OPEN ACCESS
Saudi Journal of Medicine
Abbreviated Key Title: Saudi J Med
ISSN 2518-3389 (Print) |ISSN 2518-3397 (Online)
Scholars Middle East Publishers, Dubai, United Arab Emirates
Journal homepage: http://scholarsmepub.com/sjm/

Original Research Article

# Myeloproliferative syndrome Induced Portal hypertension

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| **Received:** 07.04.2019 | **Accepted:** 15.04.2019 | **Published:** 30.04.2019
**DOI:**10.21276/sjm.2019.4.4.6

## Abstract

Myeoloproliferative syndrome can cause portal hypertension by inducing the formation of portal thrombosis. In this rectrospective study, we report all cases of portal hypertension caused by myeoloproliferative syndrome and the steps of the final diagnosis.
**Keywords:** Myeoloproliferative syndrome, portal hypertension, portal thrombosis.



## INTRODUCTION

Myeloproliferative syndromes (MPS); splanchnic venous thromboses; and portal hypertension: This triad is an inevitable continuation of events secondary to platelet and leukocyte changes, characteristics of myeloproliferative syndromes. These modifications facilitate the formation of leukoplakelet aggregates and thus the appearance of portal thrombosis which can be complicated by portal hypertension.

## OBJECTIVE

The aim of our study is to analyze the clinical, biological and therapeutic peculiarities of patients with portal hypertension secondary to portal thrombosis due to a myeloproliferative disorder.

## PATIENTS AND METHODS

This is a retrospective, descriptive study over a 16-year period from 2002 to 2018; Collected at the Department of Gastroenterology and Hepatology "Medecine C" Ibn Sina University Hospital; including 13 patients with thrombosis related to myeloproliferative syndrome complicated by portal hypertension. All our patients benefited from a complete clinical examination, Doppler abdominal ultrasonography, diagnostic and therapeutic oesogastroduodenal fibroscopy with jejunal biopsies; A blood count with crase balance and factor V, a liver test; Viral serologies: search for chronic viral hepatitis b or c; A biopsy puncture of the liver; Thrombophilia assessment (Protein C and S, antithrombin III, antiphospholipid syndrome); Paroxysmal hemoglobinuria .Homocysteinemia; Looking for signs of systemic disease; a bone marrow biopsy; JAK2 mutation investigation.

## RESULTS

Of a total of 171 patients with portal hypertension on portal thrombosis without cirrhosis; 13 patients (prevalence of 7.6%) had portal hypertension on portal thrombosis resulting from a myeloproliferative disorder. The mean age of our patients was 80.9 [1-4] years with a sex F / H ratio of [5]. The circumstances of discovery were variable: Abdominal pain in 6 patients (40%); upper gastrointestinal hemorrhage in 4 patients (33, 33%) made of melena in 01 patients and hematemesis in 03 patients; cholestatic jaundice in 2 patients (13.33%); an oedemato-ascitic syndrome in a single patient (13.33%). In the antecedents; there is evidence of hepatotoxic medication in one patient and an ischemic stroke in a patient. The concept of prolonged oral contraception in two patients. No concept of abdominal surgery in our patients. The clinical examination objectified: Signs of portal hypertension in all our patients namely splenomegaly with collateral venous circulation. The liver was clinically normal in 11 patients except two patients who had hepatomegaly overload. Abdominal ultrasound coupled to Doppler has objectified: A normal echostructure liver in all our patients without a liver nodule. Presence of a portal cavernoma and signs of portal hypertension (Splenomegaly, collateral venous circulation) in 10 patients. Presence of chronic portal thrombosis with signs of PHT (Splenomegaly, collateral venous circulation) in 03 patients. The hepatic veins were fine and permeable in all our patients. In addition, there was no intra-abdominal abscess. Oesogastroduodenal fibroscopy revealed esophageal varices in 09 patients; oesophageal varices with cardiac varices (GOV2) in 03 patients and congestive gastropathy of PHT in one patient. Jejunal biopsy was normal in all our patients.

The diagnosis of portal hypertension on portal thrombosis has therefore been carried out in all our patients. Biologically; the blood count showed hemoglobin at 17 g / l in a patient with a hematocrit elevated to 57%. Ten patients had abnormalities of the platelet line (thrombocytosis between 770,000 and 670,000 elements / mm3) and white blood cells (leukocytosis between 13,000 and 12,000 elements / mm3); 03 patients had a normal blood count. The liver test was free of cytolysis and cholestasis in all our patients. A prothrombin rate that was low; less than 50% in 05 patients. Factor V was normal in all our patients. The viral serologies B and C were negative in all our patients. Bone marrow biopdy revealed the presence of idiopathic myelofibrosis in three patients; essentialthrombocythemia in five patients; chronic myeloid leukemia in four patients and polycythemia vera in one patient. Five patients (a polycythemia vera, two chronic myeloid leukemia and 02 essential thrombocythemia) have benefited from a genetic study that objectified the presence of the mutation of the gene JAK2 in the heterozygous state. Hepatic biopsy puncture showed: hepatocyte pain with foci of myeloid metaplasia in one patient; hepatocyte suffering in 02 patients without signs of cirrhosis; without abnormalities in 10 patients. The thrombophilic balance (Protein C and S, antithrombin III, antiphospholipid syndrome) revealed the presence of protein S deficiency in 03 patients. The paroxysmal nocturnal hemoglobinuria clone search was made in 04 patients and returned negative. None of our patients had clinical signs pointing to a systemic disease (Behçet's Disease, Systemic Lupus). The etiology of thrombosis in our 13 patients was a myeloproliferative syndrome confirmed by bone marrow biopsy associated with protein S deficiency in 03 patients. The treatment was based mainly on symptomatic treatment (beta blockers, ligation of esophageal varices), anticoagulation by long-term antivitamies K in all our patients and hydroxyurea in nine of our patients. The evolution was marked by the death in four patients before they were treated. The other patients are followed regularly and did not present an extension of their thromboses with an average follow-up of six years.

