Intrasellar mixed germ-cell tumor

Case report

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Intracranial germinal tumors and teratomas typically arise from the pineal gland in the posterior region of the third ventricle, or from the infundibulum (median eminence) in the anterior region of the third ventricle.1,10 This latter site is the most rostral region of the pituitary gland and lies above the diaphragma sellae.6 The pituitary gland, beneath the diaphragma sellae within the sella turcica, has not previously been recognized as a site from which these tumors can arise. The present case documents the presence of a pluripotential germinal-cell tumor within the sella turcica, with minimal suprasellar extension. Our observations suggest that such tumors may arise within the pituitary gland as well as in the suprasellar and pineal regions.

Case Report

This 19-year-old right-handed white man was admitted to the Hershey Medical Center in July, 1981, with a chief complaint of headache and drooping of the left eyelid. His illness began 7 months prior to admission with the development of headaches, which typically occurred in the morning about 1 hour after arising, and lasted about 20 minutes. They were localized over the left eye. Two weeks prior to admission, the patient noted redness and swelling of the left eye. He was treated by an ophthalmologist with eyedrops for a presumed allergy. The swelling improved but he developed diplopia. One week before admission, he noted drooping of the left eyelid.

Examination. On admission, his general physical examination was entirely normal. He was 177 cm tall and weighed 60 kg. There was no thyromegaly or evidence for hypothyroidism. Hyperpigmentation was not present. Pubic hair and testicular and penile size were normal for an adult male. There was no anosmia. Facial sensation was normal with intact corneal and nasolabial reflexes. Cerebellar, motor, and sensory function were also normal.

Neuro-ophthalmological examination revealed total paralysis of the left lateral rectus muscle and moderate weakness of the left medial rectus, inferior rectus, and superior rectus muscles, as well as ptosis of the left upper lid. There was no proptosis. The left pupil was 2 mm larger than the right and reacted somewhat more sluggishly to both light and near stimulation. In addition, the left pupil failed to dilate with either 10% cocaine or 1% hydroxyamphetamine, indicating concomitant postganglionic oculosympathetic paresis (Horner’s syndrome). The right pupil dilated well with both 10% cocaine and 1% hydroxyamphetamine. Visual acuity was 20/20 in each eye. Color vision and visual fields (Goldmann perimetry) were normal. Fundus examination was normal.

Admission laboratory testing revealed a normal
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FIG. 1. Lateral tomogram of the sella turcica, which is symmetrically enlarged. There is thinning of the floor of the sella turcica as well as the dorsum sellae.

Asymptomatic 32-year-old man was found to have an elevated level of beta human chorionic gonadotropin (B-HCG) during a routine blood count, blood urea nitrogen, creatinine, and electrolytes. Urinalysis was unremarkable, with a specific gravity of 1.044. Basal endocrine studies demonstrated a human growth hormone (HGH) level of 1.5 ng/ml (normal less than 7.5 ng/ml), prolactin level of 104 ng/ml (normal less than 27 ng/ml), and morning serum cortisol level of 1.7 ng/dl. The thyroxine value by radioimmunoassay was 2.9 μg/dl (normal range 4.0 to 13.0 μg/dl), triiodothyronine resin uptake was 23% (normal 20% to 32%), free thyroxine index was 81 (normal 120 to 340), thyroid-stimulating hormone was 2.8 μU/ml (normal 0 to 8 μU/ml), testosterone was less than 1100 ng/dl (normal 300 to 1100 ng/dl), urinary follicle-stimulating hormone (FSH) was 17 mIU/hr (normal 190 to 1700 mIU/hr), urinary luteinizing hormone (LH) was 4100 IU/ml (normal 540 to 2500 IU/ml). The disparate LH and FSH levels led us to suspect an elevated serum level of beta human chorionic gonadotropins (B-HCG's) due to the cross-reactivity of this hormone in our LH assay. The specific B-HCG assay was elevated at 69 mIU/ml (normal 0 to 5 mIU/ml).

Skull radiographs and tomography of the sella turcica demonstrated mild enlargement of the sella, with irregular demineralization and thinning of the sellar floor and the dorsum sellae (Fig. 1). Computerized tomography (CT) demonstrated an enhancing intrasellar mass, which extended into the inferior chiasmatic cistern, slightly to the left of midline. There was no evidence of encroachment on the anterior third ventricle. Bilateral carotid angiography with additional submentovertex views demonstrated lateral displacement of the cavernous segment of the right internal carotid artery, a superior displacement of the supraclinoid carotid artery bilaterally, and a small vascular stain to the right of and posterior to the sella turcica, which was thought to represent a laterally displaced cavernous sinus.

