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A rare occurrence of primary basal ganglia germinoma in an adult patient. A case report and literature review

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ABSTRACT

Background: Basal ganglia germinomas (BGGs) represent a diagnostic and management neurosurgical dilemma. Because of the rarity of these tumors in adults, the management strategies are not well defined.

Case description: A 24-year-old man was presented with progressive left-sided hemiparesis. Cranial computed tomography (CT) and magnetic resonance imaging (MRI) demonstrated a heterogeneous lesion with few microcystic nodules, seen involving the right basal ganglia with calcification. A stereotactic brain biopsy (SBB) was obtained. Histopathology revealed BGG. The patient received whole-brain radiation therapy (WBRT) and reported marked improvement in symptoms with no recurrence during a follow-up period of four years.

Conclusion: BGG should be considered a part of the differential diagnosis in young adults presented with hemiparesis and a heterogeneous lesion in the basal ganglia. Standard recommendations for the management of such rare lesions in adults are needed.

Keywords
basal ganglia,
germinoma,
radiation therapy

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INTRODUCTION

Intracranial germinomas represent 0.5 to 3% of all intracranial tumors. [2-4,5,7] They are mostly found in the pineal and suprasellar regions. [1-7] Rarely, they arise from the basal ganglia and are sparsely reported in the literature. [1-7] Adults with an established diagnosis of basal ganglia germinoma (BGG) are exceedingly rare. [5] Only thirteen cases of primary BGG have been reported to date. BGGs are difficult to treat due to their deep anatomical position inside the brain, making them rarely susceptible to total eradication. Management practices range from stereotactic brain biopsy (SBB) to partial or more aggressive resections and even empirical radiation without a prior histological diagnosis, plus radiation therapy (XRT) and chemotherapeutic agent administration. [1-5,7]

Adult BGGs have rarely been investigated in isolation. Thus, the natural history remains mostly undefined, and the therapeutic paradigms have not been standardized yet. This article is intended to discuss a good outcome for a young adult diagnosed with BGG, using a minimal intervention strategy. We also provide a review of the relevant literature.

Case description

A previously asymptomatic 24-year-old male was presented to our facility after experiencing five months of isolated progressive left-sided weakness. The vital signs and all other systemic clinical parameters were normal. The neurological evaluation was grossly intact aside from left-sided hemiparesis (Grade 4/5 Medical Research Council) and left-sided deep tendon hyperreflexia. His gait pattern was characterized by dragging his left foot while walking.

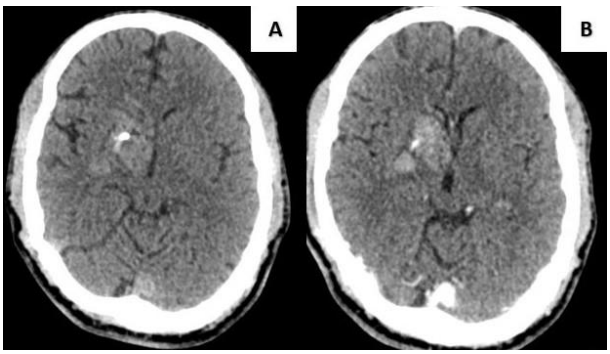

Figure 1. Preoperative cranial CT scan demonstrates a mildly hyperdense irregular lesion in the right basal ganglia with dense calcification (**A**) and a heterogenous, moderate enhancement in the postcontrast study (**B**).

Initially, a plain and intravenous contrast cranial computed tomography (CT) scan (Figure. 1) was performed, showing a mildly hyperdense lesion with moderate post-contrast enhancement and containing an area of calcification in the right basal ganglia. Cranial magnetic resonance imaging (MRI) demonstrated a heterogeneous signal intensity lesion with few microcystic nodules in the right basal ganglia with calcification on pre-contrast images (Figure. 2). The lesion showed mild hypointensity on T1-weighted images (Figure. 2A), hyperintensity on T2-weighted images (Figure. 2B) and fluid-attenuated inversion recovery images, and moderate heterogeneous patchy enhancement in postcontrast T1-weighted images (Figure. 2E). There was evidence of patchy restricted diffusion in diffusion-weighted imaging (Figure. 2C). After a negative comprehensive check-up, including spinal MRI, whole-body CT scan, HIV serology, ophthalmic examination, and positron emission tomography scan without abnormalities, amongst the differential diagnoses entertained was primary basal ganglia germinoma, followed by other less likely differentials of pilocytic astrocytoma, primitive neuroectodermal tumor, and cryptococcus meningitis.

