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SNI: Neuro-oncology

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Case Report

Preoperatively difficult-to-diagnose medulla oblongata germinoma: A case report and literature review

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Received: 15 August 2023
Accepted: 22 September 2023
Published: 13 October 2023

DOI
10.25259/SNI_682_2023

Quick Response Code:

ABSTRACT

Background: Intracranial germinomas are rare tumors, accounting for 0.5–2% of primary intracranial neoplasms. While they typically occur in the pineal gland, suprasellar region, basal ganglia, and thalamus, germinomas arising in the medulla oblongata are exceptionally rare. Diagnosis of medulla oblongata germinoma is challenging, potentially leading to misdiagnosis and poor prognosis.

Case Description: We present a case of a 29-year-old man complaining of left leg numbness. Radiological findings revealed a contrast-enhanced lesion in the medulla oblongata. The patient underwent tumor biopsy, and intraoperative pathological diagnosis (IOD) suspected the diagnosis of medulla oblongata germinoma. He underwent chemoradiotherapy after confirming the diagnosis of germinoma. Intracranial germinoma arising in the medulla oblongata differs from germinomas in other locations due to its higher incidence in individuals in their 20s and a slight female predominance.

Conclusion: When encountering lesions in the medulla oblongata, germinoma should be considered as one of the differential diagnoses, and surgical strategies including IOD should be planned accordingly.

Keywords: Germ cell tumor, Germinoma, Medulla oblongata

INTRODUCTION

Intracranial germinomas are rare, accounting for 0.5–2% of primary intracranial tumors.[5] They primarily occur in teenagers and young adults aged 20–29. Intracranial germinomas show male predominance with a ratio of 1.9-4.4:1.0.[10,11,19] The most common site of occurrence for germinomas is the pineal region (45%), followed by the suprasellar region (32%), and the basal ganglia and thalamus (13%).[2] Although extremely rare, germinomas can also arise in the medulla oblongata.[1,2,4,6-9,12-26,28-32] Preoperative diagnosis of germinoma in the medulla oblongata is difficult due to tumor rarity, and there have been reported cases where misdiagnosis led to poor prognosis.

Here, we report a case of germinoma in the medulla oblongata and summarize the epidemiology, imaging findings, treatment, and prognosis compared to previously reported cases.

CASE PRESENTATION

A 29-year-old man has been experiencing numbness in his left leg for a year. As the numbness progressed to the left side of the abdomen, he underwent gadolinium (Gd)-enhanced head

magnetic resonance (MR) imaging at a local medical facility. The examination revealed an enhanced lesion in the medulla oblongata, and the patient was subsequently referred to our hospital. There was no significant medical history or family history, and except for the left-sided numbness, no neurological abnormalities were observed. Head computed tomography (CT) showed a hypodense lesion in the central area with hyperdense areas protruding from the medulla oblongata to the surrounding tissues [Figure 1a]. Head MR imaging demonstrated a high-intensity round lesion on T2-weighted images (WI) and a circumscribed Gd enhancement surrounding the caudal low-intensity area on T1WI [Figure 1b]. A low-grade glial tumor, such as pilocytic astrocytoma, was suspected and tumor resection with duroplasty was planned.

Surgical findings

The tumor located on the dorsal side of the medulla oblongata, presumably corresponding to the nucleus gracilis, was visible through the pia mater as a brown mass [Figure 2a]. During the tumor resection after cutting the pia mater, the tumor was fragile and grayish-white in color. The border between the tumor and normal brain tissue was well-defined [Figure 2b]. An intraoperative pathological diagnosis (IOD) using a frozen section was obtained, and a diagnosis of suspected germinoma was made. Therefore, the surgery was completed with a biopsy only.

As for pathological findings [Figure 3], the tumor showed proliferation of atypical cells with relatively large nuclei and pale cytoplasm. Lymphocytic infiltration was observed. Immunohistochemistry showed that the tumor cells were positive for placental alkaline phosphatase and c-kit. The human chorionic gonadotropin beta (hCG-β) test was weakly positive, whereas the alpha-fetoprotein (AFP) test was negative. The diagnosis of germinoma was confirmed.

