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Case Report
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# Regional Recurrence of Breast Cancer in Ipsilateral Intramammary Lymph Node Six Months after Breast Conserving Surgery

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## Abstract

A 40-year-old female was diagnosed with left breast ductal carcinoma in-situ by Core Needle Biopsy (CNB) and underwent breast conserving surgery and sentinel lymph node biopsy. Final pathology reported invasive carcinoma, no special type, grade III, triple negative subtype. She started postoperative chemotherapy 2 weeks after surgery and received 4 cycles of epirubicin plus Cyclophosphamide, followed by 2 cycles of Docetaxel. The sixth chemo cycle was postponed for more than one month because of the outbreak of COVID-19. After her sixth cycle of chemotherapy, she underwent breast ultrasound and was found to have a new lesion in the ipsilateral breast. Vacuum-assisted biopsy of the lesion confirmed recurrence of breast cancer in an Intramammary Lymph Node (IMLN) and she underwent completion mastectomy. Chemotherapy regimen was changed to Vinorelbine in combination with Capecitabine due to primary resistance to anthracyclines and Docetaxel. Radiotherapy was also arranged for her.

**Keywords: Breast cancer; Breast conserving surgery; Recurrence; Intramammary lymph node; Sentinel lymph node**

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## Case Presentation

A 40-year-old, premenopausal female presented to Peking University Shenzhen Hospital with a left breast mass for 2 months. Ultrasound showed a hypo echoic mass, sized 28 mm × 27 mm × 16 mm and located 5 cm from the nipple-areolar complex (Figure 1A). Core needle biopsy was remarkable for a high-grade Ductal Carcinoma *In-Situ* (DCIS). Mammography and Magnetic Resonance Imaging (MRI) showed an irregular mass, about 23 mm × 21 mm in size, in the upper outer quadrant of left breast with no abnormal axillary lymph nodes (Figures 1B-1D). The patient underwent Breast Conserving Surgery (BCS) and left axillary Sentinel Lymph Node Biopsy (SLNB). Final pathology reported the mass as an invasive carcinoma, no special type, histology grade III, and associated with DCIS. Four axillary SLNs were negative for metastases. On Immunohistochemical (IHC), the tumor cells were estrogen/progesterone receptor negative, human epidermal growth factor receptor 2 negative, and 70% of the cells were Ki-67 positive staining.

Adjuvant chemotherapy was started two weeks after surgery with the plan of 4 cycles of epirubicin (90 mg/m$^2$) plus Cyclophosphamide (600 mg/m$^2$) followed by 4 cycles of Docetaxel (100 mg/m$^2$). The first five cycles were on time with normal dosage; however the sixth cycle was postponed for 35 days because of the outbreak of COVID-19 and travel restriction thereafter. The patient was recovering well but unfortunately, was found to have a new lesion in the same breast on a follow up ultrasound that was done in another institution due to travelling restrictions during the COVID-19 pandemic. The lesion was 12 mm × 9 mm × 8 mm in size, encapsulated, and located in the 3 to 4 o'clock direction, 2 cm from the nipple-areola complex (Figure 2A and 2B). Because of COVID-19, she could not resume care in our institution. Subsequently she underwent vacuum assisted breast mass biopsy (Mammotome), based on recommendations from her new care providers. This time, pathology reported the lesion as a lymph node with breast cancer metastasis "Intramammary Lymph Node (IMLN) metastasis" (Figure 2C and 2D). The outlook of the left breast after Mammotome is shown in Figure 3A and 3B. After travel restrictions from COVID-19, she resumed care in our institution and completion mastectomy was performed after a thorough systemic scan. X-ray of the resected breast was negative for a residual mass and the final pathology confirmed negative margins (Figure 3C). Considering the cancer as primarily resistant to Anthracycline and Taxane, Vinorelbine

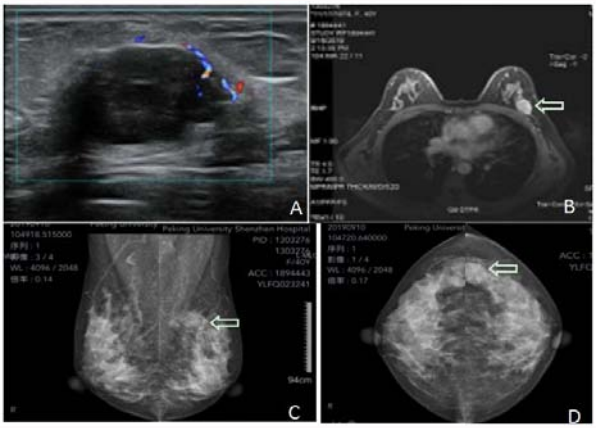

**Figure 1:** Preoperative imaging scans of the breast lesion before first surgery. Panel A: Ultrasound of breast showed a hypo echoic mass, 28 mm × 27 mm × 16 mm, 5 cm from nipple-areolar complex and 6 mm from the above skin. Panel B: Magnetic Resonance Imaging (MRI) of the breast showed an irregular shaped mass with the size of 23 mm × 17 mm in the upper outer quadrant of left breast. Panel C: External oblique position and Panel D: coronal position of breast mammography showed a slightly high dense irregular mass, 23 mm × 21 mm, in the upper outer quadrant of left breast with no abnormal lymph nodes in ipsilateral axilla.

