Idiopathic thrombocytopenic purpura and ovarian cancer

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Summary

The association of ovarian carcinoma with idiopathic thrombocytopenic purpura (ITP) is rare. There have been different case reports indicating an association between solid tumors and ITP. We report a case of a 47-year-old woman diagnosed with ovarian cancer who presented with abdominal distention and thrombocytopenia. Her clinical course and the mechanisms of thrombocytopenia are discussed.

Key words: Thrombocytopenia; ITP; Ovarian cancer.

Introduction

Maturation of the megakaryocyte generates anucleate platelets, the smallest circulating blood cells. The platelets are surrounded by a membrane covered with glucoproteins, including integrins, which are essential for the adhesion and aggregation required for hemostasis. At the site of injury, or the tumor surface, platelets may adhere and release agonists which induce the polymerization of actin monomers, resulting in shape changes. In advanced cancer, tumor-derived thrombin and ADP, and tumor stromal cells may activate platelets. Activation of platelets leads to the release of different substances from both alpha and dense granules that are essential in platelet aggregation and coagulation [1]. Thrombocytopenia in general could be caused by increased destruction, decreased production, and pooling like splenic sequestration. ITP is a diagnosis of exclusion, i.e., when other causes of thrombocytopenia are not found. ITP is an autoimmune disorder characterized by auto-reactive antibodies against platelets resulting in splenic sequestration and thrombocytopenia [2]. The association between ITP and solid tumors has been reported previously [3-8].

Patient

A case of 47-year-old female, multigravida, with a history of lower abdominal pain and progressive increase in abdominal girth of seven months duration is reported. CT scan of the abdomen and pelvis showed a right ovarian multiloculated mass 10 x 3 x 8 cm in diameter with solid and liquid components, and fluid in the cul de sac. Laboratory data showed hemoglobin 13 g/dl, WBC 7 x 10^9/l, platelet count 48 x 10^9/l, and CA 125 43.2 U/ml. Liver function tests, creatinine, CA 15-3, alpha feto protein, and beta HCG were normal. Bone marrow aspirate showed increased cellularity with adequate megakaryocytes. The diagnosis of idiopathic thrombocytopenic purpura (ITP) was established after exclusion of other causes of thrombocytopenia. Prednisone, 2 mg/kg, was started with excellent response and the steroid was stopped six weeks latter. She underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy (TAH-BSO) and the pathology revealed low-grade bilateral ovarian endometroid adenocarcinoma. The tumor was staged as IIB. She was treated with six cycles of carboplatin and paclitaxel with a decrease in the CA 125 level to 10 U/ml. Shortly after the fifth cycle her platelet count dropped again to 28 x 10^9/l with normal WBC 7 x 10^9/l and Hgb 12g/dl. She was started again on steroids with a gradual rise in platelet count to 265 x 10^9/l.

Discussion

One of the most common causes of thrombocytopenia in cancer patients is treatment with cytotoxic agents that leads to bone marrow hypoplasia, bone marrow infiltration with tumor cells, and platelet destruction caused by tumor-intrinsic factors activating the coagulation cascade. The most common non-iatrogenic mechanism for thrombocytopenia in cancer is the consumption of platelets by disseminated intravascular coagulation [9]. A low platelet count in some cancer patients has also been proposed to be due to a syndrome resembling immune thrombocytopenic purpura [3]. Circulating immune complexes have been found in some cases of breast cancer and shown to interact with platelets. The presence of platelet-activating immune complexes may lead to in vivo aggregation and thrombocytopenia [10]. The thrombocytopenia can be explained based on local recurrence of the cancer, or as a paraneoplastic syndrome [11]. The success of circulating metastases relies on extravasations; cells must therefore be equipped with an adhesive mechanism. The egress of micrometastases from the vascular system is facilitated by formation of complexes between platelets and tumor cells, as well as leucocytes. When cancer cells are injected experimentally, the decreased platelet count is a sensitive indicator of intravascular coagulation. Induction of thrombocytopenia reduces the rate of experimental metastasis, which is subsequently increased by platelet transfusion [12]. Development of thrombocytopenia in our patient could be multifactorial. However the hypercellularity of the bone marrow, increased number of megakaryocytes, absence of metastatic cells in the bone marrow, absence of associated viral infection, normal

Revised manuscript accepted for publication April 9, 2003

chemistry profile including PT and PTT, and the prompt response to steroid therapy have ruled out a secondary cause and confirmed the diagnosis of tumor associated idiopathic autoimmune thrombocytopenia.

Conclusion

ITP should be considered in the differential diagnosis of thrombocytopenia in ovarian cancer and other solid tumors after all other possible etiologies have been ruled out. ITP could be the first presentation of ovarian cancer.

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