Post-operative course

Since germinoma was not suspected before surgery, blood tests were conducted to measure AFP, hCG, and hCG-β levels on the day after surgery. The results showed an AFP of 2.0 ng/ml, HCG <0.5 mIU/mL, and HCG-β <0.28 ng/mL. Post-operative MR imaging showed no complications, and the right-side numbness remained unchanged. The patient was discharged home with a Karnofsky performance status (KPS) score of 90. Subsequently, chemotherapy using carboplatin and etoposide was initiated. After completing two cycles of chemotherapy, the contrast-enhanced lesion mostly disappeared, confirming its significant effectiveness. Therefore, radiation therapy with a total dose of 30.6 Gy in 17 fractions to all the ventricles was performed concurrently with the third cycle of chemotherapy. Post-treatment Gd-contrasted MR imaging showed no evidence of the enhanced lesion and no tumor dissemination. The patient was in good condition (KPS = 90) except for mild dysesthesia in the left extremities 6 months after the biopsy.

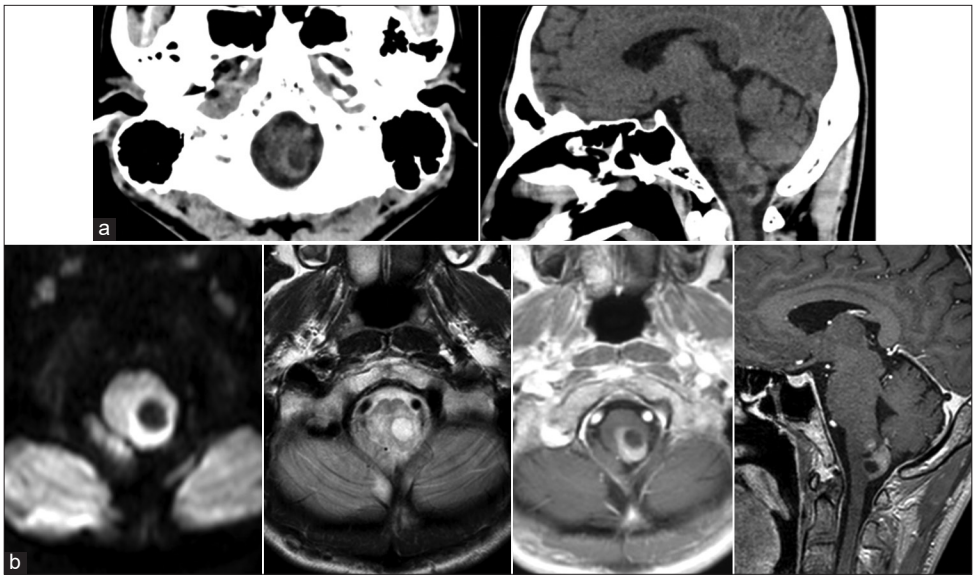

Figure 1: (a) Plain head computed tomography: axial (left) and sagittal (right) views show a hypodense lesion in the central area with hyperdense areas protruding from the medulla oblongata to the surrounding tissues. (b) Magnetic resonance imaging. The axial view on the diffusion-weighted image (WI) (left) and T2WI (middle left). Axial and sagittal views on T1WI with gadolinium contrast enhancement (middle right and right) shows a circumscribed enhanced mass.

DISCUSSION

Intracranial germinomas predominantly occur in the pineal and suprasellar regions, basal ganglia, and thalamus.[10] However, there have been reports of germinomas arising in the medulla oblongata,[1,2,4,6-9,12-26,28-32] such as in our case. A total of 29 cases have been previously reported, and including our case, a total of 30 cases are presented in Supplementary Table 1. In our case review, the male-to-female ratio of medulla oblongata germinomas was 1.0:1.3, indicating a higher prevalence in women, and the average age was 23 years (12–40). In contrast, regarding intracranial germinomas in general, with a majority of suprasellar and pineal lesions, a higher incidence in men (the male-to-female ratio was 1.9–4.4:1.0)[10,11,19] and a higher prevalence in the teenage population was observed.

