Article published online: 2022-09-20

CASE REPORT

Progressive hemiparesis in a young man: Hemicerebral atrophy as the initial manifestation of basal ganglia germinoma

Peter Yat Ming Woo, Alberto Chi Ho Chu, Kwong Yau Chan, John Ching Kwong Kwok
Department of Neurosurgery, Kwong Wah Hospital, Yau Ma Tei, Hong Kong, China

ABSTRACT

Basal ganglia germinomas are rare and patients are classically young Oriental males presenting with gradually progressive hemiparesis. Although early treatment with chemo-radiotherapy can be curative and significantly improve the quality of life, medical attention is often delayed. A young Chinese male experienced a 6-month history of right hemiparesis with magnetic resonance imaging findings of hemicerebral atrophy and lentiform nucleus microhemorrhage, highly suggestive and early signs of basal ganglia germinomas. No further imaging was performed until 2 years later when he was admitted for acute neurological deterioration and a repeat scan revealed a large infiltrative tumor pathologically confirmed to be a pure germinoma.

Key words: Basal ganglia germinoma, cerebral hemi-atrophy, gradient echo imaging, hemicerebral atrophy, Wallerian degeneration

Introduction

Primary basal ganglia germinomas are rare with fewer than a hundred cases reported.[1] Although difficult to diagnose in the early stages of disease radiotherapy can be curative.[2] Typical radiological features of advanced disease are well-described, but magnetic resonance imaging (MRI) revealing the presence of hemicerebral atrophy, a reliable early sign, is seldom reported.[2-9] We describe a patient where interval disease progression was seen 2 years after presenting with non-specific progressive hemiparesis. The initial finding of hemicerebral atrophy and subtle left globus pallidus signal changes on diffusion-weighted imaging (DWI) and gradient-echo (GRE) imaging were the first diagnostic clues of an underlying basal ganglia germinoma.

Access this article online	
Quick Response Code:	Website: www.asianjns.org
	DOI: 10.4103/1793-5482.145083

Address for correspondence:
Dr. Peter Yat Ming Woo, Room 318, Nursing Quarters, Kwong Wah Hospital, 25 Waterloo Road, Yau Ma Tei, Hong Kong, China.
E-mail: peterymwoo@gmail.com

Case Report

A 21-year-old healthy ethnic Chinese male experienced gradual onset of progressive right hemiparesis for 6 months. There were no symptoms to suggest raised intracranial pressure. On examination, the patient had mild right hemiparesis, but was able to walk unaided. There was no other focal neurological deficit; in particular there were no extra-pyramidal signs. Non-contrast enhanced MRI brain scans depicted left hemicerebral atrophy involving the basal ganglia, cerebral peduncle, midbrain as well as the left cerebral cortex. There were also subtle T2-weighted hyperintense signals at the left globus pallidus and the posterior limb of the left internal capsule [Figure 1a and b]. On DWI, there was evidence of restricted diffusion over the same region associated with susceptibility changes on GRE sequences suggesting a possible left basal ganglia tumor with previous microhemorrhage [Figure 1c and d]. Neither contrast-enhanced imaging, magnetic resonance spectroscopy nor other forms of susceptibility-weighted imaging (SWI) were performed.

How to cite this article: Woo PY, Chu AC, Chan KY, Kwok JC. Progressive hemiparesis in a young man: Hemicerebral atrophy as the initial manifestation of basal ganglia germinoma. Asian J Neurosurg 2017;12:65-8.

A private clinician assessed the patient at the time and despite the abnormal radiological findings no further investigations were arranged. After 2 years, he experienced acute symptoms of raised intracranial pressure associated with right hemiplegia. Repeat imaging revealed a large cystic lesion arising from the left globus pallidus [Figure 1e-g]. Serum concentrations for alpha-fetoprotein (AFP) and beta-human chorionic gonadotrophin (HCG) were both normal. Craniotomy with near total excision was performed and histology revealed large pleomorphic cells with prominent nucleoli and reactive lymphocytic infiltrates [Figure 2a]. Immunohistochemistry identified the tumor cells to be positive for placental alkaline phosphatase (PLAP) and strongly reactive to membranous c-kit (CD117), a distinctive feature of pure germinomas [Figure 2b and c]. A combined whole-body positron-emission tomography (PET) and computed tomography (CT) scan showed no other lesion. The patient received cranio-spinal radiotherapy and six courses of systemic vincristine, bleomycin, cisplatin and etoposide adjuvant chemotherapy. Post-operatively he experienced significant neurological recovery and could walk unaided upon discharge. At 6-month post-treatment, MRI scans showed complete disease remission [Figure 1h].

