

Metastatic breast cancer masquerading as a pituitary macroadenoma: A case report

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Abstract

The purpose of this manuscript is to report a case of symptomatic breast cancer metastasis to the pituitary gland, a described yet exceedingly rare phenomenon. A 52-year-old woman with a known history of stage-IV breast cancer treated 3 years prior with chemotherapy presented to the emergency department with 2 weeks of right-sided periorbital headache and 1 week of right-sided ptosis. Magnetic resonance imaging showed a 1.9 cm × 2.8 cm × 2.8 cm mass in the pituitary with mass effect on the right optic chiasm. Endocrine laboratory studies were largely normal, including prolactin, thyroid-stimulating hormone, insulin-like growth factor, and a minimally decreased cortisol. She underwent endoscopic transnasal transsphenoidal resection 4 days later to remove the mass without complication. Postoperative pathologic studies were positive for breast cancer metastasis, and she was subsequently started on adjuvant radiation and oral chemotherapy. While breast cancer metastases to the sella have been described in the literature before, symptomatic spread to the pituitary represents a small percentage of all breast cancer metastases, and we thus feel is worthy of further discussion.

Keywords

Otolaryngology, oncology, neurosurgery, pathology, transsphenoidal pituitary resection

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Introduction

Breast cancer remains the most common type of cancer affecting women throughout the United States, with a lifetime prevalence of around 12%.¹ Mortality is significantly higher in patients with metastasis, which are reported in up to 30% of cases.² Within this cohort of patients, bony metastases represent around 75% of all metastases, followed by the lung, liver, and brain.² Although far less common, the pituitary gland is an additional site that should be considered. Spread to the pituitary is thought to be present in about 6%–8% of breast cancer metastases, though it is reported that only about 7% of these patients will have symptoms.³ When symptomatic, patients most commonly present with diabetes insipidus (DI) as a result of effect on the posterior pituitary and secretion of vasopressin. In addition, only 1% of all resected pituitary tumors are found to be metastatic cancer.³ Providers should be aware of the possibility of metastatic disease to the pituitary in a patient with cancer history, especially breast. We believe surgical decompression for mass effect on cranial nerves is indicated, followed by possible adjuvant therapy if residual tumor is left in place.⁴ To

this end, we present the case of a woman with a history of stage-IV breast cancer who presented to the emergency department (ED) with right-sided headache and ptosis.

Case report

A 52-year-old female with a history of breast malignancy presented to the ED with 16 days of progressive headache localized around the right eyebrow, 7 days of right-sided ptosis, and 3 days of right eye photophobia, fixed and dilated pupil, and blurry vision. This patient had been diagnosed

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three and a half years prior with stage-IV estrogen receptor (ER)+, progesterone receptor (PR)+, and human epidermal growth factor receptor 2 (HER2)-invasive ductal carcinoma of the right breast. She initially underwent management with weekly paclitaxel chemotherapy for 1 year before transitioning to daily goserelin with letrozole therapy, which she remained on at the time of presentation. Routine surveillance positron emission tomography computed tomography (PET-CT) scan obtained 3 months prior to the onset of her symptoms showed increased metabolic activity in the breast mass and development of a right upper-lobe pulmonary nodule; there was no avidity in the pituitary.

At the time of presentation to the ED, our patient reported a progressively worsening headache and 1 day of acute onset of blurry vision in the right eye. Review of systems, including polyuria, was otherwise negative. Physical examination was remarkable for a sluggish, dilated right pupil to 5 mm and a reactive left pupil to 2 mm. Visual acuity was 20/50 in the right and 20/20 in the left eye. Extraocular movements, facial sensation, and visual fields were intact bilaterally.

Magnetic resonance imaging (MRI) brain was obtained and showed a 1.9 cm × 2.8 cm × 2.8 cm mildly heterogeneous mass in the sella exhibiting thinning of the nearby right optic chiasm and extension into the cavernous sinuses. The differential diagnosis remained broad at this point and included benign macroadenoma, tuberculoma meningioma, craniopharyngioma, and metastatic breast cancer. She was admitted to the neurologic intensive care unit (ICU) for further workup and treatment.

