Essential thrombocythemia as underlying cause of malabsorption syndrome

Luciana Teofili, Lorenza Torti, Alessandro Cina, Antonio Gasbarrini, Marialuisa Novi, Giuseppe Leone, Luigi Maria Larocca

Editorial Manager(tm) for Annals of Hematology
Manuscript Draft

Manuscript Number: AOHE-D-09-00489

Title: Essential thrombocythemia as underlying cause of malabsorption syndrome

Article Type: Letter to the Editor

Keywords: Essential Thrombocythemia
Malabsorption syndrome
Mesenteric ischemia

Corresponding Author: Dr Luciana Teofili, MD

Corresponding Author's Institution: Catholic University

First Author: Luciana Teofili, MD

Order of Authors: Luciana Teofili, MD; Lorenza Torti; Alessandro Cina; Antonio Gasbarrini; Marialuisa Novi; Giuseppe Leone; Luigi M Larocca

Abstract: Patients with malabsorption syndrome frequently exhibit thrombocytosis associated with iron-deficiency anemia. Indeed, in these patients, the presence of underlying Ph-negative myeloprolifative neoplasms (MPNs) is rarely suspected. Here is reported the case of a young woman with persistent thrombocytosis and with malabsorption syndrome of unknown origin. In the hypothesis of a reactive thrombocytosis, patient received iron and folic acid supplementation without platelet count normalization. When patient developed a protein losing enteropathy was admitted to the hospital and specific haematological investigations allowed the diagnosis of underling Essential Thrombocythemia. Considering the high thrombotic risk associated with MPNs, splanchnic vessel thrombosis was investigated by CT angiography, revealing the chronic occlusion of superior mesenteric artery. Interestingly, although MPNs are one of the most frequent causes of hepatic, portal or mesenteric vein thrombosis, they rarely involve mesenteric arteries. Indeed, this case underscores that, in patients with malabsorption syndrome of unknown origin, it is important to accurately exclude the primitive origin of haematological abnormalities before considering them as reactive manifestations.

Essential thrombocythemia as underlying cause of malabsorption syndrome.

Luciana Teofili, MD, PhD, Department of Hematology, Catholic University, Rome, Italy

Lorenza Torti, MD, Department of Hematology, Catholic University, Rome, Italy

Alessandro Cina, MD, Department of Radiology, Catholic University, Rome, Italy

Antonio Gasbarrini, MD, Department of Internal Medicine, Catholic University, Rome, Italy

Marialuisa Novi, MD, Department of Internal Medicine, Catholic University, Rome, Italy

Giuseppe Leone, MD, Department of Hematology, Catholic University, Rome, Italy

Luigi Maria Larocca. MD, Department of Pathology, Catholic University, Rome, Italy

Correspondence: Luciana Teofili, MD
Istituto di Ematologia,
Università Cattolica, Largo Gemelli 8,
00168 Roma, Italy.
Telephone number: 39-06-30154180
Fax number: 39-06-3017319
E-mail: lteofili@rm.unicatt.it

