CASE REPORT

Germinoma of the Corpus Callosum

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ABSTRACT

A case is described of a young man presenting with diabetes insipidus and a junctional scotoma. A diffuse infiltrating mass centred in the corpus callosum and suprasellar area is found, which on pathological examination proved to be a primary intracranial germinoma. The case illustrates that rarely the corpus callosum can be involved by this tumour and that diagnosis may be delayed in atypical presentations.

KEYWORDS: colossal mass; corpus callosum; germinoma

INTRODUCTION

Primary central nervous system (CNS) germinomas are rare tumours that typically arise within the pineal or suprasellar regions. Involvement of the corpus callosum is exceedingly rare. We describe a case of a primary intracranial germinoma manifesting as a diffuse infiltrating mass centred in the corpus callosum and suprasellar area in a young man presenting with diabetes insipidus and a junctional scotoma whose diagnosis was delayed until the pathological specimen of the tumour was obtained.

CASE REPORT

A 20-year-old previously healthy university student started noticing memory and concentration problems that eventually led him to drop out of school. His parents noted that he appeared to be depressed and lethargic, a definite change from his normal personality state. He also complained of polydipsia and polyuria. He was seen by his family physician and eventually

was diagnosed with diabetes insipidus. Computed tomography (CT) of the brain performed 2 months after the initial presentation revealed a very unusual increased attenuation in the periventricular region within the corpus callosum (Figure 1). The patient was started on desmopressin nasal spray. Differential diagnosis was between a diffuse neoplastic process (such as gliomatosis cerebri) versus a mass lesion such as lymphoma. Magnetic resonance imaging (MRI) of the brain was performed 2 weeks later, which demonstrated abnormal signal intensity, with minimal mass effect centred within the genu of the corpus callosum extending into the rostrum, with signal abnormality also seen within the splenium. There was patchy enhancement in the genu and the body of the corpus callosum and in both optic nerves and of the pituitary stalk (Figure 2). Radiologic differential diagnosis at this point included primary CNS lymphoma versus neurosarcoidosis. CT of the chest and angiotensin-converting enzyme (ACE) level were both normal.

Three months after the onset of symptoms, the patient started noticing blurred vision in both eyes. He consulted an optometrist who prescribed new glasses but they provided minimal improvement in vision.

Four months after the onset of symptoms, the patient consulted a neurosurgeon who recommended another MRI scan. An endocrine work up revealed low total and bioavailable testosterone as

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FIGURE 1 (a) Unenhanced axial head CT through the level of the corpus callosum demonstrating altered tissue attenuation and increased thickness of the genu of the corpus callosum bilaterally (vertical arrows) and thickening of the septum pellucidum (horizontal arrows). (b) Prominent infundibulum (upward arrow) and mildly thickened optic chiasm (downward arrow).

FIGURE 2 (a) Sagittal T1 image shows a mass at the inferior posterior aspect of the genu (horizontal arrow) of the corpus callosum, extending into the rostrum. Two other smaller less well defined lesions are noted along the inferior body of the corpus callosum (vertical arrows). (b) Axial T2 image demonstrates an increased thickness of the genu of the corpus callosum (arrows). (c) Axial post-gadolinium image through genu of corpus callosum shows no significant enhancement of the callosal mass (arrow) which is atypical for lymphoma. (d) Axial post-gadolinium image displays an enlarged infundibulum (long thin arrow) and increased calibre of the intracranial component of the right optic nerve.

well as low follicle-stimulating hormone (FSH) and luteinizing hormone (LH). Insulin-like growth factor (IGF)-1 levels were significantly decreased. Given the symptoms of diabetes insipidus along with very low urinary osmolality, and low FSH, LH, and IGF-1,

panhypopituitarism was diagnosed. A triple bolus test was performed, which confirmed hypogonadism, growth hormone deficiency, and inadequate cortisol reserve. Treatment included desmopressin nasal spray, testosterone gel, and hydrocortisone.

