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Case Report

Late relapse in hormone receptor (+) HER2 (-) early breast cancer: Case report

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Abstract

Background: Hormone-receptor (HR) positive breast cancers represent the majority of all breast cancers (BC). Adjuvant endocrine therapy is effective for nearly all women with ER+ and/or PgR+ tumors. Tamoxifen taken for five years has been the standard adjuvant endocrine treatment. However, despite receiving this treatment, >50% ER+ patients relapse and died from breast cancer 5–10 years after diagnosis.
Case: 50-year-old female with distant relapse BC. November 2008, radical mastectomy of the right breast. Invasive ductal carcinoma grade III T2N1M0 (stage IIb) ER+ (90%), PgR+ (90%), HER2-. Chemotherapy, radiotherapy, and Tamoxifen 2009-2014. Disease-free survival (DFS) : 8 year. January 2017, presented with cough. Chest x-ray: nodule in left lung, transthoracal biopsy: metastatic carcinoma from the breast, ER+ (50%), PgR-, HER2-.
Discussion: Identification of subpopulations likely to benefit from extended endocrine therapy is crucial. For high-risk ER+ patients, ten years endocrine therapy is an option. Evaluation of adverse event, long-term toxicity and risk of recurrence is vital. Discordant hormonal status between primary and metastatic site tumor has been reported 6-40%. Decision to change treatment based on this finding is still limited.

Keywords: *late relapse, early breast cancer, hormone receptor positive.*

Abstrak

Latar Belakang Kanker payudara reseptor hormon positif merupakan bagian terbesar kanker payudara di seluruh dunia (60% -75% ER +, 65% PgR +). Terapi endokrin ajuvan sangat efektif dan sesuai untuk hampir semua wanita dengan tumor ER + dan / atau PgR +. Selama beberapa dekade, tamoxifen yang dikonsumsi selama 5 tahun adalah pengobatan endokrin adjuvan standar, tetapi lebih dari separuh pasien dengan kanker payudara ER + akan kambuh dan meninggal akibat kanker payudara pada 5-10 tahun setelah diagnosis meskipun sudah diberikan terapi endokrin selama 5 tahun.
Kasus: Dosen wanita berusia 50 tahun dengan kanker payudara kambuh lambat. November 2008, dilakukan mastektomi radikal pada payudara kanan, hasil patologi anatomi : karsinoma duktal invasif grade III T2N1M0 (stadium IIb) ER + (90%), PgR + (90%), HER2-, kemudian kemoterapi (Docetaxel + Cyclophosphamide) dilanjutkan radioterapi dan diberikan Tamoxifen (2009-2014). Kesintasan hidup bebas penyakit : 8 tahun 1 bulan. Pada Januari 2017, pasien batuk. Rontgen dada menemukan nodul pada paru kiri dengan efusi pleura minimal, hasil biopsi transthoracal : metastasis karsinoma dari payudara, ER + (50%), PgR-, HER2-.
Diskusi: Identifikasi subpopulasi yang cenderung mendapat manfaat dari terapi endokrin yang diperpanjang dan yang tidak mendapat manfaat adalah penting. Durasi pemberian terapi endokrin penting untuk pasien ER+ dengan risiko tinggi. Pemberian terapi selama 10 tahun saat ini menjadi salah satu pilihan. Sangat penting mempertimbangkan toksisitas jangka panjang dan risiko tingkat kekambuhan. Pada pasien kanker payudara stadium awal reseptor hormon positif premenopause, pemberian terapi supresi ovarium dan exemestane mengurangi risiko kekambuhan dibanding terapi supresi ovarium dan tamoxifen. Dibandingkan dengan pemberian tamoxifen saja, terapi supresi ovarium terkait dengan peningkatan gejala menopause, disfungsi seksual, dan penurunan kualitas hidup. Biopsi pada tempat metastasis yang dapat diakses direkomendasikan untuk dilakukan. Hasil biopsi bisa ada ketidaksesuaian status hormon antara tumor primer dan metastasis dilaporkan 6-40% namun bukti penelitian masih kurang mendukung apakah mengubah terapi antikanker berdasarkan perubahan status reseptor mempengaruhi hasil klinis.

Kata kunci: *kambuh lambat, kanker payudara dini, reseptor hormon positif.*

Background

Global Cancer Report (GLOBOCAN) has reported the increasing number of cancer patient, particularly for breast cancer. In 2012, incidence of breast cancer has reached for 48.998 annually, with mortality cases of 19.750 annually. Moreover, in 2020, the incidence of breast cancer is projected to increase in a number of 58.799 of cases annually, with mortality of 23.836 of cases annually.[1]

Hormone-receptor positive breast cancer is a major type of breast cancer (60 – 75% is estrogen positive, and 65% is progesterone positive). Endocrine therapy is an effective adjuvant treatment for most breast cancer with both estrogen and progesterone positive. For latest decades, tamoxifen therapy for five years is still being drug of choice for hormone positive breast cancer.[2]

This case report will discuss about late relapse which is frequent among hormone-receptor positive breast cancer, which the late relapse is defined as recurring event after five years from initial treatment.[3] This case will also review about the effectivity of extending tamoxifen for ten years, clinical marker of late relapse, and the concordance status of hormone receptor between primary tumor and metastatic lesion.

