CASE REPORT

A state of art management of a bilateral basal ganglia germinoma: case report

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Abstract

Central nervous system germinomas are the most frequent germ cell tumors, predominantly affecting adolescents and young adults. They are generally midline tumors primarily located in the pineal gland and suprasellar regions. Basal ganglia germinomas (BGGs) are rare and generally unilateral, with only 16 histopathologically-confirmed bilateral BGGs reported to date. In this paper, we are presenting a rare case of bilateral BGG in a 14-year-old boy. The neuroradiological findings of bilateral BGGs are presented, and the strategy for their management is discussed while considering previously reported cases. A 14-year-old suffering from involuntary jerking movements of the right shoulder and arm was referred to our department. An MRI scan revealed diffuse T2/FLAIR hyperintensity in the bilateral basal ganglia, and MR spectroscopy suggested a malignant disease. A stereotactic biopsy was performed, and the histologic examination revealed germinoma. Neoadjuvant chemotherapy followed by whole ventricular radiation therapy with a boost to the tumor was initiated. Although BGGs are mostly unilateral, bilateral entities are rarely seen. Despite excellent survival rates, symptomatic outcomes may be unfavorable. Therefore, it is crucial to recognize the initial MRI findings and diagnose these tumors early to maximize symptomatic relief while minimizing complications.

Keywords: basal ganglia; germinoma; intracranial; stereotactic biopsy.

DOI: https://doi.org/10.55005/sjns.v1i1.7

Introduction

Central nervous system germinomas are the most frequent germ cell tumors (GCTs), predominantly affecting adolescents and young adults, with the overwhelming majority diagnosed under 20 years of age[1]. A strong male predominance is observed. GCTs are generally midline tumors primarily located in the pineal gland and suprasellar regions and spreading along the ventricular surfaces. However, basal ganglia germinomas (BGGs) are rare and generally unilateral, comprising approximately 5-10% of intracranial germinomas[2].

In this case report, we describe the clinical characteristics, imaging examinations, pathological characteristics, management, and outcome of an unusual case of bilateral BGG, as well as provide a literature review.

Case report

A previously healthy 14-year-old boy presented with involuntary jerking movements of his hand and right shoulder with progression over eight months. He also experienced headache, right eye twitching, loss of balance, forgetfulness, and word-finding difficulty.

An outpatient neurological evaluation was performed, and head magnetic resonance imaging (MRI) findings were unremarkable. One year later, he underwent a repeat cranial MRI due to progressive symptoms, and a bilateral cystic mass was visualized at the bilateral basal ganglia. He was then referred to our clinic for a stereotactic biopsy.

On admission, neurological examination revealed grade 3/5 right hand flexion, myoclonus of the right fingers, and right-sided eye twitching. No cognitive deterioration was noted. There was no family history of neurologic disorders in terms of neurodegenerative or metabolic diseases. Laboratory data, including serum AFP and β-hCG levels, were unremarkable.

A presurgical MRI revealed bilateral basal ganglia lesions along the 3rd ventricle associated with the anterior commissure. The lesion involved bilateral septa formations with multiple compartments. Post-contrast images showed intense peripheral enhancement. Perfusion-weighted images revealed increased perfusion parameters, most prominent in the peripheral and septal parts of the lesions.

Based on the negative tumor markers and imaging parameters, germinoma of the basal ganglia was suspected. Stereotactic biopsy of the lesion at the level of the right basal ganglia was performed (***Figure 1***).

