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Portal Thrombosis: Clinical, Etiological and Therapeutic Aspects in the Hepato-Gastroenterology Department of the Aristide Le Dantec Hospital in Dakar (Senegal)

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Abstract

Background: Portal thrombosis (PT) is a rare pathology. Its prevalence is estimated at 1%. Its consequences depend on the acute or chronic nature, the extent of the clot and the etiology. In Sub-Saharan Africa, very few studies have been devoted to it. **Patients and Method:** The objective of our work was to determine the prevalence of PT and to describe its clinical and etiological presentation as well as its therapeutic management in the Hepato-gastroenterology department of the Aristide Le Dantec hospital in Dakar. This was a retrospective, longitudinal and descriptive study during the period from January 1, 2012, to December 31, 2018. It included all patients followed in ambulatory or inpatient, who presented a PT objectively determined by a medical imaging examination (ultrasound and/or CT scan). Age, gender, clinical and radiological aspects, proposed treatments and etiology of PT were collected. **Results:** We collected 71 observations. The prevalence of PT was 1.9%. The mean age of the patients was 41 years 15 and 75 years. A predominance of men was found with a sex ratio of 2.73. The clinical manifestations were dominated by abdominal pain (74.6%), ascites (35.7%) and gastrointestinal bleeding (25.4%). Imaging allowed the diagnosis to be made in 50 patients on ultrasound and 21 patients on abdominal CT scan. PT was acute in 5 patients and chronic in 66 patients. Thrombosis was complete in 71.4% of cases and extended to the spleno-mesaraic venous trunk and the superior mesenteric vein in 2.8% and 8.4% respectively. Etiological research found cirrhosis complicated by hepatocellular carcinoma in 67.6% of cases, cirrhosis with cruoric

thrombosis in 21.1% of cases, a combined protein C and S deficiency in 1.4% of cases. No aetiology was objectified in 9.9% of cases. Treatment with beta-blockers was initiated in 32 patients. Anticoagulant treatment was performed in one patient. Evolutionarily, no recurrence of bleeding was noted. In the anticoagulated patient, PT remained stable; however, there was no portal vein recanalization. During follow-up, mortality was 74.6% and was related to the underlying pathology in all patients. **Conclusion:** PT has a prevalence of 1.9% in the Hepato-Gastroenterology Department of the Aristide Le Dantec Hospital in Dakar. The chronic form is very dominant and degenerated cirrhosis is the first etiology.

Keywords

Portal Thrombosis, Cirrhosis, Portal Hypertension

1. Introduction

Portal thrombosis (PT) is a venous thrombosis of an unusual site. It is defined as partial or complete occlusion of the portal vein lumen and/or its tributaries by a thrombus. It is a rare condition that can affect both children and adults. Its prevalence is estimated at 1% in an autopsy series in Sweden [1]. Its etiologies are heterogeneous, and a local or general cause can be identified in about 80% of cases. It is most often associated with cirrhosis, hepatocellular carcinoma, local factors (infection, surgery) or a prothrombotic state. PT can be acute or chronic. The clinical manifestations and prognosis of PT vary according to the recent or long-standing nature of the thrombosis, its extent and the underlying etiology(s). Diagnosis is based on imaging, which allows confirmation of the diagnosis, clarification of the extension of the thrombosis and searches for a local cause. In the acute phase, the goal of treatment is to permeabilize the thrombosed vessels and avoid the passage to chronicity. In the portal cavernoma stage, the aim of anticoagulant treatment is to prevent recurrence and extension of the thrombosis to the intestinal venous arches. In Sub-Saharan Africa, very few studies involving PT have been performed. We conducted a 72-month retrospective longitudinal descriptive and analytical study. The objectives of our work were to determine the prevalence of PT and to describe the etiological, clinical and therapeutic profile of patients with PT followed in the Hepato Gastroenterology Department of Aristide Le Dantec Hospital.

