Intrasellar Germinomas: A Form of Ectopic Pinealoma*

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Tumors histologically identical to the seminomas and dysgerminomas of the gonads occur intracranially and are commonly known as "atypical teratoma" or "germinoma." These tumors are also often designated as "pinealomas" because of their frequent occurrence in the pineal region and their apparent histological resemblance to the fetal pineal glands at some stage of development, despite the fact that neoplasms of the pineal parenchymal cells, although rare, are morphologically distinct from the germinomas. Similar tumors, when they occur in locations other than the pineal gland, mostly in the chiasmal region, are referred to as "ectopic pinealomas" and have been defined as a distinct group from the clinical as well as therapeutic points of view. Germinomas arising in the hypothalamic region constitute less than a third of the total intracranial tumors of similar nature and are usually limited to the suprasellar region about the optic chiasm with invasion of the neighboring structures to variable extents. Extension of the tumor to the pituitary fossa resulting in radiologically detectable enlargement of the sella turcica occurs only on rare occasions. In fact, the lack of sellar enlargement has been considered one of the features distinguishing hypothalamic germinomas from pituitary tumors. Detailed pathological studies of the intrasellar involvement by germinomas are rare; most reports deal with cases in which this involvement was observed during surgery.

We are reporting two cases of germinoma in the region of the hypothalamus and sella turcica, studied at autopsy. In each instance the tumor occupied most of the sella turcica, which was markedly expanded, and involved the hypothalamus and third ventricle. Both neoplasms closely resembled a pituitary tumor clinically as well as on macroscopic examination.

Case Reports

Case 1. A 19-year-old boy began having visual difficulties accompanied by transient episodes of frontal headaches in September, 1965. Neurological examination at that time revealed no abnormality except for a questionable weakness of the right sixth cranial nerve. No visual field defect was present. He remained stable until the summer of 1966 when his vision began to fail rapidly; within 3 months he was unable to read. In addition, he complained of fatigue, loss of hair, and chronic constipation. He underwent various endocrine function tests and was found to be suffering from panhypopituitarism. At that time, he was blind in the right eye and had a left temporal hemianopia. No other neurological abnormality was present. Skull x-ray films revealed a markedly enlarged sella turcica.

Operation. In October, 1966, the patient underwent a right frontal craniotomy; a large tumor was seen involving the pituitary fossa and hypothalamus. Biopsy of the tumor disclosed a germinoma whose details are given below. The patient never regained consciousness and died 8 days after the operation.

Autopsy findings. The unfixed brain weighed 1500 gm. The right cerebral hemisphere was swollen. A large fleshy tumor was present in the retrochiasmal region extending posteriorly to the interpeduncular fossa (Fig. 1). The tumor displaced the optic chiasm anterosuperiorly and completely obscured the structures in the floor of the third ventricle. Inferiorly, the tumor occupied most of the sella turcica which was enlarged in all dimensions. A portion of the pituitary gland was grossly recognizable as a thin rim of brownish tissue compressed by the tumor against the sellar floor (Fig. 2). The tumor extended to the cavernous sinus bilaterally. Serial coronal sections of the

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Fro. 1. Case 1. Germinoma in the retrochiasmal region extending to the interpeduncular fossa. The optic nerves are infiltrated by the tumor (black arrow). The hemorrhagic area represents the site of biopsy (white arrow).

cerebrum disclosed invasion of the anterior two-thirds of the third ventricle by the tumor (Fig. 3). Aside from an area of fresh hemorrhage at the site of biopsy, the tumor was soft, and grayish in color with small areas of necrosis. A large fresh infarct with breakdown of tissue was seen in the region of the right basal ganglia (Fig. 3). The pineal

Fig. 1. Case 1. Germinoma in the retrochiasmal region extending to the interpeduncular fossa. The optic nerves are infiltrated by the tumor (black arrow). The hemorrhagic area represents the site of biopsy (white arrow).

Fig. 2. Case 1. Midsagittal section of the sphenoid bone showing enlarged sella turcica occupied by germinoma. The pituitary gland is infiltrated as well as compressed by the tumor (arrows).

Fig. 3. Case 1. Germinoma extending to the third ventricle and infiltrating the surrounding brain. Massive infarction is seen in the region of the right basal ganglia.
gland and posterior part of the third ventricle were free of tumor.