Lab work, including prolactin, cortisol, thyroid-stimulating hormone (TSH), T4, and insulin-like growth factor (IGF) levels, were all within normal limits apart from a 9 pm cortisol of 3.6 µg/dL. Although this potentially borderline low cortisol may prompt confirmatory testing with an adrenocorticotropic hormone (ACTH) stimulation test or AM cortisol in certain situations, this was not pursued the following day in the absence of secondary adrenal insufficiency symptoms and the initiation of dexamethasone later that night. Due to concern for perilesional edema and symptomatic mass effect, she was promptly started on dexamethasone 6 mg q6h for 24 h followed by 2 days at a decreased dose of 4 mg q6h. Of note, laboratories were drawn prior to starting steroid replacement.

It was recommended that she undergo surgical resection of the pituitary mass, given the progressive nature of her symptoms, mass effect, and presumptive diagnosis of a non-functioning macroadenoma. There was also concern for pituitary apoplexy and imminent threatened vision. A repeat head MRI (Figure 1a–d) and head CT (Figure 2a, b) were obtained for pre-operative planning and again showed the sellar mass with suprasellar extension with mass effect on the surrounding optic nerves and optic chiasm, and abutment of the medial temporal lobes. A stealth-guided endoscopic transnasal transsphenoidal resection was performed 3 days after her initial presentation. Upon removal of the sphenoid contents and rostrum, a large mass was visualized protruding

through the thin bony wall. The tumor was noted to be firmer and denser than would be expected with a pituitary adenoma and was particularly adherent to the adjacent dura, almost invading it. The lower and central poles were removed by use of straight scissors and extensive scraping of the tumor off the dura; ultrasonic aspiration was not needed. Unfortunately, the tumor obstructed the normal gland and stalk, and it was difficult to evaluate the extent of suprasellar extension due to the tumor's adherence to surrounding structures. Although intraoperative frozen biopsy samples were read as pituitary macroadenoma, there remained concern for metastasis due to the patient's medical history and unusual consistency of the mass. As such, the decision was made to perform subtotal resection, with the plan for adjuvant radiation therapy if any residual suprasellar tumor remained. If pathology confirmed benign macroadenoma, she would return for complete resection via an eyebrow approach. Subtotal resection of the mass was completed and sent for permanent pathology. An intraoperative cerebrospinal fluid (CSF) leak was encountered and repaired with a combination of abdominal fat graft from the right flank and nasoseptal flap. Her postoperative course was uncomplicated, and she was discharged home 4 days later on hydrocortisone replacement therapy (20 mg in the morning, 10 mg at night) for 4 weeks after postoperative laboratories were indicative of panhypopituitarism. Encouragingly, her 2-week clinic follow-up was notable for improvements in her ptosis, pupillary dysfunction, and headache.

Final histopathological studies of the sample were read as positive for metastatic adenocarcinoma consistent with breast primary as evidenced by normal pituitary infiltration by blue tumor cells on H&E and by positive staining of CK7, GATA3, and ER (Figure 3a–e). Postoperative MRI showed residual suprasellar tumor primarily along the undersurface of the optic chiasm and prechiasmatic segment of the right optic nerve with extension into the right cavernous sinus (Figure 4a, b). Our patient subsequently underwent 5 days of external beam radiotherapy followed by oral chemotherapy.

Discussion

While breast cancer has a propensity to spread to organs such as the bone, brain, lung, and liver, it is important to also consider the pituitary. Pituitary metastases represent approximately 6%–8% of breast cancer metastases, with about 7% of these being symptomatic.³ Despite this low incidence, it is an important diagnosis to consider as it commonly denotes widespread metastasis and poor prognosis. Definitive diagnosis is a challenge as metastasis is commonly not confirmed until after surgical resection, such as in our case. Nonetheless, the clinical presentation and imaging findings are two keys which may aid in differentiating between a benign and malignant mass.

