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CT of Pineal Tumors and Intracranial Germ-Cell Tumors

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We reviewed 59 cases of pineal tumors and intracranial germ-cell tumors. Most pineal tumors occurred in the first three decades of life, with the exception of pineocytomas, which were seen at a mean age of 34. A male preponderance was noted in the various pineal tumors, except for pineocytomas. The most common tumor of the pineal region was germinoma, which usually showed high density with homogeneously intense enhancement after IV administration of contrast medium. An increased prevalence of pineal calcification was also a feature of pineal germinomas. No characteristic CT features could be found to differentiate among pineal choriocarcinoma, germinoma, embryonal carcinoma, yolk-sac tumor, pineocytoma, and pineoblastoma.

CT is useful in detecting intracranial tumors, but the definite diagnosis should depend on pathologic examination and detection of tumor markers in the serum and CSF.

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Tumors arising in the pineal region can be classified into four groups according to their cells of origin: tumors of pineal-cell origin, tumors of germ-cell origin, tumors of other cell origin, and cysts. Tumors of pineal-cell origin are also called pineal parenchymal tumors and include pineoblastoma and pineocytoma. Tumors of germ-cell origin are called germ-cell tumors and include germinoma, mature teratoma (typical teratoma and benign teratoma), teratocarcinoma, embryonal carcinoma, yolk-sac tumor (endodermal sinus tumor), choriocarcinoma, and mixed germ-cell tumors containing components of the above. The last four tumors could also be called malignant teratoids. Other cell origins include glial tumors, hemangiopericytomas, and meningiomas [1, 2].

Alpha-fetoprotein (AFP) is produced by the yolk sac in the early stage of development, and human chorionic gonadotropin (HCG) is synthesized by the chorioepithelium. Yolk-sac tumor (endodermal sinus tumor) produces AFP [3–7]. Choriocarcinoma produces HCG [3–7]. Germ-cell tumors, which contain multiple differentiated extraembryonic structures, produce both AFP and HCG; such tumors are called embryonal carcinomas [3–7]. Embryonal carcinoma has the potential to differentiate into mature or immature teratoma, teratocarcinoma, choriocarcinoma, or yolk-sac tumor [3]. Some cases of teratocarcinoma and teratoma may have elevation of AFP or HCG [2, 6, 7]. Therefore, neoplasms of germ-cell origin can be classified not only according to their morphology but also by the specific biologic marker (HCG or AFP) they produce.

Although MR imaging has become increasingly popular in the diagnosis of intracranial tumors, CT remains a useful technique for the initial screening and evaluation of the pineal region because of its ease, rapidity, and sensitivity in the detection of calcification there [8]. We reviewed CT-demonstrated masses in the pineal region and intracranial germ-cell tumors, excluding meningiomas, gliomas, and cysts involving the pineal region.

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Materials and Methods

We reviewed 59 histologically confirmed intracranial germ-cell tumors and cases of CT-detected pineal tumors since 1980, excluding those of other cell origins. We classified the cell types according to their pathologic reports and the results of examination of tumor markers in the CSF and serum.

The CT findings in these cases were analyzed carefully. We evaluated their density and presence or absence of pineal, commissural, or tumoral calcification before administration of contrast material. A calcification was considered pineal if it was seen in the usual location of a pineal gland at the center of the rhomboid CSF space, including the third ventricle and C-shaped quadrigeminal cistern. It was considered commissural if it was seen just anterior to the usual location of pineal calcification in the region of the posterior or habenular commissure. In cases of pineal gland tumor, a calcification was considered tumoral if it was in the tumor and outside the usual location of a pineal or commissural calcification. The degree of enhancement and its degree of homogeneity were evaluated after administration of contrast material.

The CT scanners that we used for examination of these pineal and related tumors were the Delta-50 FS from 1979 to 1983 and the Siemens Somatom DR3 or DRH from 1983 to 1988. The contrast media we used for IV administration were Angiografin 65%* and Telebrix 38.† Axial scans were obtained in all cases; coronal scans were obtained in some cases of suprasellar mass.

