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Radiologic features of primary intracranial ectopic germinomas

Case reports and literature review

Xin-Hua Wei, MD[a,*], Hui-Cong Shen, MD[b], Shou-Xian Tang, MS[b], Cui-Hua Gao, MS[a], Ji-Liang Ren, MS[a], Lin Ai, MD[b], Jian-Ping Dai, MD[b]

Abstract

Rationale: Germinomas are sensitive to radiation therapy and chemotherapy; therefore, correct imaging diagnosis is crucial for them. However, the imaging findings of germinomas originating from off-midline regions displayed different patterns from those originating from midline areas.

Patient concerns: The objective of this study is to describe the radiologic features of primary ectopic germinoma. We reviewed the MR and CT findings of 12 patients with histologically proven off-midline ectopic germinomas with off-midline locations.

Interventions: All of these patients underwent conventional MR images and 3 of them underwent diffusion images. Additional CT images were available in 3 patients. Analysis was focused on the shape and entity of tumors in images, signs of hemiatrophy, and the involvement of fibers in diffusion images.

Outcomes: Well-defined (8/12) and ill-defined margin masses (4/12) were identified according to the shape of the mass. Multicystic masses were seen in 11 of the 12 patients. The solid component of the tumors had a high density (3/3) with calcifications (2/3) on CT images, iso- to hypointensity in T2WI (11/12) and restricted diffusion on apparent diffusion coefficient (ADC) maps (3/3). Hemiatrophy was observed in 5 cases and progressive hemiatrophy was observed in 1 case. Other signs included mild peritumoral edema (10/12), and hydrocephalus (7/12). Additionally, infiltration of the corticospinal tract (CST) was identified on diffusion tensor imaging (DTI) (2/2).

Lessons: The results indicate that multicysitic entities and hypointensities in solid components on T2WI and hemiatrophy are the imaging features of ectopic germinomas. DTI has potential for assessing CST involvement.

Abbreviations: ADC = apparent diffusion coefficient, AFP = alpha fetoprotein, CEA = carcinoembryonic antigen, CNS = central nervous system, CST = corticospinal tract, DTI = diffusion tensor imaging, DWI = diffusion weighted imaging, FA = fractional anisotropy, HCG = human chorionic gonadotropin, PNET = primitive neurotodermal tumour.

Keywords: computer tomography, ectopic, germinoma, intracranial, magnetic resonance imaging

1. Introduction

The usual location of intracranial germinoma is in the midline areas such as the pineal and suprasellar regions.

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X-HW and H-CS contributed equally to this study.

Written informed consent was obtained from the patient for publication of this cases report and accompanying images.

HS, ST, and CG were involved in the analysis and collection of the imaging data and clinical data. LA and JD revised the manuscript. HS and XW wrote the article, which was approved by all co-authors.

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[a] Department of Radiology, Guangzhou First People's Hospital, Guangzhou Medical University, Guangzhou, Guangdong, [b] Department of Neuroradiology, Tiantan Hospital, Beijing, China.

[*] Correspondence: Xin-Hua Wei, Department of Radiology, Guangzhou First People's Hospital, Guangzhou Medical University, Guangzhou, Guangdong, China (e-mail: weixinhua@aliyun.com).

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Ectopic germinomas, which are tumors arising from off-midline areas, primarily the basal ganglia and thalamus, only constitute 5% to 10% of all intracranial germinomas and have a male predominance.[1,2]

Germinomas are sensitive to radiation therapy and chemotherapy and are among the highly curable primary brain tumors.[3] Therefore, a preoperative diagnosis is critical for developing a treatment plan for these tumors.[4] The radiologic features of germinomas in the pineal gland and supraseller region have been comprehensively interpreted.[5,6] However, the imaging findings of germinomas originated from off-midline regions displayed different patterns from those originating from midline areas. Few case reports have attempted to interpret the imaging findings of germinomas arising from unusual locations.[7–9] Some reports have suggested that the hemiatrophy was the imaging feature of germinomas arising from the basal ganglia and thalamus.[2,10,11] The explanation for this sign was attributed to the infiltration of white matter tracts by the tumors.[8] However, to our knowledge, there is no report using diffusion tensor imaging (DTI) to visualize the involved white matter fiber tracts. The goal of the present report was to identify features of ectopic germinomas on CT and MR images and longitudinal images. Additionally, DTI of tumors are discussed.

