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## Case Report

# Metastatic Breast Carcinoma with Adrenal and Pituitary Involvement: A Case Report

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**ABSTRACT**

Breast cancer commonly metastasizes to the bones, liver, lungs, and brain. However, metastasis to endocrine glands, particularly the adrenal and pituitary glands, is rare. We report the case of a 54-year-old woman with hormone receptor–positive, HER2-negative invasive ductal carcinoma of the right breast who initially showed a favorable response to standard therapy. Surveillance imaging in late 2022 revealed a left adrenal mass, subsequently confirmed as metastatic breast carcinoma. Following laparoscopic adrenalectomy, she developed primary adrenal insufficiency. By mid-2023, she presented with pituitary metastases, resulting in hypopituitarism, diabetes insipidus, and severe visual impairment. Despite targeted radiosurgery, her disease progressed rapidly, and she died in December 2024. This case illustrates an unusual metastatic pattern involving both the adrenal and pituitary glands and demonstrates the potential for aggressive clinical behavior even in hormone receptor–positive breast cancer. Clinicians should maintain a high index of suspicion for atypical metastatic sites to ensure timely diagnosis and optimize palliative care strategies.

**Key words:** Breast cancer, adrenal metastasis, pituitary metastasis

## INTRODUCTION

Breast cancer is the most commonly diagnosed malignancy in women and the second leading cause of cancer-related mortality worldwide. Invasive ductal carcinoma (IDC) accounts for approximately 80% of all invasive breast cancers. [1] Despite therapeutic advances, metastatic breast cancer carries a poor prognosis, with a median survival of 2 to 3 years. Approximately 20% to 30% of early-stage breast cancers eventually develop distant metastases, and 6% to 10% present with de novo stage IV disease. [2]

While breast cancer frequently metastasizes to the bones, liver, lungs, and brain, involvement of endocrine organs such as the adrenal and pituitary glands is exceedingly rare. [1–3] In a review of 464 patients with adrenal metastases, 90% were carcinomas, most commonly originating from the lung, gastrointestinal tract, kidney, or breast. [4] Similarly, a meta-analysis of 2,190 adrenal biopsies found that 51% were malignant, with breast cancer accounting for only 2.3% of metastatic adrenal lesions. [5]

Pituitary metastases are even rarer, accounting for approximately 1% of all pituitary tumors. [6] Breast and lung cancers are the most frequent sources, and such metastases usually occur in the context of widespread disease, often involving five or more metastatic sites, particularly bone. [2,7,8]

In this report, we describe a rare clinical case of sequential adrenal and pituitary metastases in a patient with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative IDC. Despite systemic therapy, the disease progressed

rapidly, resulting in significant endocrine dysfunction and neurological deterioration.

This case highlights the importance of recognizing atypical metastatic patterns in breast cancer and the potential for aggressive clinical behavior, even when common high-risk features are absent.

## CASE REPORT

A 54-year-old woman with a history of right breast IDC first presented in 2020 with a 4-month history of a palpable right breast lump. Core needle biopsy revealed grade III IDC, strongly positive for estrogen receptor (ER, 90%), moderately positive for progesterone receptor (PR, 30%), HER2 negative, and with a low proliferation index (Ki-67). She underwent eight cycles of neoadjuvant chemotherapy, resulting in significant tumor reduction, followed by wide local excision and axillary dissection in October 2020. Pathology staged the tumor as ypT2N1a, and adjuvant locoregional radiotherapy plus hormonal therapy with anastrozole was initiated.

During routine surveillance in November 2022, a new 6.6 cm left adrenal mass was detected on a computed tomography (CT) scan. Magnetic resonance imaging (MRI) features were suggestive of pheochromocytoma, although metastatic disease could not be excluded (**Figure 1**). A follow-up CT scan in February 2023 reinforced this suspicion, showing early contrast enhancement and rapid washout, with no evidence of local invasion or distant metastases.