Case Illustration

A 50-years old lecturer woman was known to have a distant metastasis of breast cancer. In November 2008 (42 years old), the patient complained with right breast lump which later underwent radical mastectomy on her right breast. Pathological anatomy examination concluded ductal infiltrative carcinoma grade III with estrogen receptor positive (ER 90%), progesterone positive (PR 90%), and Her-2 negative. The stage was concluded as stage IIb T2N1M0 of breast cancer. The patient then received systemic chemotherapy with docetaxel and cyclophosphamide, followed by radiotherapy. After chemo-radiotherapy, she had received hormone therapy with tamoxifen for five years from 2009 and 2014. During hormonal therapy, she underwent surveillance with relatively good compliance. In addition, she also had good quality of life without any significant adverse events of a five years tamoxifen.

In January 2017, the patient complained dry cough which did not improve but the activity level was still unrestricted. Thoracic X-Ray was evident left pulmonary nodule with minimal pleural effusion and later confirmed with PET scan which was shown a hypometabolic multiple nodules in left lung and left pleural effusion with a solid component and mild metabolic activity. A trans-thoracic fine biopsy through the pulmonary nodule concluded neoplastic cells of breast cancer. Immunohistochemistry examination showed ER positive (50%), PR negative, and Her-2 negative (figure 1, 2, and 3). The patient was still in a good performance status (ECOG 0) and subsequently received second line treatment with eribulin.

