

CLINICAL VIGNETTE

Response without Chemotherapy in a Patient with HER2-positive Breast Cancer

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Case

A 64-year-old female presented with a self-detected lump in her left breast. She underwent diagnostic mammogram and breast ultrasound which revealed a 1.2 cm mass in the left breast with axillary lymph node involvement. Biopsies confirmed high-grade invasive ductal carcinoma with HER2/neu overexpression, negative hormone receptor status, and lymphovascular invasion. She was recommended to receive neoadjuvant chemotherapy and HER2-directed therapy. However, she was reluctant to start treatment and delayed follow-up care.

Over time, her disease progressed locally, with enlarging breast masses, worsening axillary lymphadenopathy, and extensive skin involvement extending to her ipsilateral shoulder. There was no distant metastatic spread seen on PET/CT imaging, but the cancer was deemed inoperable because of the extensive area of skin involvement.

She explored alternative treatment options including cryotherapy, and was referred for multiple second opinions. She still declined chemotherapy for fear of potential side effects. She eventually agreed to undergo HER2-directed targeted therapy alone, with pertuzumab and trastuzumab. She had a rapid response, and after approximately 6 months, she achieved a complete response. The patient continues the same therapy more than one year later, with only minor side effects, has no evidence of disease.

Discussion

HER2-positive breast cancer represents a distinct subtype characterized by overexpression of the human epidermal growth factor receptor 2 (HER2/neu) protein. HER2/neu is a receptor protein involved in cell growth and division. In HER2-positive breast cancer, the HER2 receptor is overexpressed, leading to uncontrolled cell proliferation. Historically, HER2-positive breast cancer, which accounts for approximately 20% of breast cancer cases, had a poorer prognosis compared to other subtypes. However, the introduction of targeted therapies has transformed the landscape of treatment for this subtype. Over the years, research has led to significant advances in the treatment of HER2-positive breast cancer.

The standard of care for HER2-positive breast cancer involves a multimodal approach, typically including chemotherapy and anti-HER2 targeted therapy. Chemotherapy is administered to

eliminate rapidly dividing cancer cells, while anti-HER2 therapy specifically targets the HER2 receptor, inhibiting its signaling pathway.

One pivotal study that significantly influenced this standard of care was led by Dr. Dennis Slamon and colleagues. This landmark trial demonstrated the effectiveness of trastuzumab (Herceptin), an anti-HER2 monoclonal antibody, when combined with chemotherapy in HER2-positive breast cancer patients.¹ The addition of trastuzumab significantly improved disease-free and overall survival, with a 20% reduction in the risk of death, leading to widespread adoption as a cornerstone of HER2-positive breast cancer treatment.

Neoadjuvant therapy involves administering targeted therapies and chemotherapy before surgical removal of the tumor, with aim to shrink the tumor, increase the chances of breast-conserving surgery, and improve overall outcomes. The NeoSphere trial was a phase II study that evaluated the efficacy and safety of different neoadjuvant treatment regimens in HER2-positive breast cancer patients. It included four treatment arms. The trial demonstrated that docetaxel chemotherapy with pertuzumab and trastuzumab was effective in achieving high rates of pathological complete response (pCR) in the breast and axillary lymph nodes, making it an important regimen for neoadjuvant therapy in HER2-positive breast cancer. In contrast, in that trial, pertuzumab and trastuzumab without chemotherapy eradicated tumors in a proportion of women, but the pathologic complete response rate was approximately 30% lower.²

Chemotherapy remains an integral part of HER2-positive breast cancer treatment. One notable scenario where anti-HER2 therapy alone may be considered is when patients are unable to tolerate chemotherapy due to underlying medical conditions or significant side effects. The aim is to achieve favorable outcomes while minimizing chemotherapy-related toxicity. It is important to note that the use of anti-HER2 directed therapy alone without chemotherapy is not yet considered the standard of care. Observational studies and case series show clinical efficacy of this approach, and it may be appropriate for select patients.

Summary

HER2-positive breast cancer has seen significant advancements in treatment, primarily driven by the introduction of anti-HER2 targeted therapies such as trastuzumab. The current standard of care for HER2-positive breast cancer involves a combination of chemotherapy and anti-HER2 therapy, resulting in improved outcomes and survival rates. However, anti-HER2 directed therapy alone, without chemotherapy, may have a role in select cases, particularly when patients cannot tolerate chemotherapy or decline standard of care therapy.

REFERENCES

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