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Case Report

Bifocal pineal and suprasellar germinomas with posterior fossa metastases in an adolescent patient[☆]

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ARTICLE INFO

Article history:

Received 15 August 2022

Accepted 27 August 2022

Keywords:

Bifocal germinoma

Pinealoma

Suprasellar germinoma

Germ cell tumor

MRI

ABSTRACT

Central nervous system germ cell tumors are rare lesions that are more frequently seen in the pediatric age group. Intracranial germinomas are a type of these germ cell tumors and commonly arise in the pineal region, suprasellar region, or less frequently at both areas (bifocal). Common features of this tumor depend on the location of the lesion(s) and include Parinaud's syndrome, obstructive hydrocephalus, diabetes insipidus, panhypopituitarism, strabismus, and visual acuity defects. We report a case of bifocal pineal and suprasellar germinoma with posterior fossa metastases in a 15-year-old male patient. The involvement of the third ventricular floor and nonthickened inferior pituitary stalk of the suprasellar lesion suggest that it is a metastasis of a primary pineal lesion rather than a dual-primary. This distinction, with the presence of posterior fossa metastases, favors the use of more aggressive treatment with combination radiation therapy and chemotherapy for a better outcome.

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Introduction

Intracranial germinomas are a subclass of central nervous system germ cell tumors comprising <3% of all primary central nervous system tumors in the United States and Europe, with a higher occurrence in Asia, and are typically diagnosed before the age of 20 [1]. Most commonly, these germ cell tumors arise in either the pineal or suprasellar regions. Less commonly, however, bifocal tumors can occur in both regions

at initial presentation and generally carry a poorer prognosis [2]. Such bifocal lesions can be either 2 independent primary germinomas (true bifocal germinoma) or resemble one primary germinoma with metastases (false bifocal germinoma) [3].

The pathogenesis of central nervous system germ cell tumors, including intracranial germinomas, is not fully understood. One leading hypothesis states that abnormal migration of germ cells during development later form into extragonadal germ cell tumors [4]. Another theory suggests

[☆] Competing Interests: All authors have nothing to disclose.

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<https://doi.org/10.1016/j.radcr.2022.08.102>

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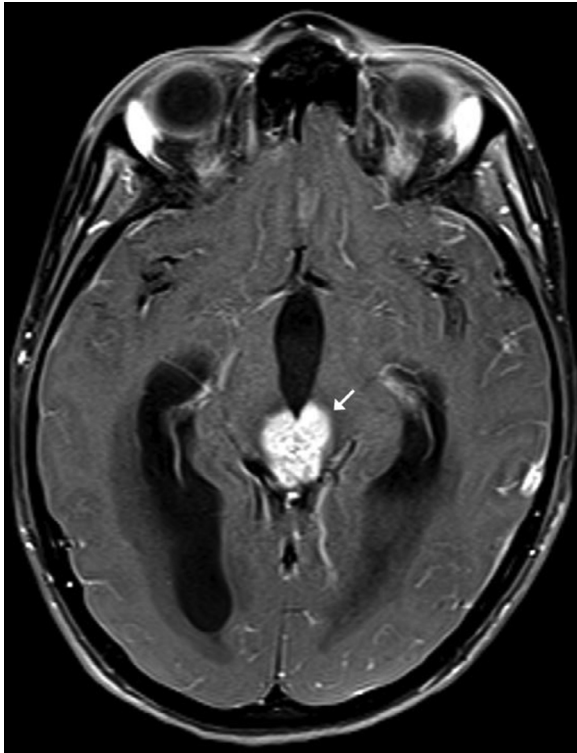


Fig. 1 – Axial turbo spin echo (TSE) contrast enhanced T1-weighted fat saturation (1.5 T; TR/TE = 582/10.0 ms; slice thickness = 4.0 mm; slice spacing = 4.0 mm) MR of the head. A pineal region mass is demonstrated (white arrow) measuring 2.2 x 2.2 x 1.6 cm.