Discussion

Primary intracranial pure germinomas tumors are uncommon representing 3% of all intracranial tumors in children and adolescents.[3,10] There is a higher reported prevalence among Oriental males with a peak incidence during the second decade of life.[3,10,11] They are believed to arise from midline totipotent cell nests arrested during their migration in rostral neural tube development. For this reason, most originate from midline structures such as the suprasellar

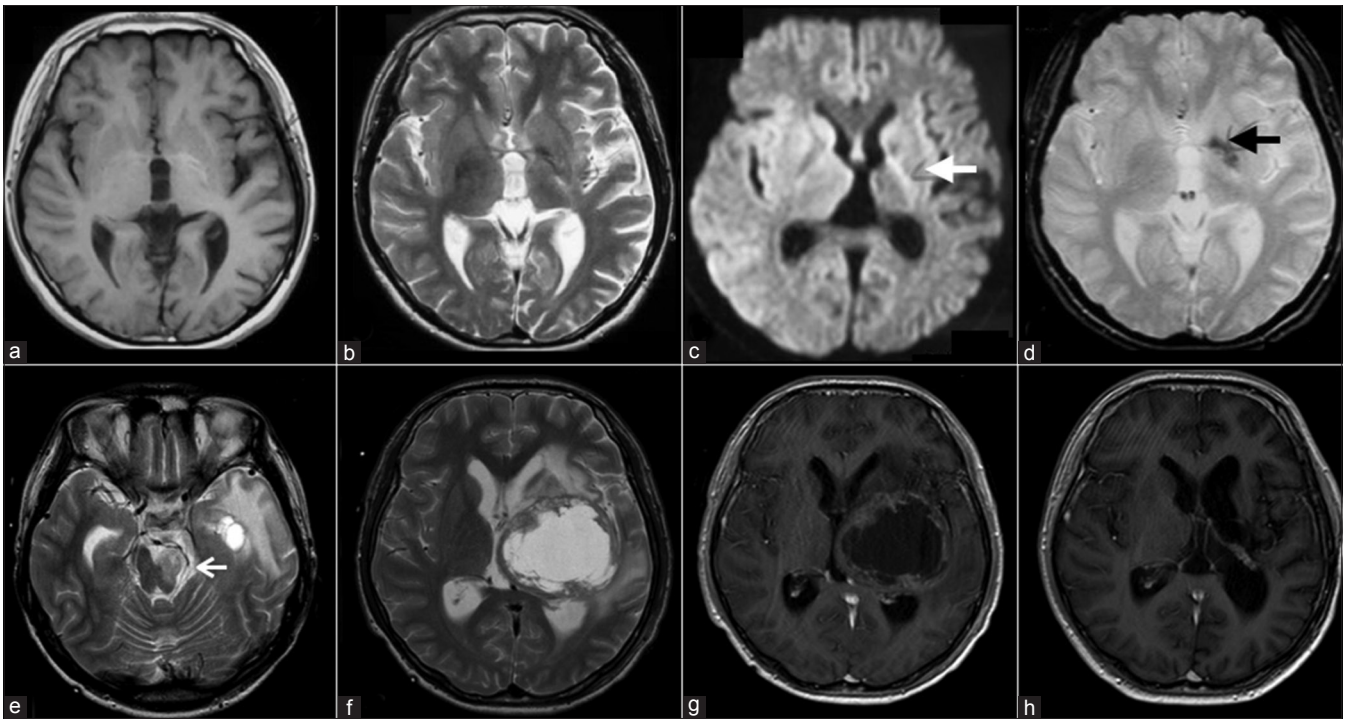

Figure 1: Initial T1W magnetic resonance imaging (MRI): Left hemicerebral atrophy with diffuse sulcal widening and prominent left sylvian fissure without ventricular enlargement (a); T2W: Subtle hyperintense signal changes at the left globus pallidus and posterior limb of the internal capsule (b); DWI: Restricted diffusion of the same areas (white arrow, c) and GRE: Hypointense signals ("blooming") (black arrow, d); 2 years later: Large left basal ganglia cystic lesion (T2W with left cerebral peduncle atrophy, white thin arrow (e); T2W (f); contrast T1W (g); 6-month post-treatment contrast T1W MRI showed no recurrent tumor (h)