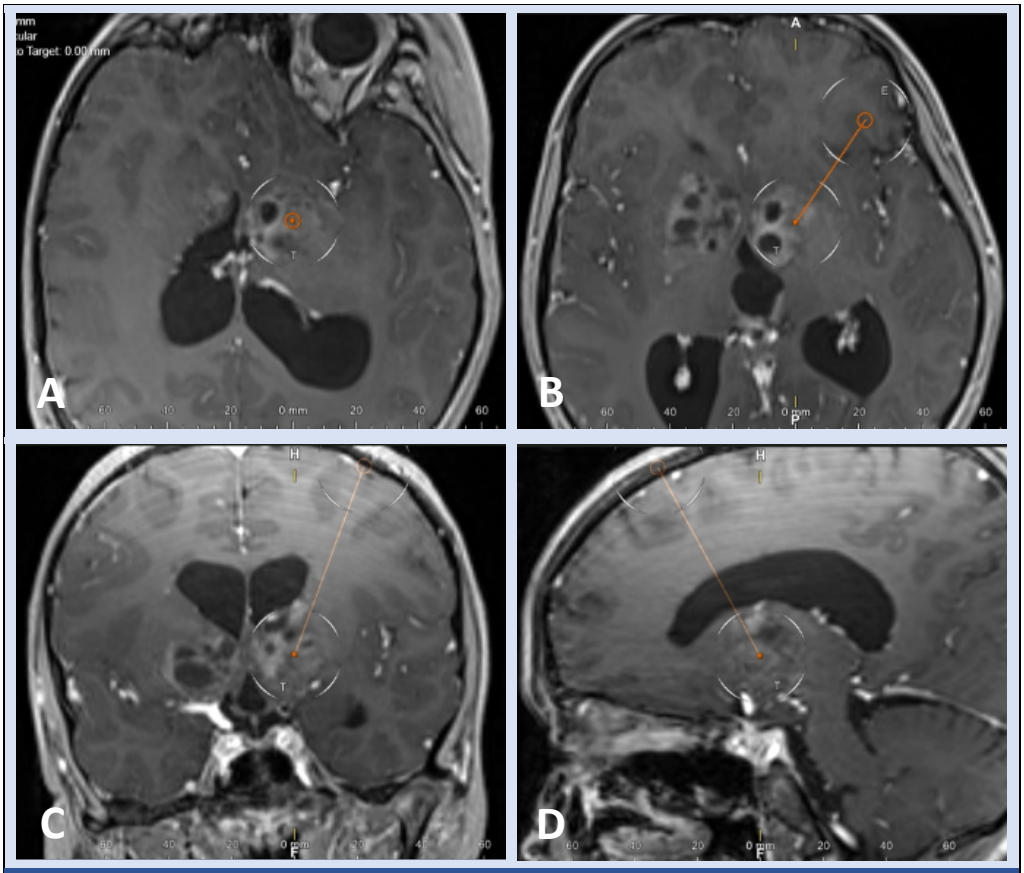

Figure 1. Stereotactic biopsy planning of the lesion located in the right basal ganglia. A. Oblique. B. Axial. C. Coronal. D. Sagital.

Histopathological investigation was consistent with germinoma. Immunohistochemical studies showed expression of SALL4, CD117, and OCT4 in tumor cells (***Figure 2***).

After the definitive pathological diagnosis, neoadjuvant chemotherapy (CTx) with carboplatin and etoposide, followed by whole ventricular radiotherapy (RT) with a boost to the tumor, was initiated. The patient remained alive at the time of writing this article with unchanged symptoms.