that misfolding during development causes the misplacement of germ cells, rather than abnormal migration [5]. Common clinical presentations of intracranial germinomas largely depend on the location of the lesion. Germinomas involving the pineal region typically cause obstructive hydrocephalus due to cerebral aqueduct compression, resulting in the typical symptoms of diplopia, vomiting, and headache, as well as Parinaud's syndrome due to midbrain involvement [6]. Suprasellar lesions typically cause endocrine manifestations such as diabetes insipidus, precocious puberty, delayed development, and amenorrhea. They also cause ocular symptoms such as strabismus, diplopia, bitemporal hemianopsia, and visual acuity deficits due to optic chiasm involvement [5,6]. Notable biomarkers for extragonadal germ cell tumors include AFP and b-HCG, however, these levels are not usually elevated with germinomas [4,6]. Here, we report a case of an adolescent male with concurrent presentation of intracranial germinomas in the suprasellar and pineal region, in addition to metastases in the posterior fossa.

Case report

A 15-year-old male presented as a transfer to our institution with a 1-year history of diplopia, 3-month history of worsening intractable headaches, vomiting, ataxia, and anomic apha-

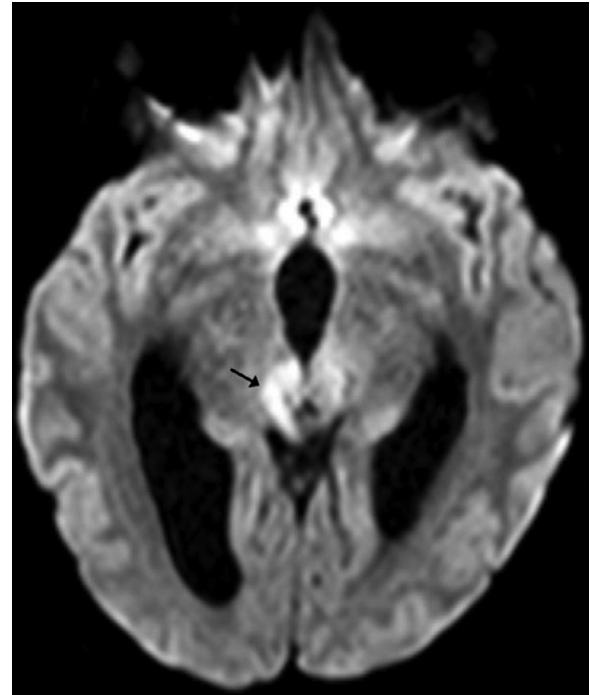


Fig. 2 – Axial diffusion-weighted imaging (DWI) (1.5 T; TR/TE = 6300/89.0 ms; slice thickness = 4.0 mm; slice spacing = 5.2 mm) MR of the head. Restricted diffusion is shown in the pineal mass (black arrow).

sia, and 1 month history of polyuria and polydipsia. Initial neurological exam was significant for dysconjugate gaze, with downward deviation in the left eye during right lateral gaze. Additionally, the right pupil measured 6 mm and was nonreactive, while the left pupil measured 4 mm and had a sluggish reaction to light.

MRI of the head demonstrated an enhancing pineal region mass with restricted diffusion (Figs. 1 and 2). An enhancing suprasellar mass was also revealed with hypothalamic and optic chiasm involvement, with no clear visualization of the posterior pituitary T1 “bright spot” and a partially empty sella (Figs. 3 and 4). Additionally, symmetric, enhancing mass-like lesions were noted at the medial aspects of both cerebellar hemispheres (Fig. 5). There was no evidence of spinal metastases on MRI.