Results

The tumors are classified by type and location in Table 1. There were 23 histologically proved germinomas without elevation of tumor markers; 14 were in the pineal region and nine were ectopic. The majority of these ectopic germinomas (eight of nine cases) were in the suprasellar region. Six pineal masses were classified as yolk-sac tumors (endodermal sinus tumors); three cases were confirmed histologically and three were presumed, with elevation of the AFP and a normal level of HCG. Four cases of pineal mass were classified as choriocarcinoma; one was biopsy-confirmed, and three were presumed to be choriocarcinoma because of elevation of HCG without elevation of AFP. Two cases were presumed to be embryonal cell carcinomas (one in the pineal and the other in the suprasellar region) because of elevation of both HCG and AFP. Three cases were histologically proved to be pineocytomas; one was proved to be pineoblastoma.

Five cases were classified as mixed germ-cell tumor: one in the pineal region, two in the suprasellar region, one in the parasellar region, and one in the basal ganglia. The pineal mixed germ-cell tumor had the histologic appearance of an epidermoid cyst but also had elevation of HCG. One case of suprasellar mixed germ-cell tumor was histologically confirmed to have components of immature teratoma and yolk-sac tumor. The other case of mixed germ-cell tumor in the suprasellar region had a histologic appearance of germinoma but also had elevation of AFP. The case in the parasellar region was histologically confirmed to have components of endodermal sinus tumor, germinoma, and mature teratoma. The mixed germ-cell tumor in the basal ganglia was found histologically to have immature teratoma and endodermal sinus tumor.

Fifteen cases of pineal mass with neither elevation of AFP nor HCG could have been germinoma, mixed germ-cell tumor, teratoma, pineocytoma, or pineoblastoma. They were categorized as unclassified. The pre- and postcontrast CT findings in these cases are listed in Table 1.

Discussion

Pineal tumors are relatively rare, with prevalences of 0.3–2.7% in the Western world [9]. In 1963, Ueki (cited in [10]) reported a prevalence of 4% (231/5794 cases) in all of Japan and concluded that pinealomas were far more common in Japan than elsewhere. In 1969, Araki and Matsumoto [10] found an even higher prevalence of 8% (136/1802 autopsies). In Mainland China, the reported prevalence of pinealomas has varied greatly, from 0.75% to 6.12% (average, 0.97%) [11, 12]. In Taiwan, the frequency of pinealoma in previous reports has ranged from 2.1% to 3.2% [9, 13–15].

The most common cell type in pineal tumors is germinoma. In our study, 14 of 23 pathologically confirmed intracranial germinomas occurred in the pineal region and were called pinealomas, or atypical pineal teratomas. Eight of these were single masses in the pineal region. Five cases were found to have multiple intracranial masses at their initial CT examination. Three of them had masses in both the pineal and suprasellar regions.

Nine cases of germinoma occurred in other intracranial locations. These have previously been called ectopic pinealomas. Intracranial ectopic pinealomas (germinomas) are most often located in the suprasellar region and thus are called suprasellar germinomas. In our study, eight of nine pathologically confirmed ectopic germinomas were in this region.

Most patients with pineal tumors and intracranial germinomas were under 30 years old, with a preponderance in the second decade. Most tumors had a male preponderance. Pineal germinomas had a male/female ratio of 13:1, while suprasellar germinomas had a ratio of 4:4. However, pineocytomas had a reversed gender ratio of 0:3 and were seen later in life than other tumors, with an age range of 20–51.

Most germinomas were of high density on plain CT: 11 of 14 pineal germinomas were of high density, as well as six of eight suprasellar germinomas. After IV administration of contrast medium, suprasellar and pineal germinomas showed intense enhancement (Figs. 1 and 2). The appearance of enhancement was homogeneous in most of the pineal germinomas (11/14) and suprasellar germinomas (six of eight). Pineal calcification in pineal germinomas was noted in 11 of 14 cases, less than the 100% prevalence reported previously [16]. In our study, there was no increase in the prevalence of pineal calcification in suprasellar germinomas (one of eight), although the prevalence has been noted to be increased in males with suprasellar germinomas [16]. In one previous report [17], a high prevalence of tumor calcification—the coarse, nodular pattern of parenchymal calcification on either side of the pineal body—was noted in pineal germinoma. However, neither our findings nor those in some other reports concur with these findings [1, 16].

