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Differentiation of Germinomas from Other Tumors in the Pineal Region with CT and MR Imaging, with Special Reference to Extension Patterns to the Thalami

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Summary. **To determine the computed tomography (CT) and magnetic resonance (MR) characteristics of pineal region germinomas, the author reviewed images from 40 patients with pineal region tumors.**

These tumors were divided into two groups: those with germinomas (n=17), and those with other tumors in the pineal region (5 with a germ cell tumor other than germinoma; 8, mixed germ cell tumor; 8, pineal parenchymal tumor; and 2, miscellaneous tumors; n=23). All cases were investigated with CT; 31 of the cases were also investigated with MR imaging. The following parameters comprised statistically significant differences between the two groups: maximum size of the tumor, tumor density of the precontrast CT, signal intensity of precontrast T1-weighted spin-echo images, and homogeneity of the tumor on both precontrast and postcontrast studies. This study found that extension patterns of pineal region tumors into the thalamus have significant implications in differentiating germinomas from other tumors of this region. Germinomas are characterized by thalamic extension without lateral displacement of the third ventricle walls due to direct compression by tumors ($P=.0034$). The analysis of tumor extension patterns, combined with the parameters mentioned above, may provide a more accurate differential diagnosis in pineal region tumors, leading to prompt and appropriate treatment.

Key words—pineal region tumors, MR imaging, CT, germinoma, germ cell tumor, thalamic extension.

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INTRODUCTION

Pineal region tumors account for approximately 0.7-1.0% of all intracranial tumors and 3-10% of brain tumors in children.[1] In Japan, the incidence of these tumors is about 3.3% of all brain tumors.[2] The pineal gland develops at the beginning of the second month of gestation as a small evagination between the posterior and habenular comissures.[3] Cellular proliferation of the neuroepithelial cells lining the diverticulum results in the development of a solid structure.[3] The pineal region includes the pineal gland, the surrounding cisterns, the posterior third ventricle, and the adjacent solid tissues of the brain stem, the thalami, and the overlying splenium of the corpus callosum.[4] Because of these embryologic and anatomic backgrounds, various types of tumors arise from the pineal region. Early initiation of radiation therapy can be very effective in achieving complete remission of germinoma. It is important, therefore, to differentiate germinomas from other types of pineal region tumor in order to provide prompt and appropriate treatment. The purpose of this paper is to define the characteristics of pineal region germinomas as they appear on computed tomography (CT) and magnetic resonance (MR) imaging. Furthermore, in the review of CT and MR imaging of several patients with germinoma, a specific extension pattern to the thalami was noted by the author. This extension pattern was analyzed in detail because, to date, only one report has evaluated the extension pattern of pineal region tumors to adjacent structures,[5] and it focused on the midbrain and the corpus callosum, not on the thalami.

MATERIALS AND METHODS

CT and MR imaging (obtained from March 1982 to December 1996) of 40 patients (35 males and 5 females, age range: 1-73 years [mean: 20.7±15.2 years]) having a pineal region tumor were retrospectively reviewed. In 34 of these patients, histopathologic diagnosis of a pineal region tumor was confirmed by surgery. Although histologic verification was not obtained in the remaining 6 patients, based on their response to radiation therapy, they were presumed to have germinomas and were included in this study.

Specimens obtained by surgical resection or stereotactic biopsy were fixed in 10% formalin, embedded in paraffin, and carefully handled in order to obtain as many sections as possible from a single specimen. Detailed histopathologic analyses were performed, with special attention paid to the evaluation of mixed germ cell tumors (GCTs). The sections were stained with hematoxylin-eosin, and immuno-histochemical methods were used when necessary.