The radiological findings were consistent with a bifocal intracranial germinoma with metastases to the posterior fossa, with resulting cerebral aqueduct obstruction and supratentorial hydrocephalus from the pineal mass (Fig. 6). Of note, there is a partially empty sella, and the suprasellar region involves the third ventricular floor with no thickening or involvement of the inferior pituitary stalk (Figs. 7 and 8). The patient was AFP and b-HCG negative with biopsy confirmation of the germinoma. Clinical manifestations of the germinoma included Parinaud syndrome, ataxia, panhypopituitarism with diabetes insipidus, and hydrocephalus.

Management involved external ventricular drainage and subsequent ventriculoperitoneal shunt placement for relief of the obstructive hydrocephalus. Treatment of the germi-

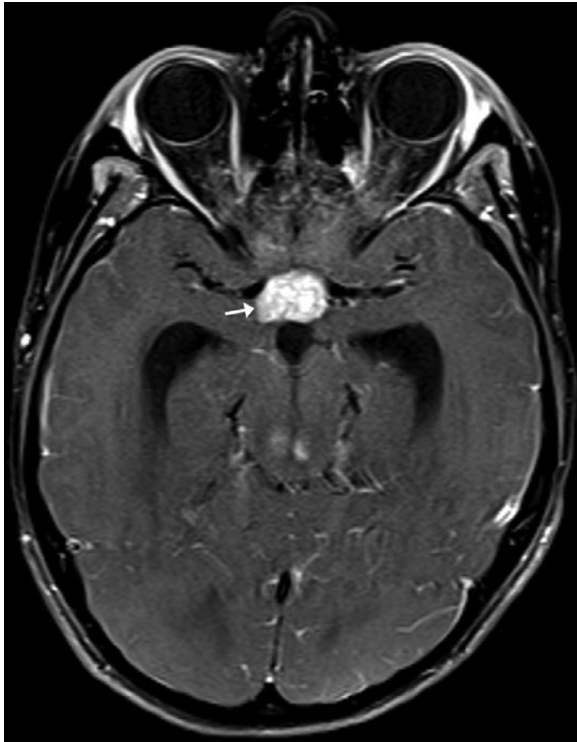


Fig. 3 – Axial turbo spin echo (TSE) contrast enhanced T1-weighted fat saturation (1.5 T; TR/TE = 582/10.0 ms; slice thickness = 4.0 mm; slice spacing = 4.0 mm) MR of the head. A mass in the suprasellar region and floor of the third ventricle (white arrow) is demonstrated, measuring 2.0 × 1.4 × 1.0 cm.



Fig. 4 – Axial turbo spin echo (TSE) T2-weighted (1.5 T; TR/TE = 9280/100.0 ms; slice thickness = 3.0 mm; slice spacing = 3.0 mm) MR of the head. Optic chiasm (thin white arrow) involvement of the suprasellar mass (thick white arrow) is demonstrated.

noma involved 4 cycles of chemotherapy with carboplatin and etoposide in combination with proton-beam radiation. The patient had a good response to treatment, demonstrating no significant enhancing or residual mass on imaging after 6 months of treatment (Fig. 7). With treatment, the patient experienced resolution of the diabetes insipidus and improvement in the ataxia and diplopia. Currently, the patient is being monitored with serial MRIs for recurrence of disease.

Discussion

Bifocal lesions, such as the one described in this case, are defined by synchronous lesions in the pineal and suprasellar areas. Such a finding is more common in males and accounts for 5%-25% of patients with intracranial germinomas at diagnosis [3,6]. Currently, 2 pathways are described for the formation of bifocal lesions. One is a dual-primary (true bifocal lesion), where both tumors arose independently, whereas the other mechanism is a false bifocal, or metastasis [3,7]. The 2 can be distinguished using features on MR, where true suprasellar tumors demonstrate a thickened pituitary stalk, especially the inferior portion, and extension into the hypothalamus with an origin at the hypophysis. However, false bifocal germinomas are described as primary pineal germinomas with

hypothalamo-neurohypophyseal axis metastasis. These originate at the floor of the third ventricle and extend to the neurohypophysis (without involvement of the inferior pituitary stalk), have a high intensity signal on T1W MRI in the posterior pituitary, and are more likely to demonstrate remote metastases to other regions [3,7]. Another discerning characteristic on MR is the shape of hypothalamo-neurohypophyseal axis. In a true lesion, this region is typically shaped in a figure-8 or bottle-plug conformation, whereas in a false lesion, it generally resembles an irregular, inverted-cone, or normal-shaped hypothalamo-neurohypophyseal axis [7].

