# CASE IN POINT

# ASYMPTOMATIC PITUITARY METASTASES

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**Pituitary metastases should be considered in the differential diagnosis of any nonfunctioning pituitary mass, as there may be no symptoms.**

The anterior pituitary gland is an uncommon site for metastases. The incidence of pituitary metastases was reported to be 3.6% in a 1981 series of 500 autopsies from Memorial Sloan-Kettering Cancer Center.[1] But symptomatic tumors are found in only 0.02% to 0.025% of the population.[1–5] In such cases, the malignancy tends to be disseminated throughout the brain.[2,3]

The most common symptoms of pituitary metastases, diabetes insipidus or visual changes, arise from the involvement of the posterior pituitary or the pituitary stalk. There are no characteristic radiologic features that distinguish a primary pituitary adenoma from a metastasis to the pituitary.

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In this article, we present the case of a relatively young man with small-cell cancer of the lung whose staging workup uncovered sellar and suprasellar masses. Although the infundibulum was involved, the patient was asymptomatic before undergoing chemotherapy and therapeutic external beam radiation to the brain, after which he developed anterior pituitary hypofunction.

## INITIAL EXAM

A 39-year-old man presented to the hospital with a cough, blood-streaked sputum, and right-sided chest pain that radiated to the back. He had a smoking history of 10 pack-years and no history of fever, weight loss, or night sweats.

On evaluation, he was found to have a large mass in the middle lobe of the right lung with bilateral hilar lymphadenopathy. A transbronchial biopsy of the mass revealed small-cell carcinoma. As part of the workup for staging, he had a computed tomography (CT) scan of the abdomen, which revealed no evidence of metastatic disease, and a bone scan, which showed diffuse uptake in the trochanteric area of the right femur, the fourth and fifth lumbar vertebrae, the left sixth rib, the left parietal area of the skull, the right scapula, and the right clavicle. A CT scan of the brain showed an enhancing mass in the sellar and suprasellar regions, but no other parenchymal brain metastases were evident.

Initial magnetic resonance imaging (MRI) of the pituitary showed two enhancing soft tissue masses: one within the sella, measuring 5 mm; the other in the suprasellar area, involving the infundibulum (Figure 1). The suprasellar lesion, which measured 1 cm in size, was at the midline and extended to the base of the anterior hypothalamus, displacing the optic chiasm upward. The patient had no clinical evidence of pituitary insufficiency (such as diabetes insipidus). Most initial laboratory data were

also normal (Table 1). He had no visual abnormalities, either clinically or by formal visual fields assessment.

## TREATMENT COURSE

The neurosurgery team recommended a biopsy of the pituitary lesion, but the patient opted not to proceed with that. Instead, he began a course of chemotherapy with etoposide 80 mg/m$^2$ IV daily for three days and cisplatin 80 mg/m$^2$ IV once.

He did not respond well to this chemotherapy regimen. A repeat CT scan of the chest three months after the initial diagnosis showed an increase in the hilar mass with pretracheal and retrocaval lymph nodes. The regimen was changed to topotecan 1 mg/m$^2$ IV daily for four days, taxol 175 mg/m$^2$ IV once, and carboplatin 80 mg/m$^2$ IV once, during the course of which he developed deep vein thrombosis of the right calf and had to be treated with warfarin. He also received radiation treatment with 3,000 cGy to the whole brain and 3,000 cGy to the right femur.

A repeat MRI of the pituitary performed four months after the initial diagnosis showed significant and almost complete resolution of the suprasellar mass and the enhancing intrasellar mass. The masses appeared to have had no lasting effect on the chiasm (Figure 2).

Pituitary reserve testing revealed evidence of cortisol deficiency with a low adrenocorticotropin level. The patient also had low levels of testosterone, luteinizing hormone, and tetraiodothyronine (T4) levels and no evidence of diabetes insipidus. He was started on a daily regimen of oral hydrocortisone 20 mg in the morning and 10 mg in the evening.

