




CASE REPORT

Relapsed breast cancer complicated by isolated brain metastasis

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Abstract

The most common etiology of malignant brain tumors is metastatic lesions. They usually present as multiple lesions at the gray-white matter junction. However, they can unconventionally present as a single space-occupying lesion mimicking meningioma.

KEYWORDS

brain metastasis, breast cancer, CK7, GATA3, solitary metastasis

1 | INTRODUCTION

Metastatic brain lesions are typically multiple and at the gray-white junction. Herein, we present a case with a remote history of in-remission breast cancer presenting with gait disturbance, vision changes, and severe headache refractory to over-the-counter medications. Imaging studies revealed a single space-occupying lesion; however, immunohistochemistry confirmed metastasis.

Despite the significant advances in diagnosis and treatment, breast cancer remains the leading cause of cancer-related morbidity and mortality in women.¹ Localized and distant metastases are commonly observed in patients with relapsed and recurrent breast cancer.² The most common sites of metastasis include lungs, bones, and liver. However, metastasis to the brain secondary to breast cancer is rare and accounts for only 5%-12% of total cases.³ Common subtypes of breast cancer complicated by brain metastases include luminal type B, triple-negative, and HER2/neu positive breast cancer.⁴ The modalities utilized to diagnose breast cancer include imaging and biopsy, followed by confirmation with

immunohistochemical analysis. The immunohistochemical hallmarks confirming the metastases as of breast origin include cytokeratin-7 (CK7) and GATA binding protein-3 (GATA3).^{5,6}

Historically, CK7 was used to identify luminal cells from myoepithelial cells in breast tissue.⁵ However, subsequent investigations discovered CK7 to be an important biomarker for breast tumor confirmation, particularly in triple-negative breast cancer.⁵ Other subtypes associated with high expression of CK7 include micropapillary carcinoma of the breast, mammary, and extramammary Paget's disease.^{5,7} On the other hand, GATA3 is an active transcriptional factor involved in cellular proliferation and differentiation in mammary glands.⁶ Recent studies have recognized GATA3 as the most sensitive (82.5%) marker in the detection of metastatic breast cancer when compared with mammaglobin (46.6%) and gross cystic disease fluid protein (GCDFFP)-15 (23.9%).⁸ In this article, we will highlight a rare presentation of relapsed breast cancer (CK7 and GATA3 positive) complicated by isolated brain metastasis.

2 | CASE PRESENTATION

A 45-year-old female patient with a past medical history complicated by breast carcinoma (grade III infiltrating ductal carcinoma, HER2/neu negative, estrogen-receptor, and progesterone-receptor positive, respectively) diagnosed 8 years ago, status post modified radical mastectomy followed by six cycles of chemotherapy and hormonal therapy presented with complaints of recent ambulatory dysfunctions, fatigue, and generalized headache. Before presentation, the patient had remained in clinical remission and had no follow-up with oncology within the previous 2 years. Physical examination was significant for broad-based gait with right lower extremity weakness (power 3/5), grossly intact bilateral sensations, and cranial nerves. The remainder of the physical examination was within normal limits. Laboratory parameters were within normal range. Brain magnetic resonance imaging (MRI) revealed a large isolated enhancing lesion in the left occipital lobe with surrounding edema and truncal herniation. The lesion was determined to have caused compression effect on optic chiasma and obliteration of left quadrigeminal cistern (Figures 1-2) consistent with features of meningioma. Because of these imaging and clinical findings, her mass was surgically excised resulting in significant symptom improvement. The histological and immunohistochemical analysis showed tumor cells of epithelial origin with a strong affinity for GATA3 and CK7 (Figure 3). The positivity of CK7 and GATA3 raised concerns for isolated brain metastasis secondary to relapsed breast cancer. Further studies were completed including bone scan and contrast computed tomography (CT) of the chest, abdomen, and pelvis (C/A/P). The bone scan was unrevealing, but the CT scan showed multiple pulmonary nodules. A diagnosis of CK7 and GATA3-positive isolated brain metastasis secondary to relapsed breast cancer was made. After discussing future treatment options and prognosis, the patient opted for 20 cycles of radiation therapy confined to the brain followed by chemotherapy. At the time of writing this report, patient was receiving radiation therapy for brain lesions. However, refused further workup and treatment for lung lesion and underlying breast malignancy was deferred.

3 | DISCUSSION

Isolated brain metastasis secondary to breast cancer is a rare initial clinical presentation. The risk of developing brain metastases ranges from 10% to 16% in advanced breast cancer patients.³ The incidence of brain metastasis due to breast cancer is on the rise due to advances in imaging modalities allowing for early detection. In addition, the use of newer antitumor therapies results in improved survival for patients diagnosed with primary breast cancer.³ Because most isolated lesions are potentially curable, early identification of intracranial neoplasm in patients with breast cancer is essential.⁹ The most common clinical manifestations associated with brain metastasis include headache (35%), vomiting (26%), hemiparesis (22%), and visual changes (13%).⁴ Radiological features on MRI that can delineate brain metastasis signs include multiple lesions, localization at gray-white matter junction and significant vasogenic edema.¹⁰ Another essential association of brain metastasis is concurrent pulmonary metastasis.¹¹ Immunohistochemical analysis can help to confirm the primary source in cases where the primary location is unknown. The co-expression of CK7 and GATA3 is highly sensitive for confirming metastatic breast cancer.¹² Similarly, in our patient, a follow-up CT revealed multiple pulmonary metastases. Immunohistochemical analysis confirmed the presence of GATA3 and CK7 that strengthened the suspicion of relapsed breast cancer as an underlying cause.

