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Contents

Semimonthly Volume 8 Number 19 October 6, 2020

OPINION REVIEW

- 4280 Role of monoclonal antibody drugs in the treatment of COVID-19
Ucciferri C, Vecchiet J, Falasca K

MINIREVIEWS

- 4286 Review of simulation model for education of point-of-care ultrasound using easy-to-make tools
Shin KC, Ha YR, Lee SJ, Ahn JH
- 4303 Liver injury in COVID-19: A minireview
Zhao JN, Fan Y, Wu SD

ORIGINAL ARTICLE

Case Control Study

- 4311 Transanal minimally invasive surgery vs endoscopic mucosal resection for rectal benign tumors and rectal carcinoids: A retrospective analysis
Shen JM, Zhao JY, Ye T, Gong LF, Wang HP, Chen WJ, Cai YK
- 4320 Impact of *mTOR* gene polymorphisms and gene-tea interaction on susceptibility to tuberculosis
Wang M, Ma SJ, Wu XY, Zhang X, Abesig J, Xiao ZH, Huang X, Yan HP, Wang J, Chen MS, Tan HZ

Retrospective Cohort Study

- 4331 Establishment and validation of a nomogram to predict the risk of ovarian metastasis in gastric cancer: Based on a large cohort
Li SQ, Zhang KC, Li JY, Liang WQ, Gao YH, Qiao Z, Xi HQ, Chen L

Retrospective Study

- 4342 Predictive factors for early clinical response in community-onset *Escherichia coli* urinary tract infection and effects of initial antibiotic treatment on early clinical response
Kim YJ, Lee JM, Lee JH
- 4349 Managing acute appendicitis during the COVID-19 pandemic in Jiaying, China
Zhou Y, Cen LS
- 4360 Clinical application of combined detection of SARS-CoV-2-specific antibody and nucleic acid
Meng QB, Peng JJ, Wei X, Yang JY, Li PC, Qu ZW, Xiong YF, Wu GJ, Hu ZM, Yu JC, Su W
- 4370 Prolonged prothrombin time at admission predicts poor clinical outcome in COVID-19 patients
Wang L, He WB, Yu XM, Hu DL, Jiang H

- 4380** Percutaneous radiofrequency ablation is superior to hepatic resection in patients with small hepatocellular carcinoma

Zhang YH, Su B, Sun P, Li RM, Peng XC, Cai J

- 4388** Clinical study on the surgical treatment of atypical Lisfranc joint complex injury

Li X, Jia LS, Li A, Xie X, Cui J, Li GL

- 4400** Application of medial column classification in treatment of intra-articular calcaneal fractures

Zheng G, Xia F, Yang S, Cui J

Clinical Trials Study

- 4410** Optimal hang time of enteral formula at standard room temperature and high temperature

Lakananurak N, Nalinthassanai N, Suansawang W, Panarat P

META-ANALYSIS

- 4416** Meta-analysis reveals an association between acute pancreatitis and the risk of pancreatic cancer

Liu J, Wang Y, Yu Y

SCIENTOMETRICS

- 4431** Global analysis of daily new COVID-19 cases reveals many static-phase countries including the United States potentially with unstoppable epidemic

Long C, Fu XM, Fu ZF

CASE REPORT

- 4443** Left atrial appendage aneurysm: A case report

Belov DV, Moskalev VI, Garbuzenko DV, Arefyev NO

- 4450** Twenty-year survival after iterative surgery for metastatic renal cell carcinoma: A case report and review of literature

De Raffele E, Mirarchi M, Casadei R, Ricci C, Brunocilla E, Minni F

- 4466** Primary rhabdomyosarcoma: An extremely rare and aggressive variant of male breast cancer

Satală CB, Jung I, Bara TJ, Simu P, Simu I, Vlad M, Szodorai R, Gurzu S

- 4475** Bladder stones in a closed diverticulum caused by *Schistosoma mansoni*: A case report

Alkhamees MA

- 4481** Cutaneous ciliated cyst on the anterior neck in young women: A case report

Kim YH, Lee J

- 4488** Extremely rare case of successful treatment of metastatic ovarian undifferentiated carcinoma with high-dose combination cytotoxic chemotherapy: A case report