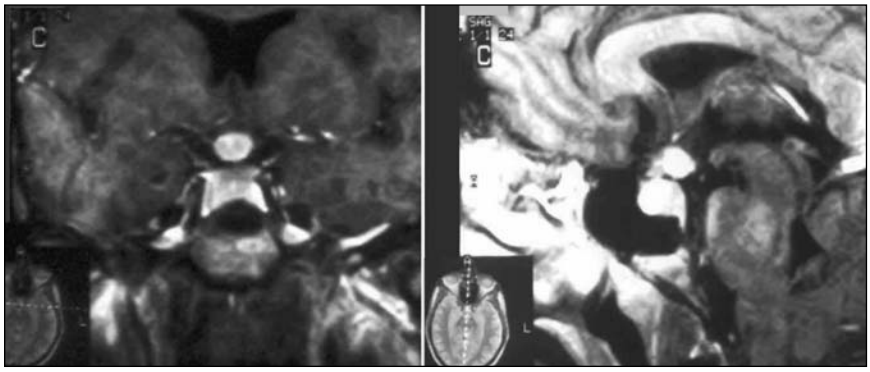

Figure 1. Magnetic resonance imaging of the pituitary at initial diagnosis. At left, the coronal view shows a metastatic lesion in the hypothalmic area close to the stalk. At right, the sagittal view shows metastatic lesions in the pituitary region and hypothalamus.

He continued with the same regimen of topotecan, taxol, and carboplatin. Initially, the right hilar mass regressed. But one year after diagnosis, the mass increased in size and invaded the mediastinum. The patient developed new metastatic lesions involving the brain parenchyma—in the posterior third ventricle, the right cerebellum, the occipital lobe, and the left midparietal region.

Thirteen months after the initial diagnosis, he developed acute paraplegia with cord compression at T7 through T8. He was treated with oral dexamethasone 16 mg/day and 3,000 cGy radiation to the dorsal spine. This, however, did not improve his functional status. He opted to have no further chemotherapy and to be placed in hospice care.

## ABOUT THE CONDITION

The pituitary is a relatively uncommon site for metastatic disease, with breast and lung cancers being the most commonly associated primary cancers (Tables 2 and 3).[1–3,5,6–11] Other cancers that spread to the pituitary include: gastrointestinal cancer (7%), prostate cancer (6%), and melanoma (2%)—and, to a lesser extent, thyroid, bladder, liver, or renal cell carcinoma; plasmacytoma; sarcoma; and leukemia.[3,4]

Presenting symptoms generally include diabetes insipidus, anterior pituitary insufficiency, and retroorbital pain.[3] Diabetes insipidus is the presenting manifestation most commonly reported,[3,12] though there also have been accounts of cranial nerve involvement and hypopituitarism.[13]

The most notable features of this case report are: (1) incidental discovery of pituitary lesions during a routine workup for lung cancer staging; (2) lack of symptoms with a lesion in the infundibulum and in close vicinity to the chiasm; (3) remarkably prolonged survival of 18 months; and (4) development of anterior pituitary hypofunction without involvement of the posterior pituitary despite the radiologic resolution of the pituitary and infundibular metastases. It is possible that radiation-induced fibrosis or persistent micrometastases in the pituitary might have contributed to this situation.