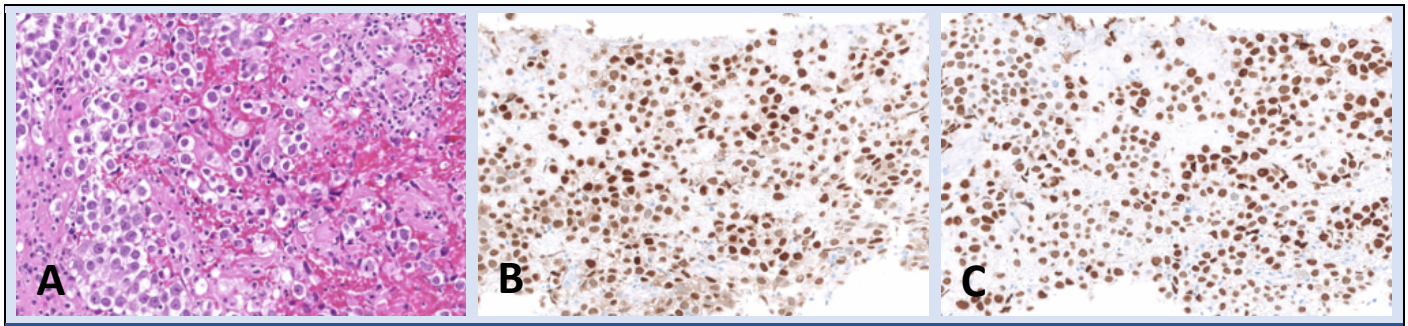

Figure 2. Hematoxylin & eosin-stained section prepared from the stereotactic biopsy specimen demonstrates a high-grade tumor composed of polygonal cells with pale/clear cytoplasm and large nuclei with prominent nucleoli A. Immunohistochemical studies revealed positivity with B. OCT4 and C. SALL4 antibodies. (Scale bar = 50 μm).

Discussion

Germinomas are the most common GCTs. Entrapment of the migrating totipotent cells during neural tube growth is considered the underlying etiology of germinomas[3]. According to the literature, the incidence of germinoma is higher in Japan and far East Asia than in western countries, with a male predominance (male-to-female ratio 20:1)[4,5]. Most of the patients are adolescents or young adults at the time of the diagnosis[1]. The most frequent locations for germinomas are pineal and suprasellar regions. BGGs are very rare, and bilateral BGGs are even more rare.

A literature review using PubMed with search terms "bilateral," "basal ganglia," "germinoma," and "germ cell tumor" revealed only 11 papers reporting 22 cases of bilateral BGGs (only 16 histopathologically-confirmed) in the English literature to date (***Table 1***)[5-15]. Kobayashi et al.[6] reported the first cases of bilateral BGGs in two boys aged 14 and 13 years in 1989. Both cases were managed with whole skull irradiation without definitive tissue diagnosis. Recently, Huang et al. [15] reported a similar case in a 8-year-old boy who presented with mild cognitive impairment, involuntary movement of his right arm, increased muscle tone of bilateral extremities without muscle weakness, and signs of precocious puberty.

Table 1. General characteristics of previously reported histopathologically-confirmed bilateral basal ganglia germinoma[5-15]

Reference	Age	Gender	Tumor location	Duration of symptoms (months)	Symptoms/Signs
Kobayashi et al., 1989	14	M	Bilateral basal ganglia	11	Slowly-progressing left hemiparesis, followed by personality and mental changes, bilateral dystonic-athetoid movements, hydrocephalus
Wong et al., 2008	13	M	Bilateral basal ganglia, thalamus	20	Left hemiparesis, drooling, speech disturbances, dysphagia, lethargy
Sonoda et al., 2008	8	M	Bilateral basal ganglia	7	Precocious puberty
Rossi et al., 2008	14	M	Bilateral basal ganglia	NA	Right hemiparesis, speech disturbance, hypertonia, hyperreflexia, mental deterioration
Ji Hoon Phi et al., 2010	13	M	Bilateral basal ganglia	30	Hemiparesis, bulbar sign, abnormal behavior, hiccup, and vomiting
	15	M	Bilateral basal ganglia	13	Hemiparesis, hiccup, and vomiting
	19	M	Bilateral basal ganglia	8	Hemiparesis, bulbar sign
	13	F	Bilateral basal ganglia, subependymal seeding	3	Hemiparesis, bulbar sign, abnormal behavior, memory disturbance, poor school performance
Tso et al., 2014	14	M	Bilateral basal ganglia, thalamus, periventricular region	12	Cognitive disturbance
Wataya et al., 2015	15	M	Bilateral basal ganglia	8	Tetraparesis, cognitive disturbance, mask-like face, speech disturbance, urinary/bowel incontinence
Konovalov et al., 2016	14	M	Bilateral basal ganglia	6	Tetraparesis, hypertonia, fatigue, drowsiness, speech disturbance
Nodomi et al., 2017	14	M	Bilateral basal ganglia	12	Left hemiparesis
Kang et al., 2020	10	M	Bilateral basal ganglia	N/A	N/A
	12	M	Bilateral basal ganglia	N/A	N/A
	19	M	Bilateral basal ganglia	N/A	N/A
Huang et al., 2020	8	M	Bilateral basal ganglia	24	Walking and writing disorders, cognitive decline, speech disturbance, nocturnal enuresis, polydipsia, polyuria, precocious puberty, and thermoregulatory problems
Present study	14	M	Bilateral basal ganglia	8	Involuntary movements of right shoulder and hand, right eye twitching, loss of balance, forgetfulness, speech disturbance, headache