Kim HB, Lee HJ, Hong R, Park SG

- 4494** Acute amnesia during pregnancy due to bilateral fornix infarction: A case report
Cho MJ, Shin DI, Han MK, Yum KS
- 4499** Ascaris-mimicking common bile duct stone: A case report
Choi SY, Jo HE, Lee YN, Lee JE, Lee MH, Lim S, Yi BH
- 4505** Eight-year follow-up of locally advanced lymphoepithelioma-like carcinoma at upper urinary tract: A case report
Yang CH, Weng WC, Lin YS, Huang LH, Lu CH, Hsu CY, Ou YC, Tung MC
- 4512** Spontaneous resolution of idiopathic intestinal obstruction after pneumonia: A case report
Zhang BQ, Dai XY, Ye QY, Chang L, Wang ZW, Li XQ, Li YN
- 4521** Successful pregnancy after protective hemodialysis for chronic kidney disease: A case report
Wang ML, He YD, Yang HX, Chen Q
- 4527** Rapid remission of refractory synovitis, acne, pustulosis, hyperostosis, and osteitis syndrome in response to the Janus kinase inhibitor tofacitinib: A case report
Li B, Li GW, Xue L, Chen YY
- 4535** Percutaneous fixation of neonatal humeral physeal fracture: A case report and review of the literature
Tan W, Wang FH, Yao JH, Wu WP, Li YB, Ji YL, Qian YP
- 4544** Severe fundus lesions induced by ocular jellyfish stings: A case report
Zheng XY, Cheng DJ, Lian LH, Zhang RT, Yu XY
- 4550** Application of ozonated water for treatment of gastro-thoracic fistula after comprehensive esophageal squamous cell carcinoma therapy: A case report
Wu DD, Hao KN, Chen XJ, Li XM, He XF
- 4558** Germinomas of the basal ganglia and thalamus: Four case reports
Huang ZC, Dong Q, Song EP, Chen ZJ, Zhang JH, Hou B, Lu ZQ, Qin F
- 4565** Gastrointestinal bleeding caused by jejunal angiosarcoma: A case report
Hui YY, Zhu LP, Yang B, Zhang ZY, Zhang YJ, Chen X, Wang BM
- 4572** High expression of squamous cell carcinoma antigen in poorly differentiated adenocarcinoma of the stomach: A case report
Wang L, Huang L, Xi L, Zhang SC, Zhang JX
- 4579** Therapy-related acute promyelocytic leukemia with FMS-like tyrosine kinase 3-internal tandem duplication mutation in solitary bone plasmacytoma: A case report
Hong LL, Sheng XF, Zhuang HF
- 4588** Metastasis of esophageal squamous cell carcinoma to the thyroid gland with widespread nodal involvement: A case report
Zhang X, Gu X, Li JG, Hu XJ

- 4595** Severe hyperlipemia-induced pseudoerythrocytosis - Implication for misdiagnosis and blood transfusion: A case report and literature review
Zhao XC, Ju B, Wei N, Ding J, Meng FJ, Zhao HG
- 4603** Novel brachytherapy drainage tube loaded with double 125I strands for hilar cholangiocarcinoma: A case report
Lei QY, Jiao DC, Han XW
- 4609** Resorption of upwardly displaced lumbar disk herniation after nonsurgical treatment: A case report
Wang Y, Liao SC, Dai GG, Jiang L
- 4615** Primary hepatic myelolipoma: A case report and review of the literature
Li KY, Wei AL, Li A
- 4624** Endoscopic palliative resection of a giant 26-cm esophageal tumor: A case report
Li Y, Guo LJ, Ma YC, Ye LS, Hu B
- 4633** Solitary hepatic lymphangioma mimicking liver malignancy: A case report and literature review
Long X, Zhang L, Cheng Q, Chen Q, Chen XP
- 4644** Intraosseous venous malformation of the maxilla after enucleation of a hemophilic pseudotumor: A case report
Cai X, Yu JJ, Tian H, Shan ZF, Liu XY, Jia J
- 4652** Intravesically instilled gemcitabine-induced lung injury in a patient with invasive urothelial carcinoma: A case report
Zhou XM, Wu C, Gu X
- 4660** Bochdalek hernia masquerading as severe acute pancreatitis during the third trimester of pregnancy: A case report
Zou YZ, Yang JP, Zhou XJ, Li K, Li XM, Song CH
- 4667** Localized primary gastric amyloidosis: Three case reports
Liu XM, Di LJ, Zhu JX, Wu XL, Li HP, Wu HC, Tuo BG
- 4676** Displacement of peritoneal end of a shunt tube to pleural cavity: A case report
Liu J, Guo M
- 4681** Parathyroid adenoma combined with a rib tumor as the primary disease: A case report
Han L, Zhu XF

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Germinomas of the basal ganglia and thalamus: Four case reports

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Abstract

BACKGROUND

The early diagnosis of basal ganglia and thalamus germinomas is often difficult due to the absence of elevated tumor markers, and atypical clinical symptoms and neuroimaging features.