The most common clinical finding in patients with symptomatic metastases to the pituitary is DI, reported in up to 71% of cases.³ This may be compared to benign pituitary

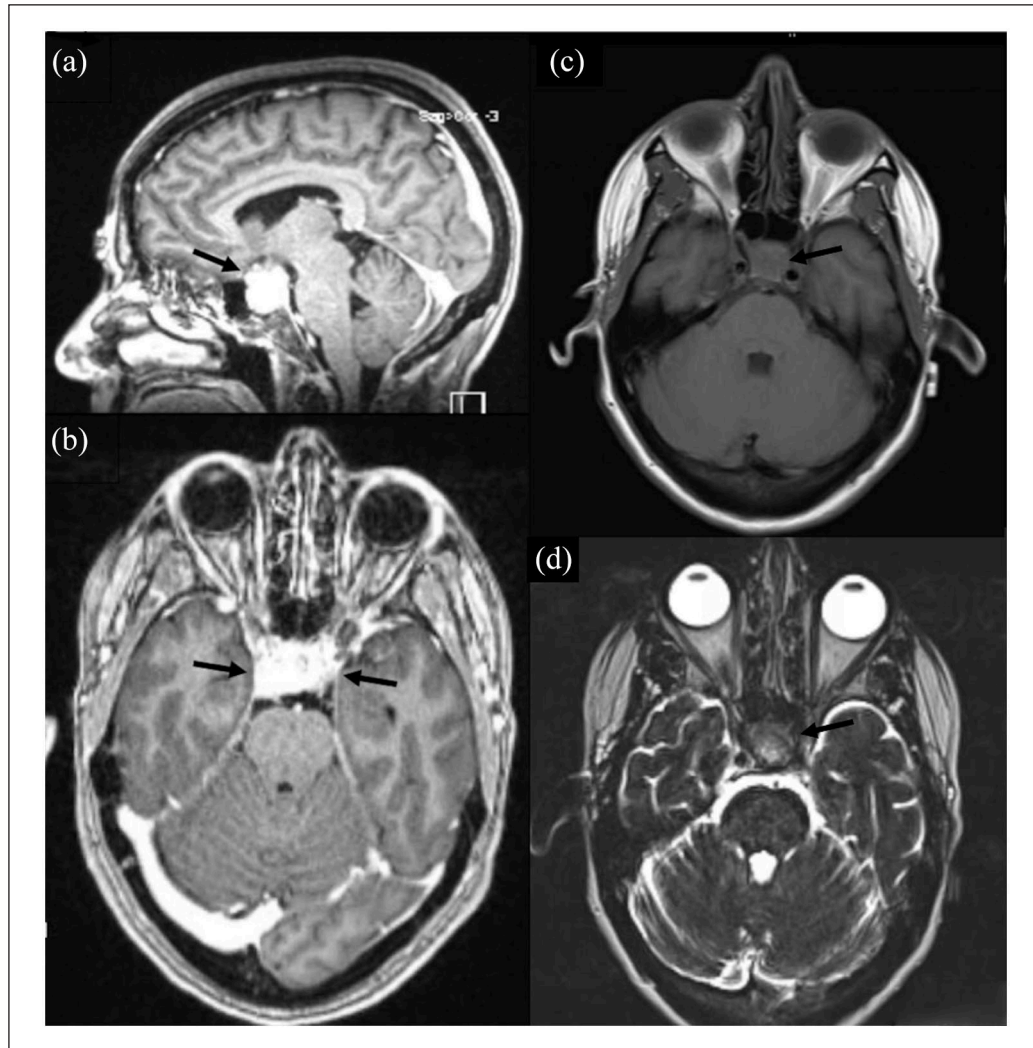


Figure 1. (a, b) Preoperative multiplanar reformation sagittal and axial MRI with contrast demonstrating an avidly enhancing sellar mass (~19 mm × 28 mm × 28 mm) resulting in mass effect on the optic chiasm and optic nerves with abutment of both medial temporal lobes. (c, d) Preoperative pre-contrast T1-weighted and post-contrast T2-weighted axial images demonstrating similar findings as described above.