MR examinations were performed on 31 patients using either a 1.5 T Siemens Magnetom H15 system or a 1.0 T Siemens Magnetom Impact system. Sagittal and axial T1-weighted spin-echo images (T1WI) (TR/TE/Excitations 500-600/12-15/2) and axial T2-weighted images (T2WI) (2500-3100/80-119/1) were obtained with a section thickness of 3-6 mm. In most cases, CT was performed with either a Siemens Somatom DR3 or Hitachi W1000, with section thicknesses varying from 1.5 to 5 mm. Postcontrast CT was obtained in all patients; postcontrast MR imaging was performed in 31 patients with the intravenous administration of contrast materials. Precontrast CT was obtained in all but 3 cases. CT and MR imaging were reviewed without knowledge of histologic findings. The following parameters were evaluated: maximum size of the tumor; homogeneity, margin, and shape of the tumor; density or signal intensity on CT and MR studies; homogeneity after contrast enhancement; the presence or absence of vascular flow void, cystic component, and hemorrhage in the tumor; central (engulfing by the tumor) or peripheral calcifications in the tumor; single or multiple intracranial lesions; and the degree of hydrocephalus. Densities or signal intensities of tumors were compared with those of the hemispheric gray matter, and were divided into 5 categories: markedly high, slightly high, iso, low and mixed. These parameters from the germinoma group (n=17) were compared with those found in the group of other tumors in the pineal region (n=23). The blood serum tumor markers (alpha-fetoprotein and human chorionic gonadotropin-beta subunit) were assayed in 38 patients, using the following parameters: serum tumor markers, sex and age.

Extension patterns of the tumor to the thalami were classified into 4 types based on axial CT and MR imaging findings as follows: type 1—bilateral thalamic extension "without lateral displacement of the third ventricle walls due to direct compression by tumors" (*without compression*); type 2—unilateral thalamic extension *without compression*; type 3—

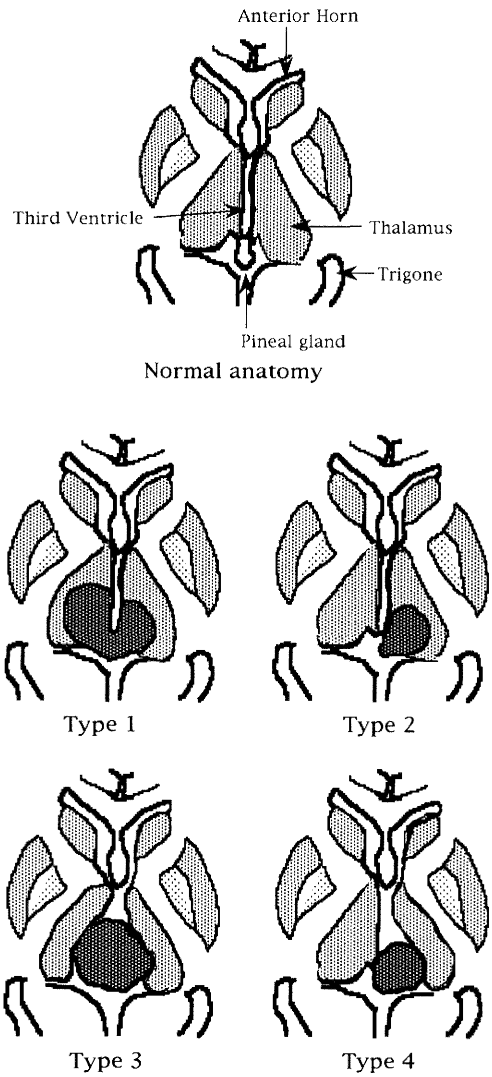

Fig. 1. Diagram of the the normal anatomy and extension patterns to the thalami. Normal anatomy at the level of pineal gland on axial CT and MR imaging. Extension patterns were classified into types 1 to 4 according to presence or absence of lateral displacement of the third ventricle walls due to compression by tumors and to unilateral or bilateral extension, respectively (●, tumor).

bilateral thalamic extension "with lateral displacement of the third ventricle walls due to direct compression by tumors" (*with compression*); type 4—unilateral thalamic extension *with compression* (Fig. 1). The frequency of thalamic extension *with compression* (types 3 and 4) and *without compression* (types 1 and 2) in the germinoma group was compared with that of the group of patients with other tumors. The frequency of bilateral extension (types 1 and 3) and unilateral extension (types 2 and 4) was also compared in both groups.