2. Case report

After obtaining approval from the research ethics board at Beijing Tiantan Hospital, China, we reviewed 12 patients with partially

Table 1

Summary of clinical data in 12 patients with ectopic germinoma.

Case No.	Age (y)	Sex	Location of tumor	Symptoms	Tumor markers AFP (ng/mL)	CEA (ng/mL)	HCG (mIU/mL)
1	16	Male	R TH,R LV,SP	Headache	Neg	Neg	Neg
2	21	Female	L LV	Headache	Neg	Neg	Neg
3	34	Male	L TH	Left hemiparesis	Neg	Neg	Neg
4	18	Male	L BG, L IC,L TH	right hemiparesis	Neg	Neg	Neg
5	31	Male	R BG, R IC, R TH	Headache	Neg	N/A	N/A
6	11	Male	R BG, R IC, R TH	left hemiparesis	N/A	Neg	Neg
7	10	Male	R BG, R IC, R TH	left hemiparesis	Neg	5.44	Neg
8	19	Male	L BG, L IC, L TH	right hemiparesis	Neg	Neg	9.35
9	21	Male	R BG, R FL	Left hemiparesis,polydipsia	Neg	Neg	Neg
10	13	Female	R BG, R IC, R TL	left hemiparesis,headache	Neg	Neg	Neg
11	30	Male	R BG,R IC,SP	left hemiparesis	Neg	Neg	Neg
12	29	Male	R BG,R IC	left hemiparesis	Neg	Neg	Neg

AFP = alpha fetoprotein, CEA = carcinoembryonic antigen (normal value: 0–3.4 ng/mL), HCG = human chorionic gonadotropin [normal value (male): 0–2.67mIU/mL], R = right, L = left, TH = thalamus, L LV = left lateral ventricle, SP = septum pellucidum, BG = basal ganglia, IC = internal capsule, FL = frontal lobe, TL = temporal lobe, Neg = negative, N/A = not available.

or completely resected and histologically proven germinomas from 2008 to 2013. Hematoxylin and eosin stain and immunohistological stain were used in histological examination. Most of the cases showed the typical of “2-cell pattern” with relatively large tumor cells and small lymphocytes in hematoxylin and eosin stain. Tumor markers including alpha fetoprotein (AFP), carcinoembryonic antigen (CEA), and human chorionic gonadotropin (HCG) were obtained in most of the cases. The tumors were enrolled for analysis from intracranial locations other than the suprasellar or pineal regions. There were 10 males and 2 females, ranging in age from 10 to 34 years (median 18.5 years old). The clinical symptoms of patients included hemiparesis, increased intracranial pressure and impaired memory. The clinical characteristics are summarized in Table 1.

Conventional MR T1WI/T2WI sequences were performed in all 12 patients, 3 of who underwent diffusion weighted imaging (DWI) /DTI examination. CT images of 3 patients were obtained. One patient had longitudinal MR scanning before and after tumor resection (10 days before and 2, 10, and 33 months after operation, respectively).

CT images were obtained using a Siemens Somatom 16-slice CT scanner (Siemens, Erlangen, Germany). MR images of 5 patients were acquired on a GE Signa 3.0T MR scanner (GE Healthcare, Waukesha, WI), and those of 7 patients were obtained using another Siemens Magnetom Trio 3.0T MR scanner (Siemens, Erlangen, Germany). Pre-contrast T1WI, T2WI and post-contrast T1WI with injection of GD-DTPA (0.2 mL/kg) were obtained. DTI was obtained using the Siemens Magnetom Trio 3.0T MR scanner with diffusion gradients applied in 30 non-collinear directions, and the following imaging parameters were used: TR 4,900 ms, TE 92 ms, matrix = 192 × 192, FOV = 230 mm^2, 4 mm slice thickness with a 1.5 mm gap and a b factor of 0 and 1000 s/mm^2.

