Basal Ganglia Germinomas in Children. Four Clinical Cases and a Literature Review


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Basal ganglia germinomas are a specific group of intracranial germinomas. Their early diagnosis is complicated due to their atypical localization and diversity of neuroimaging and clinical signs. Material and methods. We describe 4 cases of basal ganglia germinomas in boys of 11, 14, 15, and 16 years of age. The medical history data, clinical features, neuroimaging and histological characteristics of basal ganglia germinomas, and preliminary results of the treatment are presented. Conclusions. Basal ganglia germinomas are usually verified at the late stage of the disease when patients are detected with extended lesions of the basal ganglia and severe neuroendocrine and neurological deficits. This situation is associated with clinical and imaging signs that are atypical of common germinomas.

Keywords: basal ganglia germinoma, clinical signs, diagnosis.

Intracranial germinomas account for up to 0.5—2.1% of primary brain tumors [1—3]. In most cases, the disease develops in male adolescents, occurring several times more often in the Asian population than in the European one. Germinomas are usually localized in the pineal or suprasellar regions [2, 4]. The dominant symptoms usually include vision impairment and endocrine disorders if the disease is localized in the chiasm-sellar region, and symptoms of intracranial hypertension and midbrain lesions (Parinaud syndrome) when the disease is localized in the pineal region. However, germinomas have an unusual localization in the basal ganglia in 5—10% of cases [5, 6].

Germinomas are characterized by a variety of MRI manifestations — from subtle diffuse changes in the MRI signal to a large delineated space-occupying lesion uptaking a contrast agent [6—9]. Diagnosis of basal ganglia germinomas is often difficult. This is due to the localization and clinical signs atypical of this pathology. MRI at the early disease stage may miss the pathology, or the tumor looks like small lesions similar to foci of demyelination or ischemia. This is often the reason for the late diagnosis of basal ganglia germinomas [3, 9].

If germinoma is suspected, surgical treatment is limited to interventions aimed at sampling histological material and resolving intracranial hypertension because the tumor is highly sensitive to radiotherapy and chemotherapy. The prognosis for germinomas is favorable, with the overall five-year survival rate amounting to >90% [1, 4]. In the case of small germinomas of the suprasellar localization with a short disease history, many of the clinical disease symptoms regress after treatment. In particular, patients may develop vision improvement and recovery of the pituitary function. However, treatment outcomes for germinomas of an atypical localization are worse: neurological symptoms can persist after achieving disease remission, which is a consequence of the late diagnosis [9]. In this connection, the early diagnosis and correct approach to treatment of suspected basal ganglia germinoma are of great importance.

Here, we present 4 clinical cases of basal ganglia germinomas in children, which were verified by stereotactic biopsy (STB) and open tumor biopsy.

Case 1
A 15-year-old male patient Z. was sick since 2009 (since the age of 10 years) when he developed headaches, recurrent vomiting, transient weakness in the right extremities, thirst, and polyuria of up to 10 liters per day. An examination at the place of residence revealed hearing loss on the right and diabetes insipidus. MRI of the brain in 2009 did not detect any pathology (Fig. 1). The patient was prescribed desmopressin.

Two years later (2011), the patient developed a transient tremor of the right arm, dysarthria, disrupted behavior, and reduced self-criticism. In 2012, the patient experienced weakness of the facial muscles on the right, muscle weakness and decreased sensation in the right extremities, fatigue, and polyuria of up to 10 liters per day. An examination at the place of residence revealed hearing loss on the right and diabetes insipidus. MRI of the brain in 2013 revealed a space-occupying lesion of the basal ganglia on the left. In May 2013, the patient was hospitalized to the Neurosurgical Institute for stereotactic biopsy of a diffuse tumor of the basal ganglia and verification of the diagnosis. An endocrinological examination revealed, in addition to diabetes insipidus, panhypopituitarism (growth hormone deficiency, secondary hypothyroidism, hypocortisolism, hypogonadism) and hyperprolactinemia. The patient received replacement therapy with hydrocortisone and L-thyroxine. Given the characteristic endocrinological symptoms, a germinal tumor was suspected. However, a repeated MRI examination detected a decrease in the lesion size and increased strength in the right arm and leg. No signs of infiltration of the pituitary funnel or stalk were detected; signs of a partially empty sella were observed (Fig. 2). The cause of this phenomenon was not clear because the patient did not receive hormone therapy.
Given the MRI-revealed positive changes, the patient was discharged for further follow-up.

