Acromegaly associated with suprasellar and pulmonary hemangiopericytomas

Case report

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The authors report the case of a 35-year-old acromegalic woman who developed amenorrhea and decreased left vision, and who was found to have suprasellar and pulmonary hemangiopericytomas. Total removal of the suprasellar hemangiopericytoma resulted in normalization of the plasma human growth hormone (GH) level and a marked decrease in size of the pulmonary hemangiopericytoma. Immunoperoxidase studies for GH and human hypothalamic growth hormone-releasing factor (GHRF) demonstrated immunoreactive intracellular GH only in the suprasellar hemangiopericytoma, with no immunoreactive intracellular GHRF evident in either the suprasellar or pulmonary hemangiopericytoma.

KEY WORDS • acromegaly • hemangiopericytoma • suprasellar tumor • pulmonary tumor • human growth hormone

ACROMEGALY usually occurs in patients with somatotrophic pituitary adenomas. Occasionally it is found in patients with multiple endocrine neoplasia,2,25,38 tumors of amine precursor uptake and decarboxylation (APUD) cells,8,9,14,28,32,33,37 or the diencephalic syndrome.9 Recently, human pancreatic growth hormone-releasing factor (GHRF) has been isolated from a human pancreatic tumor14 and proved to be identical to human hypothalamic GHRF.22 On rare occasions, acromegaly has also been observed in association with intracranial meningioma,4,21 neurofibromatosis,1 osteosarcoma,16 and breast cancer.15,36 In this report, we describe a case of acromegaly associated with suprasellar and pulmonary hemangiopericytomas.

Case Report

This 35-year-old acromegalic housewife, who had a healthy 5-year-old son, noticed amenorrhea and a decrease of left visual acuity in early March, 1983. On March 30, 1983, she was found unconscious in the kitchen due to diabetic coma associated with the acromegaly.

Examination. On admission on April 14, 1983, excessive sweating and skin pigmentation was noted. Visual acuity was 20/500 on the left and 20/40 on the right, with a bitemporal hemianopsia. Basal plasma human growth hormone (GH) was 33.1 ng/ml, with no response to intravenous administration of glucose or insulin. Basal plasma adrenocorticotropic hormone (ACTH) was 55 pg/ml, exhibiting a slight decrease with insulin administration. Basal plasma prolactin and thyrotropin were within normal limits, and basal plasma levels of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) were slightly below normal. Fasting blood sugar was 261 mg/dl. There was no evidence of chronic liver or renal disease. The dorsum sellae was thin on plain skull films. Computerized tomography (CT) scanning revealed a round, high-density, well-circumscribed suprasellar mass compressing the third ventricle (Fig. 1 upper). Carotid angiography demonstrated opening of the left carotid siphon and elevation of the horizontal portion of the anterior cerebral artery on both sides. No tumor stain was visualized. Chest x-ray films disclosed a round mass lesion, about 5.0 cm in diameter, in the hilus of the left lung (Fig. 2 left).

Operation. A right frontal craniotomy was performed on April 20, 1983, at which time a reddish-brown tumor was found in the prechiasmal cistern. No
fluid was obtained with needle aspiration. The tumor capsule was opened and the mass excised with a ring curette. The capsule was dissected from both optic nerves and the optic chiasm. The tumor was noted to be adherent posteroinferiorly to a relatively hard yellowish-red tissue, suggesting normal pituitary gland. After evacuation of the capsule contents, the tumor was totally removed, leaving the normal pituitary gland intact.

**Postoperative Course.** Postoperatively, diabetes insipidus persisted for 2 weeks. No mass lesion was evident in the suprasellar region on the postoperative CT scans (Fig. 1 lower). Basal plasma levels of GH and glucose were 3.1 ng/ml and 126 mg/dl, respectively. Plasma ACTH responded normally to insulin administration, and plasma LH and FSH levels, although still below normal, were slightly increased by intravenous administration of 1 mg of LH-releasing hormone. Visual acuity on the left improved to 20/100.

A biopsy of the left pulmonary mass was carried out on May 4, 1983, for histological examination. The pulmonary lesion was markedly decreased in size within 3 months after total removal of the suprasellar tumor (Fig. 2 right), even though no specific treatment had been administered. No suprasellar or pulmonary mass lesion was evident on follow-up CT scans or chest x-ray films.

**Pathological Examination.** The suprasellar mass exhibited many vascular channels lined by flattened and inconspicuous endothelium. Between the channels, ovoid or slightly elongated neoplastic cells were packed (Fig. 3 left). The cells were uniform in appearance and no mitotic division was found. Neither binucleation nor multinucleation of the tumor cells was seen. A minute tissue fragment excised with the tumor demonstrated the normal histological features of the anterior pituitary lobe. Reticulin staining exhibited an abundant fine-reticulin stroma between the tumor cells, and also demonstrated the presence of neoplastic cells outside the perivascular reticulin sheath (Fig. 3 center). The pulmonary biopsy (Fig. 3 right) revealed histological features similar to those of the suprasellar specimen.

