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Letter to the Editor

Breast Carcinoma Presenting as Immune Thrombocytopenic Purpura

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Thrombocytopenia is a frequent complication of cancer and is a contraindication for aggressive antineoplastic therapy until the etiology of the low platelet count is determined and the clinical situation is successfully addressed. The association of immune thrombocytopenic purpura (ITP) with lymphoproliferative malignancies is well recognized [1], but solid tumor malignancies are rarely associated with ITP [2]. We present a 40-year-old woman with metastatic breast carcinoma and severe thrombocytopenia. Other conditions known to cause thrombocytopenia were absent, but typical features of ITP were present, such as the presence of megakaryocytic hyperplasia in the bone marrow and the dramatic response of the platelet count to steroid therapy. To the best of our knowledge, this report represents the fifth case of carcinoma of the breast presenting as ITP.

In October 1999, a 40-year-old woman presented with a 2-week history of gingival and conjunctival bleeding. There was no history of fever, photosensitivity, oral ulcers, alopecia, or arthritis. The patient had not been taking any medication before her admission. A mass measuring 3 × 2 cm was noted in the left breast. The left axillary lymph node was enlarged and the left nipple was retracted. The lung, abdomen, and vaginal examinations were unremarkable. Her hemoglobin was 117 g/L, leukocyte count, 10.4×10^9/L, and platelet count, 2×10^9/L. The peripheral blood smear showed giant platelets but no platelet clumps or leukoerythroblastosis. There was no evidence of microangiopathic hemolysis or disseminated intravascular coagulation, which may be associated with metastatic carcinoma. The patient received 28 units of random-donor platelets with no improvement in platelet count ($<10 \times 10^9$/L). The bone marrow showed increased numbers of megakaryocytes and small foci of metastatic tumor cells (Figure 1). Cytologic examination of the breast lump aspirate confirmed the diagnosis of infiltrating ductal carcinoma. The results of serologic tests for dengue virus, Epstein Barr virus, and human immunodeficiency virus were negative. The rheumatoid factor, antinuclear antibody, and lupus anticoagulant test results were negative. A diagnosis of metastatic breast carcinoma and acute ITP was made, and treatment was instituted with 1 g/d of intravenous methylprednisolone for 3 days followed by 60 mg/d oral prednisolone for 18 days. The platelet count increased to 30×10^9/L and the bleeding stopped after 7 days of steroid therapy. On day 10 of prednisolone therapy (day 17 of admission), the platelet count was 82×10^9/L and on day 22 (day 29 of admission) it was 271×10^9/L (Figure 2). After initiation

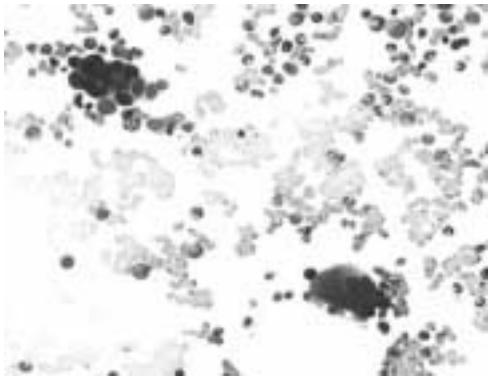

Figure 1. Asprirate of the bone marrow shows a normal-looking megakarocyte and a clump of neoplastic cells (May-Giemsa Grünwald stain; original magnification ×40).

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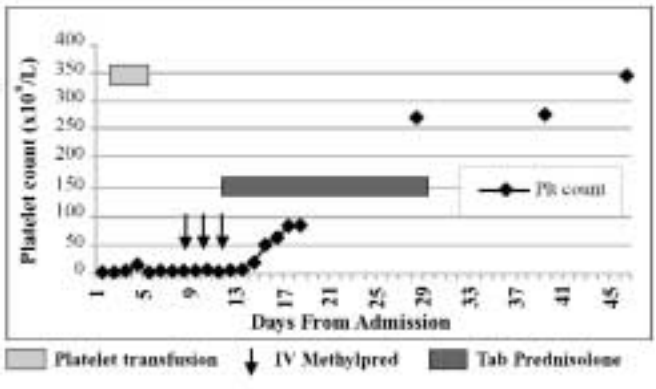

Figure 2. The relationship between steroid therapy and the platelet count of a patient with breast carcinoma and immune thrombocytopenic purpura. The dosage of IV methylprednisone was 1 g/d for 3 days and the dosage of oral prednisolone was 60 mg/d for 18 days. Plt indicates platelet; IV, intravenous.

of steroids, the patient received 60 mg of doxorubicin, but there was no change in the breast lump. Seven months later, there was partial resolution of the breast lump and the patient's platelet count remained in the normal range.

This syndrome appeared to be immune-mediated because of the presence of isolated, severe thrombocytopenia, giant platelets, and increased numbers of megakaryocytes in the bone marrow, and because the thrombocytopenia was refractory to platelet transfusions. Except in cases of severe hemorrhage, platelet transfusions are not indicated in ITP because the platelets are rapidly destroyed. The excellent response of the platelet count to steroid therapy even before treatment of the breast carcinoma supported the diagnosis of ITP. The low dose of doxorubicin administered was unlikely to affect the platelet count. The absence of clinical or biochemical evidence of systemic lupus erythematosus suggested the possible association between ITP and the underlying breast carcinoma.

Solid tumor malignancies are rarely associated with immune thrombocytopenia, although it has been reported [2-4], and can be caused by several mechanisms including marrow replacement by tumor, marrow hypoplasia secondary to chemotherapy, and platelet consumption due to activation of the coagulation cascade [5-7]. ITP has been described in patients with carcinoma of the lung, ovary, uterus, prostate, testes, bladder, and colon [1,3,8,9], and there have been 4 case reports of an association between breast cancer and ITP [2,10-12]. In most cases, there was evidence of tumor infiltration in the bone marrow. The exact mechanism for the development of immune thrombocytopenia in patients with carcinoma is unclear, but 2 possibilities are disordered immune regulation and the development of immune complexes that may bind to autologous platelets, promoting their destruction [13]. It has been shown that the platelet-associated IgG and IgM decrease after treatment with steroids and chemotherapy, and increase as the primary malignancy progresses [4]. In the present case, the brief course of chemotherapy may have contributed to the improvement of antibody levels indirectly through immune suppression.

We conclude that patients with breast cancer may develop immune thrombocytopenia and it can be successfully treated with steroid therapy, allowing specific treatment of the primary malignancy with high-dose cytotoxic therapy.

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