

Carcinoma Causing Thrombotic Thrombocytopenic Purpura and Myelonecrosis: A Very Rare Event

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Abstract We report a case of thrombotic thrombocytopenic purpura (TTP) which was explored to be the clinical presentation of carcinoma. Plasma exchange therapy failed to respond for the patient, so bone marrow aspiration and biopsy were performed to find out the reason of microangiopathic hemolytic anemia. Bone marrow examination revealed non hematopoietic cell infiltration and myelonecrosis. Carcinoma metastasis was demonstrated at bone marrow trephine biopsy. The primary tumor was found at small bowel after scanning for the source of tumor by computerized tomography.

Keywords: TTP, malignancy, plasmapheresis

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1. Introduction

Thrombotic thrombocytopenic purpura (TTP) is a rare disorder characterized by a low platelet count, microangiopathic hemolytic anemia (MAHA), fever, neurological disorders and renal dysfunction [1]. The diagnosis is supported by the presence of severe ADAMTS13 deficiency, activity being less than 5 percent [2]. TTP is most frequently associated with immune disorders, drugs and pregnancy [3]. Carcinoma is a rare cause of TTP and myelonecrosis [4]. Here, we document a case of carcinoma metastasis presenting with TTP and myelonecrosis.

2. Case Presentation

A 67-year old man living in a nursing home applied to our Hematology outpatient unit with complaints of fatigue, severe back pain and extensive bruises at his left hip and

thigh. At physical examination, he was pale, he had difficulty in breathing and there were ecchymoses around his left hip and thigh. At laboratory examination, he was anemic (7.5 gr/dl) and platelet count was 13.000/ μ l. Creatinine level was normal but lactate dehydrogenase level was high (1827 U/l). Schistocytes, polichromasia, fragmented and nucleated red blood cells and severe thrombocytopenia were observed on the blood film and he was hospitalized with a provisional diagnosis of TTP. Schistocyte rate was 6%. Coombs test was negative. ADAMTS-13 activity was 3%. Plasmapheresis with fresh frozen plasma was initiated immediately after this test. Bone marrow examination was performed as he was unresponsive to 5 courses of plasmapheresis with 1:1 volume. Bone marrow aspiration revealed signs of myelonecrosis and monoclonal nonhematopoietic cell infiltration. Pathologic evaluation of trephine biopsy revealed myelonecrosis and carcinoma metastasis (Figure 1 and Figure 2). A tumor of small intestine was seen on computerized tomography of the abdomen. The patient was referred to the medical oncology department.

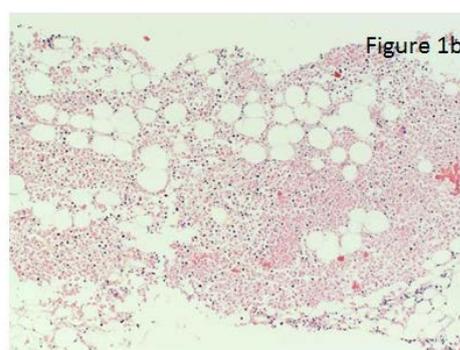
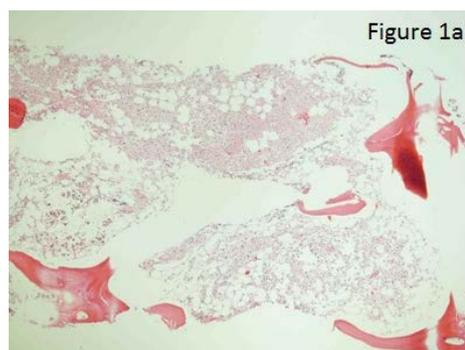


Figure 1. a- Myelonecrosis (HEx40), b-Myelonecrosis (HEx100)

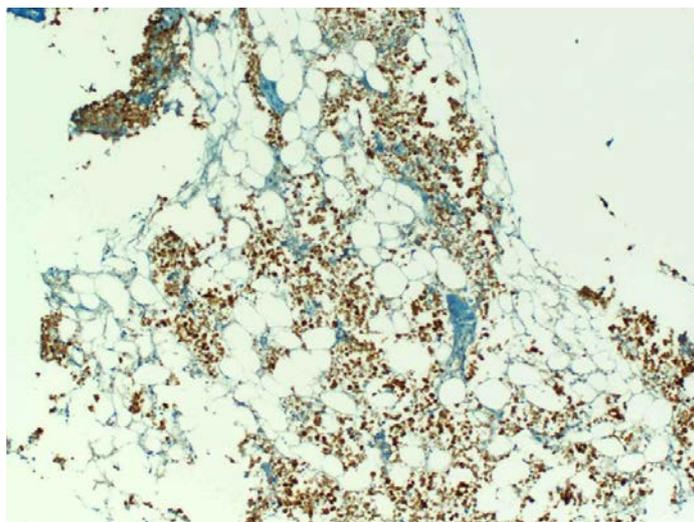


Figure 2. Positive staining of epithelial cells with pan cyokeratin showing that it's carcinoma (immunohistochemistry)

3. Conclusion

TTP has a well-known pentad of clinical features for diagnosis: thrombocytopenia, microangiopathic hemolytic anemia, neurologic and renal abnormalities, and fever [5]. In recent clinical practice, the whole pentad is not prerequisite for diagnosis of TTP. Combination of some clinical symptoms and laboratory findings leads to diagnosis as there are no specific biological markers or symptoms. Our patient had thrombocytopenia, signs of microangiopathic hemolytic anemia on blood film, he had severe back pain but he had no signs of renal failure.

TTP may be associated with predisposing situations such as cancer, pregnancy, exposure to some drugs, bone marrow transplantation and infections such as HIV-1 [6]. After demonstration of carcinoma metastasis, the patient was evaluated for the origin of malignancy and a tumor was observed at small bowel by evaluation with computerized tomography. Malignancy with or without myelonecrosis is a known but very rare cause of TTP [7,8]. Sometimes, TTP might be the first manifestation of metastatic adenocarcinoma [9]. Although there was no metastasis at radiological evaluation, TTP was also the presenting clinical condition at our patient. Bone marrow examination may yield significant information at such cases. For our patient, myelonecrosis seen at bone marrow examination rised the suspicion of bone marrow infiltration by nonhematopoietic cells. The physician should always keep this possibility in mind.

At a recent case report from our center [4], the patient was diagnosed with TTP and plasma exchange therapy was performed with no success. Upon refractoryness to this treatment modality, bone marrow examination was performed as part of routine evaluation and adenocarcinoma metastasis was demonstrated at bone marrow. Like that case and our present case, bone marrow examination may be beneficial at TTP cases that are refractory to plasma exchange therapy.

TTP was fatal in 90% of patients before the advance of effective treatment with plasma exchange therapy [5]. Mortality has decreased from 90% to nearly 10% after frequent use of plasma exchange therapy. Treatment success relies on immediate initiation of plasma exchange therapy. For this reason, early diagnosis and treatment is fundamental at TTP [10,11]. Less than 20% of patients

with cancer-associated TTP respond to plasma exchange therapy but it's still recommended for these patients [9]. Our patient received 5 courses of plasma exchange therapy but there was no improvement at neither platelet count nor LDH level. Refractoriness to plasma exchange therapy should always be taken seriously and further investigations such as bone marrow biopsy should be performed. Any possible underlying cause such as infections, drugs and malignancy should be excluded.

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