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Massive upper gastrointestinal bleeding due to splenoportal axis thrombosis in a patient with a tested JAK2 mutation: A case report and review literature

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ABSTRACT

Portal hypertension is a clinical syndrome defined as a portal venous pressure that exceeds 10 mmHg. Cirrhosis is the most common cause of portal hypertension and thrombosis of the splenoportal axis not associated with liver cirrhosis is the second cause of portal hypertension in the Western world. The primary myeloproliferative disorders are the main cause of portal venous thrombosis and somatic mutation of Janus Kinase 2 gene (JAK2 V617F) can be found in approximately 90% of polycythemia vera, 50% of essential thrombocytosis and 50% primary myelofibrosis. A 55-year-old man with JAK2 mutation-associated splenoportal axis hypertension and bleeding complications due to oesophageal varices is reported. A massive upper bleeding episode made an emergent surgery to be done immediately at seventh day. The patient was discharged home at fifteenth day after surgery.

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1. Introduction

Portal hypertension is a clinical syndrome defined as a portal venous pressure that exceeds 10 mmHg. The etiology of portal hypertension can be classified as prehepatic, intrahepatic, or posthepatic (Table 1) [1]. Cirrhosis is the most common cause of portal hypertension and thrombosis of the splenoportal axis not associated with liver cirrhosis is the second cause of portal hypertension in the Western world [2]. There are identified systemic thrombotic factors in 60% of cases and there are several etiologic factors associated in 15% of them [3].

The primary myeloproliferative disorders (polycythemia vera, essential thrombocytosis and primary myelofibrosis) are clonal disorders arising in a pluripotent hematopoietic stem cell, that causes an unregulated increase in the number of erythrocytes, leukocytes or platelets [4]. They are the main cause of portal venous thrombosis, although changes in blood in a portal hypertension context can make the diagnosis more difficult [5]. Somatic mutation of Janus Kinase 2 gene (JAK2 V617F) can be found in approximately 90% of polycythemia vera, 50% of essential thrombocytosis and 50% primary myelofibrosis [4] (Table 2).

The high incidence of gastrointestinal bleeding in patients with portal vein thrombosis and the association between oesophageal

varices and JAK2-related splanchnic vein thromboses should be kept in mind when managing such patients [6].

2. Case report

We present a 55-year-old man with JAK2 mutation-associated splenoportal axis hypertension, splenomegaly and bleeding complications due to oesophageal varices. He's on oral anticoagulants therapy. He had history of cholecystectomy 9 years ago. This patient was referred to our tertiary hospital for evaluation of long duration abdominal pain and hematochezia. He was admitted in the gastrointestinal bleeding unit.

An early endoscopy was performed within 24 h of presentation: stomach fundus was filled with blood clots and there were some isolated fundal gastric varices. (Fig. 1). Blood test revealed leukocytosis (26.000 leukocytes per mm³) and thrombocytosis (767.000 thrombocytes per mm³).

A computed tomography angiography (CTA) under fluoroscopic guidance was performed. The procedure was carried out under sedation and local anesthesia. Celiac trunk, splenic artery and upper mesenteric artery were catheterized with a 5 French (Fr) catheter. After vasodilators agents administration, intraoperative control arteriography showed absence of portal and splenic opacification, which supports thrombosis in splenoportal axis (Fig. 2).

The patient had a massive upper bleeding episode at seventh day, with tachycardia, tachypnoea, cool clammy skin, hypotension and confusion and the use of luminal tamponade with

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Table 1
Causes of portal hypertension [1].

ETIOLOGY OF PORTAL HYPERTENSION BY LOCATION		
PREHEPATIC	INTRAHEPATIC	POSTHEPATIC
Portal vein thrombosis	Cirrhosis	Budd-Chiari syndrome
Splenic vein thrombosis	Primary biliary cirrhosis	Congestive heart failure
Congenital thrombosis of portal vein	Infiltrative liver disease	Constrictive pericarditis
Arteriovenous fistula	Idiopathic portal hypertension	Tricuspid valve diseases
	Congenital hepatic fibrosis	
	Polycystic liver disease	
	Postsinusoidal venoocclusive disease	