The posterior pituitary has been reported to be involved in metastases more commonly than the anterior lobe.[2,3,5,6,12] This probably is

Continued on page 14

Continued from page 9

**Table 1. Results of laboratory tests at diagnosis and five months later**

| Laboratory test | At diagnosis | Five months after diagnosis |
|---|---|---|
| Sodium (normal: 135–145 mmol/L) | 135 mmol/L | 142 mmol/L |
| Potassium (normal: 3.3–5.1 mmol/L) | 4.7 mmol/L | 3.9 mmol/L |
| Chloride (normal: 98–108 mmol/L) | 101 mmol/L | 108 mmol/L |
| Carbon dioxide (normal: 21–32 mmol/L) | 29 mmol/L | 28 mmol/L |
| Alkaline phosphatase (normal: 50–136 U/L) | 141 U/L | 322 U/L |
| Hemoglobin (normal: 13.9–16.3 g/dL) | 14.9 g/dL | 7.9 g/dL |
| Urine specific gravity (normal: 1.001–1.030) | 1.022 | 1.014 |
| Cortisol (6:40 AM) (normal AM: 6–30 µg/dL) | — | 1.48 µg/dL |
| Adrenocorticotropic hormone (normal: 0–46 pg/mL) | — | < 10 pg/mL |
| Thyroid-stimulating hormone (normal: 0.49–4.6 µIU/mL) | — | 2.49 µIU/mL |
| Total tetraiodothyronine (normal: 4.5–12 µg/dL) | — | 4.3 µg/dL |
| Total testosterone (normal 3–12 ng/mL) | — | 0.1 ng/mL |
| Luteinizing hormone (normal: 2–12 mIU/mL) | — | 0.8 mIU/mL |
| Follicle-stimulating hormone (normal: 1–8 mIU/mL) | — | 2.3 mIU/mL |

due to the fact that the posterior lobe receives a direct blood supply by way of the superior and inferior hypophyseal arteries, whereas the anterior pituitary receives its blood primarily through the hypothalamic portal system.

Hematogenous spread may involve the hypothalamic parenchyma, infundibular stalk, and pituitary gland directly, or it may involve the sphenoid bone with secondary extension into the cavernous sinus or sella. Symptomatic metastases to the pituitary usually are seen in the setting of disseminated disease.[2,3,6] They may, however, be the initial presentation of an undiscovered malignancy.[3] The median length of patient survival following the diagnosis of pituitary metastasis has been reported to be 180 days.[3]

In many published case reports, the incidence of diabetes insipidus is low. Some authors believe that this is due to the widespread use of brain imaging techniques like CT and MRI, which allow a pituitary lesion to be detected before it progresses to the point of causing symptoms.[5]

Clinically, it can be difficult to distinguish a pituitary adenoma from a metastatic lesion. Metastatic pituitary lesions, however, are more likely than pituitary adenomas to cause cranial nerve palsies and diabetes insipidus.[1,7,14,15] Ophthalmoplegia, on the other hand, is seen in less than 2% of pituitary adenomas.

Radiologic findings on MRI and CT scan are not specific for pituitary metastases. Pituitary metastases can appear as homogenous enhancing sellar or suprasellar masses or show stalk enlargement or cavernous sinus invasion.[3] A clear determination about the etiology of the mass cannot be made on the basis of neuroimaging results, though the presence of extensive bony destruction may be a pointer in some cases.[1,3–5,7,15]

Opinions vary about how best to manage pituitary metastases. When mass lesions compress surrounding structures, surgery is recommended to relieve related symptoms. Of course, with widespread infiltration, the possibility of achieving a surgical cure is reduced. Radiation therapy also has played a palliative role.

A recent review of 35 cases found that the completeness of surgery or radiation did not affect overall survival.[3] Poorer outcomes are

