fibrillary processes (Fig. 2a). Scattered mitotic figures and pathologic vessel proliferation were seen, but necrosis was not identified. Rosenthal fibers or eosinophilic granular bodies were not seen. Immunohistochemical stains performed on formalin-fixed, paraffin-embedded tissue revealed a MIB1 proliferation index of up to 30%. The neoplastic cells showed strong, diffuse immunoreactivity for glial fibrillary acidic protein (GFAP) (Fig. 2b). In addition, approximately 70% of the tumor cells showed nuclear positivity for p53, whereas, IDH1 staining (p.R132H) was negative. On the basis of the morphologic and immunohistochemical features, a diagnosis of glioblastoma was made. Analysis of the MGMT promoter revealed no methylation in the tumor cells.

Clinical presentation case 2

This 45-year-old woman presented with 3-year history of bitemporal visual field defects, which progressed over recent months. More specifically, approximately 3–4 weeks prior to admission, she noted a slowly progressive narrowing of the left temporal visual field combined with impaired vision and fluctuating visual loss lasting a few seconds, accompanied by partial diplopia. In addition, she complained of headache, diminished appetite, amenorrhea, and lack of energy. Symptoms of diabetes insipidus, pituitary insufficiency, or weight loss were not reported. The patient reported no known family history of tumors.

Examination showed anisocoria left > right and suspicion for hypogonadotropic hypogonadism with low levels of luteinizing hormone (0.3 U/l), follicle-stimulating hormone (4.0 U/l) and estradiol (40 pmol/l). There were no further neurological deficits or signs of increased intracranial pressure. MR studies showed an intra- and suprasellar, predominantly solid, partially multicystic tumor (21 × 24 × 36 mm) (Fig. 1c, d), with ventral displacement and compression of the optic chiasm and lateral displacement of both optic nerves. The tumor extended from the upper diaphragma sellae to the tuberculum sellae, with a small component lateral to the left planum sphenoidale. The cystic components of the tumor appeared to extend into the third ventricle. The dorsal tumor border

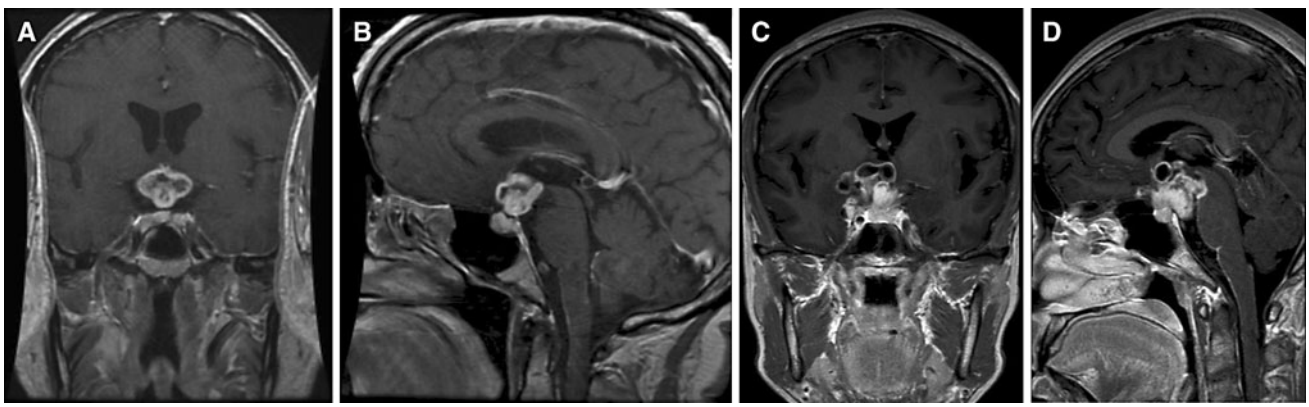

Fig. 1 T1-weighted magnetic resonance images after gadolinium injection. **a**, **b** Irregular, contrast-enhancing mass centered on the hypothalamus that extends into the sella (patient 1). **c**, **d** Suprasellar, partially cystic mass with leptomeningeal enhancement (patient 2)

