



# A case report of primary angiosarcoma of the breast

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**Background:** Breast Angiosarcoma can be divided into primary breast angiosarcoma (PBA) and second breast angiosarcoma (SBA). PBA is rare malignant breast cancer with poor outcomes. PBA usually occurs in women between 30–40 years old. PBA does not have a specific clinical manifestation. Clinically, PBA presents with a rapidly enlarging breast mass and skin involvement with skin color changes. Ultrasonography of PBA can be hypoechoic or hyperechoic, or mixed disordered areas. Microscopically, PBA can be classified into three grades according to the degree of differentiation, and the grade is related to the prognosis. And PBA can also express vascular endothelial markers. The main treatment for PBA is surgery, especially mastectomy. There are other treatments, such as chemotherapy and radiotherapy, but their effectiveness needs further confirmation. Targeted drugs may be helpful.

**Case Description:** A 32-year-old woman with main clinical presentation of a rapidly growing mass located in the upper inner quadrant of the right breast with skin involvement. PBA was diagnosed with first extended local resection, and then the patient underwent a second right mastectomy. The patient is now undergoing chemotherapy.

**Conclusions:** Since this is a rare form of breast cancer, we report this case to raise the attention of breast surgeons to avoid misdiagnoses.

**Keywords:** Primary breast angiosarcoma (PBA); breast cancer; case report

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## Introduction

Primary breast angiosarcoma (PBA) is a rare malignant tumor that originates from the lobules or surrounding capillaries of the breast. It only accounts for 0.05% of primary breast malignancies and 8% of breast sarcomas. Due to its non-specific imaging or clinical manifestation, it can be easily misdiagnosed. So, its most reliable diagnosis depends on pathology. This paper discussed a case of a young patient with PBA who was admitted to our hospital

recently. The patient was 32 years old at diagnosis and presented mainly with a fast-growing mass in her right breast. We first performed extended local resection, and after the pathology findings suggesting PBA, the patient underwent a second right breast mastectomy. In this report, we discussed the diagnosis and treatment of PBA based on recent research to enhance attention to this rare disease. We present the following article in accordance with the CARE reporting checklist (available at <https://tcr.amegroups.com/article/view/10.21037/tcr-22-1142/rc>).



**Figure 1** Preoperative appearance of the patient's right breast. The diagram shows that the black dotted line range is vascular dilatation area, about 7.0 cm × 7.0 cm; the red dotted line range for masses, about 6.0 cm × 6.0 cm. This image is published with patient consent.

## Case presentation

A 32-year-old female patient had been monitored for 2 years for a painless mass in her right breast. The mass had grown rapidly from 2 to 6 cm in the past 2 months. Her local hospital considered it might be a cavernous hemangioma. For further treatment, the patient was transferred to our hospital for the removal of the mass. Upon physical examination, a 7 cm × 7 cm vasodilated area with a cystic 6 cm × 6 cm palpable firm painless mass was identified in the upper inner portion of the right breast (*Figure 1*). The skin color was

blue-purple, and the temperature was high. Breast ultrasound showed a 2.1×1.3×1.5 cm<sup>3</sup> hypoechoic area in the upper inner quadrant of the right breast, surrounded by a 5.5×5.2 cm<sup>2</sup> moderate to the high echogenic area, with a thickness is 1.6 cm and a BI-RADS 4b classification (*Figure 2*).

On mammography: irregularly slightly high-density 5.7 cm × 6.6 cm shadow in the upper inner quadrant of the right breast, 5.0 cm from the nipple, with an unclear border (*Figure 3*). On enhanced CT + 3D reconstruction, a 60 mm × 29 mm oval mass was observed in the inner side of the right breast, and the lesion was unevenly enhanced with mostly marginal enhancement, and strip-shaped blood vessels were visible within the lesion (*Figure 4*).

