EJGO European Journal of Gynaecological Oncology

Dermatomyositis revealing a 18-year breast cancer recurrence

F. Lai-Tiong

Medical Oncology Unit Institut de Cancérologie du Gard; Rue du Professeur Henri Pujol, Nîmes (France)

Summary

Breast cancer is a well-known heterogeneous tumor, that includes inter- and intra-tumoral heterogeneity. These modifications in the phenotype can lead to modify the therapeutic strategy. The author reports the original case of a 66-year-old Caucasian woman, diagnosed with a breast cancer 18 years before. Initially it was a 32-mm, grade 2, ductal infiltrating breast carcinoma, negative for hormone receptors. The patient was treated with conservative surgery, and axillary dissection (eight positive nodes out of 21). Adjuvant chemotherapy and radiotherapy were delivered. Ten years later, the patient was diagnosed with pulmonary relapse. Biopsies were negative for hormone receptors and also for human epidermal growth factor 2 (Her2). The patient received chemotherapy. One year later, pleura effusion appeared. Biopsies of the pleura confirmed the metastasis of breast cancer, hormone receptors negative, but positive for Her2. She was then diagnosed with a paraneoplastic dermatomyositis. Eight lines of chemotherapy were given and currently the patient is continuing trastuzumab. That case illustrates the story of a very long-surviving breast cancer and its dedifferentiation. It underlies the necessity to realize new biopsies when the tumor relapses.

Key words: Dermatomyositis; Her2 positive; Breast cancer; Paraneoplastic syndrome; Dedifferentiation; Cancer recurrence.

Introduction

Breast cancer is the most common malignant disease in the world among women. Little is known about changes in the molecular profile of the metastasis and impact on clinical outcomes. Genetic events can occur at various stages of carcinogenesis and can result in phenotypic changes. In breast cancer these changes can occur in either in site at the primary invasive site or at distant metastatic site.

The author reports the case of dedifferentiation-like progression of breast cancer showing transition from negative estrogen and progesterone receptors to human epidermal growth factor 2 (Her2) positive carcinoma.

Case Report

A 66-year-old Caucasian woman was referred to us for a Her2 positive breast cancer. Nineteen years prior, the patient had been treated for a 32-mm, grade 2, ductal breast carcinoma, negative for hormone receptors. A Ki 67 labelling index at 30% was observed. The patient underwent conservative surgery and axillary lymph node dissection. Eight nodes were metastatic out of the 21 removed. She received adjuvant chemotherapy and radiotherapy.

Ten years later, pulmonary and pericardic recurrence occurred. Biopsy cores of lung and pericardium showed the presence of adenocarcinoma, negative estrogen and progesterone receptors, negative Her2 and negative TTF1, in favor of breast cancer metastasis. The patient received chemotherapy with carboplatin plus paclitaxel for a total of six courses.

One year after completion of chemotherapy, metastatic pleural effusion appeared. Pleura biopsies revealed metastasis of breast adenocarcinoma, negative for estrogen and progesterone receptors, but this time positive for Her2. The patient received six cycles of docetaxel plus trastuzumab, followed by trastuzumab maintenance.

At disease progression, she was treated with capecitabine plus lapatinib, vinorelbine plus trastuzumab, and lapatinib plus trastuzumab.

Eight years after the first recurrence, the patient presented with hand-band erythema and erythematous scaly lesions of elbows, and periungueal hyperkeratosis. She was hospitalized and the diagnosis of dermatomyositis was made. However, corticotherapy and immunoglobulins were ineffective. In parallel, a positron emission tomography (PET) for her breast cancer was performed, showing lungs, pleura, and para-aortic and jugular hypermetabolism. Ca 15-3 levels were high at 104 ng/ml. It was decided in multidisciplinary meeting to administer chemotherapy: docetaxel plus pertuzumab plus trastuzumab. After three cycles, dermatomyositis totally disappeared, and the patient was responding with chemotherapy. After six cycles of chemotherapy, disease progression was noted, but the dermatomyositis was always under control with immunoglobulin perfusions. Trastuzumab-emtansine was administered, but after three cycles, the patient was hospitalized for a pushed-dermatomyositis. Progression disease was confirmed by PET. Novel line of chemotherapy was decided. After six cycles of docetaxel plus trastuzumab, the disease was stable and the patient is continuing with trastuzumab.