Since January 2014, right hemiparesis was worsened. MRI of the brain (June 2014) revealed a significant increase in the size of a basal ganglia tumor on the left (Fig. 3a–c) as well as foci of an altered T2 signal in the pituitary funnel projection, without clear accumulation of a contrast agent (Fig. 3d).

The clinical picture at admission to the Neurosurgical Institute demonstrated decreased muscle strength in the right extremities to 3 points, impaired surface sensitivity on the right, central type paresis of the facial nerve on the right, deafness on the right; neuroendocrine symptoms in the form of panhypopituitarism and diabetes insipidus; emotional and personality disorders in the form of reduced self-criticism, disinhibition, and euphoria. Levels of blood tumor markers AFP and b-hCG were within reference values.

The patient underwent stereotactic biopsy of the tumor. The histological diagnosis was germinoma. Positive expression of PLAP (placental alkaline phosphatase) and SD117 and negative expression of AFP and hCG were detected (Fig. 4).

The patient received 4 cycles of polychemotherapy according to the protocol “Germinoma-2008” (80 mg/m² of etoposide, days 1—4; 25 mg/m² of cisplatin, days 1—4) and stereotactic radiotherapy on a “Primus” device (12 fractions of 2 Gy, TBD of 24 Gy).

According to the neurological status, an increase in the strength of the right arm and leg was observed. Control MRI revealed a complete involution of the tumor and atrophic changes in the subcortical region on the left (Fig. 5).

Brain tissue atrophy was observed at the site of a basal ganglia germinoma lysed due to chemo- and radiation therapy.

**Case 2**

A 13-year-old male patient E. was followed-up by a neurologist because of psychomotor retardation since an early age. Ambiopia developed in March 2012. The patient underwent first MRI in August 2012, which revealed no pathology. Planned MRI in January 2013 revealed a minor change in the signal in the left subcortical region. At that time, transient mild weakness in the right arm and leg developed. The patient was followed-up at the place of residence. In autumn 2013, thirst, polyuria of up to 9 liters per day, and weight loss developed. The patient was examined by a local endocrinologist who excluded diabetes mellitus and did not diagnose diabetes insipidus. Compulsive movements in the right arm developed since January 2014. Control MRI (June 2014) revealed a tumor lesion of the subcortical structures on the left (Fig. 6). An examination at the Neurosurgical Institute detected: right hemiparesis (4 points); right extrapyramidal symptoms in the form of involuntary athetoid-like movements of the right extremities; behavioral disorders in the form of disinhibition, foolishness, reduced self-criticism, and euphoria; neuroendocrine symptoms (diabetes insipidus, secondary hypocortisolism, growth hormone deficiency). The patient received replacement therapy with desmopressin and hydrocortisone, which resulted in a significant improvement in the general patient’s state. Blood tumor markers (AFP and b-hCG) were within the normal range.

The patient underwent stereotactic biopsy of the tumor.

The histological diagnosis was as follows: small fragments of glial tissue with lymphoid infiltrates and single large cells expressing PLAP and SD117. Expression of AFP and b-hCG was negative. The morphological picture corresponded to germinoma.

A diffuse neoplastic lesion was observed in the lenticular nucleus region. The lesion had a hypointense T1 signal (a) and a hyperintense T2 signal (b). The tumor had focal accumulations of a contrast agent (c). The pituitary stalk was not thickened (d).

The patient was transferred to a specialized department for chemotherapy. Control brain MRI after the second cycle of chemotherapy revealed a significant reduction in the tumor size (Fig. 7). A significant reduction in the basal ganglia tumor on the left and formation of a replacing CSF cyst were observed in association with administered chemotherapy.