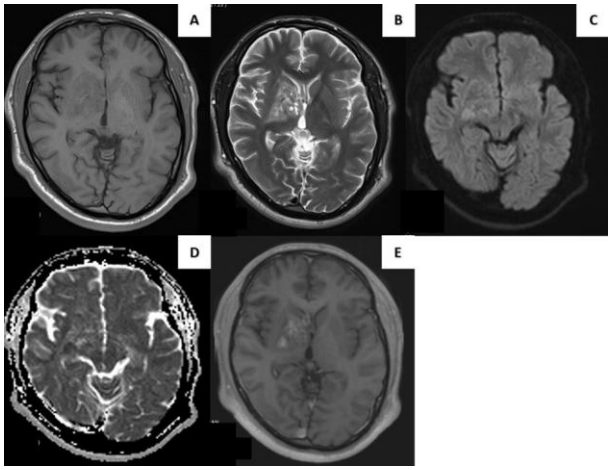

Figure 2. Preoperative cranial MRI demonstrates a right basal ganglia lesion with mild hypointensity on the T1-weighted sequence (**A**) and heterogeneous hyperintensity with microcystic nodules on the T2-weighted sequence (**B**). The lesion shows patchy restricted diffusion in the form of a patchy high signal with a high B value of DWI (**C**) and a low signal apparent diffusion coefficient (**D**). The lesion shows patchy enhancement in the postcontrast T1-weighted sequence (**E**).

SBB was performed on the patient. Histopathological evaluation (Figure. 3) revealed nests of neoplastic cells separated by thin fibrous septa. The neoplastic cells were large and polygonal with distinct eosinophilic cytoplasm and a vesicular nucleus with a conspicuous nucleolus. No fibrillary background, trophoblastic cells, rosette formation, or neutrophils were noted. Mitosis (2-4/HPF) and large areas of necrosis and hemorrhage were present in the tumor. There were a few scattered lymphocytes. The tumor cells were strongly and diffusely positive for placental alkaline phosphatase (PLAP), Beta-human chorionic gonadotropin (B-HCG), and CD117. However, they were negative for glial fibrillary acidic protein, synaptophysin, chromogranin, isocitrate dehydrogenase 1, oligodendrocyte transcription factor 2, S100, epithelial membrane antigen,

myogenin, CD 20, and CD 30. The Ki-67 index was 40-50%, and INI-1 was preserved. A diagnosis of basal ganglia germinoma was made based on histological findings.

The blood serum sample showed an elevated B-HCG of 563 mlU/mL and a normal alpha-fetoprotein (AFP) of 3.5 µg/L. The cerebrospinal fluid (CSF) sample showed an elevated B-HCG of 350 mlU/mL and a normal AFP of 1.1 µg/L. No atypical cells were detected in the CSF sample.

The patient received whole-brain radiation therapy (WBRT) using a volumetric modulated arch therapy technique with a total dose of 24 Gy in 15 fractions over four weeks, followed by a tumor boost of 16 Gy in 10 fractions over two weeks. Repeated blood serum, three months post-XRT, showed a normal B-HCG of 0.4 mlU/L. Over a four-year follow-up, the patient significantly improved after XRT and had no tumor recurrence on the MRI (Figure. 4).

Discussion

Adults with primary BGGs are uncommon, and their natural history and treatment are rarely the topic of published work.[5] We performed a literature search of the following databases on May 17, 2021: PubMed and Google Scholar. We included adult patients (age ≥ 19) with germinoma located in the basal ganglia (Striatum, Pallidum, Subthalamic nucleus, and substantia nigra) (Table. 1). Patients with a tumor mainly located in the thalamus were excluded from the review. Adding our case, thirteen patients were diagnosed with pure germinoma, and one patient was diagnosed with germinoma mixed with syncytiotrophoblastic giant cells. Six tumors were right-sided, six tumors were left-sided, and two tumors were bilateral. All of the patients were men. The median age at diagnosis was 24.5 years old (the range was 19-31 years)