CASE SUMMARY

Four male children aged 8 to 15 years were diagnosed with germinomas in the basal ganglia and thalamus by stereotactic biopsy from 2017 to 2019. All patients developed hemiplegia except patient 4 who also had cognitive decline, speech disturbance, nocturnal enuresis, polydipsia, polyuria, precocious puberty and abnormalities of thermoregulation. All four cases were alpha-fetoprotein and beta-human chorionic gonadotrophin (β -HCG) negative except patient 3 who had slightly elevated β -HCG in cerebrospinal fluid (CSF). No malignant cells were detected in the patients' CSF. Brain magnetic resonance imaging findings were diverse in these patients with the exception of the unique and common characteristics of ipsilateral hemisphere atrophy, especially in the cerebral peduncle. All patients were diagnosed with germinomas of the basal ganglia and thalamus by stereotactic brain biopsy.

CONCLUSION

Stereotactic brain biopsy is necessary to confirm the diagnosis of ectopic germinomas. Serial neuroimaging studies can not only differentiate disease but also determine the biopsy site.

Key Words: Intracranial germinoma; Stereotactic brain biopsy; Basal ganglia; Thalamus; Tumor marker; Case report

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Core Tip: Basal ganglia and thalamus germinomas are rare and early diagnosis of these tumors is usually difficult due to insidious onset, absence of elevated tumor markers, and subtle and atypical neuroimaging features. The definite diagnosis of these ectopic germinomas depends on histopathological examination. In this report, we describe four intractable cases whose histopathological diagnoses were germinomas in the basal ganglia and thalamus. Ipsilateral hemiatrophy, which was a common characteristic on neuroimaging of germinomas in the basal ganglia and thalamus, may be an important feature in differentiating these lesions from other intracranial tumors.

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INTRODUCTION

Intracranial germinomas account for approximately 50% of all central nervous system germ cell tumors and constitute 0.3%-3.4% of all brain cancers^[1,2]. They are usually located at the midline structures including the pineal and suprasellar regions. The off-midline germinomas also called ectopic germinomas are rare including those in the basal ganglia and thalamus. Germinomas in the basal ganglia and thalamus are more frequently seen in the Asian population. Intracranial germinomas have a male predominance, especially those that originate in the basal ganglia and thalamus^[3]. Pure intracranial germinomas are negative for alpha-fetoprotein (AFP) and beta-human chorionic gonadotropin (β -HCG) in both body fluid and histological staining^[3-6]. Slightly elevated β -HCG levels in the body fluid predict syncytiotrophoblastic giant cells in germinomas^[7,8]. Early clinical diagnosis of a basal ganglia germinoma is more difficult than in the midline region due to unusual localization, slow clinical course and subtle or atypical neuroimaging findings. Definite diagnosis of germinoma depends on histopathological findings. The prognosis of an intracranial germinoma is usually favorable following chemotherapy and radiotherapy. However, treatment outcome of ectopic germinoma is worse if diagnosis is delayed. Here, we describe four atypical and intractable cases which were ultimately diagnosed as germinomas by stereotactic brain biopsy and histological staining.

CASE PRESENTATION

Chief complaints

All four patients were male and the age of onset ranged from 8-15 years. Patient 1 suffered from three episodes of transient numbness of his right extremities. Patient 2 and patient 3 developed slow progressive weakness of their hemilateral legs and arms. Patient 4 gradually developed walking and writing disorders, cognition decline, speech disturbance, nocturnal enuresis, polydipsia, polyuria, precocious puberty and abnormalities of thermoregulation.

History of past illness

All four patients had no particular medical history or family history.