According to Soejima et al. [18], germinomas in the basal ganglia and thalamus have a CT appearance different from pineal or suprasellar germinomas. On plain CT, they are irregularly defined as a slightly high-density area, frequently with intratumoral cysts and calcifications. The tumor showed mild to moderate and inhomogeneous enhancement after IV

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TABLE 1: Histology and CT Findings in Pineal and Related Intracranial Tumors

Location/ Pathology	Total No.	M:F Ratio	Mean Age ± SD	Histology		Precontrast CT							Postcontrast CT					
						Density				Calcification			Enhancement			Homogeneity		
				Conf.	Pres.	Low	Iso	Mixed	High	Comm.	Pin.	Tum.	None	Slight	Intense	Yes	No	Marg.
Pineal (n = 45)																		
Germinoma	14	13:1	15 ± 7	14	0	1	0	2	11	2	11	0	0	1	13	11	2	1
Unclassified	15	9:6	15 ± 13	0	15	0	3	2	10	2	11	0	0	1	14	14	1	0
Yolk-sac tumor	6	5:1	18 ± 8	3	3	0	3	0	3	2	2	0	0	0	6	5	1	0
Choriocarcinoma	4	4:0	13 ± 2	1	3	0	0	0	4	0	3	0	0	0	4	3	1	0
Embryonal carcinoma	1	1:0	15	0	1	0	0	0	1	0	0	0	0	0	1	1	0	0
Mixed germ-cell tumor	1	1:0	9	0	1	0	0	1	0	0	0	1	0	1	0	0	0	1
Pineocytoma	3	0:3	34 ± 16	3	0	0	0	1	2	0	0	2	0	1	2	2	1	0
Pineoblastoma	1	0:1	0.2	1	0	0	0	0	1	0	0	0	0	1	0	1	0	0
Suprasellar (n = 11)																		
Germinoma	8	4:4	12 ± 7	8	0	0	1	1	6	1	1	1	0	0	8	6	2	0
Embryonal carcinoma	1	1:0	17	0	1	0	0	0	1	0	1	0	0	0	1	1	0	0
Mixed germ-cell carcinoma[a]	2	2:0	9 ± 1	1	1	0	0	1	1	0	0	0	0	0	2	1	1	0
Parasellar (n = 1)																		
Mixed germ-cell tumor[a]	1	1:0	11	1	0	0	0	0	1	0	0	0	0	0	1	1	0	0
Other ectopic (basal ganglia) (n = 2)																		
Germinoma	1	1:0	10	1	0	0	0	0	1	0	0	0	0	1	0	0	1	0
Mixed-germ cell tumor[a]	1	1:0	9	1	0	0	0	1	0	0	0	0	0	1	0	0	0	1
Total	59	43:16		34	25													

Note.—M = male; F = female; Conf. = confirmed; Pres. = presumed; Iso = isodense; Comm. = commissural; Pin. = pineal; Tum. = tumoral; Marg. = marginal.

[a] Histology of mixed germ-cell tumors showed germinoma and elevated alpha-fetoprotein (one patient) and immature teratoma and yolk-sac tumor (one patient) in suprasellar tumors; germinoma, teratoma, and yolk-sac tumor in the parasellar tumor; and endodermal sinus tumor and teratoma in the basal ganglia tumor.

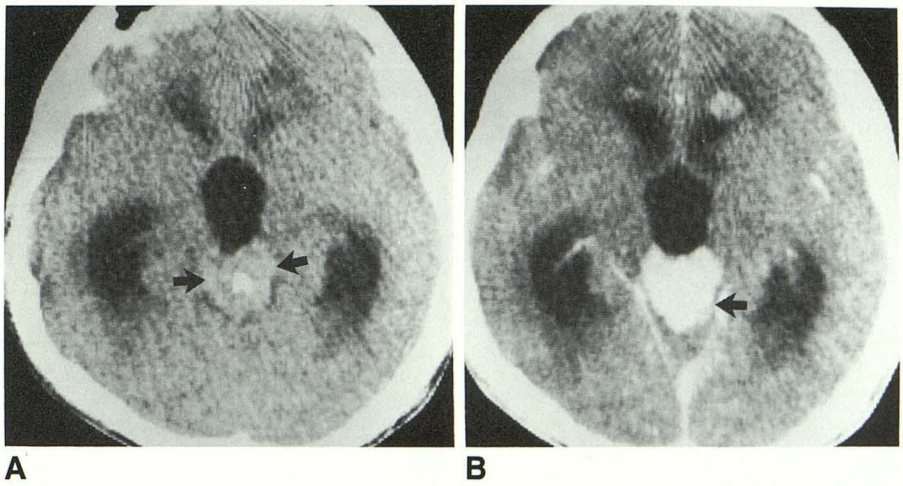


Fig. 1.—Pineal germinoma.