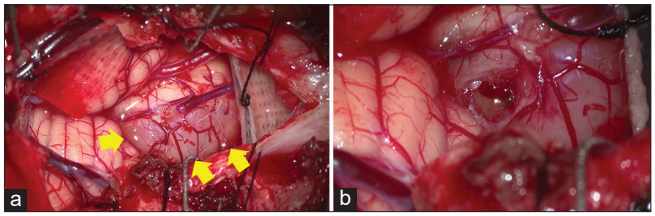

Figure 2: Intraoperative photographs. (a) The tumor covered by the pia mater was observed on the dorsal side of the medulla oblongata (yellow arrows). (b) The tumor appeared as a friable grayish-white lesion.

This suggests that medulla oblongata germinoma shows a different age distribution, occurring at a later age and being more common in women. The symptoms observed in medulla oblongata germinomas mainly involved motor and sensory abnormalities, lower cranial nerve dysfunction, and disturbances in the respiratory center, reflecting anatomical and functional impairments.

In our case review, the 1-year survival rate for the medulla oblongata germinoma was 80% [Supplementary Figure 1, calculated from the data in Supplementary Table 1]. Intracranial germinomas are generally highly sensitive to radiation therapy, resulting in high 1-year and 10-year survival rates (approximately 100% and 90%, respectively) for their intracranial locations.[11,19] However, it should be taken into account that even after 10 years, distant recurrences may occur, especially in germinoma patients who have received incomplete radiotherapy.[27] Since intracranial germinomas are known to spread through the cerebrospinal fluid, the radiation field often includes all the ventricles.[3,27] Although the limited number of cases made detailed analysis difficult, the main causes of death were cardiac arrest or respiratory failure within 8 months, and half of these cases occurred before radiotherapy or chemoradiotherapy. There was only one death due to germinoma itself after chemoradiotherapy, indicating that medulla oblongata germinomas are also chemo-radiosensitive and lead to a high patient survival

Table 1: Summary of 30 cases of medulla oblongata germinoma, including our case.

Non-contrast CT features				**Present case**
Density (*n*=7)	High or slightly high density (5 cases, 71%)	Iso density (2 cases, 29%)		Mixed density
Calcification (*n*=7)	Yes (1 case, 14%)	No (6 cases, 86%)		No
MR imaging features				
T1WI (*n*=18)	Low or slightly low intensity (9 cases, 50%)	Iso intensity (6 cases, 33%)	High, slightly high, or mixed intensity (3 cases, 17%)	Low intensity
T2WI (*n*=18)	Low or slightly low intensity (0 case, 0%)	Iso intensity (2 cases, 11%)	High, slightly high, or mixed intensity (16 cases, 89%)	High intensity
Gd-enhancement (*n*=26)	Hetero. or hetero susp. (19 cases, 73%)	Homo. or homo. susp. (7 cases, 27%)		Hetero.
Lesion boundary (*n*=24, including 3 cases data from IO finding)	Circumscribed (12 cases, 50%)	Non-circumscribed (12 cases, 50%)		Circumscribed
Cystic components (*n*=30)	Yes (16 cases, 53%)	No (14 cases, 47%)		Yes
Hydro. (*n*=30)	Obstructive hydro. (1 case, 3%)	Mild hydro. (2 cases, 7%)	No hydro. (27 cases, 90%)	No hydro.

Gray boxes indicate the majority of cases (60% or more). Hetero: Heterogeneous, Homo: Homogeneous, Hydro: Hydrocephalus, IO: Intraoperative, *n*: Number, susp: Suspected, WI: Weighted images, CT: Computed tomography, MR: Magnetic resonance