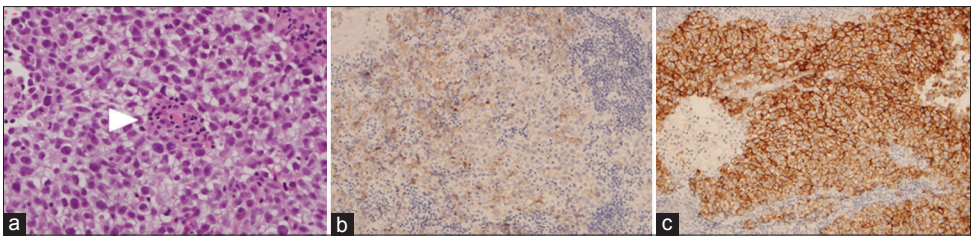

Figure 2: Photo-micrograph. H and E stain. Sheets of large pleomorphic tumor cells with enlarged nuclei, prominent nucleoli and vacuolated cytoplasm. Note hemosiderin deposition in the center (arrow head, a); Placental alkaline phosphatase reactive staining (b); and strong diffuse c-kit positivity characteristic of pure germinomas (c)

and pineal regions. Five to ten per cent of germinomas arise off-midline from the basal ganglia and are considered to be rare and "ectopic." Most originate from the lentiform nucleus and are presumed to be a result of aberrant migration of ectopic germ cells during third ventricle development.[4,12] From a single-center series in Hong Kong, China, of 432 pediatric brain tumor patients with pathological diagnoses, Wong *et al*. reported that 6 of 13 patients with basal ganglia tumors were primary germinomas.[1] They concluded that germinomas are the most common basal ganglia tumors in children.

The onset of primary basal ganglia germinomas is insidious, usually in terms of years and in a single case, the diagnosis was made after 8 years.[3,10,13] Patients present with subtle, but progressive pyramidal signs due to the tumor's proximity to the posterior limb of the internal capsule.[1] Slow infiltration of the basal ganglia and thalamus could lead to extra-pyramidal signs such as choreo-athetosis.[3] Other common symptoms include neuropsychiatric manifestations such as gradual cognitive deterioration, personality changes and psychosis when the deep limbic structures are involved.[3]

Early disease basal ganglia germinomas are elusive on imaging. CT scans may appear normal unless features of advanced disease such as intratumoral hemorrhage, calcifications or cystic degeneration are present.[4,5,14] In this case, the tumor developed into a multi-loculated complex cyst, a characteristic finding of basal ganglia geminomas, unlike their pineal or suprasellar region counterparts where solid lesions predominate.[2]

The MRI features of basal ganglia germinomas are generally non-specific: Iso-or hypo-intense on T1-weighted images and iso-or hyper-intense on T2-weighted sequences. Contrast enhancement only occurs in established disease. As illustrated in this case basal ganglia germinomas are thought to arise from small lenticular lesions and hemiparesis may even precede a demonstrable tumor. Thus, recognition of hemicerebral atrophy becomes highly important in identifying early disease. In a series of 17 patients, one-third had hemicerebral atrophy observed on MRI.[2,15] Although, this phenomenon has long been known to be associated with basal ganglia germinomas surprisingly few cases have been reported.[1,3,4,8,9,15-17] It is postulated that germinoma cells cause degeneration of ganglion cells and nerve fibers within its vicinity. Subsequent infiltration of the corticospinal and thalamo-cortical tracts elicits secondary antegrade and retrograde Wallerian degeneration of the ipsilateral cerebral hemisphere extending from the corona radiata to the internal capsule and brainstem.[1,6,16]