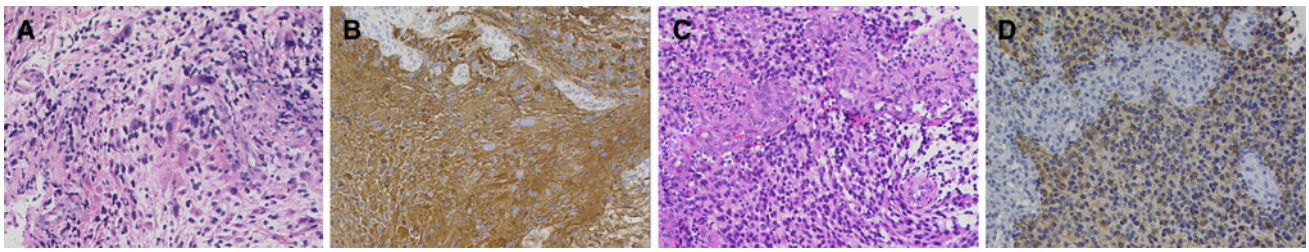

Fig. 2 Histologic features: **a**, **c** hematoxylin and eosin; **b**, **d** and glial fibrillary acidic protein (GFAP). **a**, **b** Patient 1; **c**, **d** patient 2. **a**, **c** Astrocytic tumors with microvascular proliferation typical of glioblastoma. **b**, **d** Tumor cells show positive immunoreactivity for GFAP. **a**–**d** Original magnification ×20

extended into the interpeduncular and prepontine cisterns with spread in the crus cerebri and ventrally in the pons. The imaging features were interpreted as compatible with craniopharyngioma, or less likely, germinoma or glioma.

Operation and postoperative course

The patient initially underwent a transsphenoidal partial tumor resection. Intraoperatively, the tumor appeared to be clearly separated from the tissue of the pituitary gland and partly surrounded by a greyish capsule. The tumor itself was of a light greyish yellow color with a soft consistency. However, some portions, especially toward the right lateral tumor margin, appeared firm and adherent to neighboring structures. As the intraoperative diagnosis was that of a malignant glioma, the firm tumor parts were not totally removed. Good adequate hemostasis could be achieved toward the end of the operation. Postoperatively, the patient awakened more slowly than expected and with anisocoria and right-sided hemiparesis. Emergency computed tomography (CT) scan showed blood in the tumor resection bed, so the patient underwent a pterional craniotomy for evacuation of the hematoma. Because of complications of postoperative hemorrhage after the second surgery, the patient died on the second postoperative day. No postmortem examination was performed.

Histological examination

Similar to the first case, histological examination of the biopsy revealed an infiltrating glial neoplasm composed of densely packed tumor cells with an astrocytic phenotype. The GFAP-positive neoplastic cells were moderately pleomorphic and mitotically active. Prominent microvascular proliferation and necrosis were present (Fig. 2c, d). The MIB1 proliferation index was markedly increased, with up to 15% positive nuclei. The tumor cells showed 10% immunoreactivity for p53 and negativity for IDH1 (p.R132H). Analysis of the MGMT promoter revealed no methylation in the tumor tissue.

Discussion

This report describes two well-documented examples of primary GBM arising in the suprasellar or hypothalamic/chiasmatic region. Although malignant gliomas may involve this region secondarily, tumors arising in this region are exceedingly uncommon. On the basis of the complex anatomy of the region with many different tissue types, the differential diagnosis of nonglial suprasellar lesions is extensive and encompasses both neoplastic and nonneoplastic lesions. Primary neoplasms include craniopharyngiomas, pituitary adenomas, germ-cell tumors, meningiomas, and pituicytomas, among others [7]. In addition, Langerhans cell histiocytosis [9] and hypothalamic hamartomas are recognized in this region [14, 18]. Major secondary tumors comprise metastatic carcinoma [7], melanoma [21], leukemias [10], and lymphomas [7]. Langerhans cell histiocytosis can also spread to the suprasellar region from a primary systemic site [8]. A comprehensive search of the PubMed/MEDLINE database yielded only five publications of glioblastoma centered on this region [2, 4, 6, 11, 22].

In 1973, Hoyt [11] published the first discussion of malignant gliomas of the optic nerve and established the concept of a rapidly progressive syndrome of visual loss in middle-aged men, which was often mistaken for ischemic optic neuropathy. Given the different and variably applied grading for malignant gliomas at that time, the precise pathologic diagnosis of the cases reported remains uncertain. Subsequently, Barbaro et al. [2] presented the case of a 26-year-old man with headaches and rapidly progressive visual loss that on CT scans was felt to be consistent with craniopharyngioma or cystic pituitary adenoma. Pathologic examination of the biopsy revealed a glioblastoma. Another example was reported in the optic tract of a 76-year-old man who complained of progressive deterioration of vision in his left eye over a 6-month period [22]. CT showed a suprasellar contrast-enhancing mass invading the left temporal lobe. On T1-weighted MR imaging of the head, there was inhomogeneous gadolinium enhancement with cystic areas of the expanded left optic nerve, chiasm,

and left optic tract. Expansion of the optic nerve diminished rapidly anterior to the chiasm and the intraorbital portion was of normal thickness, without enhancement [22]. In reference to this case, Pallini [19] wrote a letter to the editor that detailed a personal case of a 59-year-old woman with an optic chiasm glioblastoma. On imaging, the tumor appeared to diffusely infiltrate the hypothalamus and basal ganglia but spared the intraorbital portion of the optic nerves, similar to the cases presented in this report.