Fisher's exact probability test and Mann-Whitney's U test were used for statistical analysis of the associations between the germinoma group and other tumors. Statistical significance was set at $P<.05$.

RESULTS

Histopathologic diagnoses

Histopathologic diagnoses of 40 cases, including 6 with clinically diagnosed germinoma, are presented in Table 1. Classification of each tumor in this study was based on WHO international histologic classification of tumors.[6] In this classification, mixed GCTs are defined as any combination of histologic types of GCTs, including germinomas. In the present study, in cases with mixed GCTs, a dominant histologic component was referred to first, followed by other components, both in the text and tables.

Clinical, CT and MR imaging findings

Standard tests for association in a two-dimensional contingency table were used for analysis of the significance of the parameters. Densities on precontrast CT and signal intensities on precontrast MR imaging (Table 2) were also summarized on the two-dimensional contingency tables. The following parameters were statistically significant in differentiating germinomas from other tumors in the pineal region: serum tumor markers; maximum tumor size; density on precontrast CT; intensity on precontrast T1WI; and homogeneity in pre-and postcontrast studies both on CT and MR imaging (Table 3). In the germinoma

Table 1. Histopathologic diagnoses of pineal region tumors

Histopathologic diagnosis	No. of cases
Germ cell tumor (n=22)	
Germinoma*	17
Choriocarcinoma	1
Embryonal carcinoma	1
Yolk sac tumor	2
Mature teratoma (dominant)+Immature teratoma	1
Mixed germ cell tumor (n=8)	
Embryonal carcinoma (dominant)+Germinoma	2
Mature teratoma (dominant)+Germinoma	2
Mature teratoma (dominant)+Embryonal carcinoma	1
Mature teratoma (dominant)+Embryonal carcinoma+Germinoma	1
Yolk sac tumor (dominant)+Germinoma	2
Pineal parenchymal tumor (n=8)	
Pineoblastoma	4
Pineocytoma	4
Miscellaneous tumor (n=2)	
Meningioma	1
Carcinoma (Metastatic tumor)	1
Total	40

*: Germinomas included 6 cases of histologically non-verifiable tumors.

group, tumor markers were not elevated, and the tumors were smaller in size, showing a slightly high density on precontrast CT (Fig. 2a), a slightly high intensity on precontrast T1WI (Fig. 3a), and were homogeneous in both pre-and postcontrast studies (Figs. 2 and 3). Parameters with no statistical significance are also mentioned in Table 3.

Extension patterns to the Thalami

Fig. 1 and Table 4 show the results of the investigation of extension patterns to the thalami. Type 1 extension was seen in 7 cases of germinoma (Figs. 2 and 3), one case of mixed GCT (yolk sac tumor + germinoma), and one metastatic tumor. Type 2 extension was seen in only 2 cases of germinoma (Fig. 4). Type 4 extension was seen in one case of germinoma, one case of mixed GCT (yolk sac tumor + germinoma), and one case of pineoblastoma. The remaining 26 cases were categorized as type 3(Fig. 5). Type 1 and 2 extension patterns were classified collectively as "without lateral displacement of the third ventricle walls due to direct compression by tumors" *(without compression)*, and type 3 and 4 were classified as "with lateral displacement of the third ventricle walls due to direct compression by tumors" (*with compression*) (Table 5).

The sensitivity of the extension pattern *without compression* (type 1 and 2) in the diagnosis of pineal region germinomas was 52.9%, and the specificity was 91.3%. There was a statistically significant difference ($P = .0034$) between germinomas and other tumors in the frequency of the extension pattern *without compression* (Table 5). There was no statistically significant difference between germinomas and other tumors in the frequency of the unilateral extension pattern to one side of the thalamus (type 2 and 4).

