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Case Report

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Triple-negative Invasive Ductal Carcinoma Associated with a *PALB2* Gene Mutation

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Abstract

Among the various forms of breast cancer, invasive ductal carcinoma is a subtype often associated with hereditary genetic syndromes including PALB2. A PALB2 mutation is associated with an increased risk for several types of cancers. Here, we report the case of a young patient who presented with a breast mass that was eventually diagnosed as triple-negative invasive ductal carcinoma and was associated with a PALB2 mutation. The patient's clinical work-up, differential diagnosis, investigation, imaging, and pathology findings, and medical and surgical management are discussed.

Introduction

PALB2 (partner and localizer of *BRCA2*) is a gene located on the short arm of Chromosome 16 in humans. *PALB2* codes for a tumor-suppressor protein that regulates double-stranded DNA break repair (Figure 1). A mutation in *PALB2* has an estimated prevalence of about 1% of those with confirmed breast cancer. A bi-allelic mutation in *PALB2* leads to a subtype of Fanconi anemia, while a uni-allelic mutation leads to a predisposition to breast, ovarian, and pancreatic cancers [1-5]. It has been observed that a protein called RAD52 plays a key role in the pathogenesis of *PALB2*-associated breast cancer, and that small molecule inhibitors against RAD52 such as epigallocatechin and AICAR (5-aminoimidazole-4-carboxamide ibonucleotide) have shown promising *in vitro* results[6]. Here, we report the case of a female patient who was diagnosed with invasive ductal carcinoma, which was then found to have been associated with a *PALB2* mutation.

Figure 1: The PALB2 protein complexed with BRCA2 protein[7]. PALB2 is a homodimer consisting of mostly Beta-pleated sheets (green) and an alpha-helix (orange). PDB 3EU7. Image generated using WebMOL.

Clinical Presentation

A 34-year-old African-American, G0P0, female with a history of endometriosis, status-post bilateral salpingectomy for a recent hydrosalpinx, and endometrial polyps presented to the clinic with a palpable firm right breast mass. She was referred for further work-up.

Differential Diagnosis

The differential diagnosis of a palpable breast mass includes, but is not limited to, breast cancer, fat necrosis, galactocele, fibroadenoma, fibrocystic change, lipoma, liposarcoma, reactive lymphadenopathy.

Investigation and Imaging Findings

A diagnostic mammogram was performed, which showed a right breast mass with prominent regional lymphadenopathy (Figures 2 and 3).

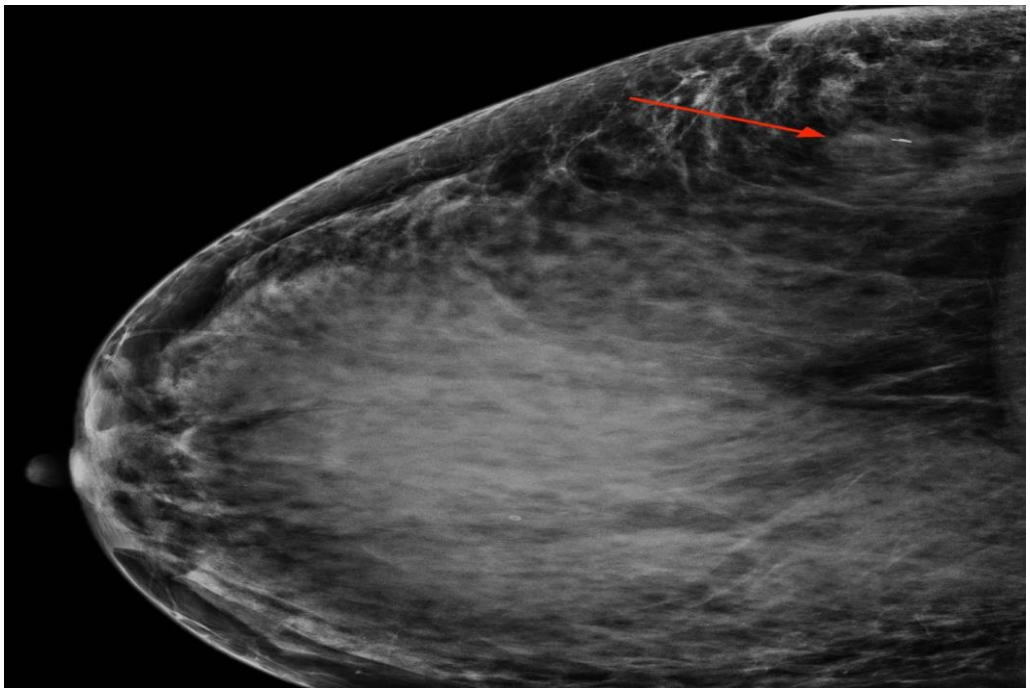

Figure 2: A diagnostic mammogram in the CC projection showing a suspicious mass in the right breast (arrow). CC, craniocaudal.

