A case of HER2-positive male breast cancer with lung metastases showing a good response to trastuzumab and paclitaxel treatment

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Abstract We present a case of advanced HER2-positive male breast cancer, which showed a good response to a combined treatment of trastuzumab and paclitaxel. A 78-year-old man was diagnosed with invasive ductal carcinoma (T4d N3 M1, stage IV). He had advanced breast cancer consisting of multiple tumors with skin involvement and redness over the entire left chest region. A computed tomography (CT) scan of the chest revealed a metastatic tumor in the left lung. Histologically, both the primary breast cancer and the metastatic lung tumor were identified as invasive ductal carcinoma that was estrogen receptor-negative (ER)(−) and progesterone receptor-negative (PgR)(−), with a HER2 score of 3+ (IHC). The patient received a combination chemotherapy using trastuzumab and paclitaxel. Two months later, a follow-up chest CT scan showed that the left lung tumor had disappeared, suggesting a good response to trastuzumab and paclitaxel. During trastuzumab treatment, no severe adverse events above grade 3 were observed. This is the first reported case of advanced HER2-positive male breast cancer in which a good response to trastuzumab and paclitaxel was demonstrated at both primary breast cancer and metastatic sites.

Keywords Male breast cancer · Trastuzumab · HER2 · Heterogeneity · Asymmetric cell division

Introduction

Breast cancer is a comparatively rare disease in men, representing less than 1% of all cases of breast cancer [1, 2].

Several studies have reported that the percentage of breast cancers with hormonal receptor (ER, PgR) positivity is higher for males than for females [1, 3]. A few studies involving limited numbers of male breast cancer patients have shown that HER2 protein was overexpressed in 15–45% of male breast cancer patients, as determined immunohistochemically [1, 2, 4–6]. Trastuzumab is used for the initial treatment for women with HER2-positive advanced and recurrent breast cancers [7–9].

Case report

We present a rare case of advanced HER2-positive male breast cancer that showed a good response to a combination therapy using trastuzumab and paclitaxel.

A 78-year-old man sought care at a hospital in November 2005 after noticing redness on his left breast. His clinical findings raised suspicion of inflammatory male breast cancer. Core needle biopsy of the left breast and the skin of the chest were performed, along with whole-body radiologic examinations. A chest CT scan revealed a tumor in the left lung. The patient underwent percutaneous CT-guided core biopsy of this tumor. Subsequently, he was diagnosed as having inflammatory male breast cancer along with lung metastasis.

The patient was referred to the Aichi Cancer Center Hospital for chemotherapy in January 2006. He presented with widespread disease of the breast that had progressed rapidly over the previous 2 months. The physical...
examination showed multiple tumors with skin involvement (redness) over the entire left breast and chest wall region (Fig. 1a). The ipsilateral axillary and cervical lymph nodes were slightly enlarged. The patient had no history of injury or infection, and neither his past medical history or his family history revealed evidence of malignancy.

On his first visit, blood tests revealed high levels of a tumor marker, carcinoembryonic antigen (CEA; 192 ng/ml) (Fig. 3). A subsequent chest CT scan revealed a solitary tumor (25 × 25 mm in diameter) in the left lung (Fig. 2a). We confirmed the histological diagnosis of breast cancer using the specimens that had been obtained by core needle biopsy at the previous hospital. Pathological findings from the left breast revealed an invasive ductal carcinoma that was both estrogen receptor-negative (ER)(-) and progesterone receptor-negative (PgR)(-), with a HER2 score of 3+(IHC).

Biopsy specimens from the left chest skin and lung tumor showed the same pathological characteristics: metastatic adenocarcinoma, ER(-), PgR(-), and HER(3+). These findings confirmed the diagnosis as inflammatory male breast cancer with lung metastasis (T4d N3 M1, stage IV).

The patient was immediately administered a combined chemotherapy of trastuzumab (4 mg/kg initially followed by 2 mg/kg, weekly) and paclitaxel (80 mg/m², 3 weeks on, 1 week off) (Fig. 3). Two months after the start of chemotherapy, the patient was injured in a traffic accident. Because of the possibility of wound infection, we stopped paclitaxel treatment, but continued the treatment with only trastuzumab every week.

After about 2 months, a follow-up chest CT scan was obtained (Fig. 2b). It showed that the primary breast cancer had nearly disappeared, the ipsilateral axillary and cervical lymph nodes were clear, and the metastatic lung tumor had completely disappeared. However, because of the status of his chest skin, his scar (Fig. 1b), and the elevated CEA levels (25.1 ng/ml) (Fig. 3), we assumed this to be a partial clinical response to paclitaxel and trastuzumab and continued with only trastuzumab on a weekly basis (Fig. 3).

No severe adverse events above grade 3 were noted [leucopenia grade 0, neutropenia grade 0, anemia grade 2, elevation of liver enzymes (GOT and GPT) grade 1, neuropathy grade 0, decrease of LVEF grade 0], and the patient was able to maintain a high quality of life between the weekly trastuzumab treatments. The appearance of the skin on his left chest continued to improve, and there were no signs of breast masses (Fig. 1c). These findings suggested that the combination therapy of trastuzumab and paclitaxel on a weekly basis was useful in treating HER2 (3+) male breast cancer.

