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Portal Vein Thrombosis in Non Cirrhotic Patients: Experience of Gastroenterology and Hepatology Department University Hospital Hassan II

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Abstract

Portal thrombosis (PT) is a rare condition of heterogeneous etiologies. The aim of our work is to study the epidemiological and etiological profile of portal thrombosis in non cirrhotic patients through the experience of our department. **Patients and Methods:** This is a retrospective study over a 9-year period (January 2009-July 2018), 54 cases of PT in non cirrhotic patients were collected in the department of Hepato-Gastro-Enterology of the HASSAN II Fez Hospital, 73 cases of PT were excluded among cirrhotic patients. **Results:** We collected 54 cases of PT cases; the average age was 45 years, with an F/M ratio of 1.42. PT was revealed by abdominal pain in 20 cases, complications of portal hypertension in 24 cases, and ultrasound discovery in 10 asymptomatic cases. Main underlying causes of PT were: A proteine S deficiency in 7 cases, Acute pancreatitis in 5 cases, colonic cancer in 4 cases, pancreatic cancer in 4 cases, Hydatic liver Echinococcoses (3 cases), anti phospholipid syndrom (3 cases), myeloproliferative syndrom (2 cases) and jak mutation 2 in 1 case, non identified etiology was reported in 20 cases (37%). Treatment was based on anticoagulation, treatment of portal hypertension complications, and etiological treatment in cases where etiological diagnosis was certainly posed. **Conclusion:** PT is a rare but serious condition, according to our study neoplastic causes are predominant followed by protein S deficiency. Etiological investigations have to be wide and early treatment is the best option to avoid extension and complication.

Keywords

Portal Thrombosis, Etiology, Anticoagulant, Non Cirrhotic

1. Introduction

Portal thrombosis is a cruoric or neoplastic obstruction, total or partial, of the portal vein and/or one of its branches, right or left, more or less extended to the spleno-mesenteric network. The incidence of recent or chronic portal vein thrombosis in adults is estimated at 0.7/100,000 inhabitants/year and the prevalence at 3/100,000 inhabitants in Europe [1] [2]. Apart from cirrhosis, multiple risk factors are identified. Nevertheless, it is advisable to remain attentive to a hidden cirrhotic cause. Finding a cause is essential for optimal patient management. An elasticity < 10 kpa can rule out cirrhosis in adults [3]. In the absence of cirrhosis, many general prothrombotic factors and/or premises are present at respectively 60% and 30% of patients (Table 1). However no cause is identified in one third of cases (1, 23). The research thrombophilia must be systematic, ideally collected before starting anticoagulant treatment, without delaying it [4] [5] [6]. The aim of this work is to study the epidemiological and etiological profile of portal thrombosis through the experience of our department.

2. Materials and Methods

This is a retrospective study over a period of 9 years (January 2009-July 2018), 54 cases of PT were collected at the Hepato-Gastro-Enterology department of HASSAN II University Hospital Fez, 73 cases were excluded because of underlying cirrhosis. Epidemiological, clinical, paraclinical, therapeutic and evolutionary data were analyzed.

Table 1. Etiological factors of portal vein thrombosis.

Study	Benjilali *et al.* 2016 [3]	Our study
Behcet disease	10; 32.2%	2; 3.7%
Oral contraceptives	4; 12.9%	2; 3.7%
Idiopatic	4; 12.9%	20; 37%
Myeloproliferative syndrom	2; 6.45%	2; 3.7%
Hereditary thrombophylia	1; 3.2%	7; 12.9%
Systemic erythematous lupus	1; 3.2%	0
Antiphospholipid syndrom	1; 3.2%	3; 5.5%
coeliac disease	1; 3.2%	2; 3.7%
cancers	0	8; 14.8%
pancreatitis	0	5; 9.2%
others	2; 6.4%	5; 9.2%

3. Results

Fifty-four patients were included, with a median age of 45 years (19 - 73 years) with a F/M sex ratio of 1.42. The majority of PT were chronic giving clinical ultrasound and CT scan data (62.96%). Abdominal pain was the predominant symptom in the acute forms (37.03%) while the signs of portal hypertension predominated in the chronic forms (37.03%). In 10 patients (18.5%), the discovery of PT was fortuitous during an abdominal imaging for other reasons.

Past medical history reported diabetes in 10 cases (18.5%); Past history of recurrent miscarriages in 7 cases (13%), 3 cases of cholecystectomy, and 3 cases of venous thrombosis of the lower limbs (5.6%).

