Ectopic pituitary adenoma of the third ventricle

Case report

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Ectopic pituitary adenomas without associated intrasellar adenomas are rare and are usually located in the
sphenoid sinus. Most have been reported without modern radiological, endocrinological, or electron micro-
scopic (EM) documentation. The case of a 47-year-old man with a third ventricular, ectopic, clinically non-
secretory pituitary adenoma, which was shown to be a gonadotrophic adenoma by immunohistochemical and
EM study, is reported. Neurological examination, extensive neurodiagnostic imaging, surgical anatomical ob-
ervation, and endocrinological evaluation showed no evidence of neoplasia outside the third ventricle.

Key Words • pituitary adenoma • third ventricle • ectopic tumor

Pituitary adenomas occur only rarely in extrasel-
lar sites that are not in continuity with the pitu-
itary. Such sites have included the sphenoid si-
num, nasal cavity, petrous temporal bone, and third
ventricle. Ectopic growth has been reported in patients
with a separate intrasellar pituitary adenoma, suggest-
ing that the ectopic growth arose from dissemination
of a primary intrasellar tumor, either spontaneously or
following surgical manipulation. In the very rare sit-
uation where ectopic pituitary adenomas have been
identified without intrasellar adenomas, it has been
hypothesized that the lesions arose from "an embry-
onic rest at the site of the obliterated craniopharyngeal
duct." Lloyd, et al., recently reviewed the nine published
reports of ectopic pituitary adenomas in patients with
normal anterior pituitary glands and added two of their
own. Seven occurred within the sphenoid sinus, one in
the nasopharynx, and one in the inferior portion of
the third ventricle. We are reporting another such case
with extensive neurodiagnostic imaging and endocri-
nological evaluation to rule out evidence of a different
tumor.

Case Report

This 47-year-old father of two children was brought
to an emergency room by a friend who explained that
the patient had been having fainting spells, headaches,
occasional blurred vision, and an unsteady gait for at
least 3 months. The patient had been living in an
automobile for months. He stated that he had used
many different drugs for nontherapeutic purposes for
at least 25 years. There was no history of temperature
intolerance, impotence, or change in weight.

Examination. Physical examination revealed a dis-
heveled patient, appearing much older than his stated
age, with matted gray shoulder-length hair and beard.
Ecchymoses and evidence of a healing abrasion in the
right orbitozygomatic region were evident. Speech was
slow but he was oriented to person, year, and month;
he answered questions appropriately but tended to con-
fabulate. He seemed content to lie supine in bed for
many hours with carphology as his only activity. His
gait was wide-based and he could stand only with
assistance. Papilledema was present in both optic discs,
otherwise the first through 12th cranial nerves were
intact bilaterally. Visual fields were normal to testing
by confrontation. There were no gaze palsies. Deep-
tendon reflexes were mildly delayed.

Radiographs of the skull were normal except for a
suggestion of flattening of the dorsum sellae; the sella
turcica was normal. Computerized tomography (CT)
demonstrated a tumor which filled the third ventricle
and was isodense with brain; however, on administra-
tion of contrast material, it enhanced in a heterogeneous
manner. On T1-weighted magnetic resonance (MR)
imaging with and without gadolinium enhancement in
FIG. 1. T1-weighted magnetic resonance images. Left: Coronal plane showing a homogeneous mass confined to the third ventricle and causing obstructive hydrocephalus. Right: Sagittal plane showing a plane of cerebrospinal fluid separating the third ventricular mass from the normally enhancing, normal-sized pituitary gland.

the coronal and sagittal planes, the lesion was confined to the third ventricle but bulged downward and posteriorly into the suprasellar and interpeduncular cisterns (Fig. 1). The tumor was slightly hypointense compared to brain before gadolinium was administered and became heterogeneously hyperintense after gadolinium injection. A distinct plane of cerebrospinal fluid separated the lesion from the pituitary gland (Fig. 1 right). Angiography demonstrated only lateral and third ventricular enlargement. Preoperative serum hormone levels were as follows: testosterone 83 ng/dl (normal 300 to 1000 ng/dl); luteinizing hormone (LH) undetectable (normal 2 to 12 mIU/ml); follicle-stimulating hormone (FSH) undetectable (normal 1 to 4 mIU/ml); thyroxine 2 μg/dl (normal 4 to 12 μg/dl); triiodothyronine resin uptake 29% (normal 25% to 35%); thyroid-stimulating hormone (TSH) 0.2 mU/liter (normal 0.5 to 5.0 mU/liter); prolactin 11 ng/ml (normal 1 to 10 ng/ml); cortisol 30 μg/dl (normal 9 to 25 μg/dl); growth hormone undetectable (normal 0 to 5 ng/ml); and alpha subunit 1.2 ng/ml (normal 0.5 to 2.1 ng/ml).