The patient was admitted with a diagnosis of a right breast mass of unknown nature, probably a cavernous hemangioma, but a stromal malignancy could not be excluded. No puncture was performed because the mass was, to some extent, cystic. To clarify the pathology, we performed an extended local excision for the first time (*Figure 5*). Postoperative paraffin pathological diagnosis was well-differentiated angiosarcoma; immunohistochemistry results: CD31 (+), CD34 (+), AE1/AE3 (-), F8-R (+), ERG (+), EMA (-), Ki-67 (index 10%) (*Figures 6, 7*). Since the patient refused breast reconstruction, she underwent "right breast mastectomy + axillary sentinel lymph node biopsy" for the second time. Postoperative pathology showed chronic inflammation of the right breast tissue with no residual tumor; sentinel lymph nodes (0/7). The patient received adjuvant chemotherapy since December 1, 2021 (paclitaxel 120 mg on d1, d8, d15; G2 hair loss) to avoid recurrence; next-generation sequencing (NGS) testing revealed no mutations in the patient's core genes and no mutations in other essential genes.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

## Discussion

### *Etiology and clinical manifestations*

Breast angiosarcomas are classified as primary breast angiosarcoma (PBA) and secondary breast angiosarcoma (SBA). However, in terms of histology, IHC (CD117,

### Highlight box

#### Key findings

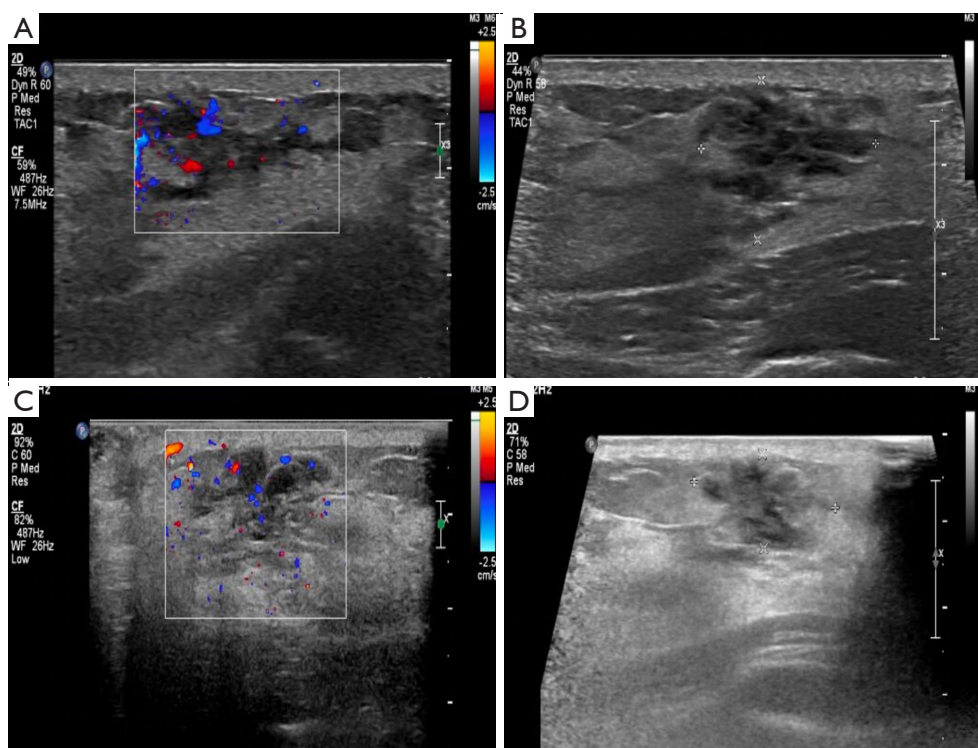
- The whole diagnosis and treatment process of the primary breast cancer patient were reported here.

#### What is known and what is new?

- Primary breast angiosarcoma usually presents with a rapidly enlarging breast mass. It does not have a specific image presentation and thus no best treatments are guaranteed. Here the clinical presentation, image presentation and pathology of this patient were reported, together with the relative references.

#### What is the implication, and what should change now?

- These findings suggest the need of further research for primary breast angiosarcoma.



**Figure 2** The ultrasound of the patient's right breast before admission. (A,B) In the ultrasound of the patient before admission, 5.5 cm × 5.2 cm high echo area can be seen, about 1.6 cm thick, internal echo is uneven; it has a range of about 2.1 cm × 1.3 cm × 1.5 cm low echo area, unclear boundary, irregular shape, and abundant point-strip blood flow, BI-RADS 4b. (C,D) The review ultrasound of the patient after admission, 5.4 cm × 5.6 cm × 2.1 cm range of high echo area can be seen, internal echo is uneven, its range of low echo area, the unclear boundary is 2.2 cm × 2.2 cm × 1.1 cm, irregular shape, abundant dot strip blood flow signal can be seen, BI-RADS 4b.