Laboratory examination showed an inflammatory syndrome in acute PT (33% of PT cases) with an average C reactive protein value of 87 mg/L (28 - 320 mg/L). The highest CRP value was 220 mg/L and was noted during a mesenteric infarction. Signs of liver injury such as cytolysis and/or cholestasis were observed in half of the cases of chronic PT mainly affecting the hepatic venous system.

The diagnosis of PT was made by abdominal Doppler ultrasound completed by angio abdominal CT scan. Radiological findings were: complete or partial clot of portal vein, cavernous transformation of the portal vein and signs of portal hypertension. Results of systematic search for underlying causes are showed in Table 1. Deficiency in protein S and C in 7 cases, pancreatitis in (5 cases), colonic cancer (4 cases), pancreatic cancer (4 cases), hydatic liver échinococcose (3 cases), anti phospholipid syndrom (3 cases), 2 cases of Behcet's diseases, Myelo-proliferative Sd (2 cases) with jak 2 mutation in (1 case), oral contraceptives (2 cases), celiac disease (2 cases), as well as 2 cases of inflammatory colitis type-Crohn. Anticoagulants were prescribed to 42 patients (78%) of cases for a period greater than or equal to one year, with treatment of the complications of portal hypertension in 24 cases, band ligation of oesophageal varices and beta-blockers for cases revealed by digestive bleeding, as well as diuretics for PT revealed by ascites, and the aetiologic treatment in cases where the aetiologic diagnosis was certainly made with discontinuation of oral contraception in women who were on oral contraception, gluten-free diet for celiac diseases, background treatment of IBD at basis of anti-TNF in the two patients and cancer treatments for tumor pathologies.

Repermeabilization of the portal vein among patients taking anticoagulant was obtained in 53% of cases, it was total in 33% of cases and partial in 20% of cases. No serious bleeding event secondary to the use of anticoagulants has been noted. The mean follow-up was 17 months (0 - 9 years). Seven patients were lost to follow-up. Five patients had died (16%).

4. Discussion

Portal venous thrombosis refers to an obstruction of the portal system by total or partial thrombosis, which can affect both sexes but with a slight female predominance in the literature (sex ratio: 1.2), and which are observed especially in

young people with an average age at diagnosis of 37 years [3]; in our series the average age was 45 years, with a sex ratio F/M of 1.42, which matches the data in the literature.

Most patients with recent vein thrombosis present with acute abdominal pain [4], however the intensity of the symptoms is very variable from one patient to another, in our series PT was revealed by abdominal pain in 20 patients (37% of cases), and of which 3 of them or 15% were already complicated by mesenteric infarction which is the most severe immediate complication of recent porto-mesenteric venous thrombosis and which can manifest itself more than abdominal pain from organ failure (shock, kidney failure, metabolic acidosis, high arterial lactate level); significant ascites or rectal bleeding [5], In patients who develop a portal cavernoma, rupture of gastroesophageal varices is one of the main complications [6], portal thrombosis has been revealed by complications of portal hypertension in 44.44% of cases (24 cases), of which 6% or 25% were ascites decompensations and 18 cases or 75% were hemorrhagic by isolated hematemesis or hematemesis associated with melena and others by isolated melena.

The etiological factors of PT can be local or systemic. Almost half of patients may have more than one etiologic factor [7]. Local factors are mainly represented by abdominal cancer, inflammation and local infections (pancreatitis, diverticulosis, cholecystitis, appendicitis, inflammatory bowel diseases) and abdominal surgery. Cirrhosis and cancer are the most common local factors, each occurring in about 30% of patients [8] [9] [10] [11]. Systemic etiological factors are mainly represented by myeloproliferative syndromes (MPS) [12], constitutional thrombophilia anomalies, antiphospholipid syndrome, paroxysmal nocturnal hemoglobinuria [13], oral contraception and pregnancy. In general, a general pro thrombotic disorder and a local factor is observed in approximately 60% and 30% of patients respectively. Several factors can be demonstrated in the same patient but in a third of cases, no cause is identified [14]. In our study, the S and C protein deficiency was retained in 7 cases, *i.e.* 12.96%, the PT was secondary to pancreatitis in 5 cases or 9.25%, to colonic Kc 4 cases or 7.40%, pancreatic Kc 4 cases or 7.40%, hydatic liver cyst 3 cases 5.55%, Anti-phospholipid antibody syndrome 3 cases or 5.55%, 2 cases of Behcet's disease, myeloproliferative Sd 2 cases or 3.70% with jak 2 mutation in 1 case or 1.85%, taking oral contraceptives 2 cases or 3.70%, celiac disease 2 cases or 3.70% as well as 2 cases of IBD type Crhon or 3.70%, the aetiology was not determined in 20 cases, ie 30.03% of cases, which showed the multiplicity of the aetiologies of PT (**Table 1**).