FIGURE 3 Automated perimetry carried out at presentation, 5 months following the onset of symptoms.

At the initial neuro-ophthalmic consultation 5 months after the onset of symptoms, the patient complained of worsening visual acuity in both eyes. Best-corrected visual acuity at the time was 20/40 in the right eye and 20/60 in the left eye. There was a left relative afferent pupillary defect. On colour vision testing, the patient correctly identified only 3 of 17 Ishihara plates with the right eye and the control plate only with the left eye. Humphrey visual fields (24-2 algorithm) demonstrated a temporal hemianopic defect in the right eye and a central scotoma in the left eye, representing a junctional scotoma (Figure 3). Ophthalmoscopy revealed optic disc pallor in both eyes, greater in the left eye.

Normal laboratory tests included complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein, ACE, antinuclear antibodies (ANA), Venereal Disease Research Laboratory (VDRL) test, and antineutrophil cytoplasmic antibodies (ANCA). CT of chest, abdomen, and pelvis was read as normal. MRI of the brain 3 months after the initial study demonstrated new enhancement in the genu of the corpus callosum and an increase in a mass-like area of increased T2 signal involving the genu of the corpus callosum, with the entire corpus callosum demonstrating increased signal on T2. There was also thickening of the optic chiasm extending along both optic nerves, with thickening of

the upper half of the pituitary stalk. The pituitary gland showed normal signal characteristics (Figure 4).

These imaging findings elicited a differential diagnosis of lymphoma, neurosarcoidosis, and gliomatosis cerebri. Lumbar puncture demonstrated normal cerebrospinal fluid constituents and normal CD4/CD8 ratio, normal flow cytometry, ACE, and negative VDRL. CT of the chest, abdomen, and pelvis was again normal. Bronchoscopy with washings did not demonstrate granulomatous disease. The need for biopsy was discussed with the patient and his family but they decided to adopt a "watchful waiting" approach despite the repeated discussions about the need for obtaining a tissue sample.

Seven months after the onset of symptoms, the patient underwent an open biopsy of the corpus callosum. Histopathological analysis of frozen sections revealed the presence of sheets of lymphocytes and was initially interpreted as high-grade lymphoma (Figure 5). However, immunohistochemistry of the permanent sections identified the phenotype of the lymphocytes as reactive T cells, and not monoclonal B cells as would be expected in lymphoma. Further analysis of deeper sections revealed large polygonal cells, which were identified immunohistochemically

FIGURE 4 (a) Sagittal FLAIR image shows significantly increased thickness, irregularity, and abnormal signal of the mass within the genu of the corpus callosum (larger arrows). Note thickened infundibulum (horizontal thin arrow) and thickened tilted optic chiasm (vertical thin arrow). (b) Axial post-gadolinium view demonstrates increased enhancement and greater extent of the callosal mass compared to the earlier MR, with greater involvement of the periventricular tissues about the frontal horns bilaterally (arrows). (c) Coronal post-gadolinium image shows an enlarged enhancing infundibulum (arrow). The infiltrating callosal mass is poorly defined. (d) Axial post-gadolinium image through the suprasellar cistern shows an enlarged enhancing infundibulum (horizontal arrow) and a diffusely enlarged optic chiasm (vertical arrow). (e) Axial FLAIR image through the suprasellar cistern demonstrating the superior aspect of the enlarged infundibulum (long arrow) and enlargement of the intracranial prechiasmatic segment of the optic nerves bilaterally (diagonal arrows). (f) Coronal postgadolinium image of the most anterior aspect of the frontal horns of the lateral ventricles surrounded by an ill defined callosal mass with minimal enhancement (thin arrows). The posterior aspect of the orbital component of the right optic nerve is enlarged (shorter arrow) by tumour extension.

as germ cells, indicating the pathological diagnosis of primary intracranial germinoma.

One month after the biopsy, visual acuity had deteriorated to counting fingers in the left eye and 20/50 in the right eye. Visual fields had also worsened (Figure 6).

