

**Case Report**

# Metachronous Adrenal Metastasis from Breast Invasive Ductal Carcinoma: A Case Report & Review of Literature

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## Abstract

Breast cancer remains the most prevalent cancer among women worldwide, despite advancements in screening programs, international awareness campaigns, and various treatment options tailored to individual patient conditions. Unfortunately, breast cancer continues to be the leading cause of death among females globally. While only a quarter of patients experience distant metastases, this aspect is a significant burden of the disease, typically peaking around two years after surgery. The most common sites of distant metastasis are the bones, followed by the liver, lungs, and brain. However, it is exceedingly rare for breast cancer to metastasize to the adrenal glands, with only a few reported cases in the literature.

In this report, we present an exceptionally rare case of right adrenal metastasis in 2019, originating from left invasive ductal carcinoma that had been treated with skin-sparing left breast mastectomy in 2014. The patient underwent laparoscopic right adrenalectomy. During post-adrenalectomy annual follow-up, while receiving chemotherapy and hormonal therapy, a computed tomography (CT) scan in 2023 revealed a suspicious left adrenal nodule. A percutaneous biopsy confirmed the origin of the nodule as metastatic breast cancer. To the best of our knowledge, there have been no reported cases of delayed distant recurrence manifesting as ipsilateral adrenal metastasis four years after right adrenalectomy for left breast invasive ductal carcinoma.

**Keywords:** Adrenal Metastasis; Ipsilateral Adrenal Metastasis; Breast Invasive Ductal Carcinoma; Post Adrenalectomy.

## Introduction

Breast cancer (BC) is the leading cause of cancer among women worldwide [1]. Approximately 20-30% of BC cases present with distant metastasis at the time of diagnosis, which often limits curative treatment options and focuses on palliation and disease control. The prognosis for these cases shows a median survival of 2 to 3 years [2]. While the relative survival rate for early-stage BC is around 99%, it drops significantly to an estimated 27% for distant recurrent BC [3]. The risk of BC recurrence is highest within the

first few years after surgical resection and remains significant from 5 to 12 years post-operatively, particularly in cases of estrogen receptor-positive (ER+) malignancies. Studies have shown that 18% of patients experience relapse after 10 years of surgery, despite receiving adjuvant chemotherapy. Distant metastasis is the most common type of recurrence, with the bone being the most frequently affected site, followed by the liver, lungs, and central nervous system [4].

Although the adrenal gland is commonly involved in metastasis originating from lung cancer, malignant colon tumors, renal cell carcinoma, and melanoma, it is exceptionally rare for a solitary

adrenal metastasis to occur from breast cancer [5]. While there are a few reported cases of solitary adrenal metastasis originating from the breast in the literature, no cases have been found reporting recurrence incidents in both adrenal glands on separate occasions.

In this report, we present an extremely rare case of left breast cancer in a patient who underwent skin-sparing mastectomy with axillary clearance 10 years ago in 2014. The patient subsequently -6 years later- underwent laparoscopic right adrenalectomy in 2020 with histopathology confirming metastatic mammary carcinoma. The patient has now presented with a left adrenal mass, and a percutaneous biopsy was performed, once again revealing metastatic mammary carcinoma.

## Case Presentation

A 43-year-old medically healthy pre-menopausal female initially presented 10 years ago in 2014 after discovering a mass in her left breast while breastfeeding. Further investigation revealed invasive ductal carcinoma, Scarff-Bloom-Richardson (SBR) grade 2 with a focal mucinous component. The tumor tested positive for estrogen receptor (ER) (>90% of cells), progesterone receptor (PR) (>70% of cells), and negative for human epidermal growth factor receptor 2. As a result, she underwent a skin-sparing left breast mastectomy with axillary lymph node dissection. The sentinel lymph node biopsy was positive intra-operatively, but the surgery proceeded smoothly without complications. She received adjuvant chemotherapy, which was later switched to hormonal therapy due to febrile neutropenia occurring four months after treatment initiation.

During regular follow-ups with normal mammograms, she visited the emergency department five years after her surgery in 2019, complaining of epigastric pain accompanied by nausea. Further investigation revealed a right adrenal mass measuring approximately 4 centimeters, suggestive of a neoplastic lesion. A fine-needle aspiration confirmed metastatic adenocarcinoma with features consistent with a primary breast tumor, and positive ER and PR status. The patient's hormonal treatment was changed from tamoxifen to letrozole, and she continued receiving zoladex. Magnetic resonance imaging (MRI) and positron emission tomography (PET) scans confirmed no other sites of metastasis. After a one-year follow-up, during which there was a partial response to hormonal manipulation, the patient underwent laparoscopic right adrenalectomy. The histopathology result, obtained two weeks later, confirmed metastatic mammary carcinoma with positive ER status.

During continued follow-up, nine years after the initial presentation, a follow-up computed tomography (CT) scan in 2023 revealed a suspicious soft tissue density in a left suprarenal nodule measuring approximately 1.5 centimeters. There were no signs of intra-abdominal metastasis. Further MRI confirmed

a left metastatic adrenal lesion with an increased size of up to 2 centimeters. While there were no signs of metastasis in the surgical bed of the right adrenal gland, the patient's hormonal manipulation was adjusted, switching from letrozole to fulvestrant. A biopsy confirmed metastatic carcinoma consistent with a breast primary. After a multidisciplinary discussion, it was deemed that the risk of left adrenalectomy for this patient was high, and she was referred for second-line chemotherapy.