***A*, Noncontrast CT scan shows high-density mass lesion (*arrows*) in pineal region with enlarged pineal calcification. Obstructive hydrocephalus is obvious.**

***B*, Contrast-enhanced CT scan. Pineal mass lesion (*arrow*) shows homogeneous, intense enhancement. Two more masses are noted in frontal horns.**

injection of contrast medium. Our one case of germinoma in the basal ganglia showed a high-density mass with slight and inhomogeneous enhancement consistent with their description (Fig. 3) [18].

Similar to germinomas, pineal choriocarcinomas and yolk-sac tumors are of high density, or isodense, with a higher prevalence of pineal calcification. After IV administration of contrast medium, these tumors showed intense enhancement and most of them were of homogeneous density (Fig. 4). No characteristic CT features could be found to differentiate among germinoma, choriocarcinoma, embryonal carcinoma, and yolk-sac tumor in the pineal region [17].

In the series of Ganti et al. [17], all teratomas demonstrated fat densities, and four of five cases of teratoma had tumor calcification linear or nodular in appearance. In our study, a fat-density structure was found on the plain CT scan in only one case of mixed germ-cell tumor, which had a component of epidermoid tumor and showed elevation of HCG (Fig. 5).

CT demonstration of calcification is well known and plays an important role in the differential diagnosis of the disease.

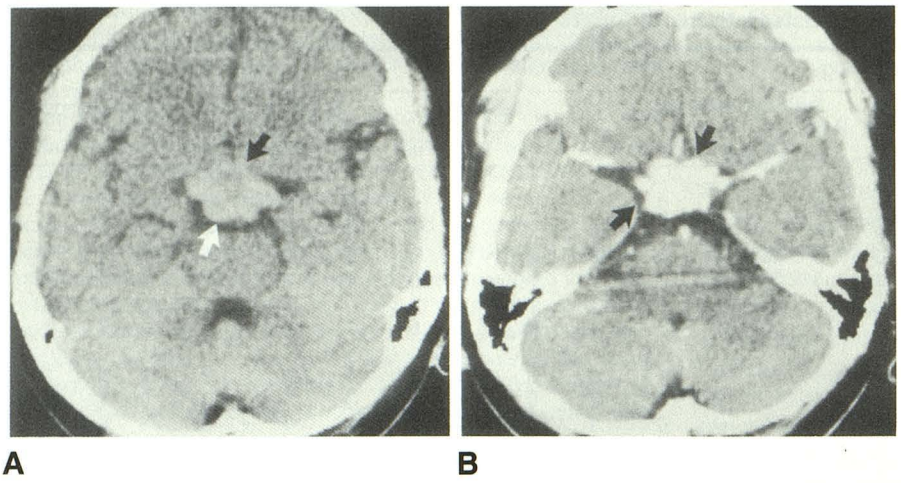


Fig. 2.—Suprasellar germinoma.
***A*, Noncontrast CT scan shows high-density mass lesion (*arrows*) in suprasellar region.**
***B*, Contrast-enhanced CT scan. Mass lesion shows homogeneous, intense enhancement (*arrows*).**