Operation. The lesion was operated on via the transcallosal approach. Grayish tissue with the consistency of a gel or very soft semisolid was protruding upward through both dilated foramina of Monro. It could easily be distinguished from choroid plexus. The lesion was attached to the upper three-quarters of both lateral walls of the third ventricle. The bulk of the lesion was removed, but there remained a layer of tumor on each side of the third ventricle. Following resection, the floor and lateral walls of the third ventricle were intact. The microscope's light transilluminated the third ventricular floor, through which the optic chiasm and both optic nerves could be clearly recognized and were seen to be uninvolved by the lesion.

Postoperative Course. The postoperative course was relatively smooth. Postoperative CT revealed a layer of abnormality, probably residual neoplasm, on both lateral walls of the third ventricle.

Two weeks postoperatively, the patient underwent a thyrotropin-releasing hormone (TRH)-stimulation test, with intravenous injection of 250 μg of synthetic TRH. At 0, 20, 30, and 60 minutes after injection, the serum TSH concentrations were 2.1, 3.3, 3.9, and 3.5 mU/liter, respectively, and the serum alpha subunit concentrations were 1.4, 2.2, 2.2, and 1.6 ng/ml. The next day the patient underwent a standard gonadotropin-releasing hormone (GnRH) test, with intravenous injection of 100 μg of synthetic GnRH. At 0, 20, 30, and 60 minutes after injection, the serum LH concentrations were less than 1.0, 12, 28, and 42 mlU/ml, serum FSH levels were less than 1, 2, 4, and 4 mlU/ml, and serum alpha subunit concentrations were 1.2, 2.6, 2.5, and 2.3 ng/ml.

The patient was treated with 6-MeV radiation, 95% isodose surface, at 180 cGy per day to a dose of 45 Gy. Three months later he was alert, could walk slowly, and had a flat affect. Family and friends reported that this was his normal personality.

Pathological Examination. Fresh tissue was fixed in 10% buffered formalin for light microscopy and immunohistochemistry. Paraffin-embedded sections were stained with hematoxylin and eosin, periodic acid-Schiff (PAS)-orange G, and Wilder's reticulin method. Immunohistochemical studies were performed using...
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FIG. 2. Photomicrograph demonstrating the characteristic monotonous, bland-cell population and prominent vascularity of the pituitary adenoma. H & E, × 212.

FIG. 3. Electron micrograph of the pituitary adenoma showing poorly developed cytoplasm, bland nuclei, and diagnostic small secretory granules. × 5800.

the horseradish peroxidase-antiperoxidase method of Sternberger, et al.13 Rabbit antisera (with the exception of the anti-alpha subunit) were obtained commercially;* the anti-alpha subunit was obtained from the National Institutes of Health and was diluted 1:200. Control tissue consisted of non-neoplastic pituitary glands. Tissue for electron microscopy (EM) was fixed in 2.5% glutaraldehyde in 0.1 M phosphate buffer (pH 7.2), postosmicated in 1% OsO4 (0.1 M phosphate buffer), dehydrated in graded ethanol acetone, and embedded in Epon-Araldite. Thin sections were stained with 2% uranyl acetate and lead citrate and were examined with a Phillips 201 electron microscope.

A vascular neoplasm consisting of sheets of monotonous bland cells with moderate amounts of cytoplasm, chromophobic by PAS-orange G stain, was seen on light microscopy (Fig. 2). Nuclei were ovoid and vesicular, and possessed inconspicuous nucleoli. No mitotic activity or necrosis was present. Reticulin staining showed the complete disruption of a normal acinar pattern. Immunohistochemical stains were negative for prolactin, growth hormone, adrenocorticotropic hormone, TSH, and FSH. Diffusely distributed, moderate immunostaining for LH and slightly stronger staining for alpha subunit were present (less than one-third of the cells were positive for each stain).