Wu-Chen et al. [23] reported that a 63-year-old man developed a malignant astrocytoma of the left optic nerve and chiasm 23 years after partial excision and radiation of a nonsecreting pituitary adenoma. In another case report, the authors described a 5-year-old boy who presented with profound bilateral visual loss and was diagnosed with an optic nerve tumor that transformed from a low-grade astrocytoma, with features most consistent with a pilocytic astrocytoma (PA), to a malignant glioma without any exposure to radiation therapy [24]. Similarly, Cirak [4] reported a 6-year-old girl who presented with visual deterioration that had progressively worsened over 2 months. MR imaging revealed a sellar, para- and suprasellar lesion, and intraoperatively, the tumor appeared to arise from the optic chiasm. In the cases presented here, optic pathway origin is unlikely because of the displacement and lack of evidence of direct involvement of those structures.

Gliomas in this location are typically low grade, such as PA of the optic nerve, which are seen mostly in the pediatric population and may be associated with neurofibromatosis (NF)1 [1]. Of interest, NF1-associated PA of the optic pathway tends to have a more benign course, and radiation therapy is generally avoided. Radiographically, PAs show variable features but are usually well-demarcated lesions. On MR, they can appear hypodense or isodense, and a few are hyperdense, with the majority showing moderate to marked enhancement [15]. On occasion, PA in this region may extend into the sellar region, and when large, they may even erode the sphenoid bone. They are rarely calcified, are usually isointense on T1, and usually lack a cystic component [5].

Pilomyxoid astrocytoma (PMA) is an uncommon, more aggressive, variant of pilocytic astrocytomas that exhibits a predilection for the diencephalic region in infants and young children (mean age 1.5 years), although it was recently reported that up to one third of patients are older children and adults [16]. Similar to PA, PMA remains a histologic diagnosis without definitive imaging findings [12]. Gross total resection is the treatment of choice, but surgery is often limited due to high morbidity and mortality rates. Patient age, rapidly progressive time course, and high-grade histopathologic features in the cases reported herein argued against consideration of either of PA or its pilomyxoid variant.

Another rare tumor that shows a predilection for the third ventricle and suprasellar region is the chordoid glioma, with approximately 50 cases reported in the literature. This entity displays distinct histological features and is hypothesized to originate along the third ventricle floor and/or the lamina terminalis [20]. The typical mucinous background and cord-like arrangement of the neoplastic cells was not observed in either of our cases. Furthermore, malignant progression has not been seen in chordoid glioma. Despite their low-grade histology, location of these tumors often precludes complete resection and recurrence, and poor outcome is inevitable [20].

Spindle-cell oncocytoma is another extremely rare and often misdiagnosed tumor of uncertain histogenesis that occurs in the sellar region [3, 17]. Radiographically, it can mimic the appearance of craniopharyngioma, and recurrences are recognized [13]. Although the histopathologic features may resemble an astrocytic tumor, the distinctive immunohistochemical profile and ultrastructure militated against this consideration in our patients.

The rarity of malignant gliomas in this location and their heterogeneous presentation on imaging renders this a difficult diagnosis prior to obtaining tissue for histological analysis. On T1-weighted images, most lesions considered in the differential diagnosis appear iso- or hypointense. The presence of protein, cholesterol, or methemoglobin may cause a high signal, which would be more likely encountered in craniopharyngioma. However, enhancement after gadolinium is seen in both craniopharyngioma and high-grade gliomas. Postoperative imaging is also crucial to monitor potential complications and recurrence.

Due to the presence of central necrosis, a rare abscess is also included in the differential diagnosis. Correlation with clinical status (infectious signs with fever in abscess) and diffusion-weighted images (diffusion restriction in abscess) help in the differential diagnosis between these two rare entities.