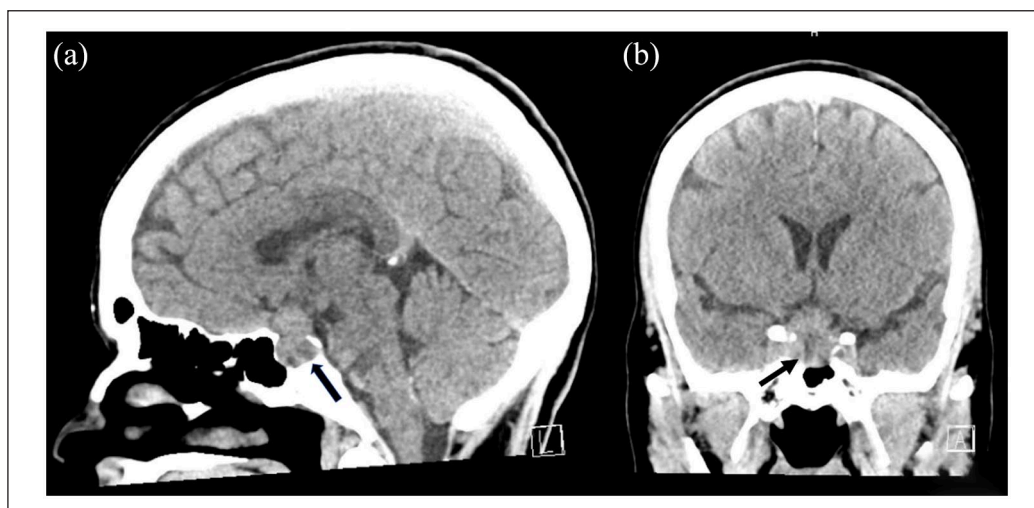


Figure 2. (a, b) Preoperative non-contrast sagittal and coronal CT demonstrating a sellar mass with an expansion of the sella and suprasellar extension.