Dear Editor,

In October 2008 we observed a 31-year old woman with 2 year-history of postprandial abdominal pain, diarrhea and peripheral oedema. Patient had no evidence of cardiac or renal failure, liver and spleen size were normal and there was not palpable lymphoadenomegalies. Liver, pancreatic and thyroid function tests and acute phase reactants were normal, antigliadin, antiendomysial and anti DNA antibodies were absent and antibodies to HCV, HBV and HIV were negative. Repeated controls of hematological parameters evidenced slight thrombocytosis and leukocytosis, in the presence of low serum ferritin. Moreover low serum protein and cholesterol, marked hypoalbuminaemia and hypogammaglobulinaemia were present. No proteinuria was found and it was hypothesized an enteric loss of protein. The stool specimens were negative for occult blood and parasitic contamination. A total body CT scan evidenced no lymphoadenomegalies, while a generalized thickening of ileal wall with mesenteric edema was present. Furthermore, no alterations of hepatic and portal veins were found. Gastrointestinal endoscopy showed jejunal mucosa covered by congested, stocky and whitish villi and biopsies of duodenal and jejunal tract documented a protein-losing enteropathy. Thrombocytosis was considered secondary to the iron deficiency and patient received two week intravenous supplementation of iron and folic acid with recovery of ferritin value. Because of thrombocytosis persisted, we decided to investigate the presence of myeloproliferative neoplasms (MPNs). The patient was proved negative for *JAK2*^{V617F} and *MPL*$^{W515K/L}$ mutations and for *BCR/ABL* rearrangement, whilst endogenous erythroid colonies were found. In addition, the HUMARA assay demonstrated monoclonal expansion of hematopoiesis. Bone marrow biopsy evidenced megakaryocytic hyperplasia and the diagnosis of essential thrombocythemia (ET) was made [1]. The high incidence of splanchnic thrombosis in patients with MPNs prompted us to a more accurate investigation of abdominal vessels [2,3]. Actually, a CT angiography revealed a significant stenosis of the superior mesenteric artery (Figure 1). The patient underwent selective mesenteric angiography and percutaneous endovascular angioplasty, with adequate revascularization. The presence of acquired or hereditary thrombophilic defects was ruled

out and therapy with low dose aspirin and hydroxycarbamide was undertaken. During the following months, the nutritive state and the clinical conditions of patient progressively improved.

The most relevant feature affecting the clinical course of Ph-negative MPNs is the prothrombotic state causing both arterial and venous thromboses and microvessel disturbances [2,3]. In particular, splanchnic vein thromboses (SVT), including both portal and mesenteric vein thromboses, are frequent presenting complications of MPNs, whilst thrombosis involving the arterial mesenteric district are rarely reported [2,3]. In these cases, malabsorption syndrome might represent the unique clinic manifestation of a mesenteric arterial flow disturbance [4]. Patients are usually olygo- or asymptomatic for a long time, although the chronic intestinal ischemia causes a progressive malabsorption syndrome resulting in weight loss in almost all affected patients [4]. Since thrombocytosis is frequently observed during the course of malabsorption syndromes [5], an underlying MPN could remain misdiagnosed even in the presence of an overt hematological picture. Importantly, in contrast to SVT, which can be sensitively diagnosed by conventional CT scan or ultrasonography, the diagnosis of mesenteric arterial occlusion requires the CT angiography with evaluation of the arterial phase, or, as a gold standard, the angiography [4].