c-Myc, P53) and survival, there is no difference between PBA and SBA (1). Primary angiosarcomas are rarer, with the breast being the most common site. The etiology of PBA is still unknown. Breast angiosarcoma is more common in young women, with a median age of 30 to 40 years old. Mostly, the first symptom is a rapidly growing painless diffuse mass, mainly on the right side. The specific clinical manifestations are localized purplish-purple, bluish-purple lesions with unclear borders, and superficial telangiectasia with skin involvement (2,3). This case presented here was a 32-year-old woman with no factors associated with SBA. Her first symptom was a painless mass with rapid enlargement. The skin on the surface of the tumor was blue-purple with telangiectasia, consistent with the clinical manifestations of PBA.

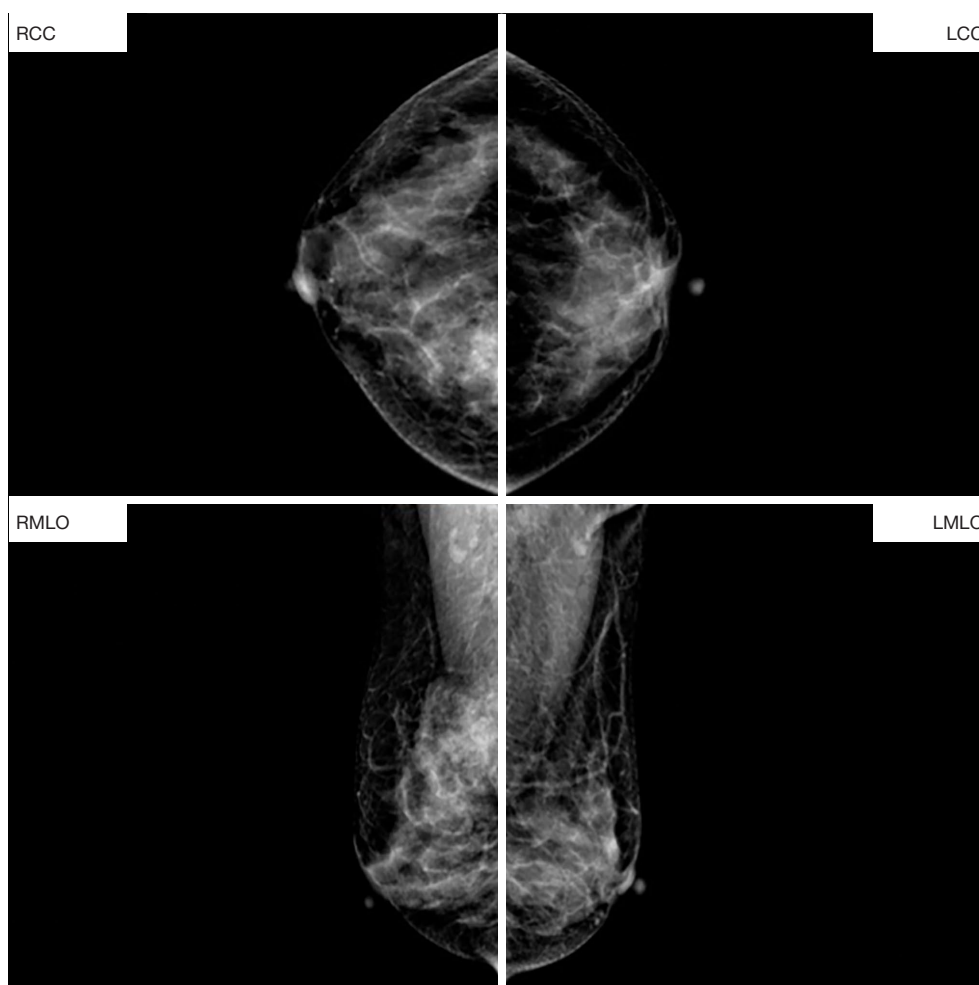
### Imaging

The ultrasound examination of PBA has no specific

findings. A disordered area with mixed echoes can be shown due to the different ratios of vessel and sarcoma (4). PBA can also present as a hypoechoic or hyperechoic mass (5). Since PBA has no apparent calcification, it usually presents as a non-calcified mass on mammography. The signal within the mass is uneven on MRI, with low T1-weighted signal intensity and high T2-weighted signal intensity, and a continuous enhancement (6). Enhanced CT and 3D reconstruction can also be a good method better visualize the vascular course and the surrounding tissue invasion of the patient.

