Renal Cell Carcinoma Metastatic to the Hypophysis

—Case Report—

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Abstract

We encountered a very rare case of renal cell carcinoma metastatic to the pituitary gland. The patient presented with complaints of headaches and visual disturbance. Physical examination disclosed bitemporal hemianopsia and panhypopituitarism. Radiological findings suggested a pituitary tumor, and surgery was performed *via* the subfrontal approach. Eosinophilic cells were present in the histological tumor specimens, which led us to the incorrect diagnosis of pituitary adenoma. After dural metastases developed, the primary renal tumor was confirmed. The intracranial metastatic lesions were removed and the primary kidney lesion was embolized.

Four other reported cases of renal cell carcinoma metastatic to the sellar region are reviewed. In one of the cases, as in ours, an erroneous initial diagnosis of pituitary adenoma was made.

Key words: pituitary tumor, metastatic renal cell carcinoma

Introduction

Renal cell carcinoma tends to metastasize to the brain, but its metastasis to the pituitary region is rare. In general, the pituitary is frequently a site of metastasis for terminal-stage malignant tumors. However, many are asymptomatic and are discovered only at autopsy. We recently treated a patient with hypophyseal metastasis of a renal cell carcinoma that caused pituitary dysfunction and mimicked a pituitary adenoma. We describe the case and review the literature.

Case Report

A 51-year-old male complained of intermittent, severe headaches beginning in January of 1984. Polydipsia was noted in February, and in March visual disturbance developed. Visual acuity in the left eye was hand movement, although that of the right eye remained normal. In June the headaches increased in severity and frequency and were accompanied by nausea and vomiting. He also noticed greater visual disturbance. Ophthalmological examination disclosed deteriorating right vision and

bitemporal hemianopsia, and he was transferred to our department. On admission, he appeared healthy and well nourished. Axillary and pubic hair was absent. He was alert and well oriented, but he answered questions slowly. The right pupil was mydriatic, with sluggish direct and indirect light reflexes. He had full ocular motion in all directions, and his visual acuity was 0.1 (20/200) in the left eye and hand movement in the right eye. Bitemporal hemianopsia was evident, and the optic discs were bilaterally atrophic. Other cranial nerves were intact and there was neither paresis nor sensory disturbance of the extremities.

The urinary volume was about 2 liters per day despite his complaint of polydipsia. Blood and biochemical studies were normal except for a high level of lactate dehydrogenase. Mild, microscopic hematuria was occasionally noted. Endocrinological study indicated panhypopituitarism, as shown in Table 1. Neither carcinoembryonic antigen nor alpha fetoprotein was elevated.

A skull x-ray showed demineralization in the sellar region. A large mass in the intra- and suprasellar region was demonstrated by computed tomography (CT) (Fig. 1). The margin of the mass appeared irregular and highly dense, and slightly enhanced with contrast medium, while the center had low density.

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Table 1 Hormonal responses to stimulating agents

	0	30	60	90	120 min
Growth hormone (ng/ml)	2	2	1	2	1
Thyroid-stimulating hormone (μ U/ml)	4.9	10.0	10.4	12.3	12.1
Prolactin (ng/ml)	5	10	8	6	7
Luteinizing hormone (mU/ml)	2	4	4	5	9
Follicle-stimulating hormone (mU/ml)	2	2	2	3	3
Cortisol (μ g/dl)	3.2	3.9	4.7	5.6	6.8

Insulin 5 units, thyrotropin releasing hormone 500 μ g, and luteinizing hormone releasing hormone 100 μ g were administered intravenously.

Fig. 1 Precontrast (left) and contrast (right) CT scans demonstrating a mass lesion in the sellar region, in which an irregular high-density area is slightly enhanced by contrast medium.

