

Atypical presentation of a central nervous system germinoma in a pediatric patient. Case presentation

Presentación atípica de un germinoma del sistema nervioso central en un paciente pediátrico. Presentación de caso

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Summary

Introduction: Germinomas, although infrequent, are the most common germ cell tumors in the pediatric central nervous system (CNS). Unlike other germ cell tumors, they do not alter hormone levels in blood or cerebrospinal fluid. They are typically located in the pineal gland and the selar-suprasellar region, and are seen as expanding masses. They rarely affect vision, unless accompanied by intracranial hypertension. ***Objective:*** This study aims to describe an atypical presentation of a CNS germinoma manifesting as decreased visual acuity, associated only with thickening of the floor and anterior wall of the third ventricle, with invasion of the optic chiasm and optic nerves, a presentation not previously described in the literature. ***Case description:*** An 11-year-old female patient with short stature presented with decreased visual acuity and dyschromatopsia. Magnetic resonance imaging (MRI) revealed thickening and contrast enhancement of the optic chiasm and optic nerves, as well as the floor and anterior wall (lamina terminalis) of the third ventricle. The neurohypophysis was not visualized. An endoscopic biopsy of the floor of the third ventricle confirmed germinoma. The patient started oncologic treatment with carboplatin and etoposide according to the COG protocol. ***Conclusion:*** This case highlights the importance of considering germinoma in pediatric patients with atypical visual and neurologic symptoms. A comprehensive evaluation, including endoscopic biopsy in atypical cases, is crucial for accurate diagnosis and appropriate treatment. It is recommended to maintain a broad differential diagnosis, especially in cases with overlapping symptoms with other pathologies. This study contributes to the understanding of the clinical variability of CNS germinomas in pediatrics, emphasizing the need for further surveillance and study of these rare cases.

Resumen

Introducción: Los germinomas, aunque infrecuentes, son los tumores de células germinales más comunes en el sistema nervioso central (SNC) pediátrico. A diferencia de otros tumores de células germinales, no alteran los niveles hormonales en sangre o líquido cefalorraquídeo. Típicamente, se localizan en la glándula pineal y la región selar-supraselar, y se observan como masas expansivas. Raramente afectan la visión, a menos que estén acompañados de hipertensión intracraneal. ***Objetivo:*** Este estudio tiene como objetivo describir una presentación atípica de un germinoma del SNC que se manifiesta como una disminución de la agudeza visual, asociada únicamente con el engrosamiento del piso y la pared anterior del tercer ventrículo, con invasión del quiasma óptico y los nervios ópticos, una presentación no descrita previamente en la literatura. ***Descripción del caso:*** Paciente femenina de 11 años de edad, con baja estatura, presentó disminución de la agudeza visual y discromatopsia. La resonancia magnética (RM) reveló engrosamiento y realce con medio de contraste del quiasma óptico y los nervios ópticos, así como del piso y la pared anterior (lámina *terminalis*) del tercer ventrículo. No se visualizó la neurohipófisis. Una biopsia endoscópica del piso del tercer ventrículo confirmó germinoma. La paciente inició tratamiento oncológico con carboplatino y etopósido según el protocolo COG. ***Conclusión:*** Este caso resalta la importancia de considerar el germinoma en pacientes pediátricos con síntomas visuales y neurológicos atípicos. Una evaluación integral, incluyendo biopsia endoscópica en casos atípicos, es crucial para un diagnóstico preciso y un tratamiento adecuado. Se recomienda mantener un diagnóstico diferencial amplio, especialmente en casos con síntomas superpuestos con otras patologías. Este estudio contribuye a la comprensión de la variabilidad clínica de los germinomas del SNC en pediatría, enfatizando la necesidad de mayor vigilancia y estudio de estos casos raros.

