

Never too old to fight breast cancer

A case report

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Abstract

Rationale: Breast cancer is the most common cancer affecting females worldwide and its lifetime risk increases with age. Human epidermal growth factor receptor gene-2 (HER-2) positive breast cancer represents about 20% of all breast cancers, 1 out of 10 is diagnosed in women over 70 years of age. It tends to be more aggressive and to spread more quickly than other subtypes, but the introduction in clinical practice of new anti-HER-2 agents combined with chemotherapy has significantly improved progression free and overall survival. Elderly patients are frequently undertreated because of concerns about their age, performance status, and comorbidities. Here, we report a case of an octogenarian patient treated with T-DM1 with brilliant results.

Patient concerns: An 87 years old woman affected with HER-2 positive breast cancer presented progression of disease with lymph node and skin metastases after 3 lines of chemoimmunotherapy.

Diagnoses: Breast cancer in elderly patient, lymph node, and skin metastases

Interventions: Chemoimmunotherapy (trastuzumab emtansine).

Outcome: Objective response of the disease and significant clinical benefit.

Lessons: This case clearly suggests that age and comorbidities do not always represent an absolute contraindication to combined treatments.

Abbreviations: HER-2 = human epidermal growth factor receptor gene-2, T-DM1 = trastuzumab emtansine.

Keywords: breast cancer, chemotherapy, immunotherapy, lymph node and skin metastases, old age

Key Points

- HER-2 positive breast cancer represents about 20% of all breast cancers. It tends to be more aggressive and to spread more quickly than other breast cancer subtypes, therefore it is associated with shortened survival.
- Combination of anti-HER-2 agents and chemotherapy currently represents an effective therapeutic strategy for HER-2 positive breast cancer patients.
- The percentage of elderly patients affected with breast cancer is growing as a result of the increasing life expectancy.
- A specific guideline that limits the indication of chemotherapy by age does not exist. Nevertheless elderly patients are frequently undertreated because of their age, performance status, and comorbidities.

1. Introduction

Breast cancer represents the most common cancer affecting females worldwide and the lifetime risk increases with age. Considering the growing life expectancy, the percentage of elderly patients is rising. Amplification of the human epidermal growth factor receptor gene (HER-2) occurs in approximately 20% of all breast cancers, 1 out of 10 is diagnosed in women over 70 years of age.^[1] It correlates with bad prognosis.^[2] In the past few years, the introduction in the clinical practice of regimens containing anti-HER-2 targeted agents (eg, trastuzumab, lapatinib, and pertuzumab), associated with standard chemotherapy, has significantly improved the outcome for these patients.^[3-7] Trastuzumab emtansine (T-DM1) is a new antibody-drug conjugate. It combines the anti-tumoral activity of trastuzumab and the powerful cytotoxic effect of the microtubule-inhibitory agent DM1. It is currently used in HER-2 positive metastatic breast cancer patients who progressed after a treatment with taxane and trastuzumab. It prolongs progression free and overall survival either in second and in later lines of treatment.^[8-10] Here, we report a case of an octogenarian patient affected with HER-2 positive metastatic breast cancer who was treated with T-DM1 after several lines of chemoimmunotherapy and achieved brilliant results.

2. Case report

The patient is an Italian 87 years old woman, diagnosed with HER-2 positive metastatic breast cancer when she was 84 years. She has no positive family history for breast/ovarian cancer. She shows, as comorbidities, hypertensive cardiomyopathy with a single episode of atrial fibrillo flutter in April 2016, hypercholesterolemia, and hypertriglyceridemia. She had no major surgeries in the past with the only exception of hysterectomy and left oophorectomy for fibromas when she was 50 years. The patient