2. Patients and Method

The study was conducted in the Hepato Gastroenterology Department of Aristide Le Dantec Hospital. The study covered the period from January 1, 2012, to December 31, 2018 (72 months). It was a retrospective, longitudinal, descriptive and analytical study involving the analysis of patient records. Our study population consisted of all patients followed as outpatients or hospitalized in the He-

pato-Gastroenterology Department of Aristide Le Dantec Hospital during the study period.

We included all patients who presented a PT objectified by an imaging examination (abdominal ultrasound and/or abdominal CT scan). We collected theage, gender, clinical and radiological aspects, proposed treatments and etiology of PT. Data entry and analysis were done with SPHINX (evaluation version) V5 and SPSS 20.0 software. MICROSOFT EXCEL 2007 software was used to design the figures; the PEARSON chi-square test and the FISHER test were used for comparison of proportions, the STUDENT test for comparison of means. The significance level was 0.05 ($p < 0.05$).

3. Results

Our study population consisted of 3736 patients. Of these patients, 71 had PT, a prevalence of 1.9%. The mean age of the patients was 41 years (15 and 75 years). There were 52 men (73.2%), with a sex ratio of 2.73. Two patients had a family history of hepatocellular carcinoma.

There was no personal or family history of thromboembolic disease, thrombophilia, or hematological pathology.

Clinical manifestations were dominated by abdominal pain (74.6%) and digestive bleeding (25.4%). The physical examination showed hepatomegaly in 62%, splenomegaly in 19.7% and ascites in 35.7% (Table 1).

Thrombocytopenia was present in 18 patients (Table 2).

The diagnosis of PT was made by abdominal ultrasound in 50 patients and by abdominal CT scan in 21 patients. Thirteen patients had undergone ultrasound and then secondary abdominal CT for further investigation. PT was acute in 5 patients (7%) and chronic in 66 patients (93%).

Thrombosis was complete in 71.4% of cases and extended to the spleno-mesenteric venous trunk and into the superior mesenteric vein in 8.4% of cases. Extension of the thrombosis to the inferior vena cava, superior mesenteric vein, and spleno-mesenteric trunk was observed in 2 patient, 6 patients, and 2 patients, respectively (Table 3).

Table 1. Socio-demographic and clinical manifestations of the patients.

Characteristics	N = 71
Age, years, mean	41
Male, n (%)	52 (73.2%)
Abdominal pain, n (%)	53 (74.60%)
Jaundice, n (%)	19 (26.80%)
Digestive bleeding, n (%)	18 (25.40%)
Hepatomegaly, n (%)	44 (62%)
Ascites, n (%)	25 (35.70%)
Splenomegaly, n (%)	14 (19.70%)

Table 2. Results of biological explorations of the patients.

Biological investigations	Average	Values Extreme
AST	120 UI/L	16 - 136 UI/L
ALT	75.2 UI/L	8 - 1204 UI/L
Bilirubin	21.3 g/L	1 - 149 g/L
Albumin	35.08 g/L	23 - 50 g/L
TP	73.83%	44% - 100%
AFP	7039.22 UI/mL	0.7 - 1,666,000 UI/mL
Platelets	241,330	76,000 - 607,000

AST = Aspartate aminotransferase; ALT = Alanine aminotransferase; TP = prothrombin level; AFP = alfa-foetoprotein.

Table 3. Results of the abdominal CT scan of the patients.

Anomalies	N (Percentages)
Complete thrombosis	50 (71.4%)
Portal cavernoma	12 (17%)
Splenic varices	10 (14%)
Superior mesenteric vein extension	6 (8.4%)
Splenic vein thrombosis	4 (5.6%)
Extension to the inferior vena cava	2 (2.8%)
Extension to the spleno-mesenteric trunk	2 (2.8%)

Upper GI endoscopy showed esophageal varices in 26 patients (36.6%), gastric varices in 4 patients (5.6%), portal hypertension gastropathy in 13 patients (18.3%).