## Discussion

The risk of distant recurrence for breast cancer is high during the first 2 to 3 years, and the most common site is the bone, followed by the liver, lungs, and brain, respectively [3]. Nevertheless, for those patients who are positive ER, the risk remains even after its peak in the first couple of years after surgery from 5 to 12 years; evidence has showed that 18% of those who received adjuvant therapy, relapsed after 10 years from surgery [3,4]. In our case, the patient had a positive ER status and developed distant metastasis 5 years after the initial diagnosis, with a subsequent metastatic incident occurring during a follow-up period of 14 years. Remarkably, both instances of metastasis originated from the adrenal gland, with the first occurrence on the contralateral side. Although literature describes cases of solitary adrenal metastasis from breast cancer after surgery, no instances were found reporting recurrence incidents involving both adrenal glands on separate occasions. According to Saphner et al., post-menopausal women had higher recurrence incident than pre-menopausal women, and in both types of women, recurrence was highest after 2 years from surgery regardless of chemotherapy treatment and status of ER [4]. However, it's important to note that our patient is pre-menopausal, which adds further complexity to her case.

In a 10 years retrospective cohort study including 13,595 patients with breast cancer, Li et al. reported an incident rate of 0.25% (34 out of 13,595) for developing adrenal metastasis from BC. The median time to progression for those 34 patients was 6.2 months and overall survival was 21.4 months [6,7]. When a patient presents with adrenal metastasis, they tend to be asymptomatic, yet signs and symptoms of adrenal insufficiency usually occur when a large part of the adrenal cortex is involved by the tumour or occurs with bilateral adrenal metastasis [1]. Our patient suffered from epigastric pain with nausea during her first adrenal metastasis incident, yet she was asymptomatic with the second incident.

For the follow-up of breast cancer after surgery, it is essential to employ appropriate investigation methods. This includes mammograms combined with complementary ultrasound for breast evaluation, CT scans for the chest, abdomen, and pelvis, and bone scans. However, when adrenal metastasis is suspected, a PET scan should be performed to identify and differentiate between malignant and benign adrenal masses. Previous studies have well-

documented the efficacy of PET scans in this regard, and it has been identified as an independent positive prognostic factor [8]. It is important to note that PET scans can have limitations, with a 25% chance of false positive results. Additionally, research by Porte et al. has demonstrated that a combination of CT and MRI scans yields a sensitivity of 100% and specificity of 80% for evaluating adrenal masses [9,10]. In cases like ours, a suspicious suprarenal mass was identified through CT scan, and confirmation was obtained through fine-needle aspiration (FNA) and PET scan during the first incident of adrenal metastasis.

As for the surgical management, laparoscopic adrenalectomy (LA) has emerged as the preferred treatment for unilateral adrenal metastasis. When compared to traditional open adrenalectomy (OA), LA has shown several advantages, including reduced length of hospital stay, decreased use of post-operative analgesia, and a higher rate of return to normal activity. However, during LA, it is important to consider the possibility of carcinomatosis and port-site metastasis, as these have been reported previously. To mitigate the risk of local and port-site recurrence, it is recommended to minimize the handling of the tumor and perform resection of surrounding fat. Shoji and colleagues have proposed several imaging features that support the decision to opt for OA over LA, including the presence of unpreserved fatty tissue between the tumor and proximal organs, irregular tumor borders, cystic features, and large tumor size [12]. A retrospective study involving 12 patients with isolated metachronous adrenal metastases from breast cancer that underwent 13 adrenalectomies in an interval of 20 years from two tertiary hospitals showed absent post-operative mortality, 17% post-operative morbidity rate, and disease-free survival at 48 months was 75%. Moreover, one of the patients included in the study underwent a contralateral laparoscopic adrenalectomy for metachronous metastases 15 months after an open adrenalectomy from the same breast cancer origin [13].

The predictive factors for survival following adrenalectomy remain inconsistent. Some studies have suggested that a disease-free interval (DFI) of more than 6 months and complete resection are favourable prognostic factors [6], while others have reported contradictory findings. In a systematic review and pooled analysis by Tawee et al. focusing on patients with non-small-cell lung cancer, the 5-year survival rates for metachronous and synchronous adrenal tumors were reported as 25% and 26%, respectively [14].

In our patient's case, it is worth noting that there was a DFI of 5 years for the first incident and 14 years for the second incident, which are relatively favourable prognostic factors. As for non-surgical treatment, a review by Spartalis et al. encompassing seven different studies and 122 medically treated patients showed poor results and low survival rates. It is important to consider that the primary tumor sites in these patients were hepatocellular

carcinomas in 81 cases, lung cancers in 25 cases, melanomas in 14 cases, lymphoma in a single case, and one case with an unknown origin [9].

In our case, the patient has already undergone chemotherapy and a right adrenalectomy. However, removing the contralateral adrenal gland carries a high risk of morbidity due to the potential development of adrenal insufficiency. It is worth noting that a combination of chemotherapy after adrenalectomy has been shown to improve responses by 58% in patients with metastatic breast cancer to the adrenal gland [15]. Nevertheless, there are currently no specific guidelines for selecting candidates for this operation, and patient management should be approached as a multidisciplinary team to determine the optimal treatment modality based on the patient's condition, tumor size, and disease-free interval [16].

## Conclusion

Adrenal metastases from breast cancer are exceedingly uncommon. We report a case of left adrenal recurrence of left breast invasive ductal carcinoma, which occurred 10 years after the initial diagnosis and 4 years after a right adrenalectomy was performed for metastasis to the right adrenal gland. Timely recognition and thorough investigation, including CT, MRI, or PET scans along with biopsy, are crucial for achieving an accurate diagnosis. The choice of appropriate treatment may vary depending on patient-specific and disease-related factors, and decisions should be made through a multidisciplinary approach.

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