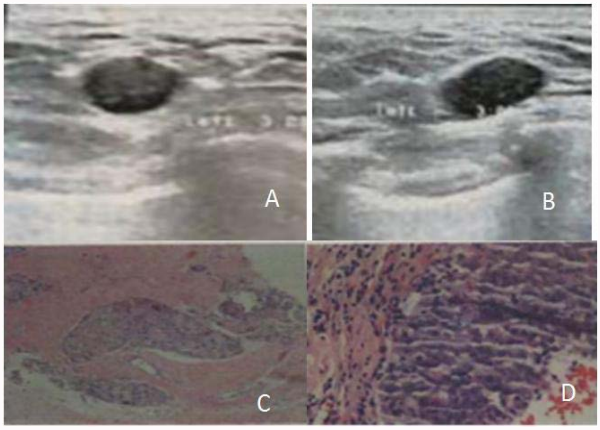

**Figure 2:** Images of neoplasm in ipsilateral breast after breast conserving surgery and six cycles of chemotherapy.
Panel A and B: Six months after BCS, ultrasound scan of the breast found a low echoic oval mass in the ipsilateral breast, 12 mm × 9 mm × 8 mm in size, with capsule, located in the 3 to 4 o'clock direction, 2 cm from nipple. No lymph hilium or lymph node cortex medulla was recognized by ultrasound, so the mass was not suspected as a lymph node during ultrasound examination. Panel C and D: H&E stain identified the mass as a intramammary lymph node with breast cancer metastasis.

in combination with Capecitabine were chosen for postoperative adjuvant chemotherapy, despite no pathogenic mutations were found on germline BRCA testing. Radiotherapy was also conducted for her.

## Discussion

In this report, we shine the light on a case, where patient care was impacted by COVID-19 pandemic. This 2019 novel coronavirus disease spread rapidly. In order to control the outbreaks, Chinese government strengthened the control of personnel mobility from late January, 2020 which had a great impact on the examination and treatment of breast cancer patients [1]. Online medical communication and discussion were gradually achieved during travel restrictions between doctors and patients, but still couldn't cover all

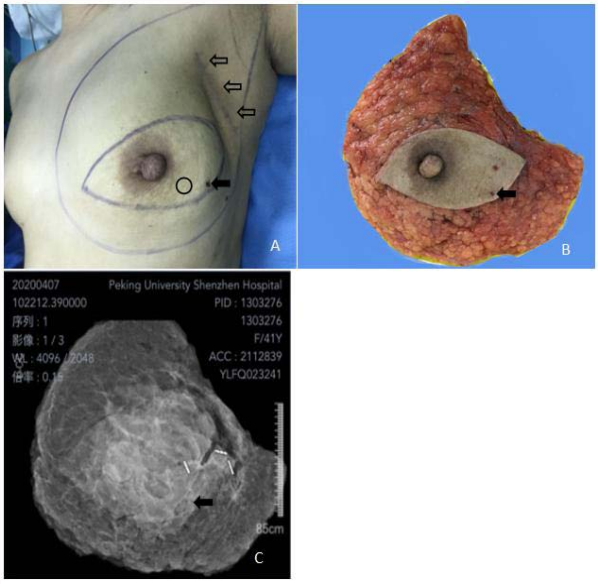


**Figure 3:** The images of left breast after Breast Conserving Surgery (BCS) and vacuum assisted breast lumpectomy (Mammotome).
Panel A: The outlook of patient's left breast. Left BCS and left axillary Sentinel Lymph Node Biopsy (SLNB) skin scar was in the outer-upper quadrant near axilla (black hollow arrows); Mammotome skin scar in the outer-lower quadrant of left breast (black solid arrow); IMLN location was inner to the Mammotomescar (black hollow circle). Panel B: Resected breast after mastectomy. Part of outer-upper quadrant of breast defect due to previous BCS. Mammotome scar (black solid arrow) was included in resected skin flap. Panel C: Resected breast X-ray scan found no residue cancer. Three metal clips marked the margin of the breast after BCS. Mammotome scar was labelled in the skin flap (black solid arrow), but vacuum resected area could be hardly recognized in the X-ray image.