The etiological factor of PT was found in 90.1%. A local cause was present in 88.7% of cases. It was cirrhosis complicated by hepatocellular carcinoma in 67.6% of cases, cirrhosis with cruciate thrombosis in 21.1% of cases. Due to lack of means, the search for prothrombotic factors was performed in 3 patients and found a combined protein C and S deficiency in one patient (1.4%). No etiology was identified in 9.9% of cases. Anticoagulant treatment with low molecular weight heparin followed by anti-vitamin K therapy was administered to the patient with protein C and S deficiency. None of our patients required thrombectomy or thrombolysis.

Treatment of portal hypertension with beta-blockers was performed in 32 patients.

Esophageal varices were ligated in 12 patients. The immediate evolution was marked by an improvement of the pain, a stop of the digestive bleeding, and a correction of the anemia.

In the anticoagulated patient, the PT remained stable, but there was no permeabilization of the portal vein. In the evolution, no hemorrhagic recurrence was noted. The average length of follow-up was 29 months (3 - 60 months). During the follow-up, mortality was 74.6% and was related to the underlying

Table 4. Correlation between etiology, age, sex, abdominal pain, GI Bleeding and completeness of thrombosis.

Characteristics		Cirrhosis	HCC	Others	p value
Sex	Male	8 (53.3%)	41 (85.4%)	3 (37.5%)	0.530
	Female	7 (46.7%)	7 (14.6%)	5 (62.5%)	0.490
Mean age (years)		40	42	37	0.745
Abdominal pain		8 (15.1%)	40 (75.5%)	5 (9.4%)	0.048
GI bleeding		6 (50%)	3 (25%)	3 (25%)	0.312
Complete thrombosis		10 (23.3%)	26 (60.5%)	7 (16.3%)	0.542

pathology in all patients.

The search for a correlation between etiology, age, sex, abdominal pain, hematemesis, and the completeness or incompleteness of the thrombosis did not find any statistically significant relationship (Table 4).

4. Discussion

PT is a rare condition. Its incidence and prevalence are estimated at 0.7 to 3.7 per 100,000 population, respectively [2] [3].

A study in Sweden of approximately 24.000 autopsies found a prevalence of 1% [1]. The prevalence of PT in our study population was 1.9%. Currently, there is an increase in the incidence of PT, due to the large number of imaging examinations performed in hospital.

PT is a pathology that can affect children and adults with a peak frequency at 6 years and 40 years. In the study, the mean age of patients was 41 years with extremes of 15 and 75 years.

Similar results were found in studies performed in Morocco, Algeria and France [4] [5] [6].

Acute and chronic PTs are different stages of the same disease.

Clinically, PT is considered acute if symptoms appear within 60 days before medical management [7]. In the past, the disease was frequently discovered in the chronic stage. Currently, due to easier access to imaging techniques, diagnosis at the acute stage in adults is more frequent. However, in our study, only 5 patients were found to have PT at the acute stage. This delay in diagnosis could be explained by the often asymptomatic nature of PT and the poor availability of imaging studies in our countries. In our series, clinical manifestations were dominated by abdominal pain which was present in 74.6% of patients. Abdominal pain was present in 77.7% of cases in the study by Abouothman and in 40% in the study by Benhaddou [8]. In the portal cavernoma stage, the revealing signs may be thrombocytopenia, splenomegaly or signs of portal hypertension discovered on endoscopy or abdominal ultrasound.

Gastrointestinal bleeding from ruptured esophageal, gastric, or intestinal varices is currently a relatively rare form of the inaugural manifestations of PT. In

adults, the risk of GI bleeding is present in 20% - 40% of cases [9]. In our series, GI bleeding was objectified in 25.40% of patients.

In the case of PT on cirrhosis, the probability of a variceal hemorrhage is multiplied by 80 to 120 times compared to cirrhotics without PT [9]. This risk of bleeding is 39% in cirrhosis associated with PT and 44% in hepatocellular carcinoma (HCC) [9]. Splenomegaly is the most consistent clinical sign in PT. It can be of any size, causing distension and discomfort. The size of splenomegaly does not correlate with the degree of portal hypertension. It is responsible for hypersplenism. Fourteen patients present splenomegaly in our series (20%).