# DISCUSSION

Portal thrombosis accounts for 07% of all causes of PH [4]. These thromboses come from a wide variety of causes. In the absence of hepatocellular carcinoma, cirrhosis, local cause (intra-abdominal septic foci, abdominal surgery, splenectomy, intra-abdominal tumors, appendicitis, diverticulitis, inflammatory bowel disease and pancreatitis) the general causes (abnormal thrombophilic balance, nocturnal paroxysmal hemoglobinuria, beetle disease, systemic disease, hyperhomocystemia,) and myeloproliferative syndromes [4], the leading cause of portal thrombosis of extrahepatic origin, should be investigated. Polycythemia veraquez; essential thrombocythaemia and myelofibrosis constitute the 03 classic SPM secondary to dysregulation of the JAK-STAT system; which in turn is secondary to many mutations such as: JAK2 V617F, CALR, or MPL [6]. These 03 entities having a clinical and biological similarity including an excessive proliferation of the figured elements of the mature blood; the possibility of progression to myelofibrosis or chronic myeloid leukemia and a particularly venous thrombotic tendency. As already mentioned; thromboses related to myeloproliferative syndrome have a predilection of the splanchnic venous system. After ruling out cirrhosis and solid cancers known as common causes of splanchnic venous thrombosis [7]; the myeloproliferative syndrome must be searched. Its diagnosis is based mainly on finding the JAK2 V617F mutation and CALR mutations, or MPL when JAK2V617F mutation is negative. This search for specific mutation can be done even in the absence of anomias of the hemogram. It is common for the myeloproliferative syndrome to be masked by hypersplenism; hemodilution or bleeding of varicose origin in patients with portal hypertension on thrombosis related to myeloproliferative syndrome: This is the case of vaquez polycythemia which is most often noted late after the occurrence of portal hypertension thrombosis [8]. This delayed diagnosis may have therapeutic implications. Osteomedullary biopsy can be diagnostic for myeloproliferative syndrome in cases where molecular mutations are absent [9]. In our study; the osteomedullary biopsy was pathological in all cases. The JAK2 mutation could only be done in 05 patients where it returned positive. Patients with portal hypertension on myeloproliferative syndrome-related thrombosis are at greater risk of developing other thromboses than patients without myeloproliferative syndrome. The risk factors for thrombosis recurrence are: budd chiari syndrome; splenomegaly and leukocytosis [10]. The treatment is based on anticoagulation; a cytoreduction; management of portal hypertension and in some cases liver transplantation.

**Anticoagulation**

Current recommendations based on expert opinion and a large number of clinical trials; recommend anti-coagulant treatment for life based on anti-vitamin K; in patients with myeloproliferative syndrome-related thrombosis [11]; taking into account the permanent risk of thrombosis recurrence in these patients. However; this anticoagulation which protects against the risk of rethrombosis; significantly increases the risk of varicose bowel bleeding after development of the portal hypertension [12]. In our study; there was no bleeding under AVK. However; thrombosis may recur despite anticoagulation [10].

**Transjugular Intrahepatic Shunt (TIPS)**

Several clinical trials have demonstrated the efficacy of TIPS in the regression of portal hypertension by MPS-related thrombosis [9]. In our

study; no patient has benefited from TIPS; however, have been eradicated by Endoscopic variceal ligation.

**Cytoreduction**

The occurrence of splanchnic thrombosis or the inferior vena cava system in a patient with myeloproliferative syndrome is indicative of a poor prognosis of myeloproliferative syndrome; thus a cytoreductive treatment; hydrea type should be instituted to improve the prognosis. However; this treatment does not necessarily reduce the risk of new thromboses [13]. In our study; 03 of our patients were put under hydrate.

Interferon can be used in young patients as a cytoreducer [10].

## CONCLUSION

The prevalence of myeloproliferative syndrome in our series is 7.6%. All our patients came to the stage of portal hypertension. Our treated patients; treatment including that of portal hypertension, anticoagulants and hydroxyurea; has well evolved after an average decline of 06 years.

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