The clinical presentation depends on the tumor's location and includes hemiparesis, raised intracranial pressure; hydrocephalus; Parinaud's syndrome; diabetes insipidus; visual disturbance; pituitary failure; precocious puberty; and speech, behavioral or psychiatric disturbances[1,11]. According to the literature, the duration of the symptoms in patients with bilateral BGG varies between 3 to 24 months, with a mean duration of 14 months. This indicates that the clinical course of this tumor group is generally slow, and that early diagnosis is mostly challenging.

Neuroimaging has a vital role in the diagnosis of germinomas. Although conventional imaging is rarely sufficient for diagnosis, germinomas are well-delineated and isointense to hypointense to gray matter on T1-weighted images, and isointense or hyperintense on T2-weighted images. Germinomas usually show strong and uniform contrast enhancement. As germinomas are highly cellular, most demonstrate significantly restricted diffusion[16]. The CT and MRI findings of BGGs are somewhat distinct from those of the pineal and suprasellar regions in terms of tumor size, cystic changes, and intratumoral hemorrhage.

Table 2. Management of previously reported histopathologically-confirmed bilateral basal ganglia germinoma[2,6-15]

Reference	Surgery	Chemotherapy	Radiation therapy	Outcome	Recurrence	Follow-up (months)
Kobayashi et al., 1989	Open biopsy + cyst evacuation	N/A	WBRT: 40.2 Gy	Mild left hemiparesis and involuntary movements, unchanged mental state, improved level of consciousness	None	24
Wong et al., 2007	STR	N/A	LBRT: 49.9 Gy; WBRT: 27.9 Gy	Tumor free, hemiplegia, slurring speech	None	153
Sonoda et al., 2008	STX biopsy	ICEx3	WBRT: 24 Gy	Cured	None	46
Rossi et al., 2008	STX biopsy	ICEx4	CSI: 24 Gy, WBRT: 16 Gy	Neurological deficits unchanged	None	16
Ji Hoon Phi et al., 2010	STX biopsy	CCG 9931	LBRT (BG): 54 Gy, WVRT: 54 Gy	Deteriorated motor functions	N/A	35†
	STX biopsy	KSPNO	LBRT (BG): 27 Gy, CSI: 23.4 Gy	Motor deficits unchanged	None	43
	STX biopsy	BEP	LBRT (BG): 50.4 Gy, WVRT: 36 Gy	Motor deficits unchanged	None	13
	STX biopsy	BEP	BG: 54 Gy, WB: 36 Gy, CSI: 21 Gy	Deteriorated motor functions	None	42
Tso et al., 2013	STX biopsy	N/A	N/A	Mild mental retardation, dystonia, and bradykinesia	None	N/A
Wataya et al., 2015	Open biopsy + ETV	CAREx3	WBRT: 24 Gy	Increased speech and activity, improved urinary incontinence	None	N/A
Konovalov et al., 2016	GTR	N/A	N/A	Improved activity level, regressed retardation, motor deficits unchanged	None	84
Nodomi et al., 2017	STX biopsy	ICE	WBRT: 24 Gy	Cured	None	10
Kang et al., 2020	STX biopsy	No	WVRT: 30 Gy + PB: 24 Gy	Cured	None	22
	STX biopsy	Yes, not known	CSI: 23.4 Gy + PB: 24 Gy	Cured	None	74
	STX biopsy	Yes, not known	CSI: 19.8 Gy + PB: 24 Gy	Cured	None	71
Huang et al., 2020	STX biopsy	N/A	N/A	Symptoms unchanged	N/A	N/A
Present study	STX biopsy	CARE	WVRT: 30 Gy + PB: 24 Gy	Symptoms unchanged	None	6