In our case, the suprasellar lesion involves the third ventricle floor and has a nonthickened inferior pituitary mass (Figs. 8 and 9), supporting the notion that it is a metastasis from a primary pineal lesion. The presence of posterior fossa metastases further supports that this is a false bifocal germinoma. In false bifocal germinomas and true bifocal germinomas with metastases, it is recommended to include craniospinal irradiation in the management, as opposed to limited radiotherapy in true bifocal germinomas with no metastases [7]. In general, however, bifocal lesions tend to have a poorer prognosis than single lesions, and it may be beneficial to treat them as disseminated disease due to failure rates of localized radiotherapy fields [2,8]. A retrospective study demonstrated that treatment outcomes for germinomas are very positive, but lower relapse rates and higher survival rates occur with craniospinal

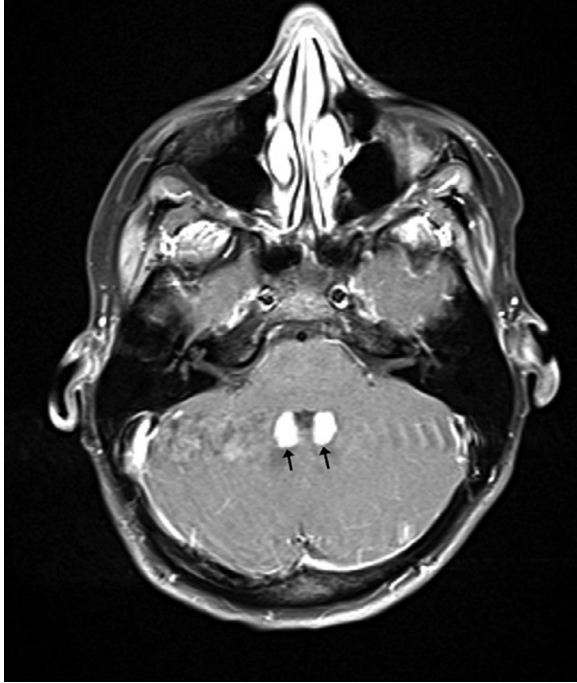


Fig. 5 - Axial turbo spin echo (TSE) contrast enhanced T1-weighted fat saturation (1.5 T; TR/TE = 582/10.0 ms; slice thickness = 4.0 mm; slice spacing = 4.0 mm) MR of the head. Symmetrical, medial cerebellar lesions in the posterior fossa (black arrows) are demonstrated.

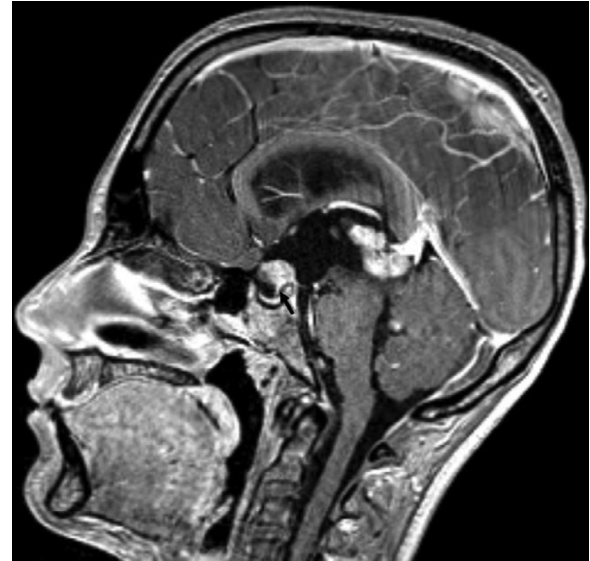


Fig. 7 - Sagittal magnetization-prepared rapid gradient echo (MPRAGE) T1-weighted (1.5 T; TR/TE = 2340/4.2 ms; slice thickness = 0.9 mm) MR of the head. A partially empty sella and a suprasellar mass with third ventricular floor involvement with no thickening of the inferior pituitary stalk (black arrow) are demonstrated.