### Pathology

PBA presents as a gray-red, spongy, hemorrhagic tumor with unclear boundaries. PBA is usually highly or moderately differentiated. Microscopically, the endothelial cells form irregular anastomosing duct lumens, forming papillary or diffuse infiltration. The endothelial cells are



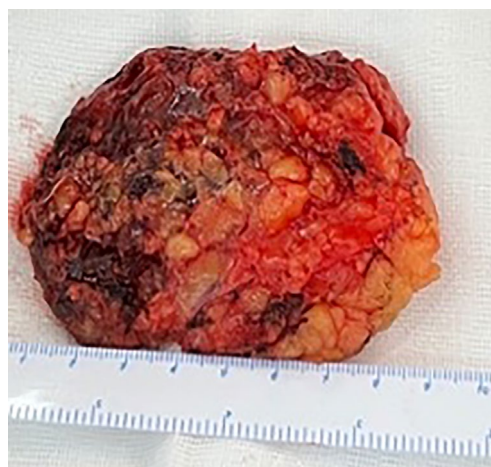
**Figure 3** The patient's right breast mammography. The distribution of bilateral breast glands was symmetrical, and the density of some glands increased. The irregular and slightly high-density shadow in the upper quadrant of the right breast was about 5.7 cm × 6.6 cm, about 5.0 cm from the nipple, and the boundary was unclear, BI-RADS 4b-c. There had no obvious enlarged lymph nodes under both armpits can be seen. RCC, right craniocaudal; RMLO, right mediolateral oblique; LCC, left craniocaudal; LMLO, left mediolateral oblique.

larger, spindle-shaped, cuboidal, or irregular, with less cytoplasm, deeper nuclei, and visible mitoses. According to their microscopical manifestation, they can be classified as well-differentiated (grade 1), moderately differentiated (grade 2), and poorly differentiated (grade 3). Well-differentiated: vascular invasion surrounding the breast tissue; moderately differentiated: vascular growth of the tumor in the breast with the increased mitotic rate; poorly differentiated: hemorrhage and necrosis appear in the tumor area. Regarding immunohistochemistry, PBA often expresses vascular endothelial markers such as CD31, CD34, ERG, and factor VIII, but if PBA is poorly

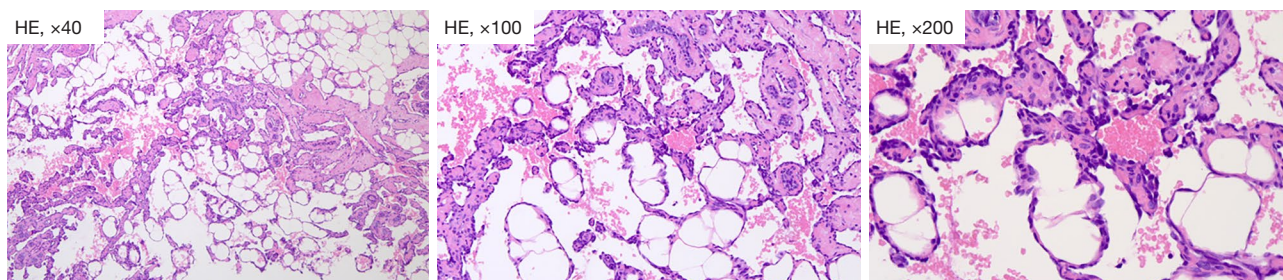
differentiated, there may be no expression of CD34 and CD31. With further research, ETS-related genes and FLI-1 gene are new markers of mammary angiosarcoma with higher sensitivity and specificity than CD31 and CD34, providing new ideas for immunohistochemistry and targeted therapy for PBA (7). NGS has become a new generation of the genetic testing method to replace Sanger sequencing, especially for soft tissue sarcoma and other diseases that are difficult to be diagnosed by morphology alone. The identification of target genes and the use of targeted drugs with NGS become a new direction in the diagnosis and treatment of sarcoma.