Bilateral carotid angiograms demonstrated upward elevation of the horizontal portion of the bilateral anterior cerebral arteries and hypertrophy of the meningohypophyseal trunk with vascular blushing and an abnormal vascular network in the sellar region. Tumor staining was observed in the capillary phase (Fig. 2). A preoperative diagnosis of pituitary tumor (specifically, a nonsecretory adenoma) was entertained. Within a few days after admission he became confused.

He underwent surgery *via* the subfrontal approach on July 16, 1984. The tumor, which protruded to the frontal base, had a dark, purplish-red, smooth capsule. It contained necrotic tissue and a large amount of clotted blood. The suprasellar portion was totally and the intrasellar portion was subtotally removed.

Histological examination revealed that much of the excised mass was composed of necrotic and granulation tissue, and some areas contained

Fig. 2 Capillary phase of right carotid angiogram showing a snowman-shaped tumor stain on the eroded, enlarged sella.

eosinophilic adenomatous cells arranged in islands (Fig. 3A). Growth hormone was identified immunohistologically in some eosinophilic cells. There were also clear cells containing abundant clear, PAS-positive cytoplasm and round, regular nuclei (Fig. 3B). There was neither mitosis nor atypism. The clear cells, like the eosinophilic cells, were arranged in islands; therefore, we surmised that the clear cells constituted a degenerative form of the eosinophilic cells and diagnosed the tumor as a chromophobe pituitary adenoma.

Postoperatively he underwent local irradiation of 41 Grey to the pituitary region and was given replacement hormones. His visual acuity recovered to 0.4 (20/50) in the right eye, although that of the left eye was 0.02 (20/1000). Diabetes insipidus was well controlled, and he was discharged in October, 1984.

Three weeks after discharge, in November of 1984, he was readmitted with headaches in the left temporal region, nausea and vomiting, and drowsiness. A CT scan revealed multiple tumors in the left temporal and frontal lobes and one in the posterior temporal region, where there was also an intracerebral hematoma (Fig. 4). Angiography demonstrated three small, round tumor stains in the left cerebral hemisphere.

A second operation was performed and six supratentorial tumors that were attached to the dura, as well as an intracerebral hematoma, were totally removed. These tumors were also dark red, hemorrhagic, and sharply demarcated from the brain. Histological examination revealed that the clear cells, in which the clear cytoplasm stained with PAS, were arranged in columns and islands in all of the tumors (Fig. 5).

Fig. 3 A: The tumor consisted of eosinophilic cells in islands arrangements. Growth hormone was detected in these cells. B: In some parts of the tumor clear cells were present, also in island formations. HE stains, $\times 200$.

The findings were very characteristic of renal adenocarcinoma, suggesting a metastatic tumor. An abdominal CT scan showed a tumor in the superior pole of the left kidney. The left renal artery was em-

Fig. 4 CT scan showing round, high-density masses in the left temporal and frontal lobes. Associated with the mass was an intracerebral hematoma in the posterior temporal region.

Fig. 5 The cells contained abundant clear cytoplasm and small dark nuclei, which are characteristic of clear cell carcinoma. PAS stain, $\times 200$.

bolized with pure ethanol, and whole brain irradiation of 44 Grey was administered. He had become alert immediately after awakening from surgery but underwent gradual mental deterioration with increasing hydrocephalus, for which a ventriculoperitoneal shunt was emplaced in February 1985. Having shown no benefit from treatment, he died in June of 1985.

At autopsy, metastatic tumors were discovered in the left lateral aspect of the medulla oblongata and the left cerebellar hemisphere. Residual pituitary tumor and metastatic lung lesions were also found.