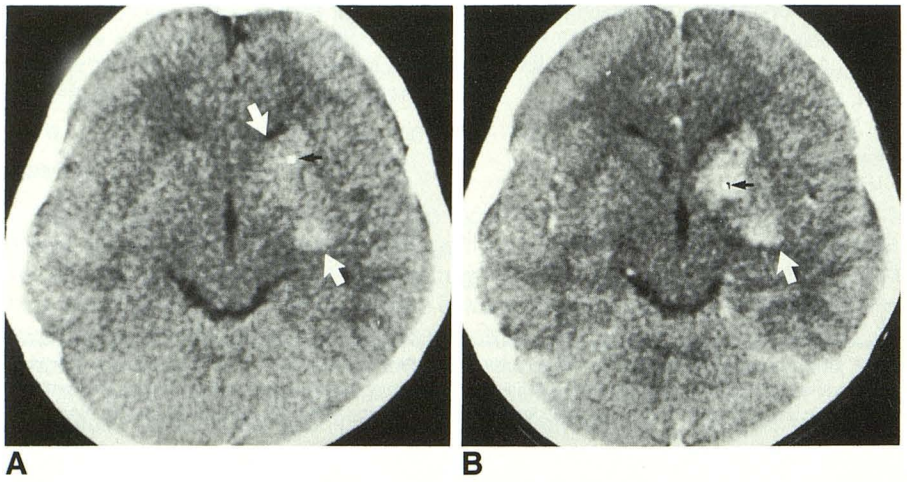


Fig. 3.—Germinoma in left basal ganglia.
***A*, Noncontrast CT scan shows high-density mass in left basal ganglia (corpus striatum) (*white arrows*). CT number in cursor (*black arrow*) measures 47 H.**
***B*, Contrast-enhanced CT scan. Mass lesion (*white arrow*) shows less obvious enhancement than in Figs. 1 and 2. CT number in cursor (*black arrow*) measures 56 H.**

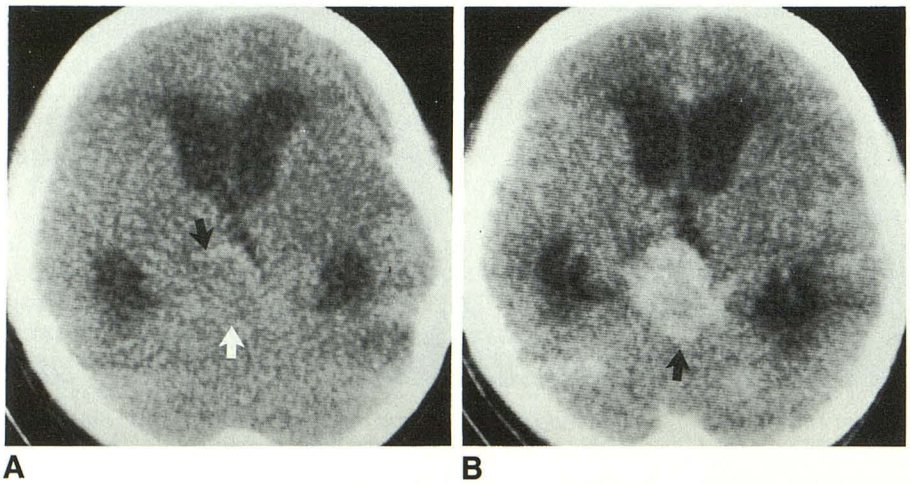


Fig. 4.—Pineal endodermal sinus tumor.
***A*, Noncontrast CT scan shows mixed high-density and isodense mass lesion (*arrows*) in pineal region. Obstructive hydrocephalus is obvious.**
***B*, Contrast-enhanced CT scan. Pineal mass lesion shows grossly homogeneous intense enhancement (*arrow*).**

Lofgren [19] found that pineal calcification is extraordinarily common in pineal tumors. The prevalence of pineal calcification in the presence of pineal tumors has varied from 27% to 75% [20]. In our series, the overall prevalence of pineal calcification in the presence of pineal tumor was 27 of 45. The frequency of pineal calcification was increased in pineal germinomas (11/14), yolk-sac tumors (two of six), and choriocarcinomas (three of four). However, no increase in pineal calcification was noted in suprasellar germinomas (one of eight). Tumor calcification was noted in four cases in our study: one suprasellar germinoma, two pineocytomas, and one mixed germ-cell tumor of the pineal gland. No tumor calcification was noted in pineal germinomas, pineal choriocarcinomas, or pineal yolk-sac tumors.

CT provided a rather clear anatomic boundary for tumor masses in the pineal region. The typical location of the pineal