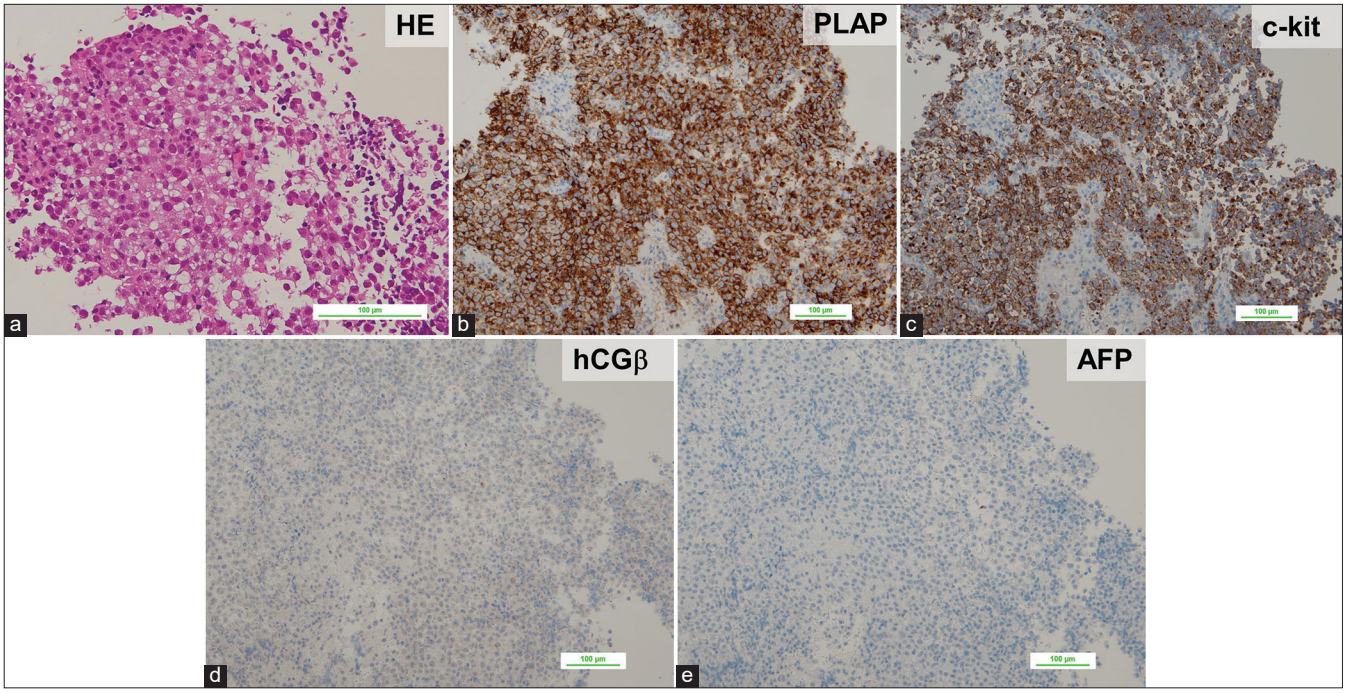

Figure 3: (a) Hematoxylin-Eosin (HE) staining showed the proliferation of atypical cells with relatively large nuclei, pale cytoplasm, and infiltrating lymphocytes. (b-e) Immunohistochemistry showed that the tumor cells were positive for placental alkaline phosphatase (PLAP) and c-kit antibodies, weakly positive for human chorionic gonadotropin beta (hCGβ) antibodies, and negative for alpha-fetoprotein (AFP) antibodies.

rate after chemoradiotherapy. Surprisingly, the 1-year survival rate for medulla oblongata germinoma treated with biopsy or partial resection (PR) was 100%, whereas it was <80% (including post-surgical complication cases before chemoradiotherapy) in patients after subtotal or gross total removal [Supplementary Figure 1], indicating that excessive resection should be avoided for medulla oblongata germinoma.

In the preoperative imaging diagnosis, including our case, ependymoma, medulloblastoma, glioma, and other lesions were considered, but not germinoma. The characteristic findings based on preoperative imaging are summarized in Table 1. Medulla oblongata germinomas typically appear as high-density lesions (71%) on CT, with rare calcification (14%). On MR imaging, the lesions often show a heterogeneous appearance (73%) on Gd-enhanced T1WI and variable signal intensity on T2WI, ranging from low to high. Well-defined borders were observed in approximately half of the cases. The finding of obvious noncommunicating (obstructive) hydrocephalus is rare (3%). Based on this summary, observation of a high-density lesion on CT can be useful in differentiating germinoma from glioma, and calcification can be somewhat useful in differentiating it from ependymoma. The absence of hydrocephalus (90%) on CT and/or MR imaging may also be a characteristic feature. While there were no specific findings on conventional MR images, distinguishing germinoma from ependymoma or medulloblastoma solely based on imaging can be challenging.