Two neuroradiologists (H-CS and X-HW) reviewed all of the MR and CT images until consensus was reached. The location, age, sex, symptoms and tumor markers were recorded. Imaging analysis was focused on shape, density/signal intensity, calcification, hemorrhage, and enhancement patterns of the tumors were explored. Other signs such as peritumoral edema, hydrocephalus and evidence of hemiatrophy were also observed. In addition, the fractional anisotropy (FA) maps, directional color FA maps, and apparent diffusion coefficient (ADC) maps were assessed in the affiliated workstation.

The general radiologic features of 12 patients with ectopic germinoma are summarized in Table 2. Two types of tumors can be identified based on the shape of the masses seen on imaging. The most common type was a well-defined mass that was

Table 2

General radiologic features of 12 patients with ectopic germinoma.

Case no.	Shape	Size (mm)*	CT Density/CA	MR T1WI	MR T2WI	DWI/DTI	CE	Edema	Hydro-cephalus	Cyst	Hemo-rrhage	Atrophy
1	D	52 × 41 × 27	High/yes	Iso	Iso	N/A	Hetero	Mild	Yes	No	No	No
2	D	40 × 45 × 35	N/A	Iso	Hyper	N/A	Hetero	No	Yes	Yes	No	No
3	L	20 × 25 × 22	N/A	Iso	Iso	N/A	Hetero	No	No	Yes	No	No
4	L	51 × 56 × 54	High/no	Iso	Hypo	N/A	Hetero	Mild	Yes	Yes	No	No
5	L	47 × 33 × 33	N/A	Iso	Hypo	N/A	Hetero	Mild	Yes	Yes	No	Yes
6 Four	L	47 × 29 × 41	N/A	Iso	Hypo	N/A	Hetero	Mild	No	Yes	No	No
7	L	38 × 33 × 45	High/yes	Iso	Hypo	RD	Hetero	Mild	Yes	Yes	Yes	No
8	L	51 × 48 × 57	N/A	Iso	Hypo	RD	N/A	Mild	Yes	Yes	No	Yes
9	L	40 × 45 × 30	N/A	Iso	Iso	RD	Hetero	Mild	No	Yes	No	Yes
10	D	42 × 36 × 72	N/A	Iso	Hypo	N/A	Hetero	Mild	No	Yes	No	Yes
11	L	34 × 16 × 38	N/A	Iso	Iso	N/A	Hetero	Mild	No	Yes	No	Yes
12	D	45 × 36 × 45	N/A	Hypo	Hypo	N/A	Hetero	Mild	Yes	Yes	No	No

CA = calcification, CE = contrast enhancement, D = diffuse mass, Four = indicate cases has total 4 times MR scanning (the table list is the first time), HIS = high intensity signal, Homo = homogeneous, Hetero = heterogeneous, Hyper = hyperintense, Hypo = hypointense, Iso = isointense, L = localized mass, N/A = not available, N/E = could not be evaluated, RD = restricted diffusion.

* Length × width × height.

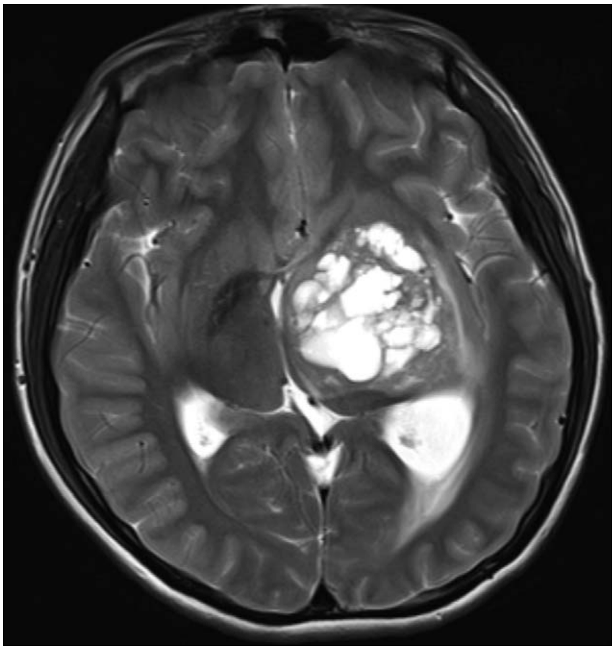

Figure 1. Case 8. The tumor is located in left basal ganglion displaying relative well-defined margin on T2WI.

relatively localized (n = 8) (Fig. 1). Another type was an ill-defined mass that had an irregular shape and disseminated to adjacent structures even in distant areas (n = 4) (Fig. 2).