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Introduction

Germinomas of the central nervous system (CNS) are more common in children and adolescents, with a male-to-female ratio of approximately 2:1. The most common locations in the CNS are the pineal and suprasellar regions, where they present with characteristic symptoms related to compression of adjacent structures. Bifocal presentation of germinoma in the CNS has also been described, which refers to the simultaneous appearance of these lesions in the CNS. The most common concomitant locations are in the sellar and pineal regions. This form of presentation increases the diagnostic suspicion of germinoma (1). The symptoms of CNS germinomas vary depending on their location. In the pineal region, patients often manifest symptoms of obstructive hydrocephalus, headache, nausea, and vomiting due to obstruction of cerebrospinal fluid flow. In the suprasellar region, symptoms may include visual disturbances, diabetes insipidus, and growth retardation resulting from compression of the optic chiasm and hypothalamus. The identification and management of CNS germinomas is critical due to their potential for cure with appropriate treatment. However, atypical presentations of these tumors can complicate early diagnosis, delaying treatment and affecting patient prognosis. Therefore, it is essential to understand the clinical and radiological characteristics of CNS germinomas, particularly those that deviate from classic patterns.

Objective

This study aims to describe an atypical presentation of a suprasellar germinoma that manifests as decreased visual acuity, associated solely with thickening of the floor of the third ventricle, with invasion of the optic chiasm and optic nerves, a presentation not previously described in the literature. This detailed case presentation highlights the clinical, radiological, and pathological features that can help clinicians recognize these unusual presentations and improve diagnostic and therapeutic approaches in patients.

Historical Context

Germinal cell tumors of the CNS have been studied since the early 20th century. Initially, it was believed that these tumors originated exclusively in the gonads, but subsequent research showed that they could also develop in the CNS due to abnormal migration of germ cells during embryonic development. Germinomas, in particular, were identified as the most common variant of intracranial germ cell tumors. During the 1970s, improvements in imaging techniques, such as computed tomography (CT) and, later, magnetic resonance imaging (MRI), allowed for better visualization of the typical locations of CNS germinomas, mainly in the pineal and suprasellar regions. This facilitated the diagnosis and characterization of these tumors in children and adolescents. Throughout the 1980s and 1990s, significant advances were made in the identification of tumor markers such as alpha-fetoprotein (AFP) and human chorionic gonadotropin (hCG), which helped differentiate germinomas from other germ cell tumors, although germinomas typically do not elevate these markers. During this period, it was observed that the response to radiotherapy and chemotherapy was remarkably effective, significantly improving the prognosis for pediatric patients. At the end of the 20th century and the beginning of the 21st century, cases of germinomas not located in the pineal and suprasellar regions, known as atypical locations, began to be documented. These rare presentations included tumors in areas such as the cerebral hemispheres, spinal cord, and brainstem. Initially, these cases were difficult to diagnose due to a lack of recognition that germinomas could occur outside their classic sites. The first reports of atypical cases began to appear in the medical literature in the 1990s and 2000s. These case studies provided valuable information about the clinical and radiological characteristics of germinomas in unusual locations. Researchers documented that although these tumors might present differently, they still responded well to standard treatment with radiation therapy and chemotherapy. Over the past decade, there has been growing recognition of atypical presentations of CNS germinomas in the medical literature. Systematic reviews and multicenter studies have been published that have attempted to group and analyze these rare cases, providing a better understanding of their clinical behavior and prognosis. In addition, the integration of genomics and molecular biology has begun to shed light on the possible reasons for these atypical presentations, suggesting differences in signaling pathways and specific mutations that may be involved. Today, it is recognized that although germinomas in atypical locations are rare, they should be considered in the differential diagnosis of CNS tumors in pediatrics. Early and accurate diagnosis remains a challenge, but increasing understanding of these atypical presentations has led to greater vigilance and improved clinical outcomes for these patients. Despite these advances, the occurrence of this tumor, as described in this case, has not been reported in the literature (2).