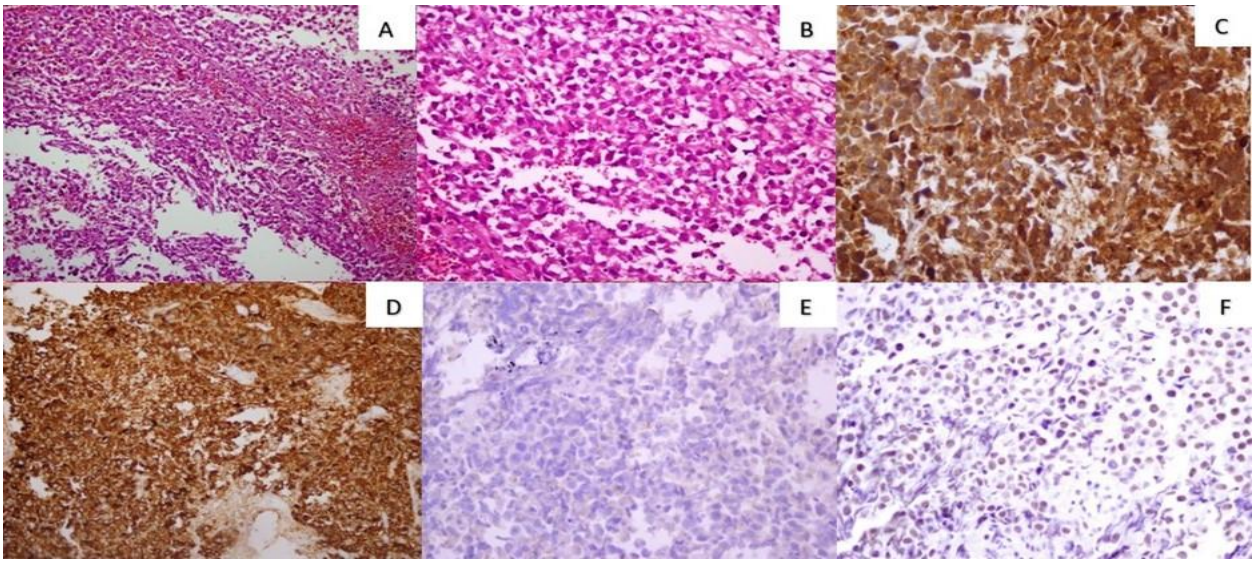

Figure 3. Histopathology of right basal ganglia germinoma. The lesion shows sheets of cells having abundant eosinophilic cytoplasm, pleomorphic nuclei with prominent nucleoli, 20x, 40x HE (A **& B**). The tumor cells are strongly and diffusely positive for B-HCG (**C**) and PLAP (**D**) immunostain and negative for synaptophysin (**E**). INI-1 is preserved (**F**).

Table 1. Clinical characteristics of reported adult cases of primary basal ganglia germinoma

Source	Age/Sex	Presentation	ICH signs ǂ	Duration (Months)	AFP (S/C)	HCG (S/C)
Elizabeth J et al. 2002	21/M	Hemiparesis, Speech difficulty	Yes	12	NA/NA	NA/NA
Sonoda Y et al. 2008	24/M	Hypokinesia	No	6.9	+/NA	-/NA
	31/M	Hemiparesis, Hypokinesia	No	6.9	-/-	-/-
	29/M	DI, Personality change	No	11.4	-/-	-/-

Phi JH et al. 2010	19/M	Hemiparesis	No	8	-/NA	-/NA
Lin JC et al. 2012	24/M	Bizarre behavior	No	0.5	-/NA	-/NA
Vialatte de Pemille C et al. 2016	21/M	Hemiparesis	No	NR	-/-	-/-
Wei X-H et al. 2016	31/M	Headache	Yes	NR	-/NA	NA/NA
	19/M	Hemiparesis	No	NR	-/NA	+/NA
	21/M	Hemiparesis, Polydipsia	No	NR	-/NA	-/NA
	30/M	Hemiparesis	No	NR	-/NA	-/NA
	29/M	Hemiparesis	No	NR	-/NA	-/NA
Woo PYM et al. 2017	21/M	Hemiparesis	No	24	-/NA	-/NA
Our case, 2021	24/M	Hemiparesis	No	5	-/-	+*/+*

ǂ ICH signs reported: Headache, Vomiting, dysphagia, Papilloedema 6th cranial nerve palsy.
**beta subunit of HCG*

Keywords: M: male; ICH: Intracranial hypertension; NR: Not reported; S: serum; C: Cerebrospinal fluid; NA: Not applicable; -: normal level; +: High level, DI: Diabetes insipidus.