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came to our attention in May 2014 complaining left breast swelling, pain, and burning sense. Physical examination showed the typical appearance of inflammatory cancer: left breast was edematous with skin redness and warmth to the touch. A bilateral mammography and an ultrasound confirmed an increased skin thickness and identified in the upper external quadrant a single hypoechoic lesion of 17 mm, with irregular margins and polymorphic calcifications. The same ultrasound showed concomitant multiple left intramammary lymph nodes while a bone scan reported 2 metastases in D9 and the left scapula. Subsequent breast needle biopsy was positive for invasive carcinoma, luminal B-like subtype (estrogen receptor 80%, progesteron receptor 0%, Ki-67 40%, HER-2 3+). The patient was initially treated with IV trastuzumab (8 mg/kg as first dose, then 6 mg/kg as subsequent doses) day 1 and vinorelbine (25 mg/mq) day 1 and 8 every 3 weeks for 15 cycles with partial response of the disease. Then she was treated for an additional year with 3-weekly subcutaneous trastuzumab (600 mg) in combination with oral letrozole. Later, due to local progression of disease with evidence of new left breast lesions and ipsilateral latero-cervical, axillary and supraclavicular pathologic lymph nodes, the patient was treated with weekly IV trastuzumab (2 mg/Kg) and paclitaxel (80 mg/mq) 3 weeks on and 1 week off for 6 cycles. Initially the disease was stable, then a further progression was evident and the patient was treated with 3-weekly IV trastuzumab and oral capecitabine. At the end of the third cycle, a significant local progression of the disease was observed: a violet skin rash developed in the left upper side of the chest wall with extension to the neck that appeared edematous, left side of the face and ear. Furthermore multiple left cervical and supraclavicular lymph nodes increased in size (Fig. 1). The primary tumor in the left breast was difficult to palpate due to the significant local inflammation and edema and the poor patient's compliance because of the pain. As a consequence of the cancer evolution, patient's general conditions had worsened: left upper arm mobility was limited because of the local condition and an intense pain in the left breast and neck. Taking into considerations all these elements together with the patient's age, comorbidities, and previous treatments administered, we decided to proceed with a further line of chemoimmunotherapy. We started T-DM1 at a just slightly reduced dosage of 3 mg/kg despite her age. The treatment was well tolerated with the exception of mild (grade 1) conjunctivitis, stomatitis, and constipation. The echocardiogram performed after the third cycle detected no significant left ventricular ejection fraction

reduction. The treatment was never delayed due to hematologic toxicity. Since the first cycle the clinical benefit was evident: the patient reported progressive improvement of left upper arm mobility and reduced pain in the breast and neck. At the physical examination the inflammatory signs gradually faded: the violet skin rash was less intense, warm, and extended, with a significant reduction of the swelling of the neck and of the dimension of the palpable lymph nodes (Fig. 2). So far, the patient has received 10 cycles of T-DM1 reaching a progression-free survival of 7 months, she is doing well, still in treatment, and happy to continue.

3. Discussion

Amplification/overexpression of HER-2 gene is present in about 20% of all breast cancers and is considered a poor prognostic factor. It usually correlates with a more aggressive disease and frequent dissemination of metastases in sites extremely difficult to reach by chemotherapy, such as brain and skin, that are reported as "sanctuary-like sites." Overall survival of HER-2 positive breast cancer has been usually shorter in comparison with other histotypes until a few decades ago when new anti-HER-2 targeted agents were introduced in the clinical practice in combination with standard chemotherapies.^[3-7] These regimens have dramatically changed the outcome of HER-2 positive breast cancer patients, both in early and metastatic setting, prolonging the disease free and overall survival. T-DM1 is a new HER-2 targeted antibody-drug conjugate including DM1, an antimicrotubule maytansine derivative conjugated to trastuzumab via a stable together linker. In both EMILIA and THERESA trials, where T-DM1 was respectively compared to lapatinib plus capecitabine and to physician's choice treatment, it was associated to a significant increase of progression free and overall survival.^[8,9] These results confirmed this new agent as the mainstay of treatment in patients progressed after a taxane and trastuzumab regimen.^[10] Our case of an elderly patient with HER-2 positive metastatic breast cancer is having a brilliant response to a fourth line of treatment with T-DM1 without serious side effects. This result is quite unexpected for 3 major reasons. The first reason is the patient's age: no specific guideline clearly reports a limit to the indication of chemoimmunotherapy for elderly patients, but physicians usually tend to undertreat these patients fearing serious side effects. Our patient was already 87 years old at the beginning of the treatment with T-DM1.



Figure 1. Clinical appearance before T-DM1.



Figure 2. Clinical appearance after 5 cycles of T-DM1.

Despite age and comorbidities, she is still very well tolerating the therapy at a just slightly reduced dose of 3 mg/kg. After 10 cycles she is happy to continue because of the evident clinical improvement. The second reason is the timing: the response was immediate. Since the first cycle the patient has reported clinical benefit, less pain, and an improved mobility of her left upper arm. The third is the entity of the response: the skin is a frequent site of metastases in HER-2 positive breast cancer but it hardly responds to the anti-HER-2 targeted therapies. It has been hypothesized that the skin acts as a “sanctuary-like site,” where a change in the tumor cutaneous microenvironment leads to a mechanism of resistance to the treatments.^[11]

4. Conclusion

We report the case of an octogenarian HER-2 positive metastatic breast cancer patient who progressed to the skin and loco regional lymph nodes after 3 different lines of chemioimmunotherapy. We decided to treat her with T-DM1 at a just slightly reduced dose considering her age. The response has been brilliant and immediate and the tolerance excellent. This case clearly suggests that age and comorbidities do not always represent an absolute contraindication to more active treatments.

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