Case description

An 11-year-old female patient with a history of short stature presented with a six-month history of decreased visual acuity and dyschromatopsia, initially treated for glaucoma without clinical improvement. MRI revealed high signal intensity on T2-weighted sequences and thickening of the optic chiasm and floor of the third ventricle (Figure 1). Optical coherence tomography showed thinning of the retinal nerve fibers. An immune-mediated disease was suspected. A lumbar puncture was performed, showing an opening pressure of 24 cm H_2O. Analysis of the cerebrospinal fluid revealed positive oligoclonal bands and negative anti-aquaporin 4 antibodies. Initial treatment with a three-day course of corticosteroid pulses was decided upon due to the suspicion of optic neuritis. There was no clinical improvement or improvement in the images. Subsequent fundoscopic examination revealed pale optic discs, with markedly worsened visual acuity: light perception in the right eye and "finger counting" in the left eye. In addition, diabetes insipidus and growth hormone deficiency were confirmed in endocrinological laboratory tests. New pulses of methylprednisolone were administered without clinical or imaging changes. An endoscopic biopsy of the lesion on the floor of the third ventricle confirmed a suprasellar germinoma with immunohistochemistry showing: SALL4, positive; PLAP, positive; and CD117, weakly and focally positive. The tumor was classified as M0. Oncological treatment was initiated with the Children's Oncology Group (COG) protocol of carboplatin and

etoposide for three consecutive days in three cycles, once a week. It should be noted that chemotherapy was decided upon due to the rapid and high response to treatment in this type of tumor in pediatrics. An 85% disease-free rate has been reported after five years (3).

Surgical Procedure

An endoscopic biopsy with neuro-navigation was chosen due to the patient's small ventricles. Under general anesthesia, with the head resting on a semilunar support, the approach was made through the right Kocher point using a 30° endoscope. Upon entering the ventricle and passing through the small foramen of Monro, a whitish lesion covering the floor of the third ventricle was observed. Samples were taken for pathological study, confirming a lesion consistent with germinoma (Figure 2). One year after diagnosis and treatment, MRI shows complete improvement of the findings (Figure 3).

Discussion

Germinomas in the pineal and suprasellar regions account for approximately 90% of intracranial germinomas in pediatric patients. However, there are rare cases in which germinomas appear in atypical locations, complicating diagnosis and treatment. In the case presented, the germinoma manifested as thickening of the optic chiasm and the floor of the third ventricle, an unusual location that poses specific challenges in differential diagnosis and clinical management, as it can mimic other pathological processes, such as immune-mediated diseases or optic gliomas, lymphomas, and other neoplasms, making early diagnosis difficult. It should be noted that immune-mediated inflammatory processes (e.g., optic neuritis) also present with severe visual acuity abnormalities. Another pathology mentioned, such as optic pathway glioma, has initial symptoms similar to the case described, and imaging studies detect thickening and pathological enhancement of the optic pathway, mainly in the optic nerve and optic chiasm. On the other hand, lymphomas in the CNS can present with selar-suprasellar morphological alterations, but—unlike the former—they respond quickly to corticosteroid therapy. Another neoplasm to highlight in the differential diagnosis in the selar-suprasellar region in pediatric patients is histiocytosis, which is usually confirmed by biopsy of the lesion.

Cases of germinomas in the corpus callosum (4), intraparenchymal (5), infundibular (6), and even medullary regions (7) have been described, but no cases such as the one reported in this study have been documented. The clinical presentation varies depending on the location of the germinoma. In the pineal region, symptoms of hydrocephalus are common, while germinomas in the suprasellar region can cause endocrine and visual disorders due to compression of the optic chiasm (8). Comparatively, the patient presents visual and endocrine symptoms due to infiltration of the chiasm and adjacent hypothalamic structures. These may overlap with other pathologies of the sellar and parasellar regions. A review of the literature has found associations between the atypical presentation of germinomas and Down syndrome. Patients with Down syndrome are at increased risk of developing certain types of tumors, including CNS germinomas. This association suggests a possible genetic and biological predisposition that may influence the onset and location of these tumors. Recognizing this association is crucial for early surveillance and diagnosis in patients with Down syndrome (9-11). The treatment of CNS germinomas has evolved significantly, improving the prognosis and quality of life of patients.