**Figure 4** Enhanced CT + 3D reconstruction. There was an oval mass on the medial side of the right breast, about 6.0 cm × 2.9 cm in size just as the arrow indicates. The lesion was unevenly enhanced, and the edge was enhanced. Strip blood vessels were found in the lesion. There was no obvious invasion of the pectoralis major muscle in the posterior hospital of the lesion.



**Figure 5** First operation: complete tumor resection. Graphical representation: Gray-yellow powder oval tissue, about 8.5 cm × 5.5 cm × 2.5 cm in size, section scattered in different sizes of gray-brown stores, about 3 cm × 2 cm × 4 cm in scope, with bleeding.



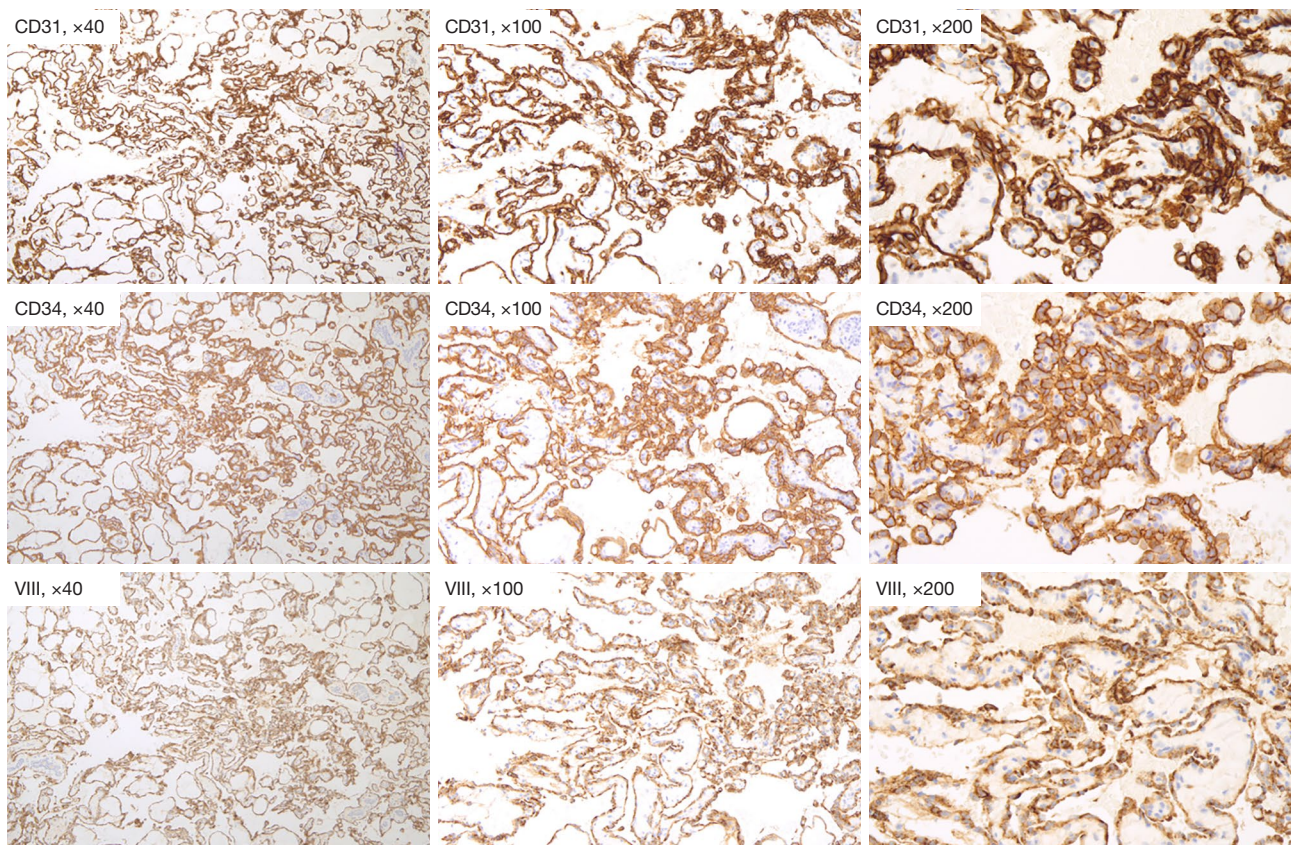
**Figure 6** The endothelial cell mitotic is rare and well-differentiated. Microscopically, the vascular lumen was anastomosed with each other, and the lumen was monolayer vascular endothelial cells. The cells were large, mostly fusiform, and red blood cells were visible in the lumen.