Discussion

Breast cancer is a well-known heterogeneous tumor that includes inter- and intra-tumoral differences [1]. Intrinsic subtypes eventually change to worse prognosis but at times patients have a chance to improve response to the treatment and survival with additional treatment by acquiring estrogen and progesterone and Her2 status [2].

Perou *et al.* proposed intrinsic subtypes using molecular

Revised manuscript accepted for publication May 10, 2016

gene expression but many other studies had supported heterogeneous tumor phenotypes of breast cancer. Intrinsic subtypes are biologically conserved distinct phenotype, because some genes are not affected by tumor progression and chemotherapy effects [3].

The method used to determine the status of hormone receptors and Her2 is important also. PAM50 is a 50-gene expression-based predictor that classifies breast cancers into four intrinsic subtypes of prognostic significance: luminal A, luminal B, Her 2-enriched, or basal-like. The PAM50 assay has been shown to be more precise concerning prognostic information compared to immunohistochemical method [4, 5].

The clinical impact of the biological heterogeneity within Her2-positive breast cancer is not fully understood. Hormone receptors and Her2 are important factors in classification of the subtypes, which are essential in the choice of therapy in breast cancer management. There has been earlier reports of instability of hormonal and Her2 status during progression tumor, especially between primary tumor and their metastasis [6, 7].

The present case is original because it reports a dedifferentiation breast cancer many times and it includes a long-surviving metastatic breast cancer story. The first cancer was positive for hormone receptors, then switched into triple negative, and finally into Her2 positive breast cancer. There is no earlier data showing in changes in the intrinsic subtypes during progressing of the tumor in the same patient.

Conclusions

The author presented an unusual case of dedifferentiation of breast carcinoma, showing transition from Her2 negative to Her2 positive, with negative hormone receptors. Some studies have argued that intrinsic subtypes in metastatic tumors is important for better treatments.

References

[1] Rosner B., Glynn R.J., Tamimi R.M., Chen W.Y., Colditz G.A., Willett W.C., Hankinson S.E.: "Breast cancer risk prediction with heterogeneous risk profiles according to breast cancer tumor markers". *Am. J. Epidemiol.*, 2013, *178*, 296.

[2] Delpech Y., Wu Y., Hess K.R., Hsu L., Ayers M., Natowicz R., *et al.*: "KI67 expression in the primary tumor predicts for clinical benefit and time to progression on first-line endocrine therapy in estrogen receptor-positive metastatic breast cancer". *Breast Cancer Res. Treat.*, 2012, *135*, 619.

[3] Perou C.M., Sørlie T., Eisen M.B., van de Rijn M., Jeffrey S.S., Rees C.A., et al.: "Molecular portraits of human breast tumours". *Nature*, 2000, *406*, 747.

[4] Bastien R.R., Rodríguez-Lescure Á., Ebbert M.T., Prat A., Munárriz B., Rowe L., *et al.*: "PAM50 breast cancer subtyping by RT-qPCR and concordance with standard clinical molecular markers". *BMC Med. Genomics*, 2012, *5*, 44.

[5] Nielsen T.O., Parker J.S., Leung S., Voduc D., Ebbert M., Vickery T., *et al.*: "A comparison of PAM50 intrinsic subtyping with immunohistochemistry and clinical prognostic factors in tamoxifen-treated estrogen receptor-positive breast cancer". *Clin. Cancer Res.*, 2010, *16*, 5222.

[6] Bogina G., Bortesi L., Marconi M., Venturini M., Lunardi G., Coati F., *et al.*: "Comparison of hormonal receptor and HER-2 status between breast primary tumours and relapsing tumours: clinical implications of progesterone receptor loss". *Virchows Arch.*, 2011, *459*, 1.

[7] Nishimura R., Osako T., Okumura Y., Tashima R., Toyozumi Y., Arima N.: "Changes in the ER, PgR, HER2, p53 and Ki-67 biological markers between primary and recurrent breast cancer: discordance rates and prognosis". *World J. Surg. Oncol.*, 2011, *9*, 131.

Corresponding Author:
F. LAI-TIONG, M.D.
Medical Oncology Unit
Institut de Cancérologie du Gard
Rue du Professeur Henri Pujol
30900 Nîmes (France)
e-mail: florencelt@hotmail.fr