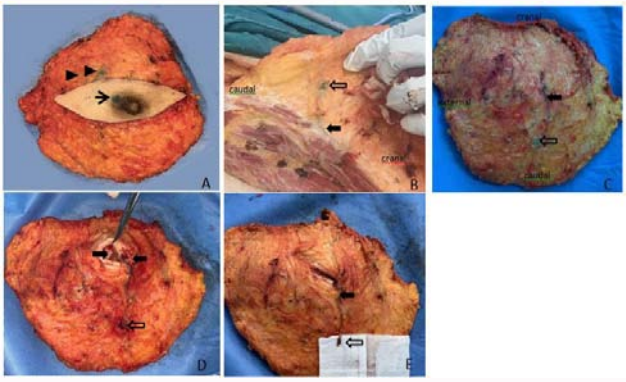

**Figure 4:** IMSLN encountered during mastectomy.
Panel A: Blue dye was injected intracutaneously (slim black arrow) in Nipple Areola Complex (NAC) for detection of axillary sentinel lymph nodes. Two lymphatic drainage tracts were blue dyed on the external upper quadrant (black solid triangles). Panel B: During resecting breast from pectoralis major muscle, blue dye lymphatic duct (black solid arrow) and intramammary sentinel lymph node (black hollow arrow), 2 mm × 1 mm in size, was encountered, which located in 6 o'clock direction inside the breast parenchyma. Panel C: The deeper layer of superficial fascial side of resected breast, lymphatic duct (black solid arrow) drained from NAC. The IMSLN (black hollow arrow) and its drainage were labeled out by blue dye. Panel D: The blue dye labeled lymphatic duct (black solid arrows) was traced to injection side in NAC. Panel E: The blue dye labeled IMSLN was 2 mm × 1 mm in size (black hollow arrow).

patients' medical care and needs. The patient reported here was one of the many who couldn't finish chemotherapy in a timely fashion and also her care in our institution was interrupted due to COVID-19

travel restrictions. COVID-19 pandemic outbreak also has impact greatly on breast patients' treatment decision-making [2]. Patients now have additional anxiety and fear for both cancer and the virus infection. Professional medical care including mental care should be provided based on a multidisciplinary team (MDT, including oncologists, pathologists, radiologists, radiation oncologists, and psychologists) or Molecular Tumor Board (MTB) [3].

We also report cancer recurrence in IMLNs after breast conserving surgery. IMLNs exist within and are completely surrounded by the breast parenchyma. They are very rare lymphatic drainage basin of primary breast cancer, as the majority of the lymphatic drainage of breast cancer drains to the Axillary Lymph Nodes (ALNs) [4]. IMLNs had long been under-evaluated during clinical practice and received less attention. The incidence of IMLNs has been reported in the range of 0.2% to 48% [5,6]. Some IMLNs can be detected by preoperative imaging scan, but majority are found incidentally during or after surgery. In very selected cases, IMLNs can be detected as sentinel lymph nodes by preoperative lymphoscintigraphy [7,8]. Figure 4 showed the IMSLN we incidentally encountered during mastectomy performed on another patient. The IMSLN and its drainage route were labeled after subcutaneous injection of blue dye preoperatively in the nipple areola complex (Figure 4).

Clinical prognosis and therapeutic approaches of IMLNs are not quite clear. In a retrospective analysis, IMLNs metastasis was associated with older age, lymphovascular invasion and high tumor grade [9]. Previous literature suggested IMLNs metastasis might be an independent poor prognostic factor, and the metastasis of IMLNs had a correlation with ALNs involvement [7]. There are no clinical trials answering whether patients with IMLNs metastasis should have Axillary Lymph Node Clearance (ALNC) or not. But in a retrospective review, 14 patients, out of 151 patients with IMLNs, had positive IMLNs but negative axillary SLNs underwent ALNC [10]. None of them had axillary lymph nodes metastasis. The study might suggest ALNC still should depend on axillary SLNs status, and no additional ALNC were needed when patients had positive IMSLNs but negative axillary SLNs. Nevertheless, there is still lack of solid evidence from large volumes of patients.

In our case, IMLN might have existed on her first admission but was missed on MRI. This IMLN could have been the IMSLN encountered during the first surgery, but due to negative preoperative imaging and breast conserving surgery limited to the outer-upper quadrant area, no surgical exploration of this node was performed. On the other hand, the characteristic of cancer in the IMLN was primary resistant to both Anthracycline and Taxane as a result it gradually progressed during chemotherapy. Primary resistance to Anthracycline and Taxane indicate poor prognosis. There are two suboptimal management steps in this patient care, one is the preoperative core needle biopsy showed DCIS instead of TNBC, which led us to do surgery first instead of neoadjuvant chemotherapy first. The second one is when the IMLN was found to be metastasis, due to travel restriction of epidemic of COVID-19 in China, she was kept in a local hospital and underwent mammotome instead of CNB and accordingly *in vivo* test of Vinorelbine and Capecitabine was not performed. As a result, on her second admission, a completion mastectomy was the only option.

In conclusion, care of cancer patients could be largely affected by COVID-19 and there is a need for better communication and facilitation of care of such fragile patient population in between institutions. IMLNs and IMSLNs should be considered both in preoperative imaging and intra-operative sentinel lymph node detection. When IMSLNs are positive but axillary SLNs are negative, ALNC could be avoided, but close axillary imaging follow-up is needed.

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