The patient received a 1-month course of fractionated whole-brain radiotherapy 6 weeks after the biopsy was performed. On last follow-up examination 10 months after the radiotherapy and 1 year after the onset of symptoms, the visual acuity was unchanged, there

FIGURE 5 H&E staining of the tumour (top panel) demonstrates large, epithelioid cells with both large and round nuclei and irregular and pleomorphic nuclei. Some prominent nests of lymphocytes are seen as well. Immunohistochemistry demonstrates large, epithelioid cells that are both D2-40 (left lower panel) and Oct4 (right lower panel) positive, consistent with a diagnosis of germinoma.

FIGURE 6 Automated perimetry carried out 8 months following the onset of symptoms and one month following the biopsy.

was still a large left relative afferent pupillary defect, mean deviation on Humphrey visual field (HVF) was unchanged in both eyes, and both optic nerve were pale. Last follow up MRI obtained 6 months after the radiotherapy demonstrated remarkably a complete resolution of all previous findings (Figure 7).

DISCUSSION

We present a very unusual case of primary intracranial germinoma centred in the corpus callosum associated with diffuse infiltration of the pituitary stalk

and optic chiasm, a presentation very rarely described in the literature. The unusual location of the tumour misled the radiologists and the difficulties with the pathological interpretation led to a significant diagnostic delay.

Most intracranial germinomas are located in the pineal and suprasellar regions. They may also originate in the basal ganglia, cerebellopontine angle, lateral ventricle, cerebellum, frontal/temporal/occipital lobes, medulla, and, very rarely, in the corpus callosum.¹⁻⁶ Because of the unusual location of the lesion, multiple neuroradiologists failed to include germinoma in the differential diagnosis.

FIGURE 7 Sagittal T1 (a) and axial T1 post-gadolinium with fat saturation (b) images show complete resolution (thin arrows) of the previous callosal and pericallosal mass with severe diffuse post-radiation thinning of the corpus callosum (thin arrows). Incidental small subdural fluid collection (thicker arrows) underlies craniotomy site.

There are only three reports of intracranial germinomas originating in corpus callosum described in the literature,^{6–8} only two of which have provided detailed descriptions.^{6,8} In one paper, Utsuki *et al.* describe two cases of intracranial germinoma involving the corpus callosum. In both cases the tumours were large with cystic components seen on the MRI, a common finding in suprasellar germinomas but that was not seen in our case.⁶ In the other report, Hieda *et al.* described a case of germinoma initially misdiagnosed as neurosarcoidosis. The MRI in that case revealed high signal intensities on T2 within the suprasellar region and in corpus callosum, and the diagnosis of germinoma was only made after histochemical analysis of the specimen.⁸

In our case, further confusion arose with the histopathological interpretation of the biopsy specimens. It is well known that the histopathological diagnosis of germinoma in adults can be difficult⁹ because germinomas usually consist of two cell populations—large, round, polygonal neoplastic germ cells and reactive infiltrative lymphocytes. The ratio of neoplastic cells to lymphocytes is variable from case to case. Because germinomas are usually surrounded by lymphocytes, on frozen sections the specimens frequently resemble large cell lymphoma or lymphocytic hypophysitis.^{9–11} The reactive lymphocytes are usually positive for T-cell markers such as CD3. In our case, the initial impression of lymphoma was based on a monomorphic population of lymphocytes and was corrected by the finding of the large neoplastic cells on permanent sections as well as the typical findings on immunohistochemistry characteristic of germinomas. Immunohistochemistry of the neoplastic cells is typically positive for placental alkaline phosphatase as well as c-kit.

Germinomas arising in the central nervous system account for not more than 1% of all intracranial

tumours. For unknown reasons, they have a significantly higher incidence in Japan.¹ They typically occur within the first two decades of life and are more common in males.¹ These tumours are believed to originate as a midline streaming of totipotent cells early in the development of the rostral part of the neural tube.^{2,3}

Clinical features depend on tumour location. For those located in the suprasellar region, the typical presentation is with diabetes insipidus, hypopituitarism, and bitemporal hemianopia.¹² For tumours located in the pineal region, hydrocephalus and dorsal midbrain syndrome are frequent findings. In our case, although most of the tumour was located in the corpus callosum, the clinical presentation was dictated by infiltration of the pituitary stalk and the compression of the optic nerves and the chiasm.