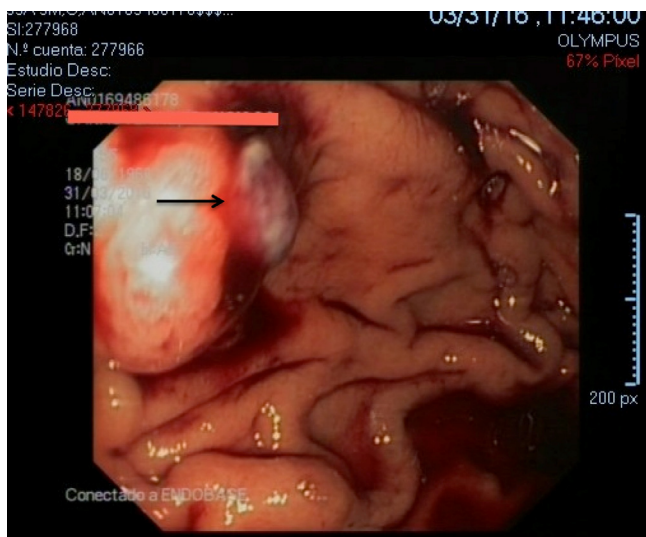


Fig. 1. Early endoscopy shows isolated fundal gastric varices (dark arrow).



Fig. 2. Angiography under CT guidance. Absence of portal and splenic opacification (thombosis).
Abbreviation: CT, computed tomography.

Table 2
Representative molecular defects in the chronic myeloproliferative disorders [4].

CHRONIC MYELOPROLIFERATIVE DISORDERS	
DISEASE	MOLECULAR DEFECT
Chronic myelogenous leukemia	BCR-ABL
Chronic eosinophilic leukemia	FIP1L1-PDGFRα
Chronic neutrophilic leukemia	BCR-ABL p230
Chronic myelomonocytic leukemia	TEL-PDGFRβ
Systemic mastocytosis	KIT D8116V
Polycythemia vera	JAK2 V617F (≈90% positive)
Essential thrombocytosis	JAK2 V617F (≈50% positive)
	MLP W515L/K (≈3% positive)
	MLP K39N
Primary myelofibrosis	JAK2 V617F (≈50%)
	MLP W515L/K (≈14%)

Sengstaken-Blakemore was a life-saving maneuver. Unfortunately, acute bleeding was uncontrolled so an emergent surgery was performed immediately. Transjugular intrahepatic portosystemic

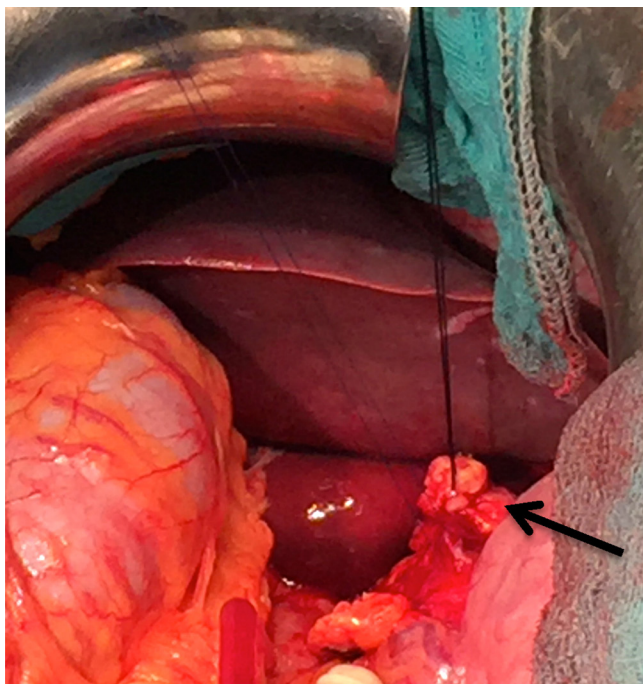
shunt (TIPS) is contraindicated because of portal vein thrombosis [7] (see Table 3).

A midline laparotomy was performed: a great stomach filled with blood and blood clots takes up most of left upper quadrant. Some fundal gastric varices are due to thrombosis in splenoportal axis. Neither esophageal nor other gastric varices were seen. A splenectomy was performed first, providing better exposure for gastric devascularization (Figs. 3 and 4). Acute upper bleeding was successfully controlled and a Sugiura procedure was not required.

The patient was discharged home fifteen days after surgery. Pathologic analysis did not reveal nothing but splenomegaly. Essential thrombocytosis was diagnosed and he is currently receiving follow-up care by haematologist. No other bleeding episodes were reported.

Table 3
Contraindications for TIPS [7].