The diagnosis of portal thrombosis is based on a first-line Doppler ultrasound which can detect the absence of flow in the portal vein, or a hyperechoic thrombus in the lumen of the portal vein, but the latter may not be visible [15]. Abdominal CT angiography has better sensitivity than Doppler ultrasound or MRI to diagnose portal thrombosis and especially to look for a local cause of recent portal vein thrombosis (acute appendicitis, acute diverticulitis, colon cancer.) as well as signs of intestinal infarction [15]. In our series all our patients benefited from

an ultrasound − Doppler + abdominal CT angiography combination for diagnostic confirmation.

The initial goal of treatment for portal vein thrombosis is to limit the spread of thrombosis and achieve recanalization of thrombosed vessels to prevent mesenteric venous ischemia in the short term and in the longer term to prevent appearance of portal hypertension and its complications. Treatment of the cause and anticoagulant therapy should be initiated as soon as possible [16].

Etiological treatment is essential as an essential part of the treatment of PT. This will involve stopping oral contraception, initiating treatment for a myeloproliferative syndrome or that of the underlying inflammatory or autoimmune disease.

Early anticoagulation is the treatment of choice for acute PT. Several studies have shown its interest in preventing extension and relapse, but also in recanalization. In a study by Plessier *et al.* [17] concerning 83 acute non-cirrhotic PT, 41 splenic vein thrombosis SVT and 55 mesenteric vein thrombosis MVT, anticoagulation prevented the extension of thrombosis in all patients and allowed a recanalization rate of 38% at 6 months and at 1 year to be obtained for PT, 54% for SVT and 61% for MVT. Although the treatment of acute PT is well established, the treatment of chronic PT remains a subject of debate as these patients develop collateral venous circulation and hypertension portal with the consequence of esophageal varices which can be complicated by sometimes fatal bleeding. A study by Condat *et al.* [18] had compared patients with a portal cavernoma and who were or were not on anticoagulants. The treated patients had significantly fewer recurrence of thrombosis compared to untreated subjects and in these patients the bleeding was not increased by the anticoagulation. This therapy should therefore be discussed on a case-by-case basis in cases of chronic DVT, taking into account the risk of extension of thrombosis and the existence of a permanent prothrombotic risk factor (namely a myeloproliferative syndrome, paroxysmal hemoglobinuria nocturnal, antiphospholipid syndrome, Behcet's disease, homozygous V Leiden factor, homozygous factor II mutation), superior mesenteric vein obstruction and history of intestinal ischemia [19]. The history of esophageal bleeding or the existence of esophageal varices well controlled by usual therapies do not constitute a contraindication to anticoagulants [19].

In our study, anticoagulants were prescribed in 78% of cases for a period greater than or equal to one year, with treatment of complications of PH in 24 cases, *i.e.* 44.44% with ligation of esophageal varices and beta-blockers for cases revealed by digestive bleeding, as well as diuretics for PT revealed by ascites, and the etiological treatment in cases where the etiological diagnosis was certainly made. Whose recanalization was observed in 53% of cases, it was total in 33% of cases and partial in 20% of cases which match the data in the literature where complete recanalization of PT under anticoagulants was obtained in 33% to 45% of cases and partial recanalization in 15% to 35% of cases [20] [21] [22].

Of course there are some limitations of the present study including the small

number of included patients, lack of some data regarding past medical history and long term follow up of some patients.

The prognosis of PT outside of cirrhosis depends essentially on the age and the underlying disease [23] [24] which constitute a real challenge for the clinician due to the multiplicity of etiologies and therefore the complexity of the disease.

5. Conclusion

Thus, the analysis of the results of our series and those of the various studies allows us to situate PT as a rare pathology but with a serious prognosis because of the risk of digestive hemorrhage by rupture of esophageal varices, and other sometimes fatal complications of where the interest of an etiological investigation and to propose an adequate treatment.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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