Microscopically, the tumor was found to be composed of spheroidal cells admixed with a variable number of lymphocyte-like cells distributed along delicate fibrovascular septa (Fig. 4). The spheroid cells were uniform in size and shape and appeared to be isolated from one another. The cytoplasm was stained faintly pink with hematoxylin and eosin. The nuclei, in general, were vesicular with prominent nucleoli and frequent mitoses. No teratomatous elements were present in this tumor. There were areas of recent hemorrhage and necrosis in the tumor at the site of biopsy. Sections representing the various parts of the hypothalamus, including the optic chiasm, showed diffuse infiltration by tumor cells to a variable extent. The neurohypophysis could not be identified. The adenohypophysis was partially infiltrated as well as severely compressed by the tumor. The sellar floor was intact. The pineal gland was free of tumor. Extensive fresh infarction was present in the right cerebral hemisphere and upper brain stem.

**Case 2.** A 13-year-old girl was seen in the endocrine clinic in June, 1968, because of her short stature since the age of 5 or 6. Her height and weight were found to be well below the third percentile for her age. The only evidence of sexual maturation was the presence of scanty pubic hair. The bone age was delayed about 2 years. Urinary gonadotropins were not detected. An arginine infusion test revealed no growth hormone response. Protein-bound iodine was normal. No abnormality was detected on neurological examination. A skull x-ray film, initially interpreted as normal, was found to show an enlarged sella turcica when it was reviewed later.

She remained apparently asymptomatic until October 9, 1968, when she had a sudden onset of vomiting and headaches followed by fever and stupor developing over a period of 12 hours.

**Examination.** On her admission to the hospital the patient was stuporous with slight neck stiffness and no focal signs. The optic discs were sharply outlined. Spinal tap showed grossly hemorrhagic cerebrospinal fluid under increased pressure. She was found to have diabetes insipidus which apparently had been present for some time but had not been discovered before. Skull films at this time again showed an enlarged sella with erosions of the floor. A carotid angiogram was suggestive of a suprasellar mass and increased intracranial pressure. The third ventricle, aqueduct, fourth ventricle, and basal cisterns were not visualized on air studies from above or below. She was treated with hydrocortisone, dilantin, pitressin, and fluid replacement. However, she remained comatose with occasional episodes of seizures and died 3 days after hospitalization.

**Autopsy findings.** The weight of the unfixed brain was 1350 gm. A large amount of fresh blood was seen at the base of the brain where a hemorrhagic mass became evident after removal of the blood clot. This mass occupied the retrochiasmal area and extended posteriorly to the interpeduncular fossa. Inferiorly, the hemorrhagic mass was continuous with a fleshy tumor which occupied most of the sella turcica (Fig. 5) and extended bilaterally to the cavernous sinuses. The sella turcica was considerably enlarged.

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**Fig. 4.** Case 1. Photomicrograph showing characteristic histologic pattern of germinoma, consisting of isolated spheroid cells interspersed by lymphocyte-like cells. Frequent mitoses are evident in the large cells. H. & E., × 240.
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in all dimensions by the tumor, which destroyed the sellar floor in some areas and bulged into the sphenoid sinus. The pituitary gland was found to be infiltrated as well as compressed by the tumor (Fig. 5). The extent of the suprasellar tumor was difficult to evaluate due to massive hemorrhage that had destroyed most of the hypothalamus and ruptured into the third ventricle through its floor (Fig. 6). Patchy areas of softening and fresh hemorrhage were present in the right basal ganglia. The pineal gland was normal and uninvolved by tumor. The cerebellar tonsils were molded by herniation into the foramen magnum.

Histologically, the tumor was a germinoma, similar to that described in Case 1 (Fig. 7). Additional features in this neoplasm consisted of the presence of massive hemorrhage in its suprasellar part and scattered discrete calcific deposits throughout the tumor (Fig. 8). The main tumor mass occupied the sella and diffusely infiltrated the pituitary gland. Portions of the adenohypophysis were surrounded by the tumor while the rest of the gland was severely compressed against the sellar floor (Fig. 8). The tumor extended to the submucosal region of the sphenoid sinus through the sellar floor. Large islands and nests of tumor cells were seen dispersed in the pools of fresh blood in the sections of the hematoma occupying the suprasellar region and the third ventricle. The hypothalamus itself showed infiltration by clusters of tumor cells. No unusual vascularity was seen in the tumor. The pineal gland showed no tumor. Diffuse anoxic changes of neurons were present throughout the brain. Fragments of necrotic cerebellar tissue were seen in the spinal subarachnoid space.