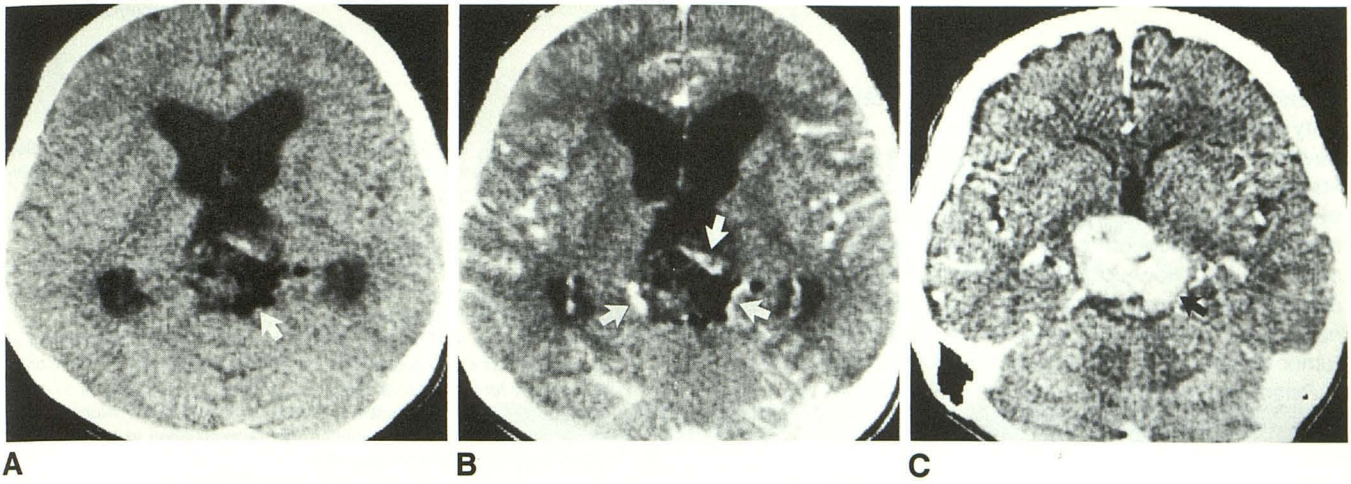


Fig. 5.—Mixed germ-cell tumor, confirmed to be epidermoid cyst histologically associated with elevated alpha-fetoprotein.
A, Noncontrast CT scan. Mixed-density mass lesion containing fat density (*arrow*) is noted in pineal region.
B, Contrast-enhanced CT scan shows slight enhancement of lesion, chiefly in its periphery (*arrows*).
C, Contrast-enhanced CT scan 4 months later. Intense enhancement (*arrow*), not present on previous scan, appears at caudal aspect of mass.

Fig. 6.—Pineocytoma.
A, Noncontrast CT scan shows mass lesion with tumoral calcification in pineal region (*arrow*).
B, Contrast-enhanced CT scan. Inhomogeneous enhancement is noted in mass (*arrow*).

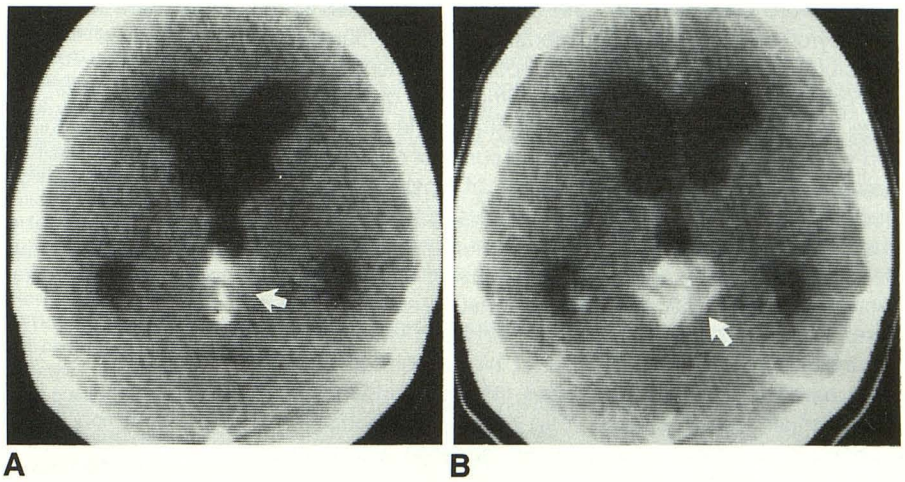
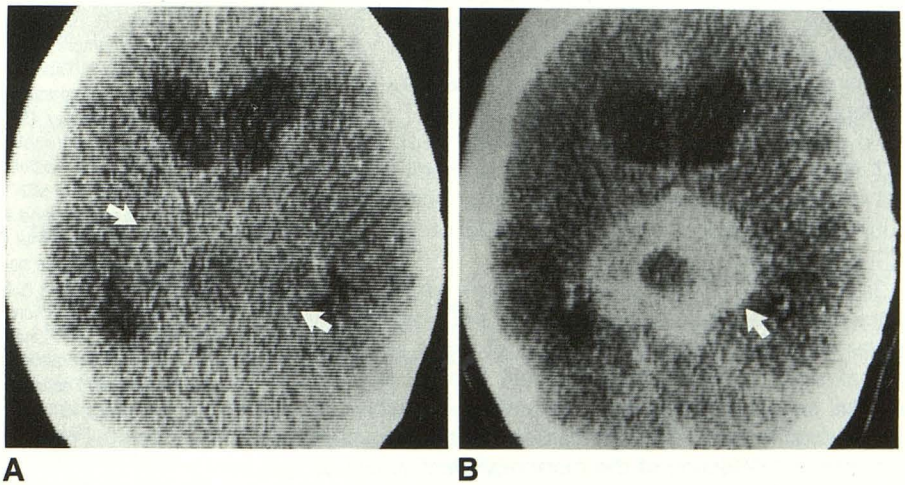