**Case 3**

A 14-year-old male patient Z developed involuntary movements of the right foot toes in summer 2006. In November 2006, the patient had episodes of weakness in the right extremities. Also, general weakness, fatigue, and drowsiness developed over time. MRI of the brain (December 2006) revealed a bilateral space-occupying lesion of the basal ganglia, with a large node on the right. Worsening of cerebral symptoms and recurrent vomiting developed over time. Somewhat later, the patient stopped talking and experienced increased weakness in the right extremities. The patient underwent decongestant and dehydration therapy at the place of residence. Control CT and MRI studies revealed an increase in the basal ganglia tumor size, expansion of the ventricular system, and periventricular edema (Fig. 8a, b).

There were detected bilateral tumors of the basal ganglia with a large node in the projection of the anterior thalamus and right caudate nucleus head and with a small node in the left lenticular nucleus. The tumors had a heterogeneous structure with hemorrhagic foci and calcifications. The tumors intensively accumulated a contrast agent. The ventricular system was expanded, with periventricular edema (a, b). Postoperative CT (c)

![Figure 1. T2-weighted MRI in the axial plane. There are no pathological signs.](image)
Figure 2. MRI reveals a small lesion with a hypointense T1 signal (a) and a hyperintense T2 signal (b) in the lenticular nucleus projection on the left. Minor contrast agent uptake is observed (c). The pituitary stalk is not changed (d).

revealed total resection of the right tumor and a small calcificated tumor on the left. The ventricular system decreased in size.

The clinical picture at admission to the Neurosurgical Institute (March 2007) was as follows: pronounced hypertensive syndrome with choked disks; tetraparesis, more pronounced on the right; extrapyramidal syndrome in the form of increased muscle tone in the right extremities (of the plastic and “thalamic hand” type on the right) and intention tremor on the left; hyperthermia, speech disorder in the form of motor aphasia, and pseudobulbar disorders. Polyuria was not observed. Blood tumor markers were not analyzed.

Given the condition severity caused by a large tumor of the basal ganglia, the patient underwent surgery for resecting a tumor of the basal ganglia region on the right, fornix, and interventricular septum.
Figure 3. Basal ganglia germinoma on the left.

a — T2-weighted MRI in the axial plane. A diffuse space-occupying lesion with a hypointense T1 signal is seen in the projection of the lenticular nuclei on the left. Infiltration of the internal capsule is observed; b — the tumor has a hyperintense FLAIR signal; c — an introduced contrast agent is heterogeneously accumulated; d — T1-weighted MRI in the sagittal plane reveals thickening of the pituitary stalk.
Germinoma is a two-cell type tumor composed of large light cells and focal clusters of lymphoid cells. Large cells are immunopositive for PLAP and CD117 (c-kit).

a — germinoma, hematoxylin and eosin staining, magnification of 200×; b — immunohistochemistry with the PLAP antibody, magnification of 100×; c — immunohistochemistry with the CD117 antibody, magnification of 300×.

Germinoma was histologically diagnosed. An immunohistochemical examination revealed positive expression of PLAP and expression of human chorionic gonadotropin in single tumor cells (Fig. 9).

A blood test for tumor markers revealed an increased b-hCG level of 85.5 mIU/mL. The CSF b-hCG level was also elevated to 142.6, the AFP level was 1.4. Given the histological examination and increased b-hCG levels in the blood and cerebrospinal fluid, germinoma with a syncytiotrophoblastic component was diagnosed.

Postoperative CT of the brain revealed total tumor removal on the right and a small residual petrified tumor on the left (Fig. 8c).

In the postoperative period, the patient’s condition improved; the activity level increased; retardation regressed.
According to the neurological status, supranuclear impairment of pharynx innervation regressed to a large extent; the patient returned to self-feeding. The range of voluntary movements of the extremities increased. Right hemiparesis and extrapyramidal symptoms on the right persisted.

Surgery was followed by chemotherapy and a course of radiation therapy. According to relatives, there was no tumor recurrence for 7 years after treatment. The patient’s condition was stable. Tetrasyndrome, more pronounced in the right extremities, persisted. The patient could walk with support and care himself.

Case 4

A 16-year-old male patient Zh. was admitted to the Neurosurgical Institute in February 2004.

Behavioral changes occurred for three years before admission. Then, episodes of motor anxiety and hyperkinesis in the extremities as well as facial asymmetry developed. Several months before hospitalization, numbness and weakness in the right arm and then right-sided hemiparesis developed. MRI of the brain revealed signs of a cystic tumor of the basal ganglia on the left.