**Discussion**

Involvement of the pituitary fossa by germinomas located in the hypothalamic region...
is generally considered to be due to direct spread of the tumor, and has been reported to be present in 20% of the cases. Lack of sellar enlargement in such cases is explained by the infiltrative nature of the tumor. Although the sella is reported to be enlarged in certain cases of hypothalamic germinomas, no anatomical correlation with the extent of pituitary fossa involvement by the tumors is available.

In both cases reported here, the tumor occupied most of the sella turcica, virtually replacing the pituitary gland. In Case 2, the tumor broke through the sellar floor and appeared in the sphenoid sinus. In both instances, the tumor involved the hypothalamus as well. A similar case reported by Russell showed atypical teratoma that completely occupied the pituitary fossa without enlarging it and projected into the third ventricle. The possibility of an intrasellar origin of germinoma in such cases cannot be excluded, although the suprasellar region is generally assumed to be the primary site of origin for this group of tumors.

Regardless of the precise site of origin, the extensive intrasellar involvement by the germinomas illustrates a remarkable feature of these tumors not adequately emphasized in the past. Consequently, such cases may present considerable diagnostic difficulty, both clinically and on surgical exploration. While diabetes insipidus, visual disturbances, and pituitary hypofunction as initial symptoms, especially in children and young adults, are considered to be characteristic clinical features of hypothalamic germinomas, various other tumors in this region, notably the pituitary adenomas and craniopharyngiomas, may produce similar manifestations. Lack of sellar enlargement, under such circumstances, has been considered evidence favoring a diagnosis of suprasellar germinoma. Our cases, which had enlarged sellae accompanied by hypopituitarism (and by visual defects in Case 1), were clinically indistinguishable from pituitary adenomas despite the rarity of such tumors in this age group. Interestingly, diabetes insipidus, one of the most characteristic findings with hypothalamic germinoma, was absent in Case 1 and was not discovered in Case 2 until the terminal stage.

Spontaneous hemorrhage occurring in a germinoma, as reported in Case 2, is extremely rare. A similar instance of massive fatal hemorrhage, however, has been reported in a hypothalamic germinoma with mixed teratomatous components. The difficulty in clinical differentiation between an intrasellar germinoma and a pituitary adenoma may be further compounded by the occurrence of hemorrhage within the tumor, in view of the fact that such hemorrhage is known to occur occasionally in chromophobe adenomas.

The diagnosis of germinoma, especially with intrasellar involvement, may not be possible on the basis of macroscopic examination alone. Evidence of gross infiltration of the hypothalamic region by the tumor may suggest the possibility of a germinoma.

Fig. 8. Case 2. Low power photomicrograph of sagittal section of the sella showing germinoma (T) surrounding and compressing a portion of the pituitary gland (P). Tumor is also seen in the submucosal region of the sphenoid sinus. Arrow indicates an area of discrete calcific deposit within the tumor. H. & E., × 24.
since most of the other tumors involving intra- and suprasellar regions tend to be encapsulated or circumscribed. Germinomas are usually easily recognized on histologic examination. On rare occasions, however, a biopsy from such a tumor may be mistaken for an inflammatory lesion due to the presence of large numbers of lymphocyte-like cells. These are often mixed with foreign body giant cells which are sometimes present in germinomas.\textsuperscript{5,14} The presence of small specks of calcium within the tumor in Case 2 appears to be unusual. Such calcific deposits in germinomas located in the sellar region, if present in sufficient amounts to be detected by x-ray, might lead to an erroneous diagnosis of craniopharyngioma.

Although suprasellar germinoma is recognized as a distinct entity, an accurate clinical diagnosis is seldom made.\textsuperscript{14} The diagnostic difficulty is greatly increased when these tumors replace the pituitary gland and enlarge the sella turcica.

**Summary**

Two cases of germinoma involving the pituitary glands and hypothalami, with enlargement of the sella turcica, have been described. In both instances, the tumor (sometimes called “ectopic pinealoma”) occupied the greater part of the pituitary fossa. This remarkable feature of extensive intrasellar involvement by a germinoma, generally considered to be a suprasellar tumor, has not been adequately emphasized previously. The diagnostic difficulties presented by such tumors with large intrasellar components have been discussed. Spontaneous fatal hemorrhage occurring within a germinoma has been described in one case.

**References**