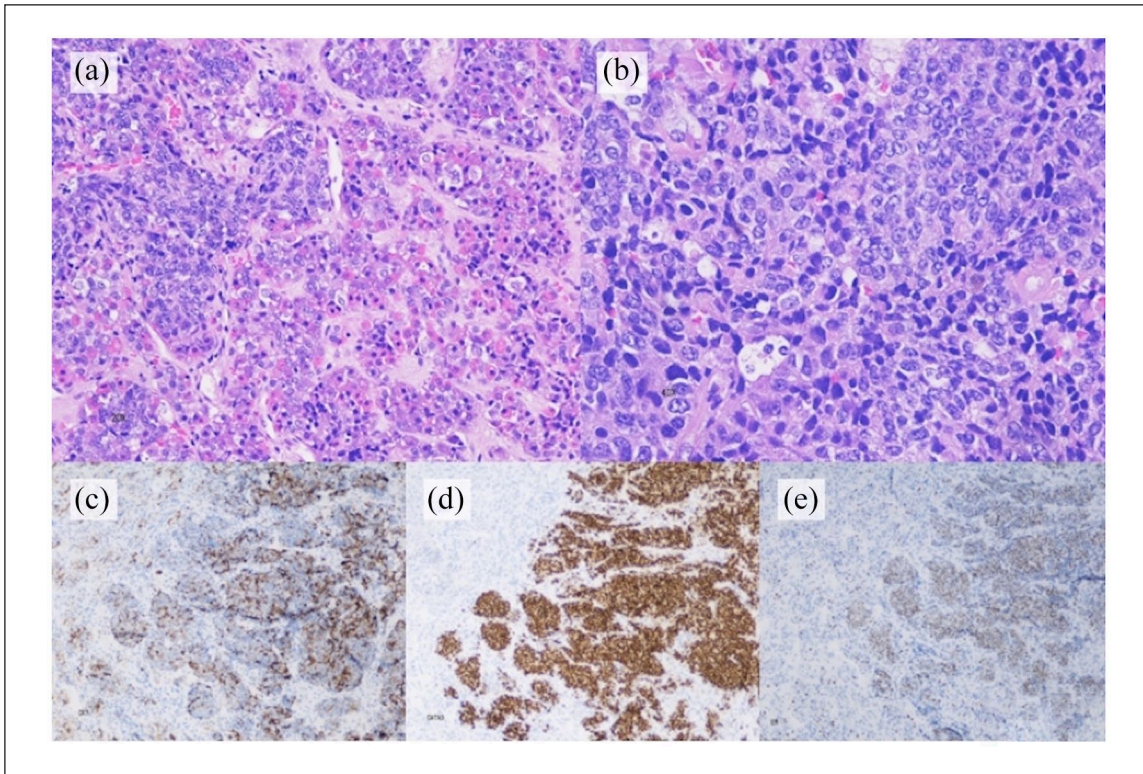


Figure 3. (a, b) Histopathologic findings. Photomicrographs showing enlarged, hyperchromatic cells with irregular nuclear membranes and nucleoli infiltrating pituitary tissue (H&E, $\times 20$, $\times 40$). (c–e) Immunohistochemical stains show the tumor cells are positive for CK7, GATA-3, and Estrogen receptor, respectively.

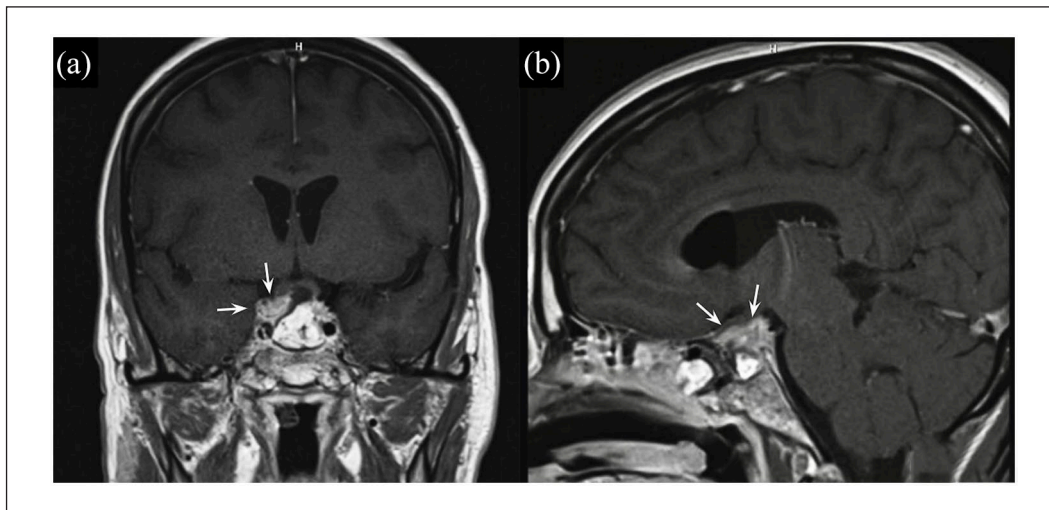


Figure 4. (a, b) Postoperative post-contrast T1-weighted coronal and sagittal MR images demonstrating contrast enhancement along the undersurface of the optic chiasm, right greater than left, and along the prechiasmatic segment of the right optic nerve with extension into the cavernous sinus, right greater than left.

adenomas, which commonly cause anterior hypopituitarism. It is thought that this relates to the fact that the posterior pituitary is perfused by the systemic circulation, as opposed to the anterior pituitary which receives its blood supply via the pituitary portal vasculature.⁵ However, anterior pituitary

dysfunction does also occur in metastatic lesions to the pituitary, resulting in low levels of prolactin, cortisol, TSH, or IGF-1.⁵ An extensive literature review yielded several reports of symptomatic breast cancer metastases to the pituitary; all of the patients in these cases presented with DI,

anterior hypopituitarism, or both.^{6–11} The patient reported in this case solely presented with signs and symptoms of mass effect, including headache, blurry vision, and dysfunction of the oculomotor nerve. Findings consistent with DI and hypopituitarism were absent. It is difficult to say whether her marginally low 9pm cortisol was representative of true hypopituitarism. Although this remains unclear, the topic of hypocortisolism and DI warrants further discussion.