STR: subtotal resection, **GTR**: gross-total resection, **STX**: stereotactic, **ETV**: endoscopic third ventriculostomy, **ICE**: ifosfamide+cisplatin+etoposide, **BEP**: bleomycin+etoposide+cisplatin, **CARE**: carboplatin+etoposide, **CYCE**: cyclophosphamide+etoposide, **CCG**: Children's Cancer Group, **KSPNO**: Korean Society for Pediatric Neurooncology, **CSI**: craniospinal irradiation, **PB**: primary boost, **WBRT**: whole brain radiation therapy, **WVRT**: whole ventricle radiation therapy, **BG**: basal ganglia, **LB**: local brain, **SS**: suprasellar, **P**: pineal, **N/A**: not available, †: patient died

The initial appearance of BGGs on CT scan is that of an irregularly defined, isodense or slightly hyperdense lesion with no mass effect[17,18]. A single calcified spot may occur first, appearing several years prior to diagnosis. MRI findings of BGGs vary. Early MR images demonstrate lesions that are mostly ill-defined, homogenous with subtle or no contrast enhancement, similar to cerebral infarctions or gliomas. However, as the disease progresses, greater contrast enhancement, internal capsule invasion, mass effect, peritumoral edema, and cystic and necrotic changes can be seen[2,9,10,17,18]. Furthermore, CT and MRI findings of ipsilateral cerebral, basal ganglia, and brainstem atrophy are common features of BGGs[19,20]. Ipsilateral cerebral hemiatrophy is due to Wallerian degeneration of thalamus and basal ganglia afferent fibers and retrograde degeneration of efferent fibers due to the damage and loss of ganglia cells and nerve fibers caused by tumor invasion and infiltration[1,19]. Cystic structural changes are thought to originate from previous hemorrhages as well as tumor enlargement and disease progression[2,20]. BBGs, however, also represent a diagnostic problem to many clinicians without these apparent imaging features. For instance, in the study by Tso et al.[10], two of the five cases were initially misdiagnosed as cerebral infarction. Definitive diagnosis was established with further imaging studies when the symptoms worsened. To overcome uncertainty in diagnosis, some other studies suggest the use of C-methionine PET that supports the MRI findings [21]. Along with the imaging modalities, serum tumor markers have a somehow limited but useful function because of the non-invasive nature[11,22].

A tissue diagnosis, through biopsy or a more aggressive surgical approach, is the accepted method of diagnosis of germinomas. After histologic diagnosis, germinomas have a high potential for curative treatment with RT. RT alone in relatively high doses and volumes frequently affords a curative choice for most patients. However, the late effects of RT have urged investigators to examine the efficacy and safety of adjuvant CTx to reduce the RT dose or field and the associated morbidity while maintaining the excellent overall survival (OS)[23,24]. The current proposed treatment includes four cycles of CTx with carboplatin and etoposide succeeded by lower dose whole ventricular RT with a boost to the tumor[25].

The outcome for subjects with germinomas is highly favorable, and several trials reported a 5-year OS of over 90%. Lesion size and pathological classification influence OS in GCTs[26]. While pineal germinomas are usually diagnosed earlier due to distinctive symptoms, BGGs are generally detected at a later stage with larger tumors due to mild or non-specific symptoms. It might be expected that BGGs would have a worse prognosis compared to pineal counterparts. However, previous studies of BGGs also revealed good OS and prognosis with CTx and RT. Among the bilateral BGGs in the literature, only Phi et al.[9] reported that one patient died after 35 months of follow-up (***Table 2***). This article also stated that treatment with only CTx frequently leads to tumor recurrence[10]. Even after treatment, symptoms generally remain unchanged, with deteriorated motor functions and cognitive and behavioral disturbances[9]. Improvement in these symptoms is strongly dependent on their severity, which is correlated, to some extent, with the diagnostic and treatment delay. For this reason, early diagnosis is crucial to maximize the potential for symptomatic improvement.

Conclusion

BGGs are mostly unilateral, but bilateral entities are also rarely seen. Despite excellent survival rates, symptomatic outcomes are often ufavorable. It is crucial to recognize the initial MRI findings and diagnose these tumors early to maximize symptomatic relief while minimizing complications.

Disclosures

Conflict of Interest: All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (**Koç University, 2020.190.IRB1.058**) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from the parents of the patient.

Funding: No funding was received for this research.

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