References

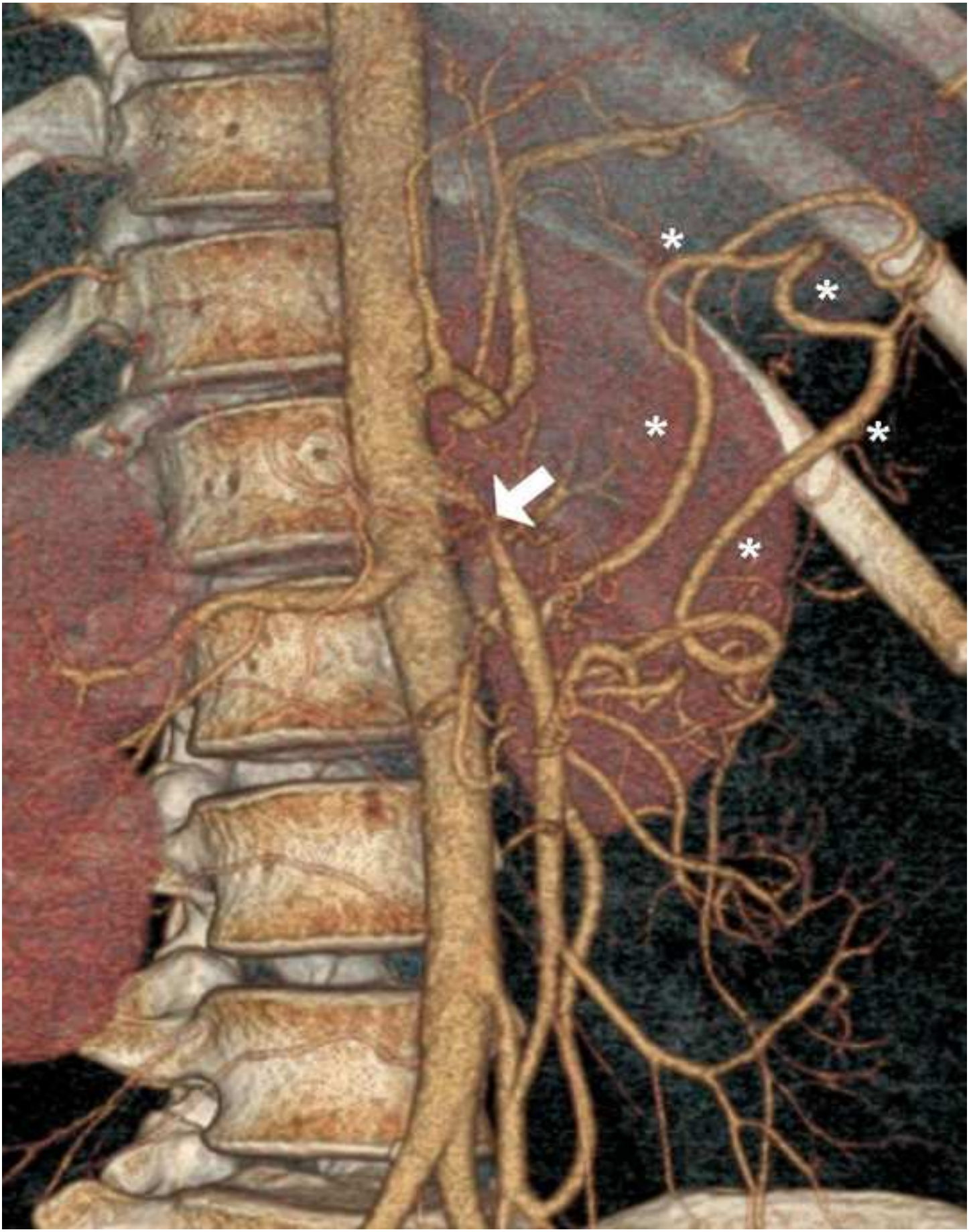
1) Tefferi A, Vardiman JW. Classification and diagnosis of myeloproliferative neoplasms: the 2008 World Health Organization criteria and point-of-care diagnostic algorithms (2008) Leukemia 22:14-22
2) Gruppo Italiano Studio Policitemia Polycythemia vera: the natural history of 1213 patients followed for 20 years (1995) Ann Intern Med. 123:656-64.
3) De Stefano V, Za T, Rossi E, Vannucchi AM, Ruggeri M, Elli E, et al. Recurrent thrombosis in patients with polycythemia vera and essential thrombocythemia: incidence, risk factors, and effect of treatments (2008) Haematologica 93:372-80.
4) Kolkman JJ, Bargeman M, Huisman AB, Geelkerken RH. Diagnosis and management of splanchnic ischemia. (2008) World J Gastroenterol. 14:7309-20
5) Halfdanarson TR, Litzow MR, Murray JA. Hematologic manifestations of celiac disease.(2007) Blood 109:412-21

Figure legend.

Figure 1. CT volume rendering oblique reconstruction showing occlusion severe stenosis of proximal superior mesenteric artery (arrow) of the celiac trunk, with a compensatory circulation throughout the hypertrophic gastroduodenal artery (asterisks).

Figure

Click here to download high resolution image



***Conflict of interest**

Click here to download Conflict of interest: Conflict of Interest Disclosure Form.doc