About 5 months later, the patient’s CEA level had increased to 53 ng/ml (Fig. 3). A chest CT scan showed reappearance of the tumor (15 × 15 mm in diameter) in his left lung (Fig. 2c). We resumed treatment with paclitaxel (80 mg/m², 3 weeks on, 1 week off) and with trastuzumab, every week (Fig. 3). About 8 months later, the appearance of his chest skin was almost normal (Fig. 1d).

About 11 months later, the CEA level had increased to 251.7 ng/ml (Fig. 3). However, the chest skin appeared to be normal. Upper and lower gastrointestinal tract testing revealed no signs of malignancy, and bone scintigraphy showed no evidence of bone metastases. However, a chest CT scan showed that the size of lung metastasis was increased (Fig. 2d). We assumed this to be indicative of progressive disease. These data highlight the discrepancy between the responses of the primary lesion (breast) and that of the metastatic lesion (lung metastases).

We modified the chemotherapy regimen to include vinorelbine (2 weeks on, 1 week off) along with trastuzumab, weekly (Fig. 3). About 14 months later, the CEA
levels increased to 903.9 ng/ml (Fig. 3). Chest CT scan suggested and increase in the size of the lung metastasis (Fig. 2e). Despite this evidence of continued disease progression, the chest wall status remained normal. We then changed to an AC (60/600) regimen (Fig. 3). The lung metastasis rapidly worsened, and about 20 months later, the patient died because of disease progression, although his skin lesion maintained normal status throughout.

Discussion

Male breast cancer is comparatively rare [1, 2] and is commonly found in elderly patients [4]. It has been reported that the percentage of hormonal receptor (ER, PgR) positivity in male breast cancer patients is higher than that in female breast cancer patients [1, 3]. HER2 overexpression is a predictive marker of tumor aggressiveness and responsiveness to trastuzumab for breast cancer [10, 11].
Trastuzumab is a human monoclonal antibody that was developed to target the HER2 receptor [7–9]. It is an initial treatment for metastatic and advanced female breast cancer patients who are HER2-positive [7, 8, 12]. To date, there is little evidence to confirm whether HER2-positive male breast cancer [6, 13] responds to trastuzumab in the same way as HER2-positive female breast cancer. This case report therefore provides useful knowledge that may be applicable to the treatment of other patients with HER2-positive male breast cancer.

In this case, the patient was a 78-year-old man who presented a widespread disease of the breast that had progressed rapidly for 1 month. Core needle biopsy demonstrated that both primary breast cancer and metastatic sites (lung) were ER(−) and PgR(−), with a HER2 score of 3+. Previously published papers had indicated that trastuzumab improved survival and quality of life when given in combination with taxanes as first-line therapy in female patients with metastatic breast cancer [7–9]. Applying a similar approach, the patient in this case was treated with combination therapy consisting of weekly trastuzumab (initially 4 mg/kg followed by 2 mg/kg every week) and weekly paclitaxel (80 mg/m²). Two months later, the breast tumor had subsided. Ipsilateral axillary and cervical lymph nodes were completely clear. The chest CT scan showed that the left lung metastasis had also disappeared. The patient continued to improve, and findings for the left breast and skin were both normal. These clinical observations carry important implications regarding the heterogeneity of breast cancer.

Of note, a discrepancy was observed in the effectiveness of the trastuzumab-based chemotherapy regimen against the primary breast cancer versus the metastatic site (lung metastasis). About 5 months later, the chest CT scan demonstrated reappearance of the tumor in the patient’s left lung. However, his primary breast cancer site continued to improve, and findings for the left breast and skin were both normal. These clinical observations carry important implications regarding the heterogeneity of breast cancer.

It has been reported that both gene expression profiles and cellular heterogeneity are preserved after breast cancer has spread to distant sites [14, 15]. HER2 status is highly preserved as breast cancers progress to metastatic disease [16]. Trastuzumab combination chemotherapy has been shown to improve survival rates for women with HER2-overexpressing metastatic breast cancer [17, 18]. However, the majority of breast cancer patients who initially respond to trastuzumab-based chemotherapy generally acquire resistance within 1 year [18, 19]. Chemotherapy results in allelic imbalances, which may contribute to the genetic alterations in breast cancer patients [20]. Asymmetric cell division results in two daughter cells with different properties. Cellular heterogeneity is linked primarily to the asymmetric cell division of cancerous cells [21]. Thus, breast cancer is a clinically heterogeneous disease with respect to its biology [15, 22].

We believe that cellular heterogeneity may explain the discrepancy in the effectiveness of treatment noted in this case. Based on this case, trastuzumab may be a useful treatment option for HER2-positive male breast cancer.

We present this rare case of advanced male breast cancer that showed a good response to trastuzumab and paclitaxel therapy. The patient’s quality of life was improved, and no severe adverse events above grade 3 were observed during therapy. This is the first reported case of advanced HER2-positive male breast cancer that showed a good response to this form of combination chemotherapy involving both primary breast cancer and metastatic sites.

References