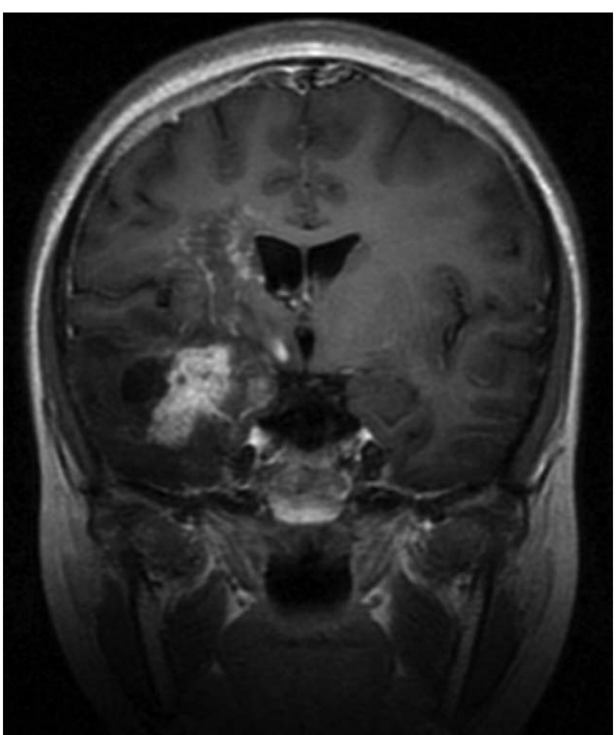

Figure 2. Case 10. The tumor with ill-defined margin is located in right temporal lobe, basal ganglion, internal capsule and thalamus with heterogeneous enhancement on post-contrast T1WI.

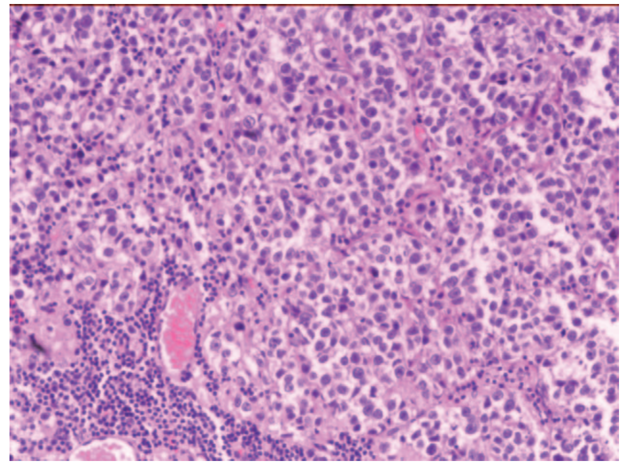

Figure 3. Case 8. Photomicrograph (original magnification, ×200; H&E stain). The tumor cells have a large nucleus, prominent nucleoli, and clear cytoplasm and display adenoid nests arrangement with cystic dilated structure. H&E stain = hematoxylin and eosin stain.

Multicystic masses were observed in 11 of the 12 patients. One case demonstrated a solid entity. The cystic component displayed low density on CT, hypointensity on T1WI, and extreme hyperintensity on T2WI (n = 11) (Fig. 1). On histopathological examination, the tumor cells composed of large polygonal tumor cells and displayed adenoid nests arrangement, part of which showed cystic dilated structure (Fig. 3). One case appeared with mixed signals on both T1WI and T2WI (Fig. 4A), indicating hemorrhage within the tumor. Accordingly, on histopathological examination, the tumor cells intermixed with foci of hemorrhage and lymphocytic infiltration (Fig. 4B). The wall of the cyst was enhanced on the postcontrast T1WI. The solid component of the masses was of higher density than the gray matter in all 3 cases on CT images, and multiple punctate calcifications were observed in 2 cases (Fig. 4C). On MR images, the solid component of the tumors was isointense compared with the gray matter on T1WI (n = 12), iso- or hypointense (n = 11) and hyperintense (n = 1) areas on T2WI (Fig. 4A), and restricted diffusion relative to gray matter on ADC maps in 3 cases (Fig. 4D). Photomicrograph showed the tumors consisted of large polygonal cells with pleomorphic nuclei accompanied by clusters of small, round basophilic lymphocytes (Fig. 4B). After the injection of GD-DTPA, the solid portion of the tumors showed marked inhomogeneous enhancement in 12 cases (Fig. 4E).