Figure 6. Basal ganglia germinoma on the left.
The clinical picture on an examination performed at the Neurosurgical Institute revealed emotional-mnestic disorders, elements of motor aphasia, right-sided pyramidal syndrome in the form of hemiparesis with reduced muscle strength up to 3 points, central paresis of the facial nerve, and impaired surface sensitivity on the right. There were no discernible neuroendocrine symptoms.

Brain MRI revealed a heterogeneous tumor of the left basal ganglia (Fig. 10a). Tumor markers were not tested. Given the presence of a large cystic tumor causing significant neurologic disorders, the tumor was resected through the frontal transcortical approach (March 2004). Germinoma was diagnosed histologically.
The postoperative period was uneventful. There was no worsening of focal symptoms. Control CT of the brain revealed partial removal of the tumor.

Given the tumor histology, the first course of chemotherapy was performed at the Neurosurgical Institute. In this connection, strength of the right extremities increased; a CT examination revealed a decreased residual tumor. After discharge from the hospital, the patient received comprehensive adjuvant treatment. MRI one year later revealed no signs of tumor recurrence (Fig. 10b). There was no tumor recurrence 10 years after the end of treatment.

**Discussion**

High sensitivity of germinomas to radiation therapy and chemotherapy limits surgery of these deep-seated tumors to sampling of biopsy material and operations aimed at elimination of intracranial hypertension. A timely diagnosis and an early onset of treatment can result in partial or complete regression of preoperative symptoms. This necessitates the early diagnosis of germinomas, which is usually not difficult in the case of a “typical” location of the tumor in the pineal and suprasellar regions.

Basal ganglia germinomas are rare. For this reason, the histological diagnosis is often unexpected if the tumor is localized in this region.

Typical manifestations of basal ganglia tumors, including germinomas, are symptoms of lesions of the internal capsule and basal ganglia (hemiparesis, extrapyramidal syndrome). In all our cases, hemiparesis of varying severity and extrapyramidal symptoms were present. In this case, hemiparesis regressed only partially or not regressed at all despite stable remission of the disease during treatment. This is associated with infiltrative growth of germinomas, a usually late diagnosis of the disease, and a late onset of therapy. In one of our cases, hemiparesis at the early stage of disease had a transitory nature, which caused a delay in stereotactic biopsy and further worsening of symptoms.

Diabetes insipidus is often the first and only symptom associated with suprasellar germinomas; in some cases, it develops before MRI visualization of the tumor [11, 12]. In our study, diabetes insipidus in case 1 was diagnosed 2 years before the emergence of hemiparesis; in case 2, diabetes insipidus developed 8 months after the onset of muscle weakness in the extremities; in cases 3 and 4, diabetes insipidus was absent. The presence of diabetes insipidus and the loss of other pituitary functions in the first two cases suggested germinoma, despite the atypical tumor localization.

The literature describes cases of the disease manifestation in the form of pathological hiccup and vomiting without hydrocephalus [10]. The cause of these symptoms is difficult to explain. Perhaps, they are related to hidden dissemination of the tumor to the medulla oblongata.

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Figure 9. a — a histological specimen of germinoma, hematoxylin and eosin staining, magnification of 200x. The arrow indicates a syncytiotrophoblast multinucleated cell; b — immunohistochemistry with chorionic gonadotropin, magnification of 200x.
Also, the disease often manifests as mental disorders [13, 14]. Three of our patients had psychopathological symptoms in the form of disinhibition, foolishness, reduced self-criticism, and euphoria. These symptoms are probably caused by lesions of the thalamic nuclei and their connections to the frontal lobes.

According to the literature, basal ganglia germinomas are characterized by a diversity of MRI signs [8, 9, 14, 15]. Ji Hoon Phi et al. identified, based on 17 cases and literature data, 4 types of MRI patterns for growth of basal ganglia germinomas — from small areas with a changed signal in the basal ganglia projection, not accumulating a contrast agent, which are often interpreted as non-neoplastic lesions (stroke, demyelination), to large space-occupying lesions with strong contrast agent uptake and a pronounced mass effect [10]. Our observations fully confirm these data. There were also reported cases of multifocal germinomas involving the basal ganglia and other brain regions [9, 16—18]. A similar case was in one of our observations. Bilateral tumor growth may indicate ependymal spread of germinoma to the contralateral side and can help in the differential diagnosis from glial tumors.