DWI showing restricted diffusion suggests the presence of a hypercellular tumor, but this is non-specific and is a shared characteristic of lymphomas.[3,4,6] Owing to the propensity for germinomas to develop an extensive vasculature micro-hemorrhages detectable on GRE and SWI may be useful. Both sequences accentuate the paramagnetic properties of blood products such as deoxyhemoglobin, intracellular methemoglobin and hemosiderin. In addition, germinoma GRE- and SWI-signal changes may be explained by two other mechanisms. Since the basal ganglia are especially rich in iron content tumor invasion could cause a disruption of its axonal transport and lead to abnormal iron accumulation within the lesion's vicinity.[7] Another hypothesis involves the possible germinoma paracrine secretion of transferrin that activates glial cell receptors to promote the transport of iron to the globus pallidus.[7] Apparently, this patient's initial subtle left pallidal DWI and GRE signal changes should have alerted the responsible clinician to arrange for an interval MRI.

Metabolic imaging shows promise of early detection in cases where MRI features are ambiguous. Fluorine 18-flurodeoxyglucose PET shows characteristic hypometabolism that is particularly useful in differentiating from high grade gliomas and lymphomas.[18] Several studies have reported that C^{11}-methionine-PET is highly sensitive for basal ganglia germinomas especially for recurrent disease.[9,18]

Immunohistochemical diagnostic biomarkers such as PLAP, AFP, HCG, c-kit/CD117 and OCT4, aid in the identification of a variety of germ cell tumors. In particular PLAP reactivity is characteristic of pure germinomas in more than 90% of cases and almost all demonstrate strong c-kit/CD117 positivity.[10] OCT4 is not only diagnostically useful, with reactivity close to 100% of germinomas, but the variance in expression carries prognostic significance with regard to 5-year progression-free survival.[19] For this patient, there was no HCG staining reactivity, a distinctive feature for germinomas with syncytiotrophoblastic elements that carry a worse prognosis. It has been proposed that a greater proportion of intracranial germinomas stain positive for vimentin and epithelial membrane antigen compared with their gonadal counterparts, but this has yet to be substantiated with larger studies and the role of these markers are typically limited to the identification of meningiomas or sarcomas.[20,21] Lymphocytic infiltration with granulomatous inflammation may confound the diagnosis and suggest sarcoidosis or infection. Familiarity with the clinical and imaging features often clarifies suspicions. Other possible differential diagnoses include non-Hodgkin's lymphomas that are readily identified with leukocyte common antigen (CD 45) positive staining. Large germinomas as in this case can trigger a gliotic reaction and mimic gliomas particularly if biopsies are taken from the periphery. Glial fibrillary acidic protein positive and PLAP negative stains promptly identifies glial tumors.

The first line treatment of primary intracranial germinomas is cranio-spinal radiotherapy and more than 90% of patients can achieve 5-year overall survival.[10] Chemotherapy is often added

to reduce radiotherapy dosages and mitigate radiation toxicity, but it is unclear whether chemotherapy alone improves survival.[10,17] Surgery is reserved for lesions presenting with mass effect or when they radiologically mimic high grade gliomas or lymphomas.[17]