Discussion

Intracranial metastasis from cancers of the urogenital system, particularly of the kidney, is well recognized. According to a Memorial Sloan-Kettering Cancer Center study,³⁾ the incidence of intracranial metastasis from renal cell carcinoma was 21% in autopsies of renal cancer patients, and other authors have reported rates ranging from 5.7 to 35%.^{5,7,8,10)} Metastatic carcinoma in the pituitary gland is mainly found at autopsy. Some autopsy series have revealed that 1 to 25% of patients who died of malignant tumors had hypophyseal metastases,^{1,2,6,9,11)} many of which were asymptomatic.^{2,6,9)} The frequency is rather high in the posterior lobe of the hypophysis.^{1,9)} The sites of primary lesions vary and include lung, breast, stomach, uterus, prostate, and urinary bladder. In females, breast cancer gives rise to the highest incidence of pituitary metastasis.^{2,6,9)} However, metastasis of renal cell carcinoma to the pituitary region was not cited in reports of autopsies.^{7,9,11)}

Table 2 Reported cases of pituitary metastases from renal cell carcinoma

Author (Year)	Age/ Sex	Initial symptom	Other symptoms	Other metastases	Radiological findings	Histological diagnosis
Post and Kasdon (1980) ¹²⁾	35/F	visual disturbance	oculomotor palsy	liver	destruction of sella, abnormal vessels	not mentioned
Anniko <i>et al.</i> (1981) ¹⁾	59/M	unknown	hypo- pituitarism, visual disturbance	contralateral kidney	destruction of sella	clear cell carcinoma
Bounguidi and Ferdegini (1983) ²⁾	53/M	hypo- pituitarism	visual disturbance	unknown	destruction of sella, abnormal vessels	clear cell carcinoma
James <i>et al.</i> (1984) ⁶⁾	75/F	visual field disturbance	hematuria	(—)	destruction of sella	clear cell carcinoma
Present case	51/M	visual disturbance	hypo- pituitarism, polyuria	dura mater, cerebellum, lung	destruction of sella, abnormal vessels	clear cell carcinoma

To our knowledge, only four cases of pituitary metastasis of renal cell carcinoma have been reported, and they are summarized in Table 2.^{1,2,6,12)} It is well known that metastatic renal cell carcinoma is often symptomatic, while the primary tumor remains asymptomatic. Renal carcinoma was diagnosed in only two of the five cases discussed here (including our own) prior to surgery for the hypophyseal lesion.^{1,6)} The most common initial symptoms of pituitary metastasis were pituitary insufficiency and visual disturbance. Only our patient developed polydipsia and polyuria. Radiological studies yielded no findings characteristic of metastatic renal cell carcinoma.^{1,2,6)} Widespread demineralization in the sellar region and blushing vessels from the meningohypophyseal artery were reported, but these findings are sometimes seen even in benign pituitary adenoma.^{4,9)}

In all examined cases the histology disclosed clear cell carcinoma. The initial histological examination led to an erroneous diagnosis of pituitary adenoma in two cases, including ours.¹²⁾ Post and Kasdon¹²⁾ attributed the misdiagnosis to the absence of histological features typical of malignant tumors, *e.g.*, nuclear atypism or mitosis, and to the lack of a tubular cell pattern. Furthermore, in our case, the specimen contained a large amount of necrotic tissue, blood clot, and some eosinophilic cells; actual tumor tissue was scant. The eosinophilic cells contained homogeneous, light-colored cytoplasm without eosinophilic granules according to hematoxylin-eosin staining. Immunohistological study revealed growth hormone in the eosinophilic cells, and so we concluded that the tumor had originated in the pituitary gland and that the clear cells were degenerated eosinophilic cells. Both types of cell were PAS-

positive and their arrangements were very similar. Unfortunately, negative fat staining of the clear cells supported our initial diagnosis. In retrospect, we speculate that the eosinophilic cells might have degenerated from pituitary cells as a result of the influence of the metastatic tumor cells.

Later, the multiple dural metastases caused us to wonder whether the pituitary metastasis might have developed from metastasis to the pituitary capsule, sellar diaphragm, or adjacent dura mater.

Our review of the literature and our own experience indicate that pituitary metastasis of renal cell carcinoma may be difficult to diagnose, both preoperatively and histologically. We caution neurosurgeons to be aware that tumors in the pituitary region may be metastatic, even if there are no symptoms of the primary tumor and no radiological evidence of their metastatic nature.

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