Physical examination

Patients 1, 2 and 3 had mild to moderate spastic paresis of unilateral limbs, brisk deep reflexes and the Babinski sign. Cranial nerve palsy was not observed. Sensory examinations were almost bilaterally symmetric. Patient 4 presented with mild cognitive impairment, involuntary movement of his right arm, increased muscle tone of bilateral extremities without muscle weakness and precocious puberty signs including enlarged testicles and penis, and the appearance of pubic and underarm hair.

Laboratory examinations

All four cases were AFP and β -HCG negative except patient 3 who had a slightly elevated β -HCG in cerebrospinal fluid (CSF, 22.9 mIU/mL, reference value 0-5 mIU/mL) (Table 1). Serum carcinoembryonic antigen and other tumor marker levels were also within the reference range. No malignant cells were detected in CSF. No other significant abnormalities in laboratory examinations were observed.

Imaging examinations

Magnetic resonance imaging (MRI) of the brain revealed local lesions in unilateral basal ganglia region in patients 1, 2, and 3. Brain MRI revealed subtle and ill-defined lesions in bilateral basal ganglia and thalamus in patient 4. The characteristics of these brain lesions are shown in Table 2 and Figure 1. In addition, patient 3 and 4 underwent both 18F-fluorodeoxyglucose-positron emission tomography (18F-FDG-PET) and 18F-fluorodopa-positron emission tomography (18F-DOPA-PET). In patient 3, 18F-FDG-PET revealed diffuse low metabolism in the left cerebral cortex, basal ganglia and thalamus (Figure 2A). 18F-DOPA-PET showed slightly low metabolism in the left basal ganglia (Figure 2B). In patient 4, 18F-FDG-PET demonstrated low metabolism in the left hemisphere and left cerebral peduncle (Figure 2C). 18F-DOPA-PET showed normal metabolism (Figure 2D).

FINAL DIAGNOSIS

All patients were diagnosed with germinomas of the basal ganglia and thalamus by stereotactic brain biopsy. Histopathological diagnoses were further confirmed by another hospital.

TREATMENT

All four patients received whole brain radiotherapy and chemotherapy at another hospital.

OUTCOME AND FOLLOW-UP

The brain lesions on MRI were reduced or disappeared and their symptoms remained stable without aggravation.

DISCUSSION

Germinomas in the basal ganglia and thalamus show a male predominance^[3,5,6,9-11]. The reason for this is unclear. They usually occur in young adolescents aged from 10 to 19 years. This may be correlated to gonad development in this age group^[3]. Basal ganglia germinomas usually have an insidious onset and slow progression. The clinical presentation of these tumors depends on their localization. The most common symptoms are progressive hemiparesis, mental status change and cognitive decline. In this report, patient 1 developed paroxysmal paresthesia which is very rare. The other 3 patients had hemiplegia. Patient 4 developed cognitive decline, diabetes insipidus, precocious puberty in addition to hemiplegia. Although patients 3 and 4 had longer duration than patients 1 and 2, the brain lesions shown by MRI were much smaller and more ill-defined. Hence, the size of the lesion did not correspond to the duration and severity of the clinical presentation. Symptoms and signs are valuable for localization and contribute to the identification of subtle lesions on brain MRI.

Tumor markers of pure germinomas including AFP and β -HCG were negative in these patients^[3-6]. β -HCG levels were slightly elevated in the body fluid of some patients which indicated syncytiotrophoblastic giant cells in the germinoma. Germinomas with elevated β -HCG in serum but not in CSF, might be associated with a poor outcome^[7,8]. It was reported that intracranial germinomas with serum β -HCG levels higher than 15 mIU/mL had a high recurrence rate^[7]. However, all the cases in that study were midline germinomas including those in the pineal region and suprasellar region or both sites. Further studies are needed to evaluate the prognosis

Table 1 Patients' characteristics

Case	Onset age (yr)	Sex	Duration(mo)	AFP (S/C)	HCG (S/C)	Histological diagnosis
1	12	M	2	-/-	-/-	Germinoma
2	10	M	3	-/-	-/-	Germinoma
3	15	M	18	-/-	-/+	Germinoma
4	8	M	24	-/-	-/-	Germinoma

AFP: Alpha-fetoprotein; HCG: Human chorionic gonadotrophin; S/C: Serum/cerebrospinal fluid. M: male