Table 2. Densities on precontrast CT and signal intensities on precontrast MR imaging

	Germinomas n (%)	Other tumors n (%)
CT (n=37)		
Markedly high	0 (0)	4 (18.2)
Slightly high	14 (93.3)	3 (13.7)
Iso	1 (6.7)	5 (22.7)
Low	0 (0)	5 (22.7)
Mixed	0 (0)	5 (22.7)
Total	15 (100)	22 (100)
T1WI (n=31)		
Markedly high	0 (0)	0 (0)
Slightly high	7 (53.8)	2 (11.1)
Iso	3 (23.1)	3 (16.7)
Low	2 (15.4)	6 (33.3)
Mixed	1 (7.7)	7 (38.9)
Total	13 (100)	18 (100)
T2WI (n=31)		
Markedly high	1 (7.7)	2 (11.1)
Slightly high	5 (38.5)	5 (27.8)
Iso	5 (38.5)	2 (11.1)
Low	0 (0)	1 (5.6)
Mixed	2 (15.3)	8 (44.4)
Total	13 (100)	18 (100)

DISCUSSION

Many radiologic papers have been published on CT and/or MR findings[4,5,7-14] and histologic types[15-22] of pineal region tumors. However, the author could find only one report[5] that evaluated the relationship between pineal tumors and adjacent structures. This report focused on the splenium of the corpus callosum and the tectum of the midbrain. Thalamic extension of pineal region tumors has not been specifically evaluated in the literature.

Germinomas are reported to be homogeneous masses with attenuation equal to or slightly higher than that of the gray matter on CT.[4] On MR imaging, these masses show iso intensity on T1WI and iso to slightly high signal intensity on T2WI,[11] and enhancement of the tumor is reported to be homogenous.[8,9,12] In the present study, germinomas showed homogeneous content on both precontrast CT (66.7%) and MR imaging (69.2%), and showed a slightly high density on CT (93.3%) and a slightly high intensity on T1WI (53.8%) compared with the gray matter. The tumors were enhanced homogeneously on both CT (76.5%) and MR imaging (76.9%). These findings were statistically significant enough to differentiate germinomas from other tumors in the pineal region. Although 76.9% of germinomas showed iso or a slightly high intensity on T2WI, identical intensity was seen in 38.9% of the tumors in the other group. There was no statistical difference in signal intensity on T2WI between the two groups. Pathologically, germinomas are highly cellular neoplasms.[8] The hyperdense areas on CT may correlate with the densely cellular nature of germinomas.[8] On MR imaging, hypercellular neoplasms generally have relatively low intensity on T2WI and approximate the intensity of normal gray matter.[23] In other re-

Table 3. Clinical, CT, and MR findings of germinomas and other pineal region tumors