Contraindications for Transjugular Intrahepatic Portosystemic Shunt (TIPS)	
Absolute contraindications	Relative contraindications
Severe elevate right heart pressure	Complete hepatic vein obstruction
Severe pulmonary hypertension	Complete portal vein thrombosis
Severe congestive heart failure	Hepatocellular carcinoma
Severe encephalopathy	Severe coagulopathy (INR greater than 5)
Uncorrectable bleeding diathesis	Severe thrombocytopenia (platelet count less than 20,000/cm ³)
Active systemic or hepatic bacterial infection	Advanced liver dysfunction (bilirubin greater than 5 mg/dL or MELD greater than 17)
Unrelieved biliary obstruction	Moderate pulmonary hypertension



Figs. 3 and 4. Images from surgery. Fundal gastric varices are ligated (arrow); specimen from splenectomy (splenomegaly).

3. Discussion

The surgery of portal hypertension has been currently abandoned because of adoption of new procedures as TIPS. The transjugular intrahepatic portacaval shunt is an interventional radiologic procedure employed as a useful treatment for the symptoms of portal hypertension since early 1970s by which a tract

is created between the hepatic and portal vein and reduces portal pressure. TIPS alleviates severe symptoms related to portal hypertension and can be a life-saving procedure in emergent upper gastrointestinal bleeding, if bleeding is uncontrolled with resuscitation, medical measures, endoscopic therapies and balloon tamponade [17].

Maintaining gastric pH above 6 optimises platelet aggregation and clot formation.

Although there is evidence of improved clinical outcome associated with post-endoscopic pharmacological management of patients at high risk of rebleeding, there is a lack of evidence to support pre-endoscopic treatment with proton pump inhibitors [8,9].

Endoscopy is an effective intervention for acute gastrointestinal bleeding and plays a critical role in the diagnosis and therapy in variceal hemorrhage. Current clinical practice involves endoscopy being undertaken in working hours within 24 h of presentation. Optimum resuscitation is essential before endoscopy in order to reduce the potential cardiorespiratory complications of the procedure [10,11].

Medical treatment includes the use of vasoactive drugs, which exert their action by reducing portal pressure and variceal pressure. Whenever a variceal bleeding is suspected, vasoactive drugs should be started as soon as possible. Literature shows that early administration of these drugs reduces the rate of active bleeding during endoscopy. The optimal duration of medical therapy is not well established. Current guidelines recommend maintaining vasoactive treatment for 2–5 days (period in which rebleeding is more frequent). Current data does not show superiority of any drugs, so the choice is based on hospital resources.

There are many vasoactive drugs to treat hemorrhage by decreasing blood flow. Published data does not permit firm conclusions about the superiority of any of them. Terlipressin is a synthetic analogue of vasopressin with few side effects. Its utility is based on reducing portal pressure and its effects are still significant four hours after administration. Terlipressin controls variceal bleeding at 48 h in 80% of cases, and has been shown to improve survival when compared to placebo. Terlipressin is limited by systemic vasoconstrictive properties that can produce ischemic complications and dysrhythmias. It should be used with caution and avoided in those patients with a history of ischemic heart, cerebral disease, vascular disease or heart rhythm disorders [12]. Octreotide, a somatostatin analog with a longer half-life, is a splanchnic vasoconstrictor and inhibitor of glucagon and other vasodilatory peptides. It inhibits acid and pepsin secretion, so reduces gastroduodenal mucosal blood flow. Published data does not show improved surveillance [14].

The surgical treatment in portal hypertension has as target to avoid rebleeding keeping liver function preserved, without encephalopathy. It has been proposed many techniques and there are two with more acceptance: distal splenorenal shunt (Warren procedure) and esophagogastric devascularization and splenectomy [15,16]. The use of beta-blockers and endoscopy must be considered as secondary prophylaxis of variceal haemorrhage: when acute bleeding is successfully controlled, the recurrence of rebleeding can be as high as 50% within the first day of first episode.

4. Conclusion

Emergent surgery in a portal hypertension context has been limited to these situations in which endoscopy and medical measures are not sufficient enough to control bleeding and TIPS are contraindicated. Nowadays, these emergent situations are only isolated cases.

Conflicts of interest

The author declares that she has no conflict of interest.

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Ethical approval

Ethical approval was not required and patient identifying knowledge was not presented in this report.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

Isabel Macías wrote the article.

Guarantor

Javier Medina Fernández.

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