Cavernous sinus venography demonstrated compression of the cavernous sinus bilaterally and good filling of adjacent venous channels (Fig. 2). These radiographic findings were thought to be consistent with a mass originating in the sella turcica, extending superiorly and laterally to the right.

Operation. On August 4, 1981, the patient underwent a transsphenoidal approach to the sellar region. The floor of the sella was markedly thinned, and in some regions absent. Upon opening the sellar dura we encountered a firm tumor mass. Frozen section diagnosis was teratoma. The tumor was removed in piecemeal fashion. Although the bulk of the tumor was firm, in the center a gelatinous region was encountered. The entire tumor was removed from the sella turcica. At the end of the procedure the diaphragma sellae could be well visualized. There appeared to be no extension of tumor above it. The walls of the cavernous sinus appeared to be thickened and, although no remaining tumor could be visualized within the sella, it could not be ascertained on inspection through the operating microscope whether or not tumor invaded the cavernous sinus wall.

Pathological Examination. Approximately 2 gm of tissue fragments were available for pathologi-

Fig. 2. Orbital venogram, frontal projection. The cavernous sinus is not opacified. It is presumed to be compressed or obliterated by a mass in the sella turcica. Small arrowheads indicate the inferior petrosal sinus, arrow the superior orbital vein, and large arrowhead the coronary sinus. The cavernous sinus lies below the coronary sinus and is not opacified.
cal examination. Histological examination revealed a mixed germ-cell tumor, consisting of immature teratoma and dysgerminoma. Teratomatous elements included tubules and cysts lined by columnar epithelium and squamous epithelium. Hair shafts and sebaceous glands were also present (Fig. 3 upper). There was abundant stroma with scattered ganglion cells, striated muscle fibers, immature cartilage, and areas of myxoid change. The dysgerminomatosus elements were comprised of scattered nests of large cells with clear cytoplasm and central hyperchromatic nuclei having prominent nucleoli (Fig. 3 lower left). Within the stroma there was an associated lymphoid infiltrate. Unusual individual syntrophoblast-like cells were present in the dysgerminoma. Immunoperoxidase staining for HCG by the peroxidase-antiperoxidase method described by Sternberger, et al., was positive within these syntrophoblasts (Fig. 3 lower right). Two different antibodies to HCG were employed. The first antibody was employed at a dilution of 1/160, and the second antibody, directed against the β subunit of HCG, was used at a dilution of 1/160.* Incubation with excess HCG abolished staining, demonstrating its specificity.

Postoperative Course. The patient did well, with subsequent resolution of his ptosis and oculomotor palsies. Replacement cortisone and thyroid hormone were initiated prior to surgery and continued postoperatively. A few days following surgery his serum β-HCG level was again determined and had decreased to 34.3 mIU/ml. Urine LH decreased to 1330 mIU/hr. Serum prolactin fell to 28.1 ng/ml. Because of the persistent elevation of serum β-HCG, a radiation course of 4000 rads in 20 fractions over 4 weeks was delivered to the sella. His subsequent β-HCG levels have been undetectable.

Provocative endocrine studies were obtained 5½ months postoperatively (2½ months after the comple-

* Antibodies to HCG obtained from Cappel Laboratories, Cochranville, Pennsylvania, and from the National Institute of Arthritis and Metabolic Diseases, Bethesda, Maryland.
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**TABLE 1**