Biochemical testing showed plasma metanephrine levels of <50 ng/L (normal: <70 ng/L) and normetanephrine levels of 268 ng/L (normal: <120 ng/L; borderline up to 320 ng/L), supporting the possibility of pheochromocytoma. Given the clinical context, the patient underwent laparoscopic adrenalectomy in February 2023 after appropriate preoperative alpha- and beta-blockade.

Unexpectedly, histopathology revealed metastatic breast carcinoma with aggressive features, including tissue invasion and high mitotic activity. Immunohistochemistry demonstrated tumor evolution, characterized by reduced ER expression (40%), complete loss of PR, and increased Ki-67 expression (20%), indicating receptor discordance with the primary tumor.

Shortly after surgery, the patient developed worsening vomiting and gastrointestinal discomfort, leading to re-admission. Hormonal evaluation showed a random plasma cortisol level of 18.67 nmol/L (normal: >170 nmol/L) and a 60-minute post-Synacthen (synthetic ACTH) cortisol of 233.5 nmol/L (normal: >550 nmol/L), confirming primary adrenal insufficiency. Corticosteroid replacement therapy resulted in rapid clinical improvement.

Systemic staging with positron emission tomography (PET) scan in May 2023 revealed a solitary scapular glenoid metastasis, with no brain lesions identified. Zoledronic acid was added to her hormonal treatment regimen.

By late 2023, the patient developed severe headaches and progressive visual loss, prompting her to seek medical attention. Clinical evaluation revealed right-eye blindness, significant left visual field loss, hypopituitarism, and diabetes insipidus (DI).

Brain MRI was performed promptly and revealed a sellar mass consistent with pituitary metastasis. PET-CT also showed new hepatic lesions. The patient declined surgical intervention and underwent Gamma Knife radiosurgery in December 2023, with palliative intent to improve symptom control and quality of life. Despite supportive care, her condition deteriorated, and she died in December 2024. **Table 1** illustrates the patient's clinical timeline and key management decisions.

## DISCUSSION

### Adrenal incidentaloma in a cancer patient: Diagnostic challenges

Adrenal incidentalomas are relatively common, with a prevalence of up to 7% in individuals aged 50 to 70 years. While approximately 4% may represent primary adrenal malignancies or metastases from other cancers, about 75% are benign, non-functioning cortical adenomas. Around 14% are functional tumors that secrete excess cortisol or aldosterone, and pheochromocytomas account for approximately 7% of cases. In patients with a known history of malignancy, up to 50% of adrenal masses are benign, emphasizing the importance of thorough evaluation, particularly in the absence of other metastatic lesions. [3,4,9,10]

In this case, MRI and CT imaging demonstrated early contrast enhancement and rapid washout–features suggestive of

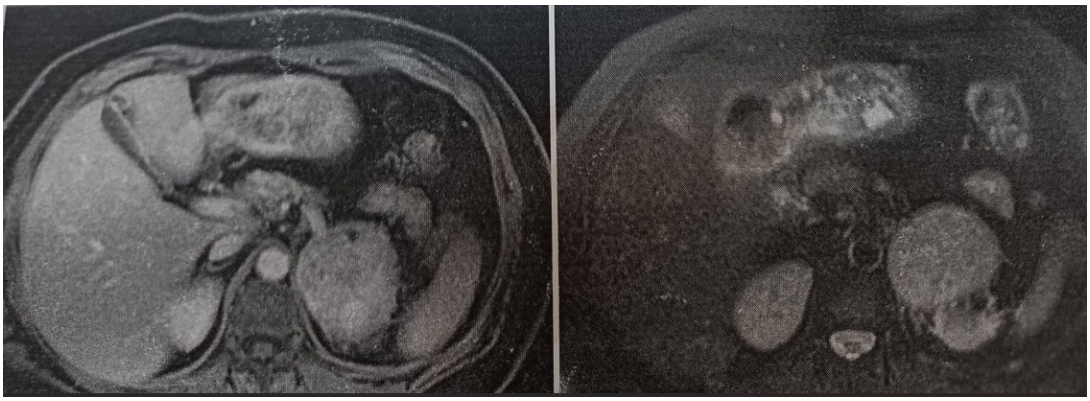

**Figure 1:** Magnetic resonance imaging showing a large mass in the left adrenal gland with high signal intensity on T2-weighted images, low signal intensity on T1-weighted images, and inhomogeneous contrast enhancement.