Parameters	Germinomas (n=17), mean±S.D. or n (%)	Other tumors (n=23), mean±S.D. or n (%)	*P* value
Age	17.7±4.2	23.0±19.5	NS
Sex			NS
Male	17 (100)	18 (78.3)	
Female	0 (0)	5 (21.7)	
Serum tumor markers			.0049
Negative	16 (100)	13 (59.1)	
Positive	0 (0)	9 (40.9)	
Maximum tumor size (cm)	2.7±1.1	3.8±1.3	.0074
Density on precontrast CT			.0002
High	14 (93.3)	7 (31.8)	
Other	1 (6.7)	15 (68.2)	
Calcification			NS
Central	3 (20.0)	2 (18.2)	
Peripheral	12 (80.0)	9 (81.8)	
Intensity on precontrast T1WI			.0166
High	7 (53.8)	2 (11.1)	
Other	6 (46.2)	16 (88.9)	
Intensity on T2WI			NS
High	6 (46.2)	7 (38.9)	
Other	7 (53.8)	11 (61.1)	
Flow void			NS
No	13 (100)	13 (72.2)	
Yes	0 (0)	5 (27.8)	
Homogeneity on precontrast CT			.0498
Homogeneous	12 (66.7)	7 (31.8)	
Heterogeneous	5 (33.3)	15 (68.2)	
Enhancement on CT			.0095
Hmogeneous	13 (76.5)	7 (30.4)	
Heterogeneous	4 (23.5)	16 (69.6)	
Homogeneity on precontrast MRI			.0130
Homogeneous	9 (69.2)	4 (22.2)	
Heterogeneous	4 (30.8)	14 (77.8)	
Enhancement on MRI			.0113
Homogeneous	10 (76.9)	5 (27.8)	
Heterogeneous	3 (23.1)	13 (72.2)	
Margin on MRI			NS
Clear	6 (46.2)	11 (61.1)	
Obscure	7 (53.8)	7 (38.9)	
Shape			NS
Round or oval	12 (70.6)	9 (39.1)	
Lobulate	5 (29.4)	14 (60.9)	
Cystic portion			NS
Yes	8 (47.1)	12 (52.2)	
No	9 (52.9)	11 (47.8)	
Intratumoral hemorrhage			NS
No	16 (94.1)	14 (63.6)	
Yes	1 (5.9)	8 (36.4)	
Multiple lesions			NS
Yes	5 (29.4)	1 (4.3)	
No	12 (70.6)	22 (95.7)	
Hydrocephalus			NS
Mild or moderate	12 (75.0)	12 (57.1)	
Severe	4 (25.0)	9 (42.9)	

NS, no significant difference.
Missing numbers were not performed on each modality or were negative in each finding.

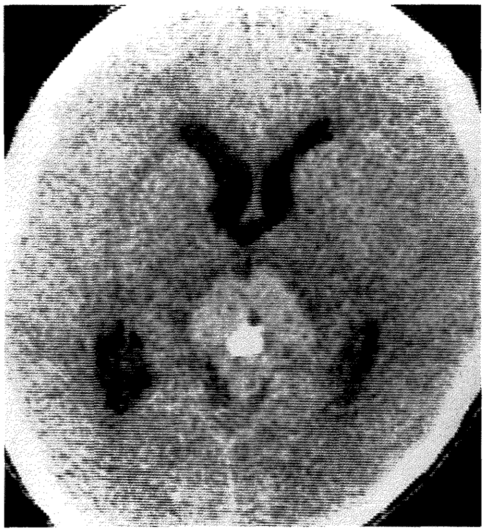

Fig. 2a.

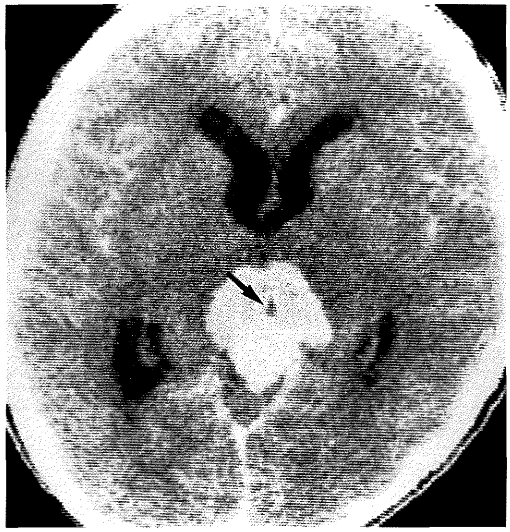

Fig. 2b.