Fig. 6 - Sagittal magnetization-prepared rapid gradient echo (MPRAGE) T1-weighted (1.5 T; TR/TE = 2340/4.2 ms; slice thickness = 0.9 mm) MR of the head. The pineal, suprasellar, and cerebellar lesions (black arrows) are shown. Enlargement of the lateral ventricle (white arrow) can also be seen due to compression of the cerebral aqueduct, resulting in obstructive hydrocephalus.

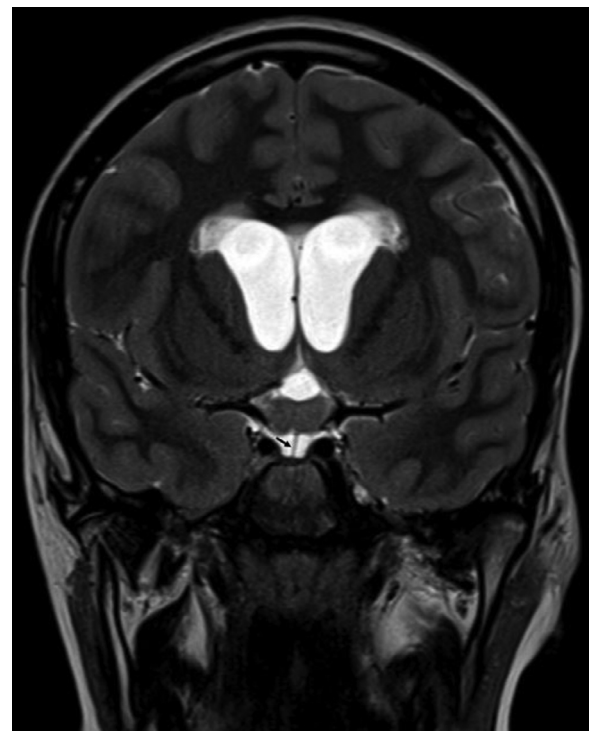


Fig. 8 - Coronal turbo spin echo (TSE) T2-weighted (1.5 T; TR/TE = 6600/95.0 ms; slice thickness = 3.0 mm; slice spacing = 3.0 mm) MR of the head. A suprasellar mass with a nonthickened inferior pituitary stalk (black arrow) is demonstrated.

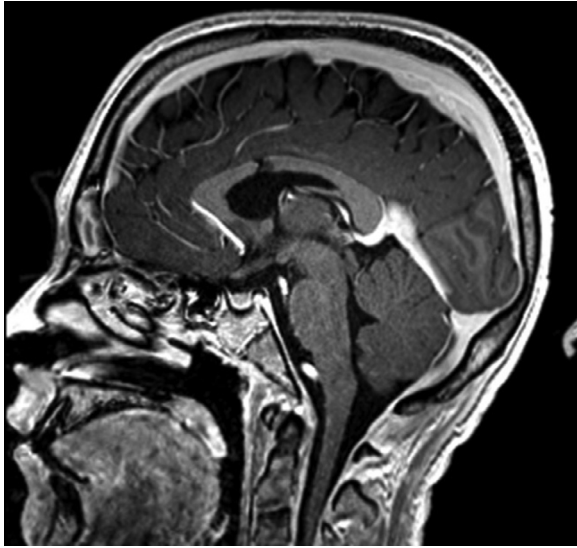


Fig. 9 – Sagittal magnetization-prepared rapid gradient echo (MPRAGE) T1-weighted (3.0 T; TR/TE = 2000/2.3 ms; slice thickness = 1.0 mm) MR of the head. No residual enhancement of the pineal, suprasellar, and cerebellar lesions is demonstrated after 6 months of chemotherapy and proton-beam radiation. Resolution of the hydrocephalus can also be seen as the lateral ventricle has returned to normal size after ventriculoperitoneal shunting.

irradiation with chemotherapy [1]. If whole ventricle irradiation is used instead of craniospinal irradiation, however, then it is recommended to also use chemotherapy with treatment [2].