**Table 1:** Summary of clinical features and investigations, and key decisions.

| Date | Clinical features and investigations – Key results | Clinical decision/action |
|---|---|---|
| Early 2020 | Palpable right breast lump, 4-month duration. Core needle biopsy: Grade III IDC, ER 90%, PR 30%, HER2−, low Ki-67 | Neoadjuvant chemotherapy ×8 → Wide local excision + axillary dissection |
| October 2020 | Final pathology: ypT2N1a invasive carcinoma | Radiotherapy + Anastrozole |
| November 2022 | Surveillance CT scan: 6.6 cm left adrenal mass | Further evaluation initiated (MRI + hormonal workup) |
| February 2023 | • MRI and repeat CT scan: Early contrast enhancement and rapid washout; no local invasion<br>• Plasma metanephrines <50 ng/L (normal <70),<br>• plasma normetanephrines 268 ng/L ↑ | • Suspicion for pheochromocytoma or metastasis<br>• Biopsy deferred; pheochromocytoma risk considered |
| | • Laparoscopic adrenalectomy<br>• Histology: metastatic breast carcinoma (ER 40%, PR 0%, Ki-67 20%) | Diagnosis confirmed; receptor discordance noted |
| | Postoperative endocrine panel:<br>Cortisol: 18.67 nmol/L (↓)<br>Post-Synacthen: 233.5 nmol/L (↓) | Adrenal insufficiency diagnosed; corticosteroids initiated |
| May 2023 | PET scan: Solitary glenoid metastasis; no brain lesions | Continued hormonal therapy; added zoledronic acid |
| Late 2023 | • **Symptoms:** Headache, visual symptoms<br>• **Evaluations:** Right-eye blindness, left visual field loss; signs of hypopituitarism and DI<br>• Brain MRI confirmed pituitary metastasis | Gamma Knife radiosurgery initiated; multiple sessions delivered. |
| 2024 | Progressive clinical decline; patient died (Dec 2024) | |

IDC: invasive ductal carcinoma; ER: estrogen receptor; PR: progesterone receptor; HER2: human epidermal growth factor receptor 2; Ki-67: proliferation index; DI: diabetes insipidus; ypT2N1a: pathologic stage after neoadjuvant therapy.

pheochromocytoma. Borderline-elevated normetanephrine levels supported this possibility, although the low metanephrine level and absence of systemic metastases complicated interpretation. [10–12] Similar diagnostic challenges have been reported. For instance, a 57-year-old woman with concurrent breast cancer and pheochromocytoma had adrenal imaging initially suggestive of metastasis, but histopathology confirmed pheochromocytoma. [13] Another report from 2023 described an undiagnosed pheochromocytoma leading to adrenal crisis during breast cancer surgery. [14] These cases highlight the importance of including pheochromocytoma in the differential diagnosis when evaluating adrenal lesions in oncology patients, even in the presence of a known primary malignancy. [5,10,11]

Given the isolated nature of the adrenal lesion, the absence of other systemic metastases, and the diagnostic uncertainty due to overlapping imaging features with pheochromocytoma, a surgical approach was justified. Adrenalectomy provided definitive histopathological confirmation while offering potential therapeutic benefit. This decision aligns with current evidence supporting adrenal metastasectomy in well-selected patients with oligometastatic breast cancer. [10,15]

**Histopathology and postoperative course: Evolving tumor biology**

Histopathology of the adrenal metastasis showed reduced ER expression and complete loss of PR, indicating receptor discordance from the primary tumor. Such changes reflect the evolving biology of metastatic breast cancer and are linked to endocrine resistance and poorer outcomes. Reassessing receptor status in metastatic lesions is crucial for guiding treatment decisions. [16]