Electron microscopy showed elongated cells with centrally placed nuclei, finely dispersed chromat, and inconspicuous nucleoli, often near the nuclear membrane. Stacks of rough endoplasmic reticulum were seen in some cells and the Golgi apparatus was neither dilated, prominent, nor honeycomb-like. Mitochondria were not abundant and the small, sparse secretory granules averaged 150 nM in size and tended to be near the cell borders (Fig. 3).

Discussion

Low preoperative serum levels of thyroxine and testosterone suggested that the patient had preexisting hypothyroidism and hypogonadism. Corresponding low or normal baseline levels of serum TSH, FSH, and LH localized the defect to the hypothalamic-pituitary axis. The mildly elevated prolactin level, blunted but positive TSH response to TRH, normal LH response to GnRH, and normal alpha subunit responses to TRH and GnRH strongly suggested that the patient's pituitary gland was responsive to stimulatory factors. The site of the endocrine defect was therefore the hypothalamus and not the pituitary gland; hence there existed no endocrinological evidence for an intrasellar lesion.

The anterior pituitary gland, which is thought to derive from Rathke's pouch, may leave residual cells along its ontological pathway, commonly in the sphenoid sinus. Rarely, these remnants give rise to adenomas in the absence of detectable intrasellar adenomas (11 currently accepted cases have been reported in the literature).8 Slightly more often, adenomas have been reported in both ectopic and intrasellar sites, the former probably resulting from dissemination of the latter9,10 or possibly as a result of a similar response of both ectopic and intrasellar pituitary tissue to a common stimulus for neoplastic change.

The intrasellar pituitary gland of our patient appeared normal on detailed MR imaging. As noted by Cushing9 and nicely reviewed by Kepes and Fritzlen,7 adenomas occasionally arise from cells of the pars tuberalis located high on the hypothalamic-hypophyseal stalk and expand above the diaphragma sellae without

* Rabbit antisera were obtained from Cambridge Research Laboratories, Cambridge, Massachusetts.
compromising the sella and its normal pituitary gland. Such a growth pattern was seen in the case of Kepes and Fritzlen, with neoplastic tissue found at the base of the brain and in the region of the optic chiasm. Our patient showed no evidence of involvement of the optic chiasm or pituitary stalk. Therefore, this case differs from those described by Cushing and by Kepes and Fritzlen and it seems highly probable that the cells of the pars tuberalis were not the source for the adenoma in our patient. It is possible that the neoplasm in this case and that of Rothman, et al., and the rare third ventricular craniopharyngioma reported by Cashion and Young arose from aberrantly migrated cells of the craniopharyngeal duct.

Since the pituitary gland was not biopsied, we cannot exclude the possibility of a microadenoma in an intrasellar location, but detailed neurodiagnostic imaging and endocrinological tests showed no evidence of a secretory adenoma or of primary hypopituitarism. Relevant to this possibility is the case of Corenblum, et al., who reported a patient with acromegaly and an ectopic pituitary adenoma within the sphenoid sinus in whom growth hormone levels failed to normalize following removal of the adenoma. Exploration and biopsy of the anterior pituitary gland failed to disclose an identifiable intrasellar pituitary adenoma; however, an intrasellar mass was discovered 1 year later.

In a review by Horvath and Kovacs of 30 gonadotrophic adenomas of the human pituitary, all of the tumors presented as macroadenomas, mostly grade III and grade IV with suprasellar extensions; this type of adenoma constitutes 4.1% of all human pituitary adenomas and occurs equally in men and women. On EM, our patient's tumor resembled the gonadotrophic adenomas which tend to occur in men and are similar to null-cell adenomas with poorly developed cytoplasm. Our patient is therefore unique with respect to tumor location and clinical presentation but not with respect to tumor immunohistochemical and electron microscopic features. This is the fifth reported case of an ectopic pituitary adenoma (all others occurred in the sphenoid sinus) to be studied by immunohistochemistry, and the only one to be documented by EM. Our EM immunohistochemical studies illustrate the morphological and secretory similarity of ectopic pituitary adenomas with the far more common intrasellar pituitary adenomas.

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References


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