Table 2 Neuroimaging findings before stereotactic brain biopsy

Case	MRI findings									18F-FDG-PET	18F-DOPA-PET
	Contrast enhancement	Mass effect	Hemorrhage	Calcification	Cyst formation	Ipsilateral hemiatrophy	SWI	MRS	DTI		
1	Y	Y	N	Y	Y	Y	Hypo	Low NAA	Nor	Low	Low
2	Y	N	N	N	N	Y	N/A	N/A	N/A	N/A	N/A
3	Y	N	N	N	Y	Y	N/A	N/A	Interrupted	N/A	N/A
4	N	N	N	N	N	Y (Bi)	Nor	Nor	N/A	Low	Nor

MRI: Magnetic resonance imaging; SWI: Susceptibility weighted imaging; MRS: Magnetic resonance spectroscopy; DTI: Diffusion tensor imaging; 18F-FDG-PET: 18F-fluorodeoxyglucose-positron emission tomography; 18F-DOPA-PET: 18F-fluorodopa-positron emission tomography; Hypo: Hypointense; NAA: N-acetylaspartate peak; Nor: Normal; N/A: Not applicable; Bi: Bilateral.

of basal ganglia germinomas with elevated β -HCG. All our cases were AFP and β -HCG negative except patient 3 who had a slightly elevated level of β -HCG in CSF. Although these tumor markers are usually negative in germinomas, they serve to differentiate germinomas from other germ cell tumors.

According to the literature, typical brain MRI signs of basal ganglia germinomas are usually cystic formation, amorphous calcification, focal hemorrhage, peritumoral edema, contrast enhancement and ipsilateral cerebral and brain stem hemiatrophy^[12-14]. None of our four cases presented all of the above typical neuroimaging characteristics. One patient had calcification, two patients exhibited cystic formation, and three patients had contrast enhancement. All these patients developed ipsilateral hemisphere atrophy especially in the cerebral peduncle. None had intratumoral hemorrhage. Although the MR images of case 1 shared overlapping features with craniopharyngioma, the location of the tumor was useful in differentiating it from craniopharyngioma. In cases 2-4, it was easy to miss the lesions on brain MRI. The most atypical case was patient 4 who showed bilateral involvement and did not present with the above signs except bilateral hemisphere atrophy. As shown in the literature, ipsilateral hemiatrophy is the predominant feature of basal ganglia germinoma^[3,15]. Wallerian degeneration of the conduction tract is hypothesized to be the etiology of hemiatrophy^[15]. In our report, patients 1 and 3 underwent diffusion tensor imaging examination which further supported this hypothesis. Why only germinomas rather than other brain tumors lead to ipsilateral hemiatrophy requires further investigation. Previous reports revealed that susceptibility weighted imaging (SWI) might be more sensitive in detecting early basal ganglia germinoma than conventional MRI, and MR spectroscopy (MRS) was helpful for monitoring the effects of treatment^[6,16]. Patient 1 had similar SWI and MRS findings to those in the literature. A preoperative computed tomography scan was helpful in evaluating hemorrhage and calcification. Patients 3 and 4 underwent both 18F-FDG-PET and 18F-DOPA-PET. It seems that both these techniques had limited use for germinoma. Further studies are needed to confirm the value of PET examination in the diagnosis of germinoma. The reason why patient 4 had the longest clinical course before definite diagnosis was the limited findings on radiological examination.

According to the above findings, germinomas originating from atypical regions are not easy to diagnosis, especially in patients with small and ill-defined brain lesions.

