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CASE REPORT

Treatment of Breast Cancer Accompanied by POEMS Syndrome: A Case Report[△]

Jian-yu Dong, Yan Yan, Min-feng Liu, Zhao-ze Guo,
Jing-yun Guo, and Chang-sheng Ye*

Breast Center, Nanfang Hospital, Southern Medical University,
Guangzhou 510515, China

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POLYNEUROPATHY, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes (POEMS) syndrome is a rare paraneoplastic syndrome characterized by the presence of a monoclonal plasma cell disorder, peripheral neuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and typical skin abnormalities. The cause of POEMS syndrome is unknown.¹ Although numerous cases with POEMS syndrome have been reported, the POEMS syndrome patients with malignant tumor were seldom reported. Here, we present a rare case with breast cancer accompanied by POEMS syndrome.

CASE DESCRIPTION

A 52-year-old woman who was admitted to the Department of Neurology, Nanfang Hospital on December 27, 2011 presented with progressive weakness and numbness in the legs for one year. She also suffered peripheral edema

of the four extremities, ascites, bilateral pleural effusion, and mild pericardial effusion. Physical examinations revealed the motor strength in the upper and lower extremities was 2/5, decreased sensation of the bilateral lower extremities and a steppage gait. A nerve conduction velocity test was conducted and confirmed demyelinating polyneuropathy. Immunofixation electrophoresis showed monoclonal gammopathy of IgA λ . Abdominal ultrasonography revealed splenomegaly. Serum thyroid hormone test showed hypothyroidism. Skin change was hyperpigmentation of the lower lip.

The clinical manifestations, lab and imaging study results fulfilled the criteria of diagnosis of POEMS syndrome, and the diagnosis of POEMS syndrome was further confirmed *via* multidisciplinary consultation 2 months after admission. The patient was transferred to Hematology Department on February 8, 2012. She received chemotherapy in the form of melphalan and prednisone (melphalan 14 mg/d per os on days 1 to 4 and prednisone 40 mg per os on days 1 to 4), cycled every 4 weeks for 7 cycles from February 2012 to July 2012.

After the 1st cycle of chemotherapy, the ascites, bilateral pleural effusion, and pericardial effusion disappeared. After 4th cycle, the peripheral edema was cured and a

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*Corresponding author Tel: 86-20-62787172, E-mail: ycsnfyy@163.com

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recovery of limb weakness was observed. After 7 cycles a significant and meaningful improvement of neuropathy was observed. Physical examination indicated that the motor strength in the upper and lower extremities was improved from 2/5 to 4/5. In order to sustain long-term improvement, the patient underwent autologous peripheral blood stem cell transplantation (SCT) on December 29, 2012.

The patient visited Breast Surgery Department on March 3, 2013 presented with a palpable lump in the right breast for 1 month. Physical examination confirmed a firm, fixed, non-movable lump situated at the 10 o'clock position of the right breast, measuring approximately 4.5 cm. Breast ultrasonography revealed an ill-defined irregular hypoechoic density lesion in the right breast, measuring 2.8 cm×1.5 cm×3.4 cm. Diagnostic mammography showed a 4.9 cm×2.8 cm high density mass with spiculated margin in the upper outer quadrant of the right breast, amorphous calcifications distributed in clusters within the mass. The lesion was classified as BI-RADS category 4 and a further biopsy was suggested. She had no family history of breast cancer and had a natural menopause at 49 years old.

On March 5, 2013, a core needle biopsy was performed, and frozen section was reported as invasive ductal carcinoma, so the patient underwent right-sided modified radical mastectomy on March 6, 2013. Pathology result: invasive ductal carcinoma, Grade 2, metastasis in 4 axillary lymph nodes. Immunohistochemistry testing showed: estrogen receptor-positive, progesterone receptor-positive, human epidermal growth factor receptor 2 (2+), Ki-67: 30%. Unfortunately, no further fluorescence *in situ* hybridization (FISH) or chromogenic *in situ* hybridization (CISH) was performed following the rejection of the patient to provide consent over financial concerns, and the patient could not receive target therapy with the same reason. The staging evaluation was performed, and there was no evidence of distant metastases. The tumor was finally staged as pT2N2M0, stage IIIA.

A multidisciplinary consultation was applied to discuss the proper and safe treatment plan. Both epirubisin and cyclophosphamide (EC) were the effective and commonly used regimens for treatment of hematology-oncology and breast cancer patients, so the patient was suggested to receive EC followed by docetaxel chemotherapy: epirubisin 90 mg/m² docetaxel administrated intravenously (IV) on day 1, cyclophosphamide 600 mg/m² IV on day 1, cycled every 21 days for 4 cycles, followed by docetaxel 100 mg/m² IV on day 1, cycled every 21 days for 4 cycles.