### Diagnosis

Diagnosing PBA can be challenging because its manifestation is nonspecific. It could resemble a fibroadenoma on preoperative examination (8). Clinically, PBA should be considered in young women aged 30s to 40s with rapid enlargement of breast mass with or without pain, especially accompanied by skin color changes. As for radiologist diagnosis, it can be an uneven oval area both on MRI and CT. Ultrasonography can be a mixed echo area with or without posterior shadowing. Most young women's breasts are high in density, so mammography is inappropriate for identifying this tumor. However, the most authoritative diagnosis of PBA is pathology.

### Treatment and prognosis

The prognosis of PBA is very poor, and patients undergoing surgery at the earliest may prolong the life (9). Abdou concluded that tumor size and grade are reliable predictors of prognosis, and survival is significantly lower for high-grade tumors or those spanning greater than 5 cm (3,10). However, Alessandra concluded that grade does not affect prognosis (11). Masai conducted a retrospective analysis of patients with breast angiosarcoma from 1997 to 2012 at the National Cancer Center Hospital in Tokyo, Japan, and found that the 5-year survival rate for PBA was 50%, and the 3- and 5-year disease-free survival rates were 20% and 0% bone (12). Among the six patients with confirmed PBA, 1 case



**Figure 7** Immunohistochemical staining. CD31 and CD34 are cell membrane staining, and VIII is cytoplasm staining. It can be seen that CD31, CD34 and VIII staining of vascular endothelial cells were positive.

had local recurrence, and 4 had distant metastatic recurrence; the metastatic sites were lung, liver, and bone (12). Sher *et al.* found that 55% of PBA patients recurred after 40 months (13). These studies suggest that PBA has a poor prognosis and a high rate of metastasis or recurrence.

The treatment of PBA is mainly surgery. Breast surgery mainly includes extended local excision, mastectomy, and modified radical mastectomy. The preferred surgical method for PBA is mastectomy (14,15). However, some investigators believe that if the resection margin of local excision can reach R0 (complete tumor resection with negative microscopic resection margin), the prognosis of local extended breast tumor resection is better than that of mastectomy and also improves the overall survival rate of PBA. Axillary lymph node dissection is not routinely recommended because PBA is predominantly vascular with little lymph node involvement, even in advanced stages (16,17). Losanoff *et al.* suggested that a sentinel lymph node excision biopsy should be performed, and axillary lymph

node dissection should be determined based on the biopsy results (18). In the case presented here, the mass was too large to obtain R0, and ultrasound showed the axillary lymph nodes were enlarged, so we chose mastectomy + sentinel lymph node biopsy.

There are different views regarding postoperative adjuvant therapy for PBA. Darre *et al.* think chemotherapy and radiotherapy should be considered for large tumors of grade 3 (9). Abdou believes that although adjuvant chemotherapy improves local recurrence-free survival in high-grade PBA, it does not significantly improve survival outcomes (3). However, Torres concluded that adjuvant chemotherapy prolongs survival and reduces the local recurrence rate in patients with angiosarcoma of the breast (19). Sher found that anthracycline-ifosfamide and gemcitabine-taxane chemotherapy regimens were beneficial in patients with PBA (13). Regarding postoperative radiotherapy, Torres suggested that patients with PBA with skin or muscle involvement should be treated with

adjuvant radiotherapy (19). Sher pointed out that the poor effect of adjuvant therapy in improving prognosis in some studies was due to a small sample size and patient selection bias (13). In addition to the common chemoradiotherapy, Painter believes PIK3C-a inhibitors may be a new target for treating patients with PBA (20).

## Conclusions

In conclusion, PBA is a rare breast malignancy with a bad prognosis. Most patients are young women. The typical clinical manifestation is a rapid enlargement of the painless mass. Due to its non-specific clinical and imaging manifestation, the diagnosis can be confused. Surgery is the most recommended treatment for PBA, with mastectomy being the first choice. The efficacy of adjuvant therapy needs to be further explored. Meanwhile, we believe that further in-depth research on specific markers and target genes of PBA in the future may facilitate further improvement of PBA treatment.

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## Footnote

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is

available for review by the editorial office of this journal.

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