<table>
<thead>
<tr>
<th>Authors, Year</th>
<th>Age (yrs), Sex</th>
<th>Cranial Nerve Dysfunction</th>
<th>Sella</th>
<th>Endocrinopathy</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Russell, 1944 Case 3</td>
<td>14, M</td>
<td>II</td>
<td>enlarged</td>
<td>diabetes insipidus: growth failure</td>
<td>died: tumor filled sella, replaced diaphragm &amp; extended to foramen of Monro, dysgerminoma with dermoid cyst</td>
</tr>
<tr>
<td>Horrax &amp; Wyatt, 1947 Case 2</td>
<td>12, M</td>
<td>none</td>
<td>enlarged</td>
<td>diabetes insipidus</td>
<td>died 16 mos post surgery: intra- &amp; suprasellar tumor, dysgerminoma</td>
</tr>
<tr>
<td>Kageyama &amp; Belsky, 1961 Case 4</td>
<td>9, M</td>
<td>III</td>
<td>enlarged</td>
<td>diabetes insipidus; hypoadrenal precocious puberty</td>
<td>died: 8-cm tumor in pituitary region, cavernous sinus invaded, pituitary stalk thickened, teratoma, choriocarcinoma</td>
</tr>
<tr>
<td>Simson, et al., 1968</td>
<td>11, M</td>
<td>III, IV, VI</td>
<td>enlarged</td>
<td>—</td>
<td>at surgery tumor found anterior to chiasm &amp; elevated rt optic nerve, extended into sella &amp; cavernous sinus, dysgerminoma</td>
</tr>
<tr>
<td>Ghatak, et al., 1969 Case 1</td>
<td>19, M</td>
<td>II, VI</td>
<td>enlarged</td>
<td>panhypopituitarism</td>
<td>died: sella filled with tumor, cavernous sinus invaded, intracranial extension, dysgerminoma</td>
</tr>
<tr>
<td>Case 2</td>
<td>13, F</td>
<td>none</td>
<td>enlarged</td>
<td>panhypopituitarism</td>
<td>died: sella filled with tumor, massive suprasellar extension, dysgerminoma</td>
</tr>
<tr>
<td>Guiffré &amp; Di Lorenzo, 1975</td>
<td>10, F</td>
<td>II, III, VI</td>
<td>enlarged</td>
<td>diabetes insipidus; panhypopituitarism, increased gonadotropins</td>
<td>intra- &amp; suprasellar tumor, teratoma at initial surgery; died 4 mos later, choriocarcinoma found at autopsy</td>
</tr>
</tbody>
</table>

Discussion

The patient’s clinical presentation suggested the presence of an intrasellar lesion with cavernous sinus involvement. Intrasellar involvement with mixed germ-cell tumors has been reported in seven previous cases (Table 1). In two cases no cranial nerve dysfunction was found. As in the present patient, involvement of the cranial nerves within the cavernous sinus was present in four cases. Three patients manifested visual impairment, but in only one was vision disturbed without concomitant oculomotor dysfunction.

Pituitary dysfunction has also been noted with intrasellar teratomas or germinal tumors. Four of the previously reported patients had diabetes insipidus. All these patients were found, either at postmortem examination or at craniotomy, to have extensive suprasellar (chiasmal and hypothalamic) involvement by tumor. Only two of the previously reported cases demonstrated panhypopituitarism. One further patient had increased gonadotropin secretion and one demonstrated precocious puberty at presentation. Our patient demonstrated hypothyroidism and probable depressed adrenal activity. Diabetes insipidus was not present. Prolactin was elevated, presumably as a result of functional pituitary disconnection from the hypothalamus. Gonadal function was presumably maintained by a β-HCG secretion from the tumor; as pituitary gonadotropins were depressed, serum β-HCG levels were elevated and β-HCG was demonstrated within syntrophoblasts in the dysgerminomatous tumor elements.

Radiological studies in previously reported cases have been limited but, as in our case, all demonstrated sellar abnormalities. In six cases the sella was enlarged, in one the dorsum sellae was eroded. In our case, cavernous sinus involvement was demonstrated by angiography and venography.
In previously reported cases, suprasellar (chiasmal, infundibular, and hypothalamic) involvement by tumor has been extensive. Even in the case of Giuffrè and Di Lorenzo,3 the tumor expanded above the sella and "protruded between the optic nerves." Hence, it has not been possible to ascertain whether these tumors arose from the infundibular region of the anterior third ventricle and invaded the pituitary gland, or whether they arose in the pituitary gland and extended rostrally into the brain. We believe that our patient developed a mixed germ-cell tumor within the sella turcica, with subsequent invasion of the cavernous sinus but without invasion of the brain. This belief is based on the following findings: 1) there was no disturbance of visual acuity or fields; 2) there was no diabetes insipidus; 3) although the tumor could be visualized within the suprasellar cistern on the CT scan, the diaphragma sellae was ballooned upward at surgery, and could be seen to return to its normal position with evacuation of tumor from the sella during surgery; 4) the diaphragma sellae was intact, and no tumor could be seen at surgery to pass through it. For the above reasons we believe that this pluripotential tumor arose from the pituitary gland.

References

10. Takeuchi J, Handa H, Nagata I: Suprasellar germi-

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