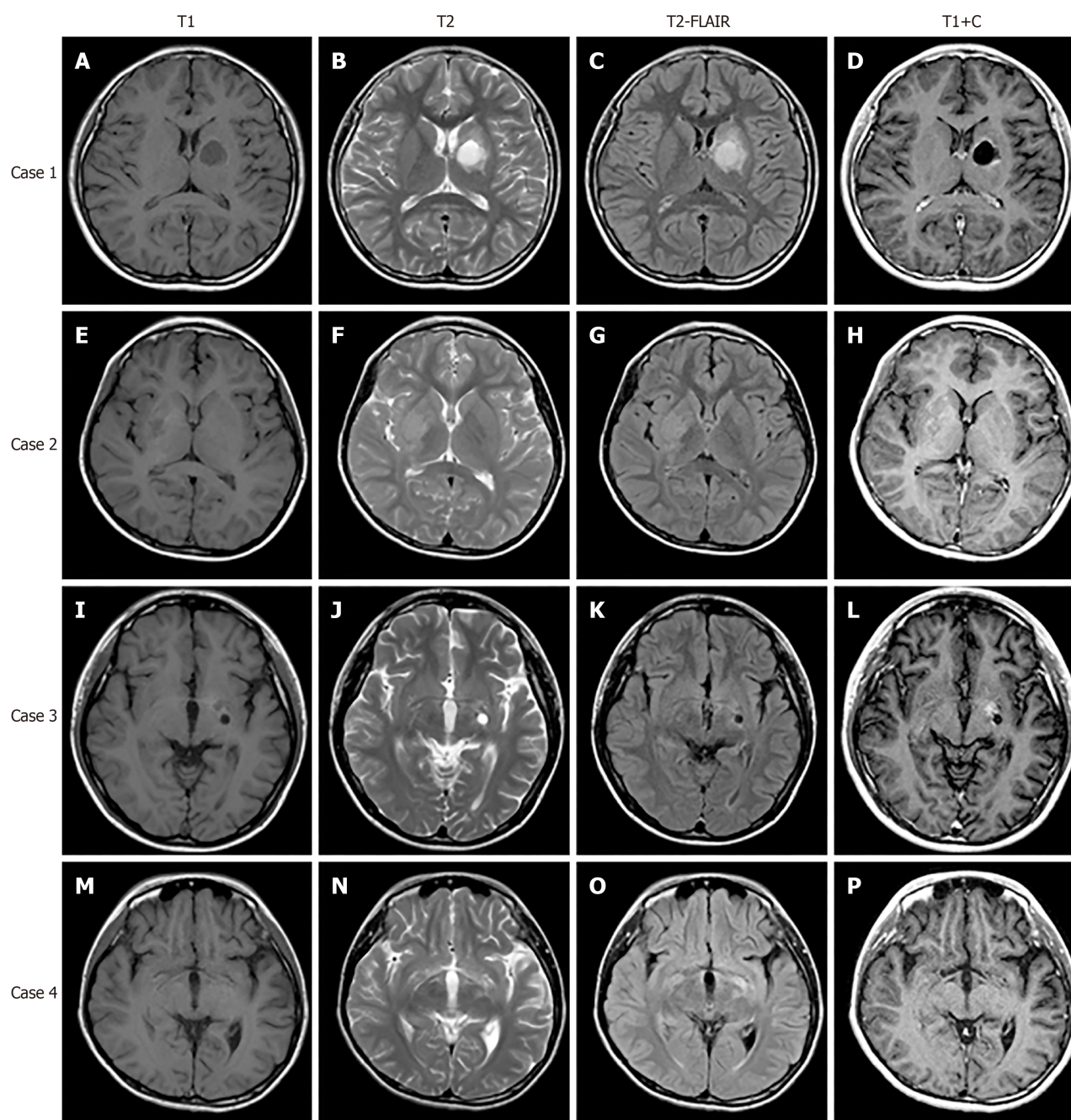


Figure 1 Appearance of germinomas on conventional magnetic resonance images. A-D: Case 1. A round space occupying lesion in the left basal ganglia and thalamus was hypointense on T1 and hyperintense on T2/T2-fluid-attenuated inversion recovery (FLAIR) with annular enhancement around the cystic component. Mild ipsilateral hemiatrophy appeared; E-H: Case 2. An irregular lesion in the right basal ganglia was slightly hypointense on T1 and isointense to hyperintense on T2/T2-FLAIR with mild heterogeneous enhancement and ipsilateral hemiatrophy; I-L: Case 3. An ill-defined lesion was hypointense on T1 and hyperintense on T2/T2-FLAIR in the left basal ganglia beside malacia foci. The left hemisphere showed mild atrophy. Heterogeneous enhancement was shown after gadolinium administration; M-P: Case 4. The subtle lesions were isointense on both T1 and T2/T2-FLAIR around bilateral internal capsule and thalamus. Bilateral cerebral atrophy was revealed which was predominant on the left side. No enhancement was found. T1+C: Contrast-enhanced T1-weighted imaging; FLAIR: Fluid-attenuated inversion recovery.

Stereotactic biopsy was valuable for early diagnosis. Serial neuroimaging studies are needed not only for disease differentiation but also for determining the biopsy site.