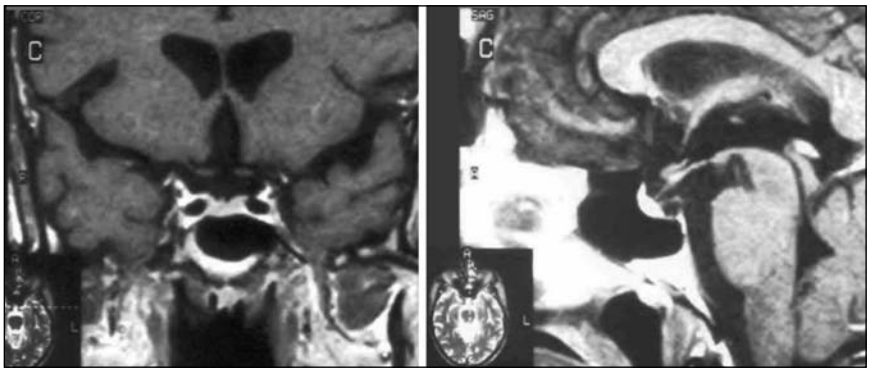

Figure 2. Magnetic resonance imaging of the pituitary following chemotherapy and radiation to the brain. Both the coronal view at left and the sagittal view at right show a complete resolution of pituitary and hypothalamic legions.

associated with age over 65, small-cell carcinoma, and a short period of time from diagnosis to development of pituitary metastases.[3] In the setting of disseminated cancer and pituitary metastases, management decisions should be based on an assessment of the patient's overall clinical status and prognosis as well as the risks and benefits of therapy.

Pituitary metastases should be considered in the differential diagnosis of any nonfunctioning pituitary mass. While there are no specific clinical or radiologic criteria that distinguish metastatic pituitary lesions from pituitary adenomas, symptoms and bony abnormalities may provide clues. Keep a high index of suspicion—especially if the patient has preexisting cancer. Evaluation is similar to that of any pituitary incidentaloma and includes evaluation of pituitary hormone function and visual fields. ●

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**Table 2. Findings from autopsy series reports involving pituitary metastases[1,6,8–10]**

| Autopsy series | No. (%) of pituitary metastases | Most common symptoms | Pituitary lobe involvement | Primary cancers |
|---|---|---|---|---|
| Abrams et al, 1950[8] | 18 (1.8%) | Not available | Not available | Breast, lung, stomach |
| Delarue et al, 1964[10] | 33 (12%) | Diabetes insipidus (3%) | Posterior mostly | Not available |
| Roessmann et al, 1970[9] | 5 (8.3%) | Not available | Not available | Breast, lung, colon |
| Teears et al, 1975[6] | 88 (Not applicable) | Diabetes insipidus (6.8%) | Postpituitary (50%), anterior pituitary (12%), both postpituitary and anterior pituitary (11%) | Breast, lung, stomach |
| Max et al 1981[1] | 18 (3.6%) | Not available | Not available | Lung, melanoma, germ cell |

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**Table 3. Findings from case series reports involving pituitary metastases[1–3,5,7,11]**

| Case series | No. of cases | Most common symptoms | Pituitary lobe involvement | Primary cancers |
|---|---|---|---|---|
| Duchen, 1966[11] | 12 | Diabetes insipidus (17%) | Postpituitary (33%), anterior pituitary (25%), both postpituitary and anterior pituitary (42%) | Breast |
| Houck et al, 1970[2] | 11 | Diabetes insipidus (81%) | Postpituitary (55%) | Breast |
| Max et al, 1981[1] | 2 | Diabetes insipidus and anterior hypopituitarism (50%), visual symptoms (50%) | Sellar plus suprasellar extension | Prostate, lung, carcinoid |
| Kattah et al, 1985[7] | 10 | Ophthalmoplegia (90%); diabetes insipidus (10%) | Parasellar (80%) | Breast, nasopharynx, lung, colon |
| Branch et al, 1987[5] | 14 | Headache (69%), anterior hypopituitarism (64%), visual field defects (50%), ophthalmoplegia (43%), diabetes insipidus (28%) | Sellar plus suprasellar extension (69%), sellar or with lateral extention (31%) | Breast, lung, plasmacytoma |
| Morita et al, 1998[3] | 36 | Diabetes insipidus (61%), anterior hypopituitarism (47%), Panhypopituitarism (22%) | Sellar (61%), suprasellar (39%), stalk (31%), cavernous sinus (8.3%), hypothalamus (5.5%) | Breast, lung, prostate |

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