Thus, the absence of hydrocephalus on CT and/or MR imaging, a high-density lesion without calcification on CT scan, and the higher prevalence in women with an onset in the 20s may provide some assistance in the differentiation from ependymoma and medulloblastoma; however, it is extremely difficult to diagnose medulla oblongata germinoma preoperatively. As mentioned above, a biopsy or PR is recommended for medulla oblongata germinoma to prevent fatal complications, such as cardiac arrest or respiratory failure. Therefore, in cases where the diagnosis of germinoma cannot be definitively ruled out based on preoperative imaging and intraoperative findings, IOD using a frozen section should be performed, and excessive resection should be avoided in confirmed or suspected germinoma cases.

CONCLUSION

Intracranial germinoma occurring in the medulla oblongata differs from germinomas in other locations, as it has a higher incidence in individuals in their 20s, a slight female predominance, and no evidence of hydrocephalus or calcification. When encountering lesions in the medulla oblongata, germinoma should be considered as one of the

differential diagnoses, and surgical strategies including IOD should be planned accordingly.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The author(s) confirms that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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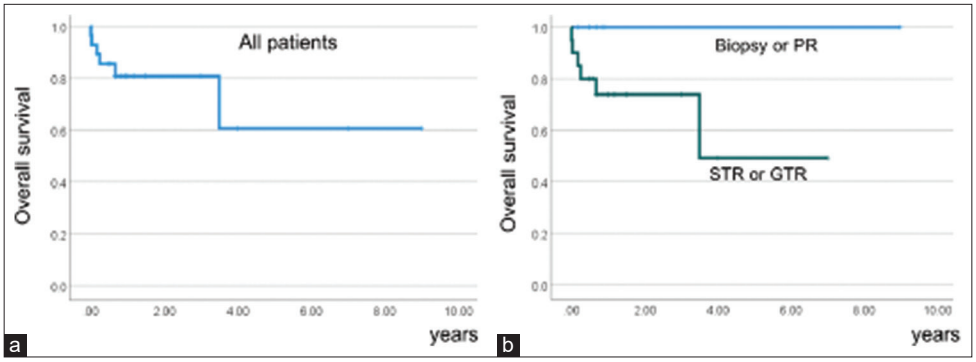
How to cite this article: Karita H, Koiso T, Muroi A, Sakamoto N, Zaboronok A, Ishikawa E. Preoperatively difficult-to-diagnose medulla oblongata germinoma: A case report and literature review. Surg Neurol Int 2023;14:366.

SUPPLEMENTARY

Supplementary Table 1: Summary of 30 cases of medulla oblongata germinoma, including our case.