CONCLUSION

The diagnosis of germinomas in the basal ganglia and thalamus is often delayed due to the absence of elevated tumor markers, and atypical clinical symptoms and neuroimaging features. The association of a focal lesion in the basal ganglia or

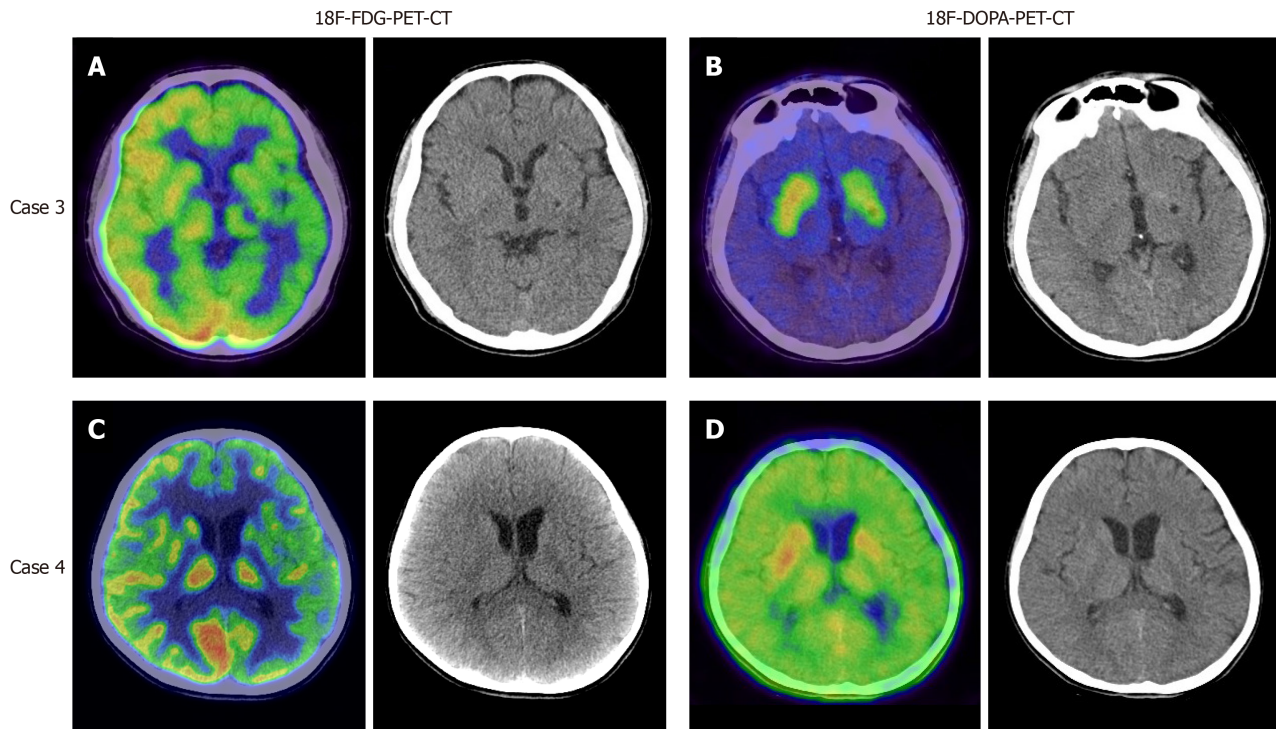


Figure 2 Appearance of germinomas on positron emission tomography-computed tomography. A: 18F-fluorodeoxyglucose-positron emission tomography-computed tomography (18F-FDG-PET-CT) detected diffuse low FDG uptake in the left hemisphere in case 3; B: 18F-fluorodopa-positron emission tomography-computed tomography (18F-DOPA-PET-CT) detected low uptake of DOPA in the left basal ganglia in case 3; C: 18F-FDG-PET demonstrated low uptake in the left hemisphere in case 4; D: 18F-DOPA-PET-CT showed normal metabolism in case 4. 18F-FDG-PET-CT: 18F-fluorodeoxyglucose-positron emission tomography-computed tomography; 18F-DOPA-PET-CT: 18F-fluorodopa-positron emission tomography-computed tomography.

thalamus of children with progressive hemiparesis, neuroendocrine and neuropsychiatric symptoms and ipsilateral hemiatrophy could prompt the diagnosis of ectopic germinoma. Histological examinations are necessary to confirm the diagnosis of an atypical lesion. Serial neuroimaging studies not only differentiate diseases but also determine the biopsy site.

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