References

1. Alshail E, Rutka JT, Becker LE, Hoffman HJ (1997) Optic chiasmatic–hypothalamic glioma. Brain Pathol 7:799–806
2. Barbaro NM, Rosenblum ML, Maitland CG, Hoyt WF, Davis RL (1982) Malignant optic glioma presenting radiologically as a "cystic" suprasellar mass: case report and review of the literature. Neurosurgery 11:787–789
3. Borges MT, Lillehei KO, Kleinschmidt-DeMasters BK (2011) Spindle cell oncocytoma with late recurrence and unique neuroimaging characteristics due to recurrent subclinical intratumoral bleeding. J Neurooncol 101:145–154
4. Cirak B, Unal O, Arslan H, Cinal A (2000) Chiasmatic glioblastoma of childhood. A case report. Acta Radiol 41:375–376
5. Curran JG, O'Connor E (2005) Imaging of craniopharyngioma. Childs Nerv Syst 21:635–639

6. Dinh TT, Wang YY, Rosenfeld JV, Cherny M (2007) Glioblastoma of the optic chiasm. J Clin Neurosci 14:502–505
7. Glezer A, Paraiba DB, Bronstein MD (2008) Rare sellar lesions. Endocrinol Metab Clin North Am 37:195–211
8. Grois N, Tsunematsu Y, Barkovich AJ, Favara BE (1994) Central nervous system disease in Langerhans cell histiocytosis. Br J Cancer Suppl 23:S24–S28
9. Hervey-Jumper SL, Ghori A, Ziewacz JE, McKeever PE, Chandler WF (2011) Langerhans cell histiocytosis of the optic chiasm: case report. Neurosurgery 68:E556–E561
10. Hon C, Law RW, Shek TW, Au WY (2005) CNS manifestations of malignancies: case 1. Conjunctival relapse of acute lymphoblastic leukemia heralding pituitary and CNS disease. J Clin Oncol 23:4225–4226
11. Hoyt WF, Meshel LG, Lessell S, Schatz NJ, Suckling RD (1973) Malignant optic glioma of adulthood. Brain 96:121–132
12. Johnson MW, Eberhart CG, Perry A, Tihan T, Cohen KJ, Rosenblum MK et al (2010) Spectrum of pilomyxoid astrocytomas: intermediate pilomyxoid tumors. Am J Surg Pathol 34: 1783–1791
13. Kloub O, Perry A, Tu PH, Lipper M, Lopes MB (2005) Spindle cell oncocytoma of the adenohypophysis: report of two recurrent cases. Am J Surg Pathol 29:247–253
14. Kollias SS, Barkovich AJ, Edwards MS (1991–1992) Magnetic resonance analysis of suprasellar tumors of childhood. Pediatr Neurosurg 17:284–303
15. Kornreich L, Blaser S, Schwarz M, Shuper A, Vishne TH, Cohen IJ et al (2001) Optic pathway glioma: correlation of imaging findings with the presence of neurofibromatosis. AJNR 22: 1963–1969
16. Linscott LL, Osborn AG, Blaser S, Castillo M, Hewlett RH, Wieselthaler N et al (2008) Pilomyxoid astrocytoma: expanding the imaging spectrum. AJNR 29:1861–1866
17. Matyja E, Maksymowicz M, Grajkowska W, Olszewski W, Zieliński G, Bonicki W (2010) Spindle cell oncocytoma of the adenohypophysis—a clinicopathological and ultrastructural study of two cases. Folia Neuropathol 48:175–184
18. Maixner W (2006) Hypothalamic hamartomas—clinical, neuropathological and surgical aspects. Childs Nerv Syst 22:867–873
19. Pallini R, Lauretti L, La Marca F (1996) Glioblastoma of the optic chiasm. J Neurosurg 84:898–899
20. Pomper MG, Passe TJ, Burger PC, Scheithauer BW, Brat DJ (2001) Chordoid glioma: a neoplasm unique to the hypothalamus and anterior third ventricle. AJNR 22:464–469
21. Wang YY, Norris A, du Plessis D, Gnanalingham KK (2011) Melanoma of the sellar region. J Clin Neurosci 8:154–156
22. Woiciechowsky C, Vogel S, Meyer R, Lehmann R (1995) Magnetic resonance imaging of a glioblastoma of the optic chiasm. Case report. J Neurosurg 83:923–925
23. Wu-Chen WY, Jacobs DA, Volpe NJ, Dalmau JO, Moster ML (2009) Intracranial malignancies occurring more than 20 years after radiation therapy for pituitary adenoma. J Neuroophthalmol 29:289–295
24. Zoeller GK, Brathwaite CD, Sandberg DI (2010) Malignant transformation of an optic pathway glioma without prior radiation therapy. J Neurosurg Pediatr 5:507–510