Thrombotic Thrombocytopenic Purpura Secondary to an Occult Adenocarcinoma

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Thrombotic thrombocytopenic purpura (TTP) is characterized by microangiopathic hemolytic anemia (MAHA) and thrombocytopenia. TTP is generally idiopathic, and the association with adenocarcinomas is extremely infrequent [1, 2].

We report a case of a 69-year-old woman with TTP syndrome secondary to metastatic cancer and normal ADAMTS13 (von Willebrand factor [vWF]-cleaving protease) activity and propose the pathogenetic events underlying this unusual association.

The patient was admitted to our hospital because of anemia (hemoglobin level 7.8 g/dl, mean cell volume 90 fl, reticulocyte count was 12%) and thrombocytopenia (platelet count 124 × 10^3/mm^3). Other laboratory findings were: serum aptoglobin <8 mg/dl, lactate dehydrogenase 1,733 UI/l, and alkaline phosphatase 603 UI/l. Partial thromboplastin time and prothrombin time were normal. Direct and indirect Coombs’ tests were negative. A peripheral blood smear study demonstrated the presence of schistocytes and erythroid and myeloid precursors, with no evidence of dacryocytes. A diagnosis of TTP was established, and a program of daily plasma exchange started, but TTP did not resolve after 2 weeks.

Since the increase of alkaline phosphatase could be a sign of bone disease, total body scintigraphy (99mTc) and bone marrow study were performed to rule out TTP secondary to cancer. In fact, total body scintigraphy revealed an increased diffuse uptake in all bone segments, while bone marrow aspirate and biopsy revealed neoplastic cells, suggesting metastasis of mucin-producing adenocarcinoma.

Concomitantly, another set of investigations was performed to find the origin of the neoplasm. Total body computed tomography scan revealed enlarged lymph nodes in the mediastinum; small metastatic lesions of liver, spleen, and bone; and some renal and splenic ischemic lesions. However, these and other investigations (gastroscopy, mammography, and bronchoscopy) could not document any primary neoplastic lesion. A diagnosis of TTP secondary to occult adenocarcinoma diffusely metastatic to bone marrow was established, but a few days later the patient died.

Only a few cases of TTP secondary to metastatic adenocarcinoma are known in the literature [2-7]. The mechanism of secondary TTP is different from the idiopathic mechanism. Idiopathic TTP is believed to be caused by the deficiency of ADAMTS13, which results in the accumulation of unusually
large vWF multimers, which then causes platelet agglutination and microvascular thrombi.

In contrast, in cancer-associated TTP, ADAMTS13 activity and the multimeric pattern of vWF are normal, as in our case. The pathogenesis of secondary TTP remains poorly understood [8, 9]. Probably, tumor cell emboli could generate endothelial damage with platelet aggregation. MAHA is considered to be caused by mechanical fragmentation of red blood cells traversing the injured microvasculature [3]. The role of plasma exchange in these patients should be re-evaluated [8].

**REFERENCES**


3 Gonzalez N, Rios E, Martin-Noya A et al. Thrombotic thrombocytopenic purpura and bone marrow necrosis as a complication of gastric neoplasm. Haematologica 2002;87:ECR01.


In conclusion, patients with TTP who do not initially respond to plasma exchange must be investigated suspecting an underlying disorder. Moreover, if alkaline phosphatase is increased, such as in our case, bone marrow biopsy could be performed to rule out bone marrow metastasis. Finally, the assay of ADAMTS13 activity can help to discriminate between idiopathic and secondary TTP.

**DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST**
The authors indicated no potential conflicts of interest.