An interesting endocrinologic phenomenon exists where symptoms of DI can be masked in patients with central glucocorticoid deficiency.¹² This occurs through a complex mechanism that results in an unmasking of the underlying DI upon cortisol replacement. This is clearly seen in a report by Chin et al.¹² wherein they describe a patient with metastatic lesions to the pituitary, resulting in hypocortisolism and other anterior pituitary deficiencies. Similar to our patient, she was started on dexamethasone for perilesional edema. Shortly after administration, she was found to have polyuria and a rapid increase in serum sodium from 130 to 163 mmol/L, prompting the initiation of desmopressin. Our patient, however, did not develop these overt signs and symptoms of DI following administration of dexamethasone and did not require treatment with desmopressin, which points to the absence of underlying DI. Thus, the relative lack of either of these entities in our patient represents an exceedingly rare situation.

Despite this patient's unusual clinical presentation, a close inspection of her MR images demonstrates subtle findings that support her eventual diagnosis of metastatic cancer. A review of 36 cases of pituitary metastases by Morita et al.⁵ found that the four most common radiologic findings include a homogeneous enhancing sellar mass, suprasellar enhancing mass, stalk enhancement, and cavernous sinus invasion. While our patient's mass was mildly heterogeneous with its central hypodensity, it did in fact display the other findings. Possibly even more critical in the discussion of her imaging is the rapid growth of the mass. As previously mentioned, a PET scan performed only 3 months prior showed no evidence of disease in the pituitary. This rapid growth again supports the diagnosis of metastasis as opposed to a benign adenoma. Despite this, it is important to acknowledge that imaging findings may have substantial overlap and cannot be relied upon as the sole data point when making a diagnosis.¹³

Accurate diagnosis of these pituitary masses is essential as it affects future treatment and goals of care discussions. Some pituitary masses have well-established therapies. For example, prolactinomas are typically amenable to medical treatment with dopamine agonists, while larger, non-functioning adenomas are treated with surgical resection.¹⁴ To our knowledge, there have been no trials where surgical and medical management have been compared for metastatic breast cancer to the pituitary. That being said, we support the idea that the best management is patient-centered and geared

toward their specific goals. In this case, our patient was primarily suffering from symptoms related to mass effect on the optic chiasm, optic nerve, and oculomotor nerve. Surgical management in these patients has been proposed to provide good symptomatic relief despite a lack of evidence that resection decreases mortality.^{5,7,13} Neoadjuvant radiation and chemotherapy is commonly used in these patients as well, though there are no current guidelines or evidence-based recommendations on this topic.⁵

Conclusion

This case serves as a call to all providers to maintain an open mind when presented with a complex clinical scenario. In a patient with a history of cancer, especially breast, metastatic spread to the pituitary should be considered. While patients with metastatic cancer to the pituitary typically present with concurrent DI, this case serves as a reminder that its absence should not be used as a disqualifier. Even then, however, it is important to remember the possibility of a masked DI in the presence of central hypocortisolism and the potential for its unmasking upon normalization of cortisol levels. Apart from these endocrinopathies, patients may also present with mass effect as was seen in this case. Our patient developed cranial nerve deficits, indicating the need for acute decompression, and our otolaryngology and neurosurgical teams worked together to surgically remove the rapidly growing pituitary mass. We suggest that treatment of these masses should be prompt if resulting in neurological deficit and may require adjuvant therapy following surgery.

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Data availability

The authors confirm that the data supporting the findings of this study are available within the article.

Declaration of conflicting interests

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Ethical approval

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Statement of informed consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

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