Conclusion

Early stage intracranial primary basal ganglia germinomas should be considered when MRI findings reveal hemicerebral atrophy or ill-defined lentiform nucleus lesions in young Oriental males with progressive hemiparesis. Recognition of this phenomenon will prevent delayed treatment and irreversible neurological deficit in a tumor with an otherwise favorable prognosis.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Wong ST, Yuen SC, Fong D. Pathophysiological mechanism of ipsilateral cerebral and brainstem hemiatrophy in basal ganglia germ cell tumors: Case report. Childs Nerv Syst 2009;25:693-9.
2. Phi JH, Cho BK, Kim SK, Paeng JC, Kim IO, Kim IH, *et al*. Germinomas in the basal ganglia: Magnetic resonance imaging classification and the prognosis. J Neurooncol 2010;99:227-36.
3. Villani A, Bouffet E, Blaser S, Millar BA, Hawkins C, Bartels U. Inherent diagnostic and treatment challenges in germinoma of the basal ganglia: A case report and review of the literature. J Neurooncol 2008;88:309-14.
4. Kim DI, Yoon PH, Ryu YH, Jeon P, Hwang GJ. MRI of germinomas arising from the basal ganglia and thalamus. Neuroradiology 1998;40:507-11.
5. Soejima T, Takeshita I, Yamamoto H, Tsukamoto Y, Fukui M, Matsuoka S. Computed tomography of germinomas in basal ganglia and thalamus. Neuroradiology 1987;29:366-70.
6. Okamoto K, Ito J, Ishikawa K, Morii K, Yamada M, Takahashi N, *et al*. Atrophy of the basal ganglia as the initial diagnostic sign of germinoma in the basal ganglia. Neuroradiology 2002;44:389-94.
7. Lou X, Ma L, Wang FL, Tang ZP, Huang H, Cai YQ, *et al*. Susceptibility-weighted imaging in the diagnosis of early basal ganglia germinoma. AJNR Am J Neuroradiol 2009;30:1694-9.
8. Rushing EJ, Sandberg GD, Judkins AR, Vezina G, Kadom N, Myseros JS, *et al*. Germinoma: Unusual imaging and pathological characteristics. Report of two cases. J Neurosurg 2006;104:143-8.
9. Lee J, Lee BL, Yoo KH, Sung KW, Koo HH, Lee SJ, *et al*. A typical basal ganglia germinoma presenting as cerebral hemiatrophy: Diagnosis and follow-up with 11C-methionine positron emission tomography. Childs Nerv Syst 2009;25:29-37.
10. Mufti ST, Jamal A. Primary intracranial germ cell tumors. Asian J Neurosurg 2012;7:197-202.
11. Tamaki N, Lin T, Shirataki K, Hosoda K, Kurata H, Matsumoto S, *et al*. Germ cell tumors of the thalamus and the basal ganglia. Childs Nerv Syst 1990;6:3-7.
12. Kobayashi H, Yamada H, Sakai N, Andoh T, Shinoda J. Germ cell tumor arising in the basal ganglia in a female – Case report. Neurol Med Chir (Tokyo) 1990;30:123-6.
13. Takeda N, Fujita K, Katayama S, Uchihashi Y, Okamura Y, Nigami H, *et al*. Germinoma of the basal ganglia. An 8-year asymptomatic history after detection of abnormality on CT. Pediatr Neurosurg 2004;40:306-11.
14. Oyama N, Terae S, Saitoh S, Sudoh A, Sawamura Y, Miyasaka K. Bilateral germinoma involving the basal ganglia and cerebral white matter. AJNR Am J Neuroradiol 2005;26:1166-9.
15. Ozelame RV, Shroff M, Wood B, Bouffet E, Bartels U, Drake JM, *et al*. Basal ganglia germinoma in children with associated ipsilateral cerebral and brain stem hemiatrophy. Pediatr Radiol 2006;36:325-30.
16. Nagata K, Nikaido Y, Yuasa T, Fujimoto K, Kim YJ, Inoue M. Germinoma causing wallerian degeneration. Case report and review of the literature. J Neurosurg 1998;88:126-8.
17. Tang J, Ma Z, Luo S, Zhang Y, Jia G, Zhang J. The germinomas arising from the basal ganglia and thalamus. Childs Nerv Syst 2008;24:303-6.
18. Sudo A, Shiga T, Okajima M, Takano K, Terae S, Sawamura Y, *et al*. High uptake on 11C-methionine positron emission tomographic scan of basal ganglia germinoma with cerebral hemiatrophy. AJNR Am J Neuroradiol 2003;24:1909-11.
19. Wanggou S, Jiang X, Yuan X, Ren C, Zeng Y, Li G, *et al*. Prognostic value of OCT4 in primary intracranial germinoma: A single institute analysis of 31 cases. Br J Neurosurg 2012;26:237-46.
20. Nakagawa Y, Perentes E, Ross GW, Ross AN, Rubinstein LJ. Immunohistochemical differences between intracranial germinomas and their gonadal equivalents. An immunoperoxidase study of germ cell tumors with epithelial membrane antigen, cytokeratin, and vimentin. J Pathol 1988;156:67-72.
21. Ji X, Chao X, Fei Z, Zhao Y. Primary frontoparietal lobe convexity germinoma with dural invasion mimics meningioma. Neurosciences (Riyadh) 2011;16:276-80.