Evidence of ipsilateral cerebral and brainstem hemiatrophy including widened dilatation of the Sylvian fissure (Fig. 5), shrinkage of the cerebral peduncle, and decreased volume of the caudate nuclei were detected in 42% (5/12) of the cases. One case underwent longitudinal MR scanning before and after the operation (10 days before, and 2, 10, and 33 months after tumor resection). No definite hemiatrophy could be observed on the first preoperative MR images; however, progressive atrophy of the ipsilateral cerebrum and cerebral peduncle were observed in the serial follow-up MR images. Mild peritumoral edema was seen in 83% (10/12) of the cases. Hydrocephalus was observed in 58% (7/12) of the cases.

Two cases showed obviously infiltrated white matter by tumors on directionally encoded FA color map, which primarily involved the corona radiation and the corticospinal tract (CST). In addition, the CST in the pons showed marked decreased FA on the color FA map (Fig. 6A) but minimal high signal on T2WI compared with the contralateral intact side (Fig. 6B).

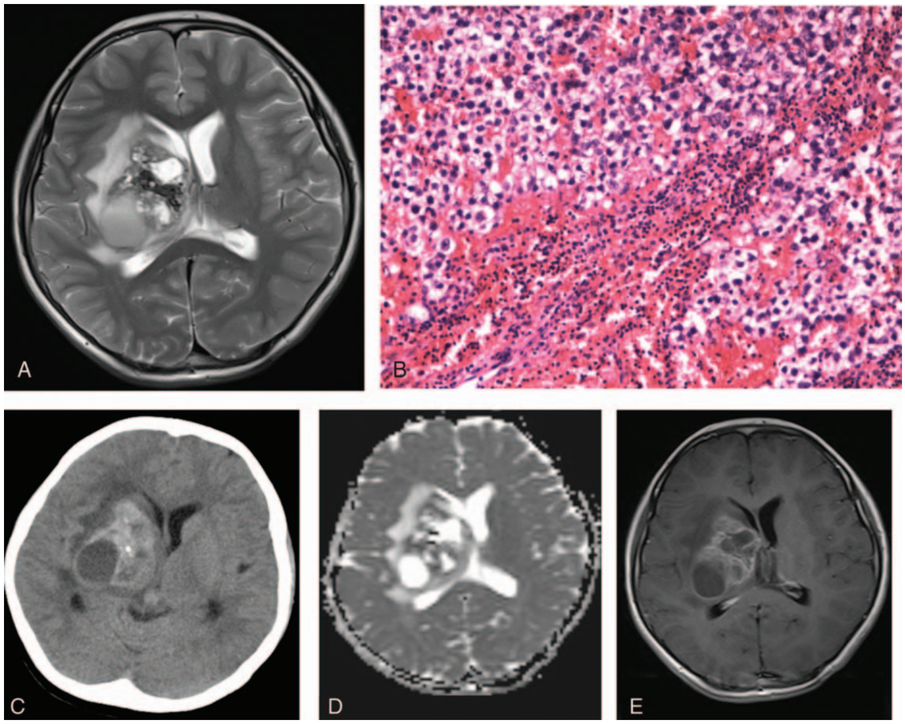

Figure 4. (A) Case 7. The mass in right basal ganglion shows heterogeneous entity, of which the solid component shows hypointensity on T2WI. (B) Case 7. Photomicrograph (original magnification, ×200; H&E stain) shows the tumor cells consisted of large polygonal cells with pleomorphic nuclei accompanied by clusters of small, round basophilic lymphocytes intermixed with foci of hemorrhage. (C) Case 7. The solid component of the mass presents high density compare with gray matter with multiple punctate calcifications inside the mass on unenhanced CT image. (D) Case 7. The solitary component of the mass indicates restricted diffusion on ADC map. (E) Case 7. The solitary component of the mass is enhanced obviously on post-contrast T1WI. ADC = apparent diffusion coefficient, CT = computed tomography, H&E stain = hematoxylin and eosin stain.

