

# Confused Response to Neoadjuvant Therapy in Breast Cancer

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## ABSTRACT

Neoadjuvant chemotherapy (NAC) brings a series of benefits for patients with mammary neoplasms. While literature shows its effectiveness, the utilization of NAC remains highly variable. Herein, we analyze our clinical experience with the use of NAC in an infiltrating ductal carcinoma with evident axillary lymphadenopathy. In this rare case, response to NAC is seemingly inconsistent in the breast and the axilla for the same tumor.

**Key words:** Axillary macrometastasis, breast cancer, chemotherapy, neoadjuvant treatment, patient management

## INTRODUCTION

Neoadjuvant chemotherapy (NAC) offers a series of advantages in patients with breast cancer, making it an important treatment option to be taken into account by multidisciplinary teams. Although a review of the current scientific evidence suggests its efficacy, the use of NAC remains highly variable.<sup>[1]</sup> Herein, we analyze our clinical experience with the use of NAC in a mammary ductal carcinoma, with the aim of helping multidisciplinary teams to identify patient suitability for neoadjuvant support.

Following radiographic marking for both lesions, NAC was initiated (Adriamycin, cyclophosphamide, and docetaxel), which resulted in complete radiographic response (mammography and ultrasonography, since magnetic resonance imaging was unfeasible). During surgery, the tumor area was excised under harpoon guidance, and then, the clip-marked axillary lymphadenectomy was also removed and analyzed. The pathology study confirmed a complete pathological response (CPR) in both the breast and marked lymph node, but not in the rest of the axilla, where another lymph node developed macrometastasis and tumor-related capsular rupture [Figure 1].

## CASE REPORT

We would like to contribute our experience regarding the findings in a 45-year-old female patient with a cochlear implant and no other relevant conditions who had a breast nodule identified during routine examination. The study showed a 12 mm tumor with evident axillary lymphadenopathy, which was found to be an infiltrating ductal carcinoma 100% estrogen receptor positive, 5% progesterone receptor positive, human epidermal growth factor receptor type 2 (HER2) negative, with Ki67 at 30%, and axillary metastasis.

## DISCUSSION

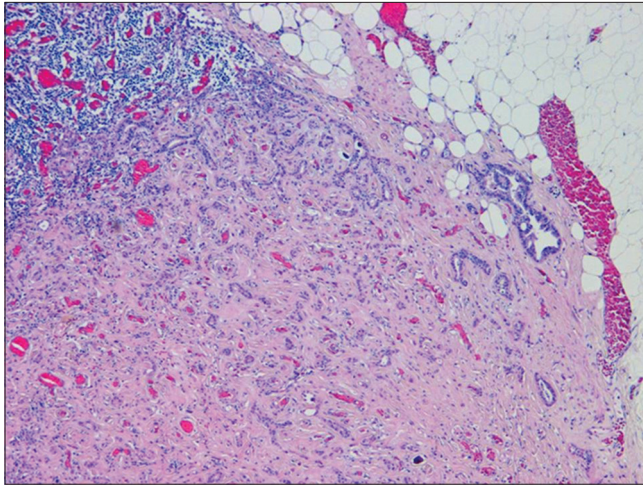
Progression during neoadjuvant therapy is a truly strange clinical finding even for a very experienced surgeon, with a rate of 3% in a meta-analysis of 1928 cases published by Caudle *et al.*, in 2011.<sup>[2]</sup>

In this case, response to NAC is seemingly inconsistent in the breast and the axilla for the same tumor. NAC facilitates surgery, assesses response to therapy, and provides a prognostic factor more effectively than systemic therapy after surgery.<sup>[3-6]</sup> It is consequently very important for the specialized team

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**Figure 1:** Hematoxylin and eosin stained section of tumor bed showing macrometastasis and tumor-related capsular rupture

to take into account the advantages and possible risks when selecting subjects who may gain from NAC.

While extensive agreement exists regard the group of patients most likely to benefit from NAC, its use in clinical practice varies widely. In any case, a number of factors must be allowed for when selecting patients for NAC:

- Patients presenting with inoperable locally advanced breast neoplasm
- Young age
- High tumor volume-to-breast ratio
- All early-stage breast cancer patient, as they could probably benefit from NAC before surgery
- Axillary lymph node-positive disease
- Biological features of primitive cancer (positive HER2, high grade, hormone receptor negative, and triple-negative breast cancer).

The efficacy of NAC is assessed by evaluating the clinical and radiological response during and after therapy and the pathological response after surgery. With nuances, CPR is defined as the complete clearance of the infiltrating component both in the breast and the axilla; hence, it represents a significant predictive factor for survival and disease-free interval.<sup>[7-9]</sup>

CPR primarily depends on molecular phenotype. Good CPR rates are obtained in 31–60% of HER2 subtypes, 34–40% of triple-negative tumors, and <10% of luminal A and B types.<sup>[3,4,7]</sup> Furthermore, in luminal B tumors, CPR also depends on the Ki67 proliferation index and histologic grade; our patient had a high Ki67 at 30%.

Both the sentinel node biopsy and clip-marked node biopsy offer a relevant number of false-negative results for axillary node metastasis after NAC.<sup>[1,10]</sup>

Therefore, in the absence of comparative studies with adequate follow-up to provide true guidelines, potential residual disease in the axilla,<sup>[4,5]</sup> the effect of radiotherapy, and the impact of it all on overall survival make up the big enigma regarding breast cancer today. On the other hand, the fact that overall survival is in itself high for breast cancer raises concerns regarding some “non-inferiority” studies.

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