Fig. 7.—Pineocytoma.
A, Noncontrast CT scan. Slightly hyperintense mass lesion with low density is within pineal region (*arrows*).
B, Contrast-enhanced CT scan. Intense enhancement is noted in majority of mass, except in central low-density part (*arrow*).



tumor is posterior to the third ventricle, at the center of CSF-containing rhomboid structures including the third ventricle and quadrigeminal cistern. It has an intimate relationship to the posterior thalamus and the deep cerebral veins, such as internal cerebral veins and vein of Galen [21]. The deep-seated central location and intimate relationship of the pineal tumors to the deep cerebral veins have constituted a surgical challenge and a high operative morbidity and mortality following direct surgery [22–24]. Fortunately, there have been remarkable improvements in the diagnosis and treatment of

pineal tumors: (1) the advent of CT, with a rather high sensitivity in the detection of pineal tumors [1, 2, 17, 19], and development of CT-guided biopsy [25]; (2) the use of microsurgery in direct surgical resection; (3) the routine examination of tumor markers in the CSF and serum for detection of more malignant components other than pure germinoma, as well as for serial follow-up after treatment [4, 26]; and (4) the development of new chemotherapeutic drugs for more malignant pineal tumors such as embryonal carcinoma, yolk-sac tumor (endodermal sinus tumor), or choriocarcinoma [4, 26].

Pineocytoma is a tumor of pineal cell origin that arises from the large cells of the pineal parenchyma, whereas the pineoblastoma arises from the small cells. Pineoblastomas are often histologically indistinguishable from retinoblastomas, medulloblastomas, and neuroblastomas. These morphologically similar malignant tumors have been classified as primitive neuroectodermal tumor [27]. Tumors of pineal cell origin are much less common than tumors of germ-cell origin [17]. In our series, only three of 22 histologically confirmed pineal tumors were pineocytomas, and one was a pineoblastoma. Pineocytomas occurred preponderantly in female patients in our study as well as in previous reports. Zimmerman et al. [1] reported two cases of pineocytoma, both of which had large deposits of calcification at the site of the pineal gland and were of high density with marked contrast enhancement. Ganti et al. [17] reported eight cases of pineocytoma, with isodensity or hyperdensity before contrast administration and marked enhancement in all cases. Two of our three cases were of high density and one was of mixed density, with a central lucency on plain CT. After contrast enhancement, two cases showed intense enhancement and one showed slight enhancement (Figs. 6 and 7). Four of five cases of pineoblastoma reported by Ganti et al. had moderate enhancement with a small central lucency. Two cases of pineoblastoma reported by Zimmerman et al. were isodense with marked contrast enhancement.

Extension of pineal tumors can occur via three different pathways: direct continuity, seeding via the CSF, and occasionally via the bloodstream. In our study, five of 14 cases of germinoma involving the pineal region were found to have multiple masses intracranially at their initial CT examination. Two cases demonstrating a single pineal mass at the initial CT study were shown to have multiple seedings on a later CT examination. Similarly, four suprasellar germinomas were found to be multiple or to have intracranial seeding at the first CT examination.

In conclusion, CT is still a valuable examination for detecting intracranial masses, including those in the pineal and suprasellar regions. Differential diagnosis of mass lesions in the pineal region should include germ-cell tumors, pineal parenchymal tumors, tumors from other cells, and cysts. CSF and serum examination of tumor markers should be undertaken routinely for detection of the more malignant tumor components such as embryonal carcinoma, choriocarcinoma, and endodermal sinus tumor. The differential diagnosis of suprasellar germinoma should include pituitary adenoma, craniopharyngioma, suprasellar meningioma, chiasmal glioma, metastasis, and third ventricular tumors [28, 29]. The definite diagnosis of suprasellar or parasellar germ-cell tumors depends on tissue examination.

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