The onset of adrenal insufficiency shortly after surgery was unexpected, as the contralateral adrenal gland typically compensates for the loss of function. However, postoperative adrenal insufficiency has been documented in the literature. [10,11] For example, a 68-year-old man developed chronic adrenal insufficiency following unilateral adrenalectomy due to postoperative stress overwhelming the remaining adrenal gland. [17] In a study of 100 patients with primary aldosteronism, 27% developed adrenal insufficiency after surgery, with nearly half requiring long-term steroid replacement. [18] Additionally, a recent meta-analysis found that 22% of patients without prior cortisol excess developed adrenal insufficiency after surgery. [19]

Reduced adrenal reserve, unrecognized subtle contralateral adrenal dysfunction, or stress-induced unmasking of latent adrenal insufficiency may contribute to these outcomes. In our patient, another possible explanation for the reduced adrenal reserve is the presence of micrometastases to the pituitary gland. [17–19]

Pituitary lesions, particularly small metastases, may be missed on PET imaging due to low metabolic activity or limited anatomical resolution. [20] In retrospect, an earlier MRI might have identified the lesion sooner and potentially improved

symptom control, although it remains uncertain whether this would have significantly altered the overall prognosis. Given the rarity of pituitary metastases in breast cancer and the absence of neurological symptoms at the time, brain imaging was not initially indicated. [7,15]

This case highlights the need for increased clinical awareness and a low threshold for pituitary MRI in breast cancer patients with comparable clinical presentations. While pituitary metastases are generally visible on imaging, micrometastases can be difficult to detect due to their small size and lack of immediate clinical symptoms; the disease often progresses before significantly affecting the hypothalamic-pituitary axis. [7] In our patient, the onset of headache and progressive visual loss raised clinical suspicion for central nervous system involvement, prompting MRI evaluation, which subsequently confirmed pituitary metastasis.

**Metastases to both adrenal and pituitary glands: A rare occurrence**

Metastases involving both the adrenal and pituitary glands are rare, even in advanced breast cancer. Typically, cases present with either adrenal or pituitary metastases, but involvement of both sites simultaneously is exceedingly uncommon, with very few documented reports.

One notable case described a 32-year-old woman with stage IV breast adenocarcinoma that had metastasized to axillary lymph nodes, bone, and the right adrenal gland. Five months after undergoing chemotherapy and mastectomy, a PET scan detected a pituitary mass. [21] Another report detailed a 57-year-old woman with a history of bilateral breast cancer who developed central DI, partial anterior pituitary failure, and primary adrenal insufficiency due to metastases, five years after her initial diagnosis. [22]

In our case, the patient initially presented with an isolated adrenal metastasis; however, early pituitary micrometastases likely contributed to subsequent hypoadrenalism. Disease progression led to hypopituitarism, DI, and visual disturbances several months after subtle initial symptoms, indicating slowly evolving pituitary involvement. Despite a negative PET scan in May 2023, a more sensitive MRI might have improved the detection of pituitary metastases. [20]

This case emphasizes the importance of considering pituitary metastasis in breast cancer patients presenting with unexplained hypoadrenalism following unilateral adrenalectomy. Early recognition and management may improve clinical outcomes.

## CONCLUSIONS

This case highlights the rare occurrence of breast cancer metastasizing to two endocrine glands—the adrenal and pituitary. It underscores the need to consider pituitary metastases in breast cancer patients who present with unexplained hypoadrenalism following unilateral adrenalectomy. Early recognition, appropriate imaging, and tailored management are essential to reduce complications and optimize clinical outcomes.

## LEARNING POINTS

- The adrenal gland can be the first site of distant metastasis in breast cancer, even in the absence of widespread disease.
- In cancer patients, new-onset adrenal insufficiency after unilateral adrenalectomy may indicate underlying pituitary metastasis and warrants prompt endocrine and neuroimaging evaluation.
- Receptor status discordance between primary and metastatic breast tumors can influence prognosis and treatment response, highlighting the need to reassess receptor status in metastatic sites.
- PET scans may miss pituitary lesions—MRI is essential in patients with suggestive symptoms.
- Pituitary metastases may present with devastating clinical sequelae and are often associated with poor prognosis

## PATIENT CONSENT

Written informed consent was obtained from the patient for the publication of this case report and all associated images.


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None.


## CONFLICT OF INTEREST

None.

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