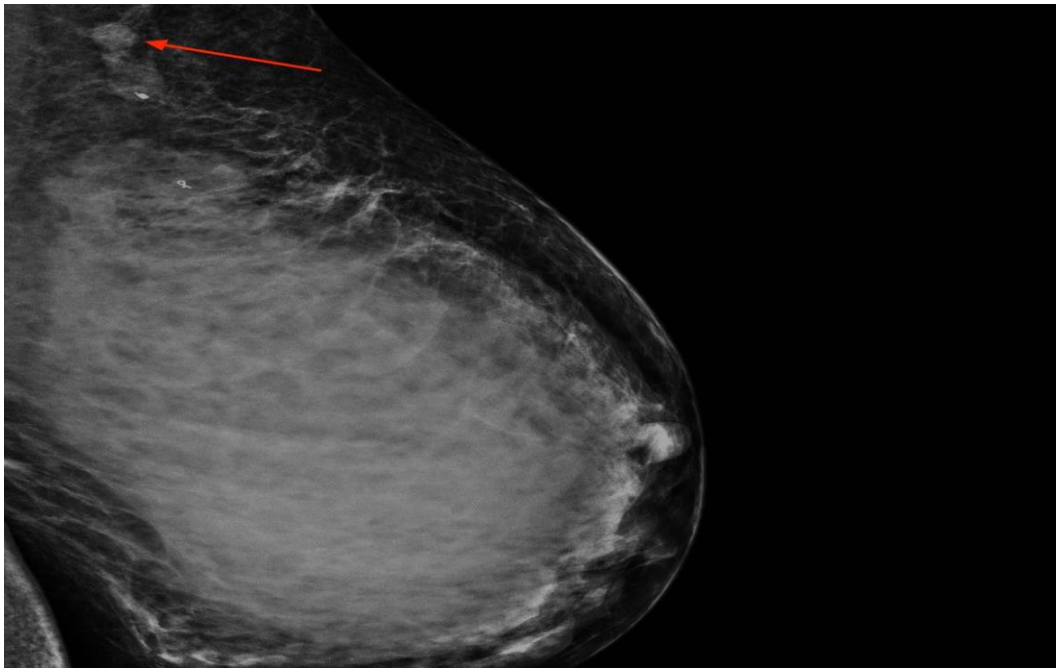

Figure 3: A diagnostic mammogram in the LM projection showing a suspicious mass in the right breast (arrow), along with prominent lymphadenopathy. LM, lateromedial.

A breast ultrasound was also performed, which showed a right breast mass with heterogeneous echogenicity and increased flow with vascular Doppler studies (Figure 4).