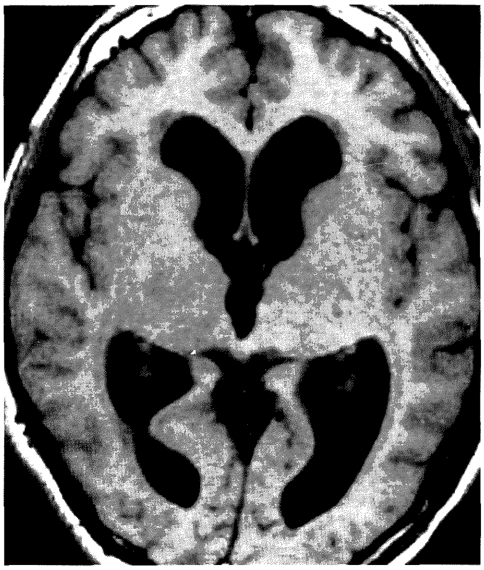

Fig. 3a.

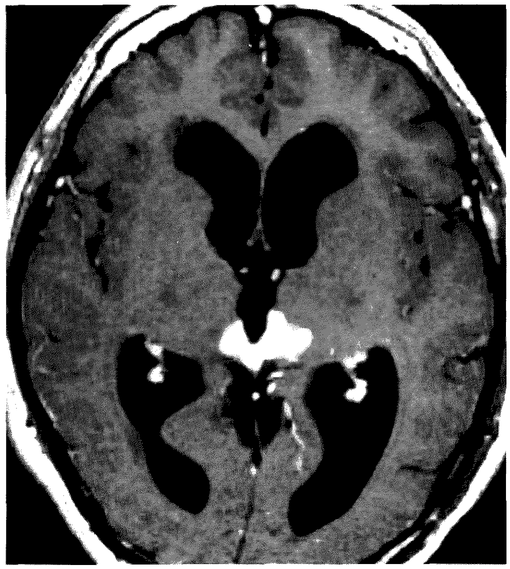

Fig. 3b.

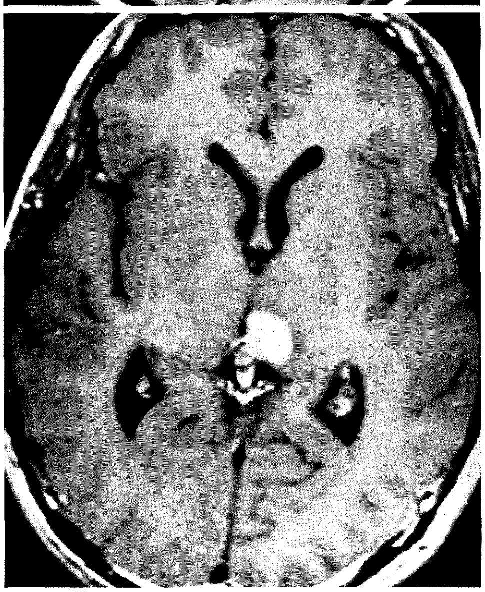

Fig. 4.

Fig. 5.

Table 4. Extension patterns to the thalami

Type	Germinomas (n=17), n(%)	Other tumors (n=23), n (%)
1	7 (41.2)	2 (8.7)
2	2 (11.7)	0 (0)
3	7 (41.2)	19 (82.6)
4	1 (5.9)	2 (8.7)

Table 5. Extension patterns to the thalami divided into "with" or "without" compression

Compression	Germinoma (n=17), n (%)	Others (n=23), n (%)
No (type 1 and 2)	9 (52.9)	2 (8.7)
Yes (type 3 and 4)	8 (47.1)	21 (91.3)

There was a significant difference in the frequency of thalamic extension *without compression* between germinoma patients with other tumors in the pineal region ($P = .0034$).

ports,[12,14] however, germinomas have shown various densities and intensities. One of these reports assesses the densities and intensities of germinomas compared to white matter, and another does not compare these with other structures.