Determination of appropriate treatment for isolated brain metastasis in breast cancer patients is dependent on the patient's performance status and the extent of extracranial disease. Adjuvant whole-brain radiation therapy (WBRT) and surgical excision are widely used options in such cases.¹³ Stereotactic radiosurgery (SRS) is another approach that can be beneficial in patients with the stable extracranial disease.¹⁴ In patients with extracranial lesions, especially pulmonary metastatic disease, the options are limited to palliative care or mastectomy. As our patient had multiple pulmonary metastases, the patient and oncology team decided on WBRT along with palliative care for pulmonary symptoms. However, prognosis is dismal for patients with distant metastatic disease undergoing WBRT for brain metastasis with a median

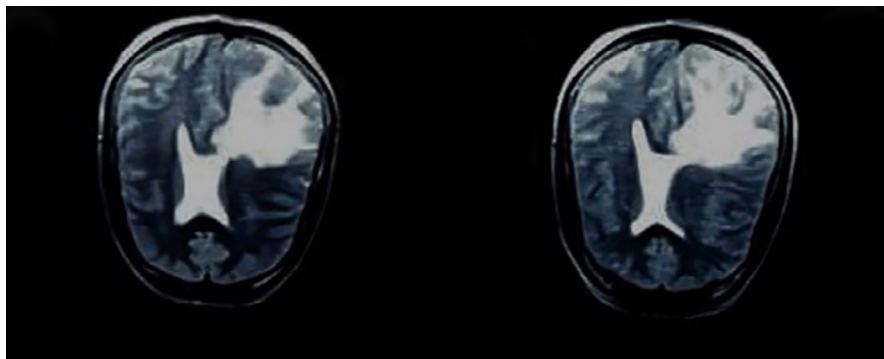


FIGURE 1 Magnetic resonance imaging scan results of solitary space-occupying lesion (axial view)

FIGURE 2 Magnetic resonance imaging scan results of solitary space-occupying lesion (sagittal view)

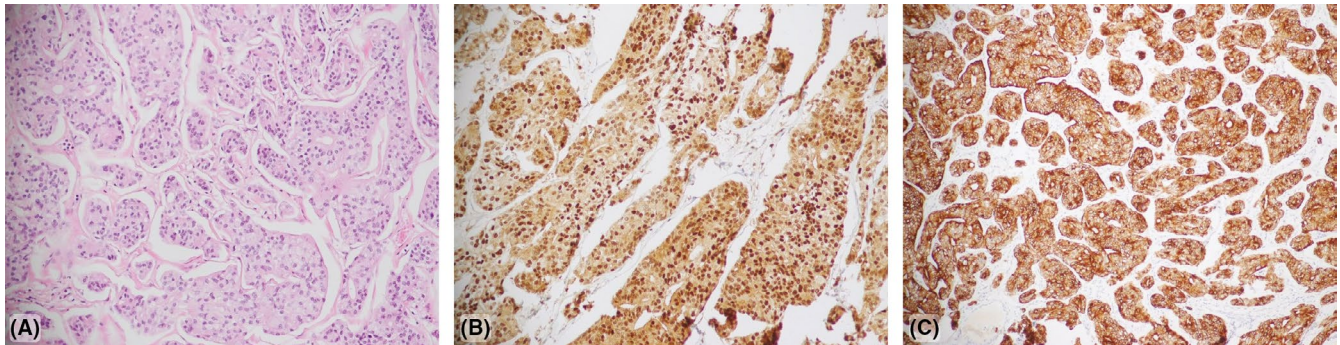


FIGURE 3 Histopathology examination of the lesion under a microscope (panel A), positive immunohistochemical stain for GATA3 (panel B), and positive immunohistochemical stain for CK7 (panel C)

survival rate ranging from 4-6 months.¹⁵ Those who had undergone surgery showed fewer recurrences (20% vs 52%) with better survival (40 weeks vs 15 weeks) and significant improvement in quality of life.¹⁶ Given the dismal prognosis and limited treatment options, a regular follow-up, even in the setting of disease remission, is recommended to detect early recurrence or metastases.

4 | CONCLUSIONS

Relapsed breast cancer can unconventionally present as solitary brain metastasis. CK7 and GATA3 are usually confirmatory immunological markers for the suspected diagnosis of metastatic breast cancer even in the absence of an identifiable lesion on initial presentation. Therefore, it is imperative to have immunohistochemistry confirmation along with detailed history, clinical, and imaging findings for an accurate diagnosis. The extent of metastatic disease and the patient's functional status can guide the provider in choosing future management options.

ACKNOWLEDGMENTS

Published with written consent of the patient.

CONFLICT OF INTEREST

The authors report no conflict of interest.

AUTHOR CONTRIBUTIONS

HE: involved in conception of idea, manuscript writing, and final approval. HI: involved in acquisition of data, manuscript writing, and final approval. MKS and MMS: involved in critical revision, manuscript writing, and final approval. AW: involved in manuscript writing and final approval.

ETHICAL APPROVAL


This manuscript did not receive any financial support.

DATA AVAILABILITY STATEMENT

The data will be made available on request due to ethics and privacy.

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How to cite this article: Ehsan H, Imtiaz H, Sana MK, Sheikh MM, Wahab A. Relapsed breast cancer complicated by isolated brain metastasis. *Clin Case Rep*. 2021;9:887–890. <https://doi.org/10.1002/ccr3.3699>