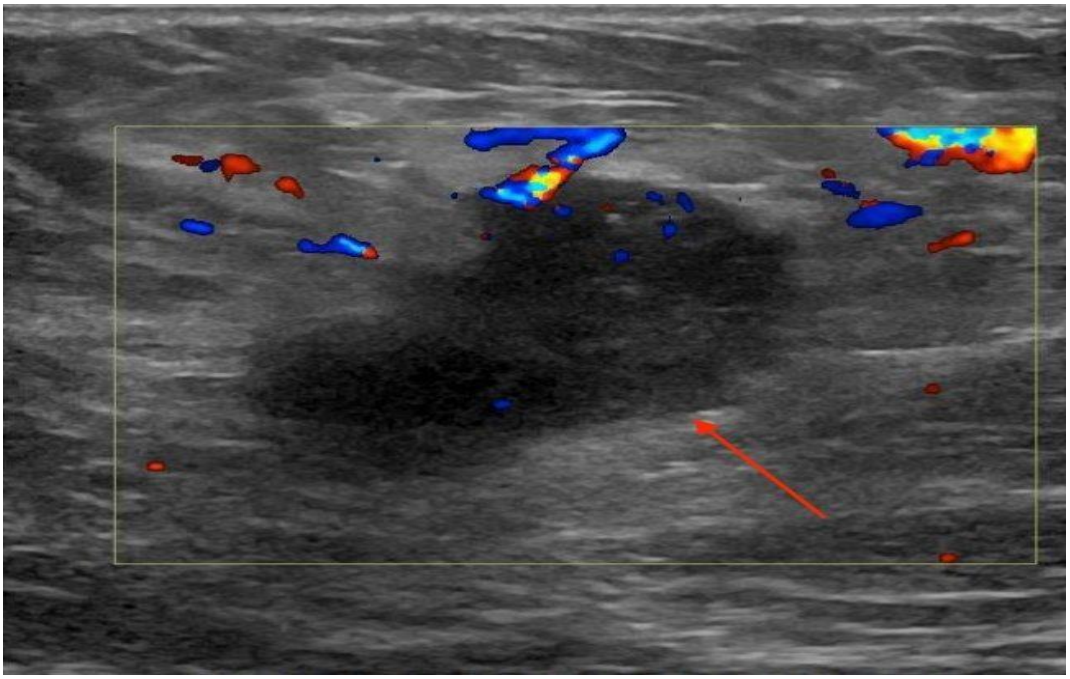

Figure 4: A breast ultrasound showing a heterogeneous mass with varying internal echogenicity, associated with increased Doppler flow in the right breast (arrow).

Next, an ultrasound-guided core needle biopsy of the mass and an axillary lymph node was performed for definitive diagnosis. On pathology, the patient was diagnosed with invasive ductal carcinoma, which was negative for the estrogen receptor (ER), progesterone receptor (PR), and HER2-neu (triple-negative). There was also evidence of ductal carcinoma in-situ with comedo necrosis. Axillary lymph node sampling was negative for metastatic disease.

Given the suspicion for possible metastatic disease, a CT scan and a PET scan of her head and neck, chest, abdomen and pelvis were performed, which confirmed the evidence of the mass in the chest window but did not lend support for concurrent metastatic disease elsewhere in the body (Figures 5,6, and 7).