Table 2. Magnetic resonance imaging findings before stereotactic brain biopsy of reported adult cases with primary basal ganglia germinoma

Source	MRI Findings						
	Enhancement	Mass effect	Hemorrhage	Cyst formation	Calcification	DR	Other
Elizabeth J et al. 2002	+	+	+	+	NR	NR	Multiple lesions
Sonoda Y et al. 2008	+	+	-	-	-	NR	-
	+	-	-	-	-	NR	-
	+	+	-	-	-	NR	Multiple lesions
Phi JH et al. 2010	-	-	-	-	-	NR	Bilateral
Lin JC et al. 2012	+	-	NR	+	NR	NR	Bilateral
Vialatte de Pemille C et al. 2016	+	-	NR	NR	NR	NR	Multiple lesions
Wei X-H et al. 2016	+	+	-	+	NR	NR	CA, multiple lesions
	NR	+	-	+	NR	Yes	CA, multiple lesions
	+	-	-	+	NR	Yes	CA, multiple lesions
	+	-	-	+	NR	NR	CA, multiple lesions
	+	+	-	+	NR	NR	Multiple lesions
Woo PYM et al. 2017	NR	+	+	+	NR	Yes	Early CA
Our case, 2021	+	+ *minimal*	-	+	+	Patchy	None

Keywords: NR: Not reported; DR: Diffusion restriction; CA: cerebral atrophy.

Table 3. Treatment protocols and outcome of adult patients with primary basal ganglia germinoma

Source	SBB	Surgery	XRT					CTX	Outcome	Recur -rence
			Type	Total (Gy)	Fractions	Duration (weeks)	Boost (Gy/Fractio-ns/weeks)			
Elizabeth J et al. 2002	No	TR	Yes (Type NR)	NR	NR	NR	NR	Yes	Minimal improvem ent	No

Sonoda Y et al. 2008	Yes	No	LB	60	NR	NR	NR	Yes	Partial response	No
	Yes	No	No	-	-	-	-	Yes	Complete response	Yes
	Yes	No	No	-	-	-	-	Yes	Complete response	Yes
Phi JH et al. 2010	Yes	No	BG + WV	50.4 + 36	NR	NR	NR	Yes	Complete remission	No
Lin JC et al. 2012	Yes	No	CSRT	NR	NR	NR	NR	Yes	Complete resolution	No
Vialatte de Pemille C et al. 2016	Yes	No	CSRT	24	NR	NR	16/NR/NR	No	NR	NR
Woo PYM et al. 2017	No	NTR	CSRT	NR	NR	NR	NR	Yes	Complete resolution	No
Our case, 2021	Yes	No	WBRT	24	15	4	16/10/2	No	Mark improvement	No

Keywords: SBB: Stereotactic brain biopsy; TR: Total resection; LB: Local brain; BG: Basal ganglia; WV: Whole ventricle; NTR: Near-total resection; NR: Not reported; XRT: Radiation therapy; CSRT: Cerebrospinal radiation therapy; WBRT: Whole-brain radiation therapy; CTX: Chemotherapy.