3. Discussion

The third ventricle development might cause displacement of ectopic germ cells from the midline, which could explain the occurrence of germ cell tumors in the off-midline structures.[12]

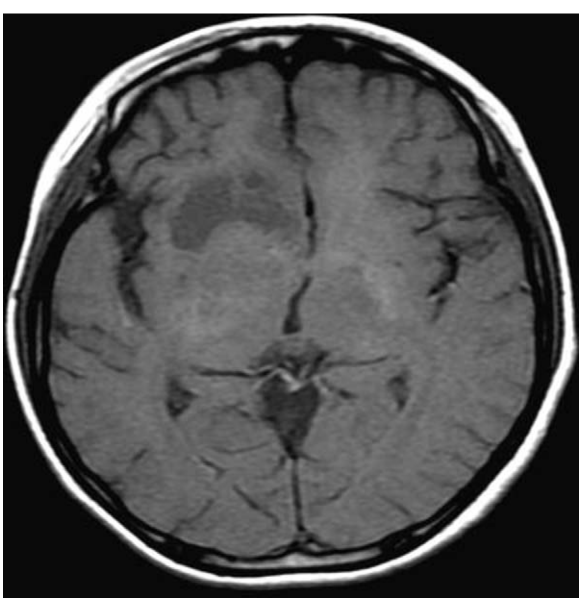

Figure 5. Case 9. Dilatation of right side sylvian fissure is seen on pre-contrast T1WI.

Clinical presentation of ectopic germinoma depends on the location, duration and histological type of the tumor. Mild hemiparesis, mental deterioration, nausea, and vomiting are common symptoms at the time of admission. These mild symptoms do not correlate with its average size.[13] Seven of the 12 cases in our group presented with signs of hydrocephalus on image, but only 3 patients complained of headache. In keeping with previous surveys,[2,12,14] absolute male predominance was observed in the present study, with a male to female ratio of 5:1.

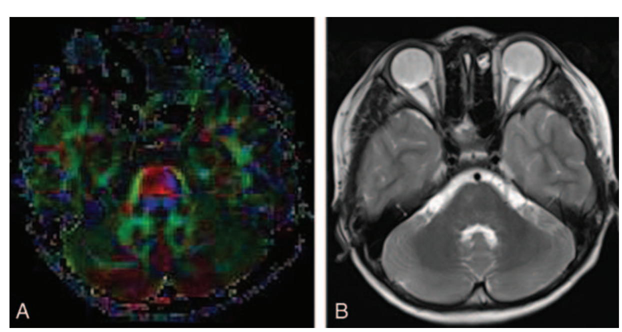

Figure 6. (A) Case 7. Decreased FA on right CST of in the pons on directional color FA maps. (B) Case 7. The pathway of right CSF in the pons shows mild high signal intensity on T2WI. CSF=cerebral spinal fluid, CST=corticospinal tract, FA=fractional anisotropy.

According to the gross imaging appearance of tumors, 2 main type(s) of tumors, that is, those with well- or ill-defined margins, were observed in this group. The distinct shape of the tumor may be related to different pathologies and growth activity and may exert diverse effects on treatment and prognosis of patients.

Coinciding with most of the previous reports,[2,15] the solid component of tumors have a high density. Moreover, calcified foci were most commonly observed in ectopic germinomas. Accordingly, the solid component of ectopic geminomas commonly showed relative isointensty on T1 and iso- or hypointensity on T2WI compared with gray matter.[16] The characteristic imaging findings of solid component of germinoma may be related to the relatively high nuclear to cytoplasmic ratio of neoplastic cells, which is similar to the pathologic basis of lymphomas.[17] The diffusion-weighted imaging technique has been applied to evaluate primary central nervous system (CNS) neoplasms such as lymphomas and primitive neurotodermal tumours (PNETs) based on molecular (Brownian) motion and cellularity of tumors.[18,19] However, only a few cases have described the diffusion imaging manifestation of germnomas arising in midline region.[20,21] In the present study, restricted diffusion was observed in the solid component of three (3/3) cases on ADC maps. The imaging findings can be explained by the pathology features of germinomas, which are characterized by variable proportions of cellular sheets or lobules of uniform germinoma cells with large round nuclei with prominent nucleoli.[20] Unlike in lymphoma, restricted diffusion was not the rule in germinomas which commonly contained prominent necrosis or cystic degeneration.[20] Unfortunately, few cases with DTI or DWI are available in the present group. The specific diffusion imaging features of germinomas need to be explored in more depth and with more cases.