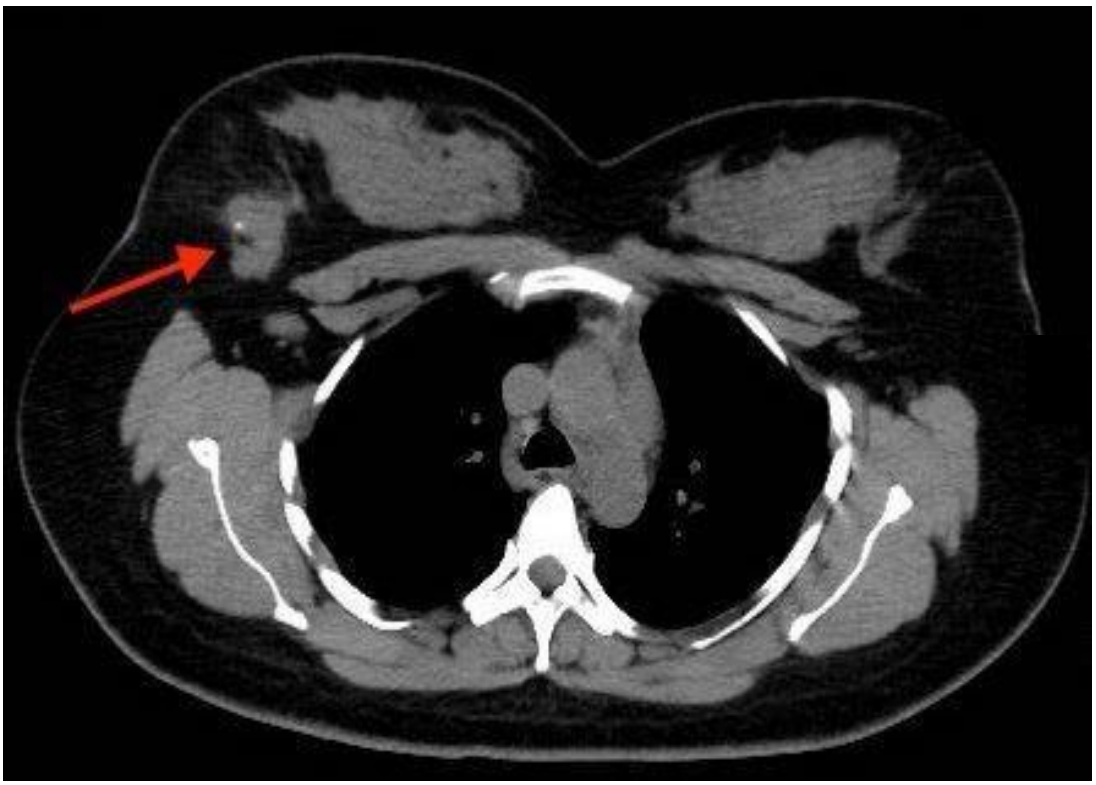

Figure 5: A CT scan showing a soft tissue density (arrow) in the region of the suspected mass.

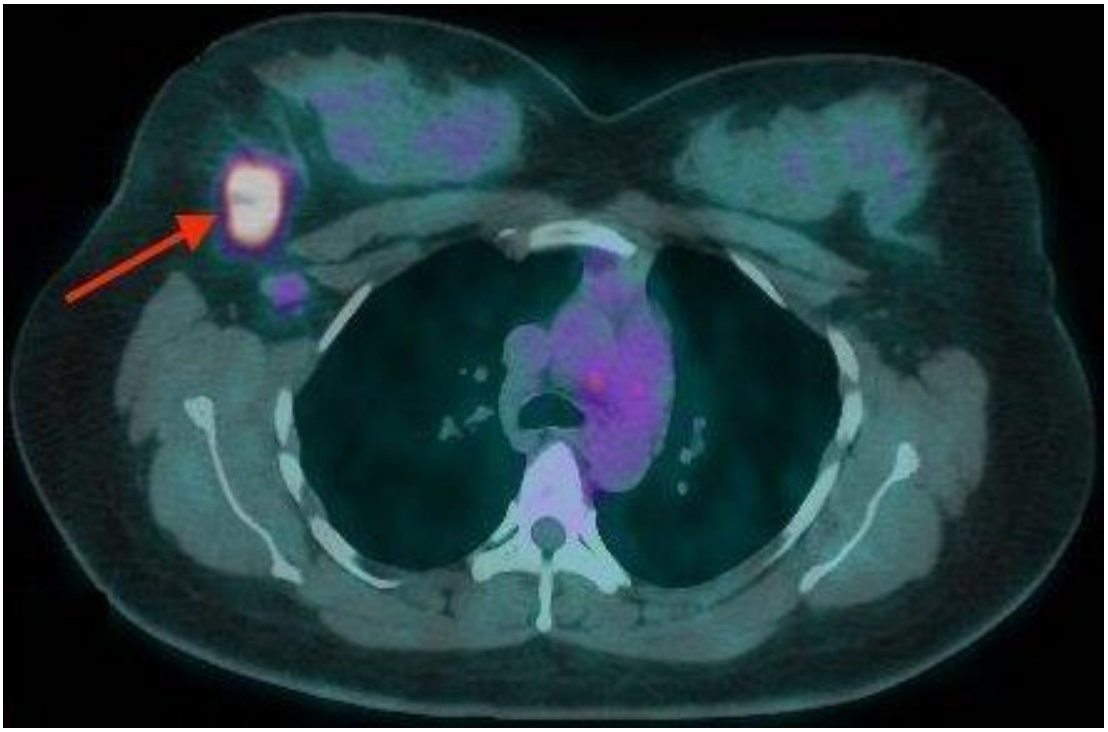

Figure 6: A PET scan in the axial projection showing increased uptake in a soft tissue density (arrow) in the region of the suspected mass.