Author	Age	Sex	Preoperative diagnosis	Operation	Chemotherapy	Radiotherapy	Outcome	Follow up
Saito *et al*., 1983	14	F	n.d.	GTR	No	Yes (n.d.)	Death	2 mos.
Poungvarin *et al*., 1991	17	M	n.d.	STR	No	Yes (n.d.)	Death (recurrent chest infection)	92 days
Hashimoto *et al*., 1992	19	M	n.d.	Biopsy	No	CS	CR	2 mos.
Tashiro *et al*., 1993	30	F	n.d.	STR	CDDP, VP-16	No	n.d.	14 mos.
Sugiyama *et al*., 1994	32	F	n.d.	PR	No	PF, WS	CR	9 yrs.
Israel *et al*., 1996	40	F	n.d.	STR	CDDP, VP-16, BLM	WV, Tumor bed	CR	18 mos.
Nakajima *et al*., 2000	18	F	n.d.	PR	CBP, VP-16	GK	CR	8 mos.
Yoshida *et al*., 2003	33	M	EPM	STR	CBP, VP-16	No	SD or more	7 mos.
Yen *et al*., 2003	16	F	n.d.	STR	No	PF, WS	CR	7 yrs.
Kakani *et al*., 2006	16	F	EPM, glioma, MB	STR	No	No	Death (sudden cardiac arrest)	12 days
Yang *et al*., 2009	12	M	n.d.	STR	CDDP, cyclophosphamide	Yes (n.d.)	CR	6 mos.
Akimoto *et al*., 2009	30	F	Highly malignant tumor	STR	Yes (n.d.)	Yes (n.d.)	CR	12 mos.
Akimoto *et al*., 2009	24	M	n.d.	PR	Yes (n.d.)	Yes (n.d.)	CR	8 mos.
Madden *et al*., 2009	12	M	Low-grade astrocytoma	STR	CBP, VP-16	CS, Boost (tumor)	CR	12 mos.
Madden *et al*., 2009	21	M	n.d.	GTR	CBP, VP-16, BLM	PF, Boost (tumor)	Death (disease)	3.5 yrs.
Neelima *et al*., 2010	24	F	n.d.	GTR	No	Yes (n.d.)	n.d.	n.d.
Yasuhara *et al*., 2011	27	F	EPM, astrocytoma, MB	PR	ICE	WV, Boost (tumor)	CR	11 mos.
Shuto *et al*., 2012	28	M	Glioma	STR	CBP, VP-16	PF, WS	CR	3 yrs.
Nakatsuka *et al*., 2012	31	F	n.d.	STR	CBP, VP-16	WV, residual tumor	CR	6 mos.
Hao *et al*., 2013	14	M	Glioma	STR	CDDP, VP-16, BLM	GK	CR	4 yrs.
Hao *et al*., 2013	22	F	EPM, glioma	STR	No	GK	Death (pneumonia)	8 mos.
Khan *et al*., 2013	25	F	EPM, PA, PNET	PR	No	CS, Boost (tumor)	Almost CR	10 mos.
Yip *et al*., 2014	22	F	MB, EPM	GTR	No	WV	CR	12 mos.
Budohoski *et al*., 2016	23	F	PA, MB, EPM	GTR	No	CS, Boost (PF)	CR	12 mos.
Garg *et al*., 2019	17	M	MB	STR	No	No	Death (sudden cardiac arrest)	5 days
Seifert *et al*., 2020	12	F	EPM, glioma, MB	GTR	CBP, VP-16	Yes (n.d.)	CR	18 mos.
Minh Thong and Minh Duc, 2020	12	M	EPM	GTR	Yes (n.d.)	Yes (n.d.)	Alive (n.d.)	1 week
Tai *et al*., 2021	25	M	EPM, MB, METs	STR	CDDP, VP-16	Yes (n.d.)	CR	8 mos.
Albiña *et al*., 2022	33	F	Glioma, EPM, meningioma	PR	No	WV, Boost (tumor)	CR	6 mos.
Present case, 2023	29	M	Low grade astrocytoma including PA	Biopsy	CBP, VP-16	WV, Boost (tumor)	CR	6 mos.

BLM: Bleomycin, Boost: Boost (to tumor, cavity or primary lesion) of irradiation, CBP: Carboplatin, CDDP: Cisplatin, CR: Complete remission, CS: Craniospinal, EPM: Ependymoma, VP-16: Etoposide, , F: Female, GK: Gamma knife, GTR: Gross total removal, , M: Male, MB: Medulloblastoma, METs: Metastatic brain tumors, mos.: Months, n.d.: No description, PF: Posterior fossa, PNET: Primitive neuroectodermal tumor, PR: Partial resection, PA: Pilocytic astrocytoma, SD: Stable disease, STR: Subtotal removal, WV: Whole ventricles, WS: Whole spine, yrs: years



Supplementary Figure 1: (a) A survival curve of all patients with previously reported medulla oblongata germinomas, including ours. (b) Survival curves of patients who underwent biopsy or partial resection (PR) and patients who underwent subtotal removal (STR) or gross total removal (GTR). ($P = 0.122$, logrank test).