A Case of Granulocyte-Colony Stimulating Factor–Producing Spindle Cell Carcinoma of the Breast

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Clinical Practice Points

- This is the first report to describe a very rare case of spindle cell carcinoma of the breast that produced granulocyte-colony stimulating factor (G-CSF).
- Removal of the tumor induced an immediate decrease in the white blood cell count and fever.
- In addition, immunohistochemistry for G-CSF provided proof of G-CSF expression of this breast carcinoma.
- Patients with G-CSF–producing tumors usually have a poor prognosis, just as do those with spindle cell carcinoma of the breast.
- Consequently, our patient rapidly developed distant metastases.
- A G-CSF–producing tumor should be considered, including in the breast, when a patient with cancer shows continuous leukocytosis and hyperthermia without a focus of infection.

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Introduction

Spindle cell carcinoma of the breast is rare; it represents approximately 0.3% of all invasive carcinomas.[1] These tumors show greater aggressive behavior and mortality than with common invasive breast cancer. In addition, hormonal receptors and human epidermal growth factor receptor 2 (HER2) will all typically be negative in spindle cell carcinomas.[1-3] Therefore, the treatment options for spindle cell carcinoma of breast are limited. The median survival of patients with spindle cell carcinoma has been reported to be 18 months.[1]

Granulocyte-colony stimulating factor (G-CSF) is recognized as a naturally occurring glycoprotein that stimulates the proliferation and maturation of precursor cells in the bone marrow into fully differentiated neutrophils.[4] G-CSF also mobilizes hematopoietic stem cells into the peripheral blood.[5] Exogenous G-CSF is routinely used during cancer chemotherapy to promote neutrophil proliferation and mobilization to decrease the incidence of infection.[6] In addition, G-CSF can be used to mobilize hematopoietic stem cells from healthy donors to harvest stem cells for transplantation.[7]

Several G-CSF–producing malignant tumors have been reported in the lung,[8-11] urinary bladder,[12,13] digestive organs,[14-19] and thyroid gland,[20-22] but not in the breast. We present a rare case of a G-CSF–producing spindle cell carcinoma of the left breast.

Case Report

A 58-year-old woman noted a mass in her left breast in 2009. One year later, it had begun to enlarge rapidly and had progressed to ulceration accompanied with bleeding. Eventually, she lost consciousness owing to hemorrhagic shock and was transported to our hospital.

Examination of her vital signs showed she had a temperature of 38°C, her pulse rate was 52 beats/min, and her blood pressure was 128/77 mm Hg. On physical examination, she had a huge and exophytic tumor approximately 14 cm in size occupying the entire left breast, with an ulcerative lesion with necrotic tissue and hemorrhage present. No fixation to the pectoral muscle was noted (Figure 1).

The laboratory tests revealed a hemoglobin and hematocrit value of 2.8 g/dL and 9.6%, respectively, a white blood cell count of

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Figure 1 Physical Examination Showed a Huge and Exophytic Tumor Approximately 14 cm in Size That Was Occupying the Entire Left Breast and Presented With an Ulcerative Lesion With Necrosis Tissue and Hemorrhage. The Tumor Was Not Attached to the Pectoral Muscle

63.2 × 10^3/μL, with 94% neutrophils, and a platelet count of 57.3 × 10^4/μL. Blood chemistry testing showed that her renal and hepatic function and all tumor markers were within the normal ranges.

A computed tomography (CT) scan showed that the tumor size was 17.1 cm × 8.0 cm, and the pectoralis major muscle did not seem to have been invaded by the tumor (Figure 2A). Some of the left axillary and subclavian lymph nodes were enlarged, with a maximum size of 2.1 cm (Figure 2B). These findings indicated lymph node metastasis. Core needle biopsy of the breast tumor revealed proliferation of large spindle-shaped cells with severe atypical nuclei and necrotic changes. These results suggested that this tumor was a spindle cell carcinoma of the breast (Figure 3).

Because we suspected that the hyperleukocytosis and hyperthermia were induced by bacterial infection of the tumor, we treated the patient with antibiotics and irrigation. However, her white blood cell (WBC) count remained high (30.0-40.0 × 10^3/μL), and her temperature continued to be > 38°C. Other sites of infection (eg, pneumonia, urinary tract infection) were not detected radiographically or by CT or culture. As another cause of hyperleukocytosis, leukemia was doubtful, and examination of the bone marrow aspiration and specimens revealed normocellular marrow and hypercellularity of neutrophils. Finally, we strongly suspected a G-CSF–producing tumor, because the serum G-CSF level was elevated to 116 pg/μL (normal value, < 30 pg/μL), and no infection site was found.

Because this tumor was diagnosed as an advanced spindle cell carcinoma of the left breast with ulceration accompanied by hemorrhage, we performed total mastectomy and axillary lymph node dissection without skin grafting to control the hemorrhage and to cure the breast cancer.

Macroscopic findings showed a huge breast tumor with a peduncle that bulged in a cauliflower-like shape. The tumor was 22.0 cm in size, and skin invasion was observed. An ulcerative lesion with hemorrhage and necrosis was present on the surface of this tumor (Figure 4A). Histologic examination by hematoxylin-eosin (HE) staining revealed large spindle-shaped cells with variant and bizarre nuclei arranged in a solid nest. Lymphatic and venous permeation was notable (Figure 4B). Three lymph nodes were involved. Immunohistochemical examination for epithelial

Figure 2 (A) A Computed Tomography Scan Showing a Tumor Size of 17.1 cm × 8.0 cm. The Pectoralis Major Muscle Appeared Not to Have Been Invaded by the Tumor. (B) Several Left Axillary and Subclavian Lymph Nodes Were Enlarged, Indicating Lymph Node Metastasis