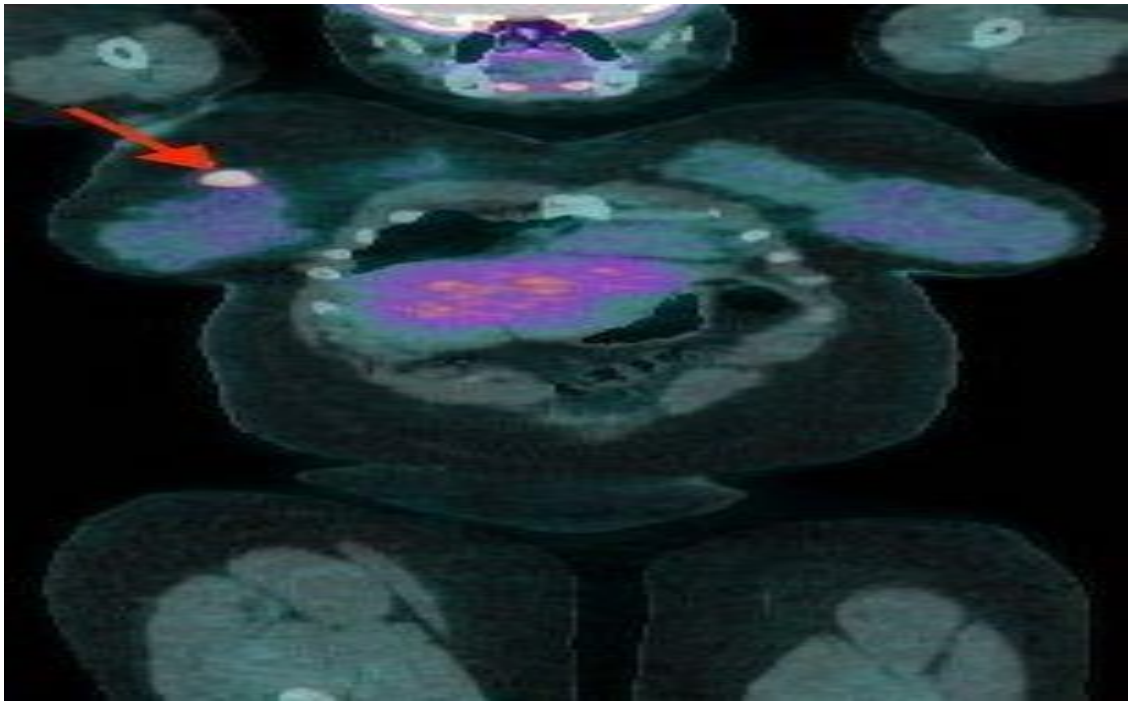

Figure 7: A PET scan in the coronal projection showing increased uptake in a soft tissue density (arrow) in the region of the suspected mass, but otherwise showing no abnormal uptake elsewhere.

The patient's disease was conclusively staged as T2 N0 M0 triple negative invasive ductal carcinoma of the axillary tail of right breast.

Outcome, follow-up, and discussion

The patient was informed about this diagnosis and was started on neoadjuvant chemotherapy consisting of four cycles of carboplatin and taxane, followed by four cycles of dose-dense Adriamycin-cyclophosphamide.

After surgical consultation, the patient decided that she would undergo an initial right lumpectomy and sentinel lymphadenectomy with mastopexy of the left breast with delayed nipple sparing mastectomy and reconstruction approximately four to five months later.

Conclusion

In the evaluation of a young patient presenting with an early-onset breast mass, the clinician must consider a genetic abnormality associated with breast cancer. Among various genetic mutations such as *ATM*, *BRCA1*, *BRCA2*, and *HNPCC*, a *PALB2* mutation is associated with increased risk for breast cancer, epithelial ovarian cancer, pancreatic cancer, and Fanconi anemia. Several tailored small-molecule inhibitors have shown promising *in vitro* results against *PALB2*-associated breast cancer, and clinical trials on these molecules should be monitored closely in the near future. For a patient diagnosed with invasive ductal carcinoma, surgical management, adjuvant chemotherapy, and close monitoring and follow-up is necessary.

Learning Points

1. Various genetic syndromes are often implicated in hereditary forms of breast cancer, including *BRCA1, BRCA2, HNPCC, ATM,* and *PALB2.*
2. *PALB2* mutations are rare and are associated with an increased risk for several types of cancers, including epithelial ovarian, breast, and pancreatic cancers.
3. Small-molecule inhibitors targeting the PALB2 protein-associated biochemical pathway are potentially promising future developments in chemotherapeutics.
4. In a patient diagnosed with triple-negative invasive breast cancer, surgical management, adjuvant chemotherapy, and close monitoring and follow-up is necessary.

Acknowledgments and Conflicts of Interest: None

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