The cystic formation is uncommon in the early stage of ectopic geminomas arising in off-midline region;[2,8] however, because most of our cases represent the late stage according to the size of the neoplasm, 92% (11/12) of the cases manifested multiple small cysts and few fused large cysts located in the central or peripheral regions of the tumors. Multiple small cysts could be observed in tumors that were even less than 2 cm in diameter. However, it is not a common sign observed in midline germinomas or in other tumors occurring in the basal ganglion or thalamus.

However, in small case series, calcifications are usually reported and proposed as an imaging feature of ectopic germinomas.[2,22–24] In our group of cases, 2 of the 3 cases with available CT images showed calcifications within the tumors. MR is limited in detecting calcifications alone using conventional sequences. Several case reports have shown that evidence of ipsilateral cerebral and/or brain stem hemiatrophy is highly suggestive of germinomas of the basal ganglia or thalamus.[2,8,11,25–27] However, the pathological mechanism of hemiatrophy in germinomas is not clear.[26] Obliteration of the perforating arteries was proposed as the underlying pathophysiological mechanism of hemiatrophy in ectopic germinomas. In addition, the proposed mechanism of hemiatrophy is the result of tumor involvement of the internal capsule fibers or thalamic ganglion cells with the subsequent interruption of thalamocortical connections.[2,11] Currently, the assessment of fiber tracts involved in intracranial tumors using the DTI technique has been well documented.[28,29] However, to our knowledge, there is no report about the manifestations of DTI in ectopic germinomas. Our results showed that the tumors prefer to infiltrate the intracranial projection fibers such as the corona radiate and that CST in 2 ectopic germinomas arose in the basal ganglion and internal capsule. As the upper part of the CST was infiltrated by tumors, obvious shrinkage of the lower segment of the CST in pons was noted. Therefore, our results from DTI support the inference that destruction of the pyramidal tract may be the potential pathologic mechanism of hemiatrophy and Wallerian degeneration in ectopic germinomas. In addition, DTI has a potential value in therapeutic planning and predicting the prognosis of the patients.

Even with effective tumor treatment, the clinical deficits cannot be improved for patients with ectopic germinoma.[10,23,30] Our imaging findings most likely provide evidence for this clinical problem. Aggravated ipsilateral atrophy of the brain and cerebral peduncle can be observed in the patient who underwent longitudinal MR studies over 2 years.

Ectopic germinoma features on imaging usually mimic high-grade astrocytoma and lymphoma occurring in the similar regions. Unlike germinomas, high-grade astrocytomas commonly show high signal intensity on T2WI and relative low density on CT compared with normal gray matter. Cystic formation and/or necrosis are commonly observed in high-grade astrocytomas but seldom in tumors with multiple small cysts. In addition, hemiatrophy is more often observed in germinomas. Some reports have even suggested that hemiatrophy can also be present in astrocytoma.[31] Another differential diagnosis is lymphoma, which often manifests as iso- or hypointesity on T2WI, which is similar to germinomas. However, lymphoma commonly occurs in patients who are older than 50 years of age, whereas germinomas occur in patient in their 20s. Moreover, uniform enhancement is commonly observed in lymphomas, except when it occurs in immunodeficient patients.

There are some limitations in our report. First, as a retrospective review, not all patients had CT and DTI examinations, so the imaging features of ectopic germinoma could not be investigated extensively. Second, the comparison study between imaging findings and pathology could not be completely conducted in each case.

In conclusion, the rare clinical entity of ectopic germinomas most commonly occurs in male patients in their 20s. The imaging features of these tumors include multicystic appearance, high density on CT, iso- to hypointensity on T2WI and restricted diffusion on ADC map for the solid component of the tumor. Signs of hemiatrophy support such a diagnosis. Moreover, the DTI can help visualize the infiltration and Wallerian degeneration of CST and the ability to predict the prognosis of the patient.

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