Other statistically significant parameters for differentiating germinomas from other tumors in the pineal region were serum tumor markers and tumor size. Tumor markers were negative in all germinoma cases. The most striking finding in this study was that the extension pattern *without compression* was statistically significant ($P = .0034$) in differentiating germinomas from other tumors. Germinomas are usually poorly defined, not encapsulated, soft, and friable, on macroscopic, pathologic specimens, and tend to extensively infiltrate adjacent structures.[1,4,24) These characteristics reflect on the specific findings of the thalamic extension pattern on CT and MR imaging. Tanaka et al. reported some patients with pineal germinomas that extended along the wall of the third ventricle.[7] This pattern resembles the type 1 thalamic extension in the present study.

Unilateral extension into one side of the thalamus was not statistically significant in differential diagnosis. However, the type 2 extension pattern (extension to one side of the thalamus *without compression*) was found exclusively in 2 cases of germinoma. Further studies are needed to determine whether this finding is characteristic of germinomas.

While vascular flow void in the tumor and multiplicity in intracranial were also not statistically significant parameters, these parameters should be taken into consideration in differentiation between germinomas and other tumors. Vascular flow void detected on spin-echo MR imaging may reflect hypervascularity of the tumor seen on conventional angiography. Large vessels in hypervascular tumors appear as linear or serpentine regions of signal void within and about masses on spin-echo images and are an important sign for the diagnostician.[23] In the present study, this finding was evident in 27.8% of patients in the group with other tumors, these being one choriocarcinoma, one teratoma (Fig. 5), one meningioma, one case of yolk sac tumor, and one case of pineocytoma. Germinomas did not demonstrate vascular flow void. On cerebral angiography, tumors with vascular flow void on spin-echo MR imaging proved to be hypervascular tumors, showing such characteristics as many feeding arteries, tumor stains, and prominent drainage veins. No previous report has described vascular flow void in pineal region tumors. However, some teratomas and choriocarcinomas on angiography show fine vascular brushes in the early arterial phase and tumor stain with

Fig. 2. A 14-year-old boy with germinoma. **a**. Precontrast CT shows a homogeneous and slightly high density mass engulfing a large calcification centrally. Symmetrical extension into bilateral thalami *without compression* is also seen, **b**. Post contrast CT shows homogeneous enhancement of the mass with a tiny and non-enhancing cystic lesion (*arrow*) anterior to the calcification.

Fig. 3. A 21-year-old man with germinoma **a**. Axial precontrast T1WI (600/15) demonstrates a slightly high intensity mass in the pineal region extending into bilateral thalami, **b**. Postcontrast T1WI (600/15) with intravenously administrated Gd-DTPA shows a homogeneously enhanced mass. The third ventricle walls were not displaced laterally due to compression by tumor.

Fig. 4. A 15-year-old boy with germinoma. Gd-DTPA enhanced T1WI (500/26) discloses a pineal region mass extending into the left thalamus. The third ventricle walls are not compressed laterally by the tumor. This pattern of extension was categorized as type 2 in this study and was seen in only 2 cases of germinoma.

Fig. 5. A 12-year-old boy with teratoma. Axial T2WI (3000/90) shows a markedly heterogeneous and lobulated mass with mixed signal intensity. Bilateral thalamic extension *with compression* is recognized. Vascular flow void in the tumor is also seen *(arrows)*.

irregular vessels in the intermediate phase.[25,26] Multiple lesions were identified in 29.4% of germinomas in which the suprasellar region, ventricular wall and basal ganglia were involved. In other tumors, however, multiple lesions were found in 4.3%.

In conclusion, statistically significant parameters that are useful in differentiating germinomas from other tumors in the pineal region are: tumor size; density on precontrast CT; intensity on precontrast T1WI of MR imaging; and homogeneity on both precontrast and postcontrast studies. In addition, the most striking and characteristic feature of germinomas was the extension pattern to the thalami without lateral displacement of the third ventricle walls due to direct compression by tumors. A combination of these parameters could be helpful in differentiating pineal region germinomas from other tumors in the pineal region and lead to the initiation of prompt and appropriate treatment.

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