The patients has received the melphalan and prednisone chemotherapy followed by autologous SCT

before, therefore, she has a high risk to acquire severe bone marrow suppression. We monitored the side effects by complete blood count test every other day and the intervention with granulocyte colony stimulating factor (G-CSF) was recommended when the neutropenia was detected. I-III degree bone marrow suppression was observed in each cycle and cured by G-CSF. There was no other severe side effects occurred during the whole treatment.

After the chemotherapy, she received the radiotherapy to the chest wall, axilla, infraclavicular and supraclavicular lymph nodes area with a dose of 50 Gy in 25 fractions over 35 days. She received exemestane 25 mg per os daily as initial endocrine therapy. After following up for 24 months, no recurrence and distant metastasis were detected and POEMS syndrome was stable.

DISCUSSION

Though significant advances have been made in the diagnosis and treatment of POEMS syndrome over the last decade, its pathogenesis is still not well understood. The course of POEMS syndrome is usually chronic, with a median survival time of nearly 14 years.² The patients would have an excellent prognosis if the diagnosis is made early and appropriate therapy is applied.¹ The diagnosis of POEMS syndrome relies on a set of clinical manifestations and lab studies, and it was very difficult to make an early diagnosis. Multidisciplinary collaboration is commonly essential for the diagnosis.

Many kinds of treatment methods have been proved effective, and melphalan-dexamethasone is an effective and well-tolerated treatment, especially for older patients or the patients with organ dysfunction who could not tolerate SCT. SCT was suggested to be preferred treatment for POEMS syndrome patients with normal organ function,² and it has resulted in a high response rate and durable remission. In our case, the patient suffered severe systemic diseases and was not eligible for SCT. After 7 cycles of chemotherapy, the general situation improved significantly which permitted the patient to undergo autologous SCT.

It was clear that the risk of secondary solid tumor increases steadily with time since allogeneic SCT, ranging from 1.2% to 1.6% at 5 years. The two main risk factors for secondary cancers after allogeneic SCT are irradiation and chronic graft-versus-host disease (GVHD).³ A retrospective analysis of 3337 female patients who received allogeneic SCT was performed, 52 survivors developed breast cancer at a median follow-up of 12.5 years.⁴ GVHD did exist in autologous SCT patients though it occurred not as much as allogeneic SCT.⁵ The immunosuppressive state induced by

melphalan-dexamethasone may further enhance the risk of cancer in patients with POEMS syndrome. In our case, the patient found a 4.5-cm lump in the right breast just 1 month after SCT, so it seemed like a primary breast cancer rather than secondary carcinoma.

Breast cancer is the most common malignancy in women in the world. The American Cancer Society estimates that 292 130 Americans will be diagnosed with invasive breast cancer in 2015.⁶ The favorable prognosis benefits from the early detection and effective treatments, including: surgery, cytotoxic chemotherapy, radiation therapy, endocrine therapy and biologic therapy.

The selection of anti-cancer agents is complicated, both the effectiveness and toxicities should be considered seriously. We tried to seek the regimens which could benefit not only for breast cancer but also POEMS syndrome. After multidisciplinary consultation, we recommend EC followed by docetaxel regimens to the patient, and all regimens were preferred first-line agents in adjuvant chemotherapy of primary breast cancer. These agents also were commonly used in hematological malignancies. Patients with SCT may experience unexpected toxicity after classical chemotherapy, in particular unexpected hematologic toxicity. We just recommended the traditional every-3-week schedule, although in patients without previous SCT dose-dense doxorubicin and cyclophosphamide followed by paclitaxel every 2 weeks showed survival-benefit when compared with 3 weeks.⁷

Tamoxifen has been widely used as endocrine therapy for patients with hormone receptor-positive breast cancer for four decades and approved as chemoprevention for more than ten years. Four cases which focused on the treatment of POEMS syndrome with tamoxifen have been reported separately since 1989, among them, two cases were effective and the others were failed.⁸⁻¹¹ The clinical efficacy and mechanisms in the treatment of POEMS syndrome with tamoxifen are not clear. Since it has been proved that exemestane showed a greater clinical benefit than tamoxifen in premenopausal patients with early breast cancer, we recommended exemestane to the patient instead of tamoxifen.

In conclusion, chemotherapy followed by SCT is an effective therapy for POEMS syndrome. The carefully selected adjuvant regimens are relatively safe to the patient who has undergone SCT. Multidisciplinary colla-

boration is essential in the diagnosis and treatment of rare diseases.

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