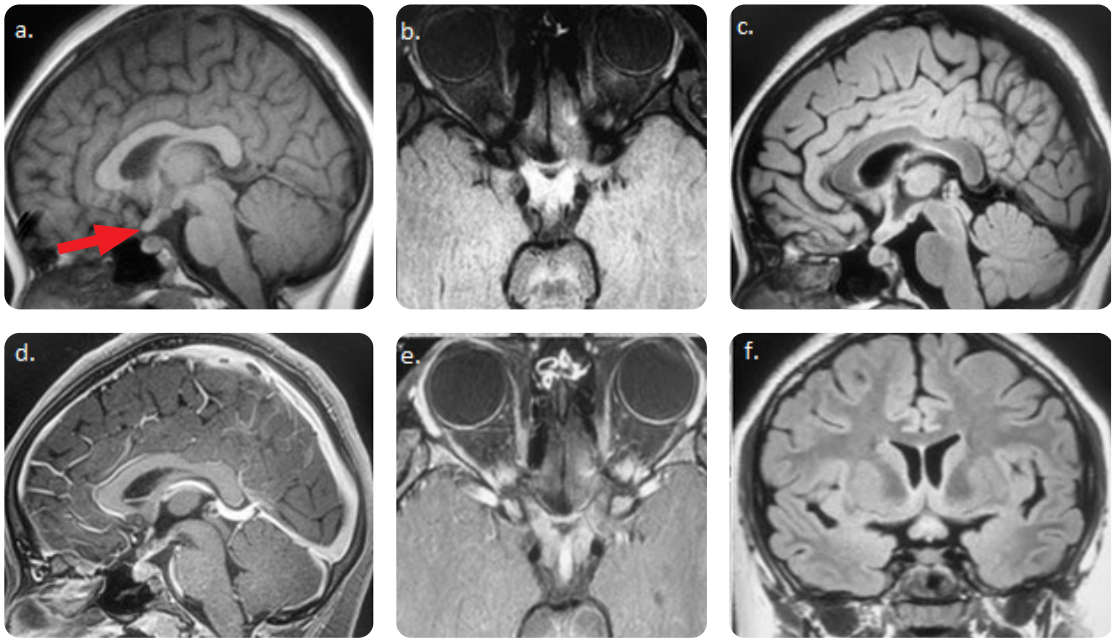


Figure 1. MRI of the sellar region in sequences with T1 information. a) Without contrast medium. d) With contrast medium. T2FLAIR sequence (b) axial; (c) sagittal, (f) coronal, and (e) SPIRT1 sequence axial. Absence of high signal in sequence with T1 information corresponding to the neurohypophysis. Thickening and contrast enhancement of the optic chiasm, the posterior segment of the optic nerves, and the anterior wall-floor of the third ventricle.

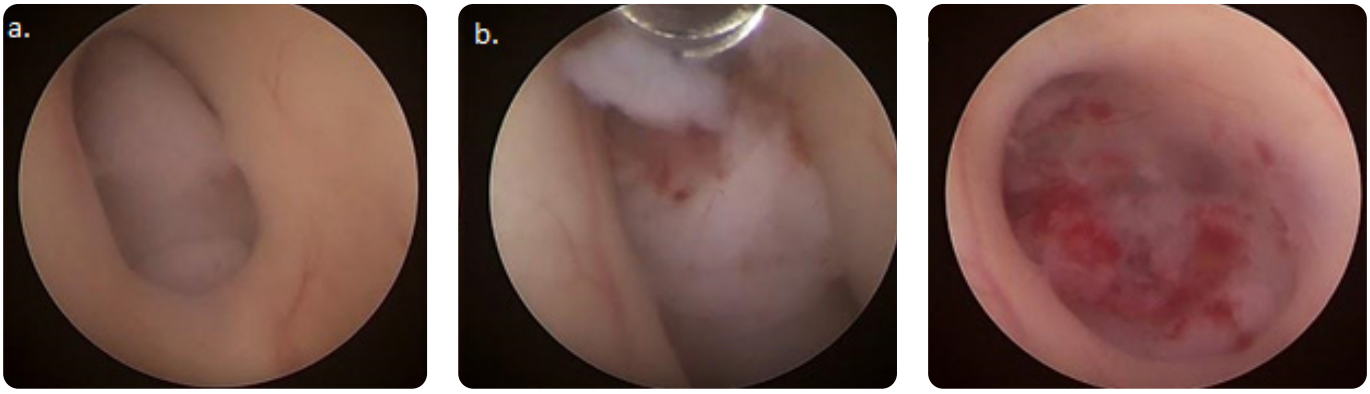


Figure 2. Endoscopic view of the lesion covering the floor of the third ventricle. Whitish lesion a) before; b) during, and c) after endoscopic biopsy.