The differential diagnosis of callosal masses includes glioblastoma multiforme, lymphoma, oligodendroglioma, “tumefactive” multiple sclerosis, gliomatosis cerebri, and lipoma. When there is a substantial suprasellar component to the mass, the differential diagnosis extends to pituitary adenoma, meningioma, saccular aneurysm, craniopharyngioma, pilocytic astrocytoma, sarcoidosis, Langerhans cell histiocytosis, lymphocytic hypophysitis, metastatic cancer, and leukaemia.

Our case serves as a reminder that central nervous system germinoma can present as a callosal mass and this entity should be kept on the differential diagnosis especially if a suprasellar mass is also present. CNS germinomas in most cases are entirely treatable by radiation therapy and diagnosing them early can prevent permanent damage to the visual system as occurred in our case.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

Note: Figure 5 of this article is available in colour online at www.informahealthcare.com/oph

REFERENCES

- [1] Matsutani M, Sano K, Takakura K, Fujimaki T, Nakamura O, Funata N, Seto T. Primary intracranial germ cell tumors: a clinical analysis of 153 histologically verified cases. *J Neurosurg* 1997;86:446–455.
- [2] Uchino A, Takase Y, Nomiyama K, Egashira R, Kudo S. Acquired lesions of the corpus callosum: MR imaging. *Eur Radiol* 2006;16:905–914.
- [3] Moon WK, Chang KH, Kim I, Han MH, Choi CG, Suh DC, Yoo S-J, Man CH. Germinomas of the basal ganglia and thalamus: MR finding and a comparison between MR and CT. *Am J Radiol* 1994;162:1413–1417.
- [4] Kyritsis AP. Management of primary intracranial germ cell tumors. *J Neurooncol* 2010;96:143–149.
- [5] Villani A, Bouffet E, Blaser S, Millar BA, Hawkins C, Bartels U. Inherent diagnostic and treatment challenges in germinoma of the basal ganglia: a case report and review of the literature. *J Neurooncol* 2008;88:309–314.
- [6] Utsuki S, Oka H, Tanizaki Y, Kondo K, Fujii K. Radiological features of germinoma arising from atypical locations. *Neurol Med Chir (Tokyo)* 2005;45:268–267.
- [7] Liang L, Korogi Y, Sugahara T, Ikushima I, Shigematsu Y, Okuda T, Takahashi M, Kochi M, Ushio Y. MRI of intracranial germ-cell tumours. *Neuroradiol* 2002;44:382–388.
- [8] Hieda S, Fukui T. [Germinoma presenting with personality and socio-behavioral abnormalities may challenge differential diagnoses]. *Brain Nerve* 2008;60:949–953. Japanese.
- [9] Taxy JB. *Biopsy Interpretation: The Frozen Section*. 1st ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2009.
- [10] Fehn M, Bettendorf M, Lüdecke DK, Sommer C, Saeger W. Lymphocytic hypophysitis masking a suprasellar germinoma in a 12-year-old girl: a case report. *Pituitary* 1999;1:303–307.
- [11] Nishiuchi T, Imachi H, Murao K, Fujiwara M, Sato M, Nishiuchi Y, Kushida Y, Haba R, Shindo A, Tamiya T, Ishida T. Suprasellar germinoma masquerading as lymphocytic hypophysitis associated with central diabetes insipidus, delayed sexual development, and subsequent hypopituitarism. *Am J Med Sci* 2010;339:195–199.
- [12] Endo H, Kumabe T, Jokura H, Tominaga T. Stereotactic radiosurgery followed by whole ventricular irradiation for primary intracranial germinoma of the pineal region. *Minim Invasive Neurosurg* 2005;48:186–190.