According to the MRI data [15, 19, 20], basal ganglia germinomas are also characterized by atrophic changes in the brain at the lesion site. In this connection, it should be noted that a series of repeated brain MRI in one of our cases revealed a reduction in the basal ganglia lesion size with time, with a subsequent substantial lesion increase. The reason for this phenomenon was not clear because the patient did not receive hormone therapy that could facilitate edema reduction and partial regression of neurological symptoms. We did not find similar cases in the literature.

Because of a variety of the neuroradiologic signs of basal ganglia germinomas, examination of tumor metabolism using PET with C11-methionine can help in the differential diagnosis [7, 10, 21, 22].

Surgical treatment of basal ganglia germinomas is limited to stereotactic biopsy. In two of our cases, direct neurosurgical intervention was performed in association with a serious condition of patients caused by a severe mass effect and occlusion of CSF pathways. In case 3, right tumor resection led to worsening of left-sided hemiparesis, while right hemiparesis substantially regressed due to chemotherapy. In case 4, hemiparesis regressed in the postoperative period.

There are few publications on long-term treatment outcomes in basal ganglia germinomas [9, 10].

According to the data given therein, survival of patients was somewhat lower than that of patients with germinomas located along the midline. In 2010, Ji Hoon Phi reported a disease-free survival of 66% and overall survival of 77% in a series of 17 patients [10]. Y. Sonoda (2008) observed 3 tumor recurrences and 1 death in a group of 10 patients [9]. A possible cause for an unfavorable outcome is a late diagnosis of basal ganglia germinomas when the disease acquires a disseminated form, with the spread through the ventricular ependyma and subarachnoid spaces of the CNS. Also, a cause for recurrence may be an insufficient area of radiation therapy, which should involve the entire ventricular system in these cases [10, 17, 23, 24].

Conclusions

Basal ganglia germinoma is a very rare pathology. According to our experience and published data, basal ganglia germinomas are often diagnosed at a late stage due to atypical clinical symptoms and a variety of neuroimaging signs. Establishing the diagnosis can be facilitated by disease manifestations in boys during the second decade of life; MRI signs of a bilateral basal ganglia lesion; neuroendocrine symptoms present in some of these patients despite the lack of MRI signs of a suprasellar lesion; psychopathological
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doi: 10.1017/S0022321609005735.


doi: 10.1007/s00415-008-0811-0.


Commentary

Intracranial germ cell tumors (GCTs) account for 0.8—2.2% of all CNS tumors in children under 18 years of age. Germinomas occur 2 times more often than other GCTs. In 80% of cases, intracranial GCTs are localized in the pineal and suprasellar regions, which underlies clinical symptoms of the disease — endocrine disorders and hypotension symptoms. A basal ganglia localization of germinoma is rare, accounting for about 5% of intracranial germinomas.

The clinical picture of basal ganglia germinomas is represented by hemiparesis and extrapyramidal syndrome; mental disorders can occur. A diagnostic method for germinomas, as well as for all CNS tumors, is MRI. Tumor markers AFP and HCG are not elevated in “pure” germinomas, and only syncytiotrophoblastic germinomas are characterized by a minor increase in the hCG level.

The MRI picture of basal ganglia germinomas is atypical and can miss tumor lesions.

Establishing the diagnosis of basal ganglia germinoma is a challenge for a common practitioner because of the rare tumor localization, absence of elevated tumor markers, and atypical clinical and MRI signs. The late diagnosis of germinoma is the cause for delayed treatment and, as a result, deterioration of treatment outcomes and persistence of neurologic symptoms.

The article will be useful for practitioners because it describes the features of a clinical picture and neuroimaging and gives grounds for the diagnosis and treatment.

The authors indicate the advisability of tumor biopsy for establishing the diagnosis instead of tumor resection that may cause worsening of neurological symptoms, recommend using methionine PET for diagnostic purposes, and confirm their findings by published data.

The conclusions as well as the published data demonstrate that the treatment efficacy depends on the timely diagnosis and treatment.

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