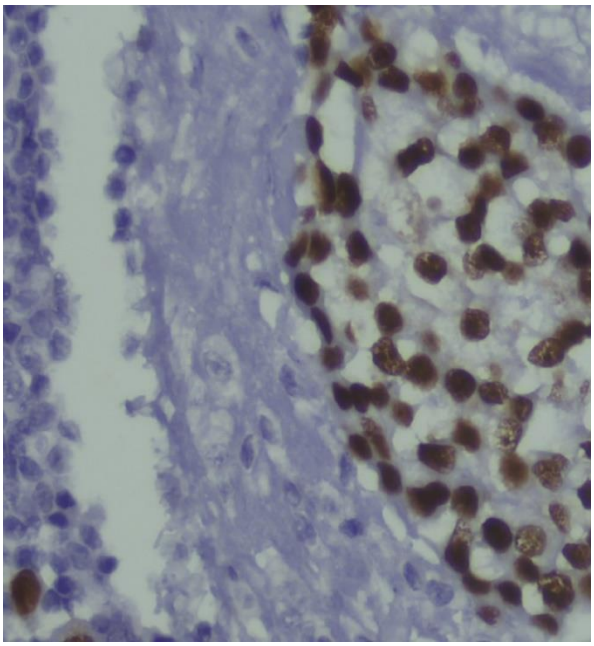

Figure 1. Immunohistochemical examination showing 50% ER positive tumor cells

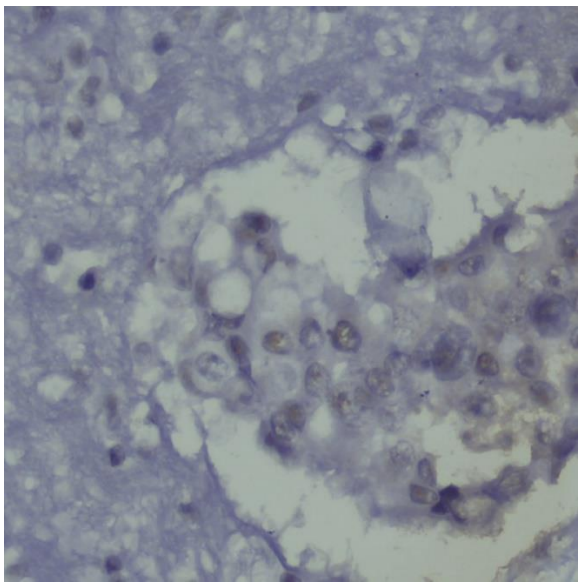

Figure 2. Immunohistochemical examination showing PR negative tumor cells

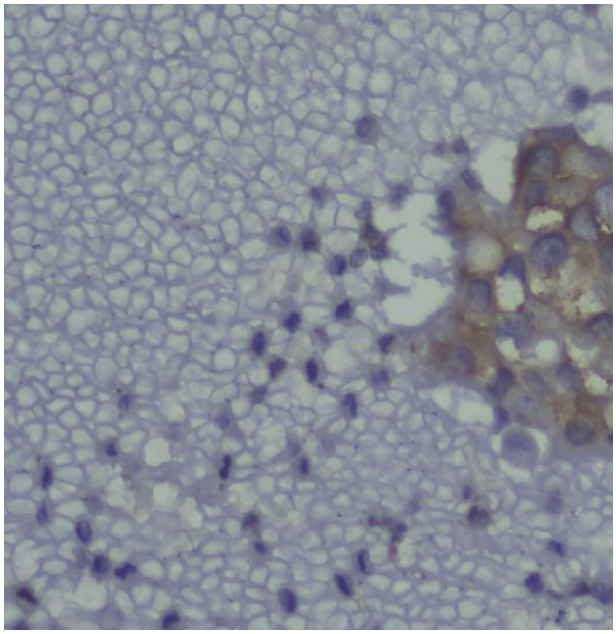

Figure 3. Immunohistochemical examination showing Her-2 negative tumor cells

Discussion

Breast cancer is heterogeneous disease with varying pattern of recurrence. It also has been evidenced as a spectrum of disease with several subtypes such as luminal, Her2, and basal.[4] The onset of late recurrence is also varies in each subtype. For instance, ER negative/Her2 positive breast cancer is known for a three times higher risk of relapse for initial 5-7 years of disease compared with ER positive.[5] Nevertheless, the latter type tends to have higher risk of relapse after 5-7 years among all age groups compared with ER negative.[6]

According to the presented case supplemented with other study results showed that the duration of endocrine treatment is an important aspect for ER positive breast cancer prognosis due to higher risk of late recurrence. The ATLAS study compared a group of ER positive breast cancer with five years and ten years of tamoxifen, later evidenced a significant reduction in mortality with superior reduction in ten years of tamoxifen. A ten years duration of tamoxifen significantly decreased relapse case compared with five years arm (617 in 3428 subjects vs 711 in 3418 subjects, p = 0002), cancer-specific mortality reduction (331 vs 397 of dead cases, p = 0,01), and reduction of overall mortality (639 vs 722 of dead cases, p = 0,01). However, the adverse events were known to increase in ten years tamoxifen arm, particularly among postmenopausal women. The ATLAS study showed that ten years tamoxifen decreased half of overall mortality for 10-14 years after the diagnosis.[7]

Ovarian Function Suppression (OFS) treatment has a significant role in reducing recurrence rate among early hormone receptor positive breast cancer in premenopausal women. According to TEXT and SOFT study, it has been evidenced that adjuvant endocrine treatment in form of OFS and exemestane significantly reduced recurrence rate compared with OFS and tamoxifen. However, OFS plus tamoxifen insignificantly reduced recurrence rate compared with tamoxifen only. Compared with tamoxifen only, the combination of OFS and tamoxifen increased the menopausal symptoms substantially, sexual dysfunction, and decreased the quality of life.[8,9]

It is essential to know precisely the risk stratification of breast cancer recurrence and predict survival of hormone-receptor positive breast cancer. According to St Gallen's International Conference of Breast Cancer in 2009, nodal status, tumor size, grade and histological type, peritumoral vascular invasion, HER2 and hormone receptor status are categorized as the most useful clinical markers for management of breast cancer.[10] Registry data reported by Danish Breast Cancer Cooperative Group (DBCG) showed similar mortality as general population among 3,197 of hormone receptor positive and early stage breast cancer patients with aged of 60 years or older, small tumor size (≤10 mm), no lymph node involvement, and favorable grade of ductal or lobular carcinoma.[11]

From the presented case, it has been known the concordance expression of hormone receptor between the primary site and metastatic lesion, which were ER positive and Her-2 negative. There are many potential benefits to perform biopsy for metastatic lesion, such as concluding the diagnosis, excluding the possibility of any other primary tumor, and confirming the concordance expression of hormone receptor status between primary and metastatic lesion. Indeed, it has been reported discordance rate between primary and metastatic lesion in 6-40% of cases.[12] Moreover, the discordance rate of hormone receptor expressions for ER, PR, and Her-2 are 20%, 33%, and 8% respectively.[13] The BRITS and DESTINY study showed the result of biopsy causes management changes in 14.2% of cases but the clinical effect was still unknown.[14] Exposure of previous treatment can change the molecular profile of metastatic tumor cells, including in breast cancer, and may induce drug resistance which makes the subsequent treatment challenging.[15]

Conclusion

It is important to identify subgroup of early-stage, hormone-receptor positive breast cancer patients who might benefit from extended endocrine therapy to prevent the late recurrence. Therefore, clinical markers such as age, nodal status, tumor size, and histopathology could be utilized to stratify the risk. Extending the endocrine therapy for ten years to ER+ with high risk breast cancer patients may reduce the risk of late recurrence. Effectiveness of ovarian function suppression (OFS) treatment is potentiated by combination with exemestane in premenopausal breast cancer patients. Weighing the side effects and long-term toxicity against the recurrence risk is essential. Re-biopsy of recurrent metastatic lesion in breast cancer is beneficial albeit lacking evidence to change treatment when found any discordant expression of hormone receptor which actually aims to improve patient outcomes.

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Conflict of Interest

The authors have no conflict of interest to declare.

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