For immunohistochemical studies, formalin-fixed paraffin-embedded sections were dewaxed and stained by the peroxidase-antiperoxidase technique. In addition, before immunoperoxidase staining for GHRF,
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deparaffinized hydrated sections were incubated in a solution of 0.02% trypsin in phosphate-buffered saline, pH 7.2, for 30 minutes at 37°C to unmask the antigenicity of GHRF, as described by Brozman. The specific rabbit antibodies used were anti-GH and anti-GHRF. After immunohistochemical staining, the sections were counterstained with Mayer’s hematoxylin. Immunoreactive GH was detected in only a few scattered neoplastic cells in the suprasellar hemangiopericytoma (Fig. 4), and was not found in the pulmonary hemangiopericytoma. Immunoreactive GHRF was not found in either the trypsin-treated suprasellar or the pulmonary hemangiopericytoma. Controlled incubation with the immunoglobulin fraction of serum from non-immunized rabbits did not show any positive cells in either the suprasellar or the pulmonary hemangiopericytoma.

Discussion

Hemangiopericytomas, tumors composed of the pericytes of blood vessels, may occur in practically any location in the body where there are capillaries. The histological features of the suprasellar and pulmonary tumors in our case are characteristic of hemangiopericytoma. These tumors have a rapid growth potential and sarcomatous tendencies; recurrence has been reported in about 80% of patients with hemangiopericytoma of the meninges, even when the tumor was believed to have been completely removed. Extraneural metastases are found in up to 25% of patients with hemangiopericytoma of the meninges.

As is true of other central nervous system tumors, bone and lung are the most common sites for metastases. A total of 36 cases of primary hemangiopericytoma of the lung have been reported. In addition, the occurrence of multiple primary hemangiopericytomas has been described. In the present case, the suprasellar hemangiopericytoma was GH-positive, whereas the pulmonary hemangiopericytoma was GH-negative. Recently, Burchiel, et al., and Fischer, et al., reported cases of mixed functional microadenoma and

![Fig. 4. Immunoperoxidase staining of a specimen from the suprasellar hemangiopericytoma reveals the presence of scattered intracellular immunoreactive human growth hormone. × 280.](image)

![Fig. 3. Photomicrographs of specimens from the suprasellar and pulmonary hemangiopericytomas. × 70. Left: Suprasellar hemangiopericytoma specimen showing many vascular channels lined with flattened endothelium. Ovoid or slightly elongated tumor cells, rather uniform in appearance, are packed together between the vascular channels. H & E. Center: Suprasellar hemangiopericytoma specimen with reticulin fibrils found around the vascular channels and between the tumor cells. Reticulin stain with nuclear fast red counter-stain. Right: Biopsy specimen from the pulmonary hemangiopericytoma showing several vascular channels lined with inconspicuous endothelium. Ovoid or slightly elongated tumor cells, similar to the suprasellar tumor cells, are clustered between the vascular channels. H & E.](image)
gangliocytoma of the pituitary fossa in which some of the adenoma cells that were intermingled with ganglialoma cells were immunoreactive for GH by immunoperoxidase staining, and the basal plasma GH levels were 7.6 to 7.7 ng/ml. In our case, the incidental removal of a pituitary microadenoma associated with the hemangiopericytoma cannot be excluded, but no histological evidence of a somatotrophic adenoma was evident in the suprasellar tumor. The synthesis and release of GH have been identified in tumors outside the central nervous system. It would be reasonable to assume that GH-producing cells in the suprasellar hemangiopericytoma were responsible for the increased plasma GH level in the present case. Tumors of the APUD series, principally carcinoids, have produced GHRF-active fractions, and relief of acromegaly has occurred after removal of the tumors. Immunoactive GHRF was not demonstrated immunohistochemically in either the suprasellar or the pulmonary hemangiopericytoma in our case. 

It is interesting that our patient's pulmonary hemangiopericytoma was markedly decreased in size on the chest x-ray film obtained after total removal of the suprasellar hemangiopericytoma, despite the fact that she received no specific therapy. The primary postoperative change was the normalization of plasma GH and glucose levels. Talwalker, et al. demonstrated an undoubted effect of prolactin and GH on the development of breast cancer. Capanna and Gherlinzoni reported the consecutive occurrence in an acromegalic patient of cancers of the breast and sigmoid colon, with rapid and massive spread of the latter neoplasm after interruption of all therapy for acromegaly. However, there is little clinical evidence linking high levels of circulating GH with an increased frequency of tumors. Since the mean survival time of patients with intracranial hemangiopericytomomas is 7 years after initial operation, long-term follow-up review is required.

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