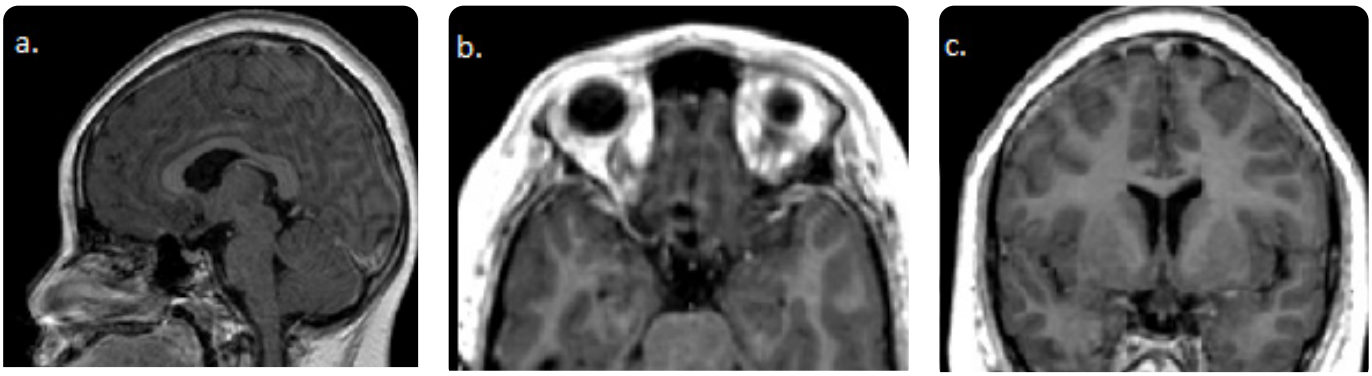


Figure 3. MRI with T1 information and contrast medium administration in a) sagittal, b) axial, and c) coronal planes, one year after diagnosis and subsequent treatment. Compared to the previous study: complete improvement of findings indicative of neoplasia. The optic chiasm and optic nerves appear normal.

Current modalities include:

- **Radiotherapy.** The use of focused radiotherapy has gained popularity to reduce the long-term side effects of craniospinal radiotherapy, with an efficacy of 90%.
- **Chemotherapy.** It is used as a complement to radiotherapy to reduce the necessary radiation dose and limit toxicity. Protocols include drugs such as cisplatin, etoposide, and cyclophosphamide.
- **Surgery.** Endoscopic or stereotactic biopsy, depending on the center and the neurosurgeon in charge, is mainly used to confirm the histological diagnosis. Surgical resection is rarely necessary due to the high sensitivity of these tumors to radiation therapy and chemotherapy.

For diagnosis and follow-up, the complementary reference study is MRI. MRI with gadolinium provides excellent delineation of the tumor's extent. In addition, tumor markers in the cerebrospinal fluid are not altered in this type of tumor, making them useful tools for differentiating them from other germ cell tumors. The prognosis for patients with CNS germinomas is generally favorable, with 5-year survival rates exceeding 90%. However, long-term follow-up is essential to manage the side effects of treatment, which may include endocrine dysfunction, neurocognitive deficits, and risks of secondary neoplasms (12, 13).

Conclusion

The atypical presentation of germinomas in the optic chiasm and floor of the third ventricle, although rare, underscores the importance of considering this diagnosis in similar cases. The combination of advanced imaging techniques, such as contrast-enhanced MRI, together with the evaluation of tumor markers in the cerebrospinal fluid, is crucial for differentiating these tumors from other pathologies. While standard treatment with radiation therapy and chemotherapy has proven highly effective, rigorous follow-up is required to address potential long-term sequelae. The prognosis for patients with CNS germinomas is generally favorable, emphasizing the importance of comprehensive, multidisciplinary management.

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