In summary, an intracranial bifocal germinoma is an exceedingly rare condition that is often diagnosed in patients less than 20 years old. The diagnosis of this condition is supported through clinical, radiological, biological markers. Generally, the prognosis for germinomas is overall excellent, with treatment consisting of radiotherapy and chemotherapy. The distinction of true and false bifocal germinomas can be made radiologically and can have implications for more aggressive treatment to allow for better outcomes.

Patient consent

Informed consent was obtained from the legal guardian of this patient regarding the publication of the clinical information and diagnostic images in this case.

REFERENCES

- [1] Lo AC, Hodgson D, Dang J, Tyldesley S, Bouffet E, Bartels U, et al. Intracranial germ cell tumors in adolescents and young adults: a 40-year multi-institutional review of outcomes. *Int J Radiat Oncol Biol Phys* 2020;106(2):269–78. doi:[10.1016/j.ijrobp.2019.10.020](https://doi.org/10.1016/j.ijrobp.2019.10.020).
- [2] Kang YM, Lee YY, Lin SC, Chang FC, Hsu S, Lin CF, et al. Bifocal lesions have a poorer treatment outcome than a single lesion in adult patients with intracranial germinoma. *PLoS One* 2022;17(3):e0264641. doi:[10.1371/journal.pone.0264641](https://doi.org/10.1371/journal.pone.0264641).
- [3] Esfahani DR, Alden T, Dipatri A, Xi G, Goldman S, Tomita T. Pediatric suprasellar germ cell tumors: a clinical and radiographic review of solitary vs. bifocal tumors and its therapeutic implications. *Cancers (Basel)* 2020;12(9):2621. doi:[10.3390/cancers12092621](https://doi.org/10.3390/cancers12092621).
- [4] Kong Z, Wang Y, Dai C, Yao Y, Ma W, Wang Y. Central nervous system germ cell tumors: a review of the literature. *J Child Neurol* 2018;33(9):610–20. doi:[10.1177/0883073818772470](https://doi.org/10.1177/0883073818772470).
- [5] Echevarría ME, Fangusaro J, Goldman S. Pediatric central nervous system germ cell tumors: a review. *Oncologist* 2008;13(6):690–9. doi:[10.1634/theoncologist.2008-0037](https://doi.org/10.1634/theoncologist.2008-0037).
- [6] Jorsal T, Rørth M. Intracranial germ cell tumours. A review with special reference to endocrine manifestations. *Acta Oncol (Madr)* 2012;51(1):3–9. doi:[10.3109/0284186X.2011.586000](https://doi.org/10.3109/0284186X.2011.586000).
- [7] Zhang H, Qi ST, Fan J, Fang LX, Qiu BH, Liu Y, et al. Bifocal germinomas in the pineal region and hypothalamo-neurohypophyseal axis: primary or metastasis? *J Clin Neurosci* 2016;34:151–7. doi:[10.1016/j.jocn.2016.06.009](https://doi.org/10.1016/j.jocn.2016.06.009).
- [8] Chung SY, Han JW, Kim DS, Yoon HI, Suh CO. Treatment outcomes based on radiation therapy fields for bifocal germinoma: synchronous or disseminated disease? *PLoS One* 2019;14(10):e0223481. doi:[10.1371/journal.pone.0223481](https://doi.org/10.1371/journal.pone.0223481).