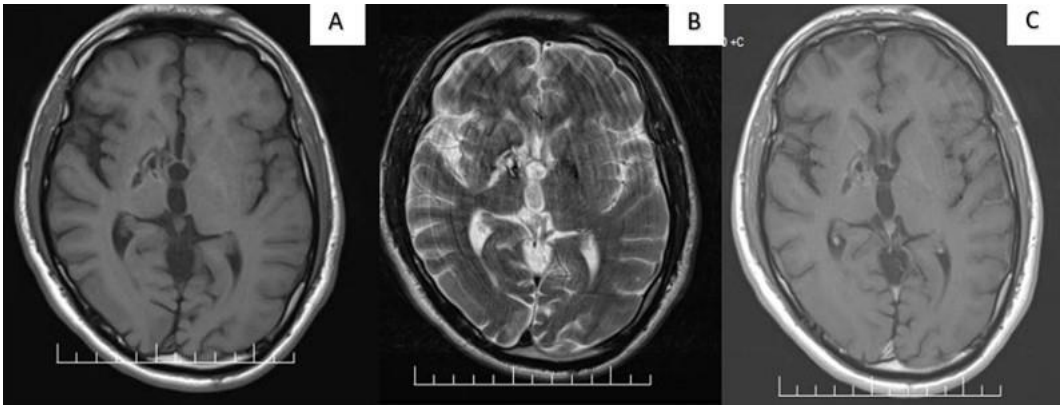

Figure 4. Cranial MRI of the previously treated basal ganglia germinoma at the last follow-up demonstrates stable disease with surrounding gliosis and post-radiation changes with secondary ex-vacuo dilation of the ipsilateral frontal horn of the lateral ventricle in T1 and T2-weighted images (A **& B**). No new lesion was detected in the post-contrast T1-weighted image (**C**).

Presenting symptoms included hemiparesis (71.4%), hypokinesia (14.2%), psychiatric symptoms (14.2%), diabetes insipidus (14.2%), headache (7.14), and speech difficulty (7.41%). Signs and symptoms of increased intracranial pressure such as headache, vomiting, papilledema, dysphagia, and sixth cranial nerve palsy were found in two patients at the initial presentation. Diabetes insipidus due to the coexisting suprasellar lesion was evident in two patients. At the onset of symptoms, patients seek medical attention after a median of 9.3 months (range: two weeks to two years). Serum AFP and HCG were measured in (13/14) cases. Elevation of serum AFP and HCG was detected in one patient and two patients, respectively. CSF testing for AFP and HCG was not routinely performed.

In all patients, cranial MRI was required for radiological diagnosis (Table. 2). Eight patients had multiple lesions - in the internal capsule (4 cases), thalamus (3 cases), frontal lobe (2 cases), septum pellucidum (1 case), pineal (1 case), suprasellar (2 cases), corpus callosum (1 case), frontotemporal gyri (1 case) regions, as well as the basal ganglia. In five individuals, the initial study revealed ipsilateral cerebral hemiatrophy, indicating wallerian degeneration. The patterns seen in the MRI were varied and were related to the duration of the disease before admission. The MRI patterns ranged

from a subtle patchy lesion seen in the T2-weighted sequence with no contrast enhancement to a large lesion with a mass effect and vivid contrast enhancement. Some BGGs displayed hemorrhagic and cystic components or calcification. Hydrocephalus was evident in four cases.

Reported therapeutic strategies are outlined in (Table. 3). SBB was performed in seven cases and craniotomy in two (reported 1 Transylvanian approach) patients. Postoperative imaging in craniotomy patients revealed one complete resection and one near-total resection. Seven patients received XRT (3 craniospinal, 1 whole-brain, 1 basal ganglia with whole-ventricle, and 1 local brain technique). Seven cases received platinum-based antineoplastic regimens to mitigate XRT toxicity. However, chemotherapy alone did not seem to improve survival.

Follow-up imaging (> 3 months) was available for eight patients. While most reported marked improvement in symptoms, some reported poor neurological outcomes. In general, all treated tumors by XRT tend to show no recurrence on subsequent imaging or progression to the contralateral side.

Our patient, for example, is notable for being: 1. diagnosed in an adult patient, 2. diagnosed in a middle Eastern patient, 3. located in the basal ganglia, 4. not associated with ipsilateral cerebral atrophy, and 5. successfully managed with a minimal treatment strategy, 6. showed no recurrence during the follow-up period. As far as we know, such a case has never been described before.

Conclusion

BGGs are rare entities, and a high degree of suspicion is needed for their diagnosis, especially in young adults with hemiparesis and a heterogeneous basal ganglia lesion on cranial MRI. Early detection of such lesions is critical, as a delay in intervention may result in poor neurological recovery. SBB followed by WBRT seems to be a minimal and safer treatment strategy for managing such lesions.

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