Ascites are uncommon in PT and occur transiently in the aftermath of GI bleeding, renal failure, or severe sepsis in an elderly subject. Ascites were present in 25 patients (35.7%). Most patients in the study had advanced cirrhosis and ascites are the main complication of cirrhosis.

Ultrasound is the key examination for diagnosis. It is a simple, non-invasive, accessible and reproducible examination. It allows demonstrating the direct image of the thrombus as an echogenic intraluminal material. This technique is generally sufficient for the diagnosis of PT in 60% to 100% of cases. However, it remains "operator-dependent" and sometimes difficult to interpret. In these situations, CT is interested because of the study of the liver and its vascularization. In our series, the diagnosis of PT was made by abdominal ultrasound in 70% of cases. CT has the advantage of being a sensitive method for the diagnosis of PT and the search for the extension of the thrombosis within the portal system, as well as in the mesenteric venous network. It is also relevant in the etiological diagnosis, especially for local causes. In our study, extension to the superior mesenteric vein, spleno-mesenteric trunk and inferior vena cava were present in 8.4%, 2.8% and 2.8% of cases, respectively.

The etiologies of PT are multifactorial. It may be a local cause, a prothrombotic condition, or a combination of both. A local cause is found in 40% of cases and a general cause in 60% of cases according to the series [10]. In our series, a local cause was present in 93% of cases. A Moroccan study conducted between 2004 and 2008 found a local cause in 75% of cases [4].

Analysis of cross-sectional studies of patients with cirrhosis shows an overall prevalence of extrahepatic PT of 10% to 15% [11] [12].

The prevalence of PT increases with the severity of cirrhosis, from approximately 1% in patients with compensated cirrhosis [13] to 8% - 25% in liver transplant candidates [11] [14].

In patients with cirrhosis, portal vein obstruction is most often related to HCC invasion. Rarely the thrombus is of cruciate origin [15]. In our study, cirrhosis complicated by cruciate thrombosis was present in 21.1% of patients. In advanced cirrhosis, slowing of portal vein flow and increased portal pressure are the cause of PT formation in cirrhosis [15]. Cruoric thrombus in the portal vein is often partial and changes in appearance and location during follow-up. The few longitudinal studies available show that in almost half of the cases the sub-

sequent examination shows a decrease in thrombus size and an increase in 15% of the cases [16] [17]. In our study, cirrhosis was present in 70.8% of patients and cirrhosis was decompensated in 96.8% of cases.

In cases of cirrhosis, in most cases, partial thrombosis (mean prevalence of 10%) and much more rarely thrombosis completely occluding the lumen (mean prevalence of 3%) was present [9]. Contrary to what is described in the literature, in our series, thrombosis was complete in 71.4% of cases. The Moroccan study found similar rates (80%) of complete thrombosis [4].

In compensated cirrhotic patients, the coexistence of an underlying thrombophilia could be considered. Indeed, cirrhotic patients with PT have an increased prevalence of mutations in the factor V Leiden gene and the prothrombin gene compared to those without PT [18]. It is important to assess for thrombophilia in cirrhotic patients who present with PT. In our study, two patients had compensated cirrhosis. However, in these patients, the thrombophilia work-up could not be performed because of its high cost. In our study, cirrhosis complicated by HCC was present in 67.5% of cases and PT was complete in 60.5% of cases on ultrasound.

PT is a frequent complication of HCC, associated with a poor prognosis. Approximately 10% - 40% of patients with HCC have PT at diagnosis and approximately 35% - 44% will have PT at the time of death or liver transplantation [19]. The presence of PT in HCC exposes a higher risk of metastasis, reduces treatment options, and results in decreased survival compared to patients without PT. In patients with PT treated with supportive care, studies have reported overall survival ranging from two to four months, compared with 10 - 24 months in HCC patients without PT [19] [20] [21]. Incomplete thrombosis has a better prognosis than complete thrombosis.

The management of patients with HCC complicated by PT remains particularly challenging.

Liver transplantation is generally contraindicated in these patients because of the high recurrence rates. Curative liver resection is controversial and rarely used in expert US and European centers, but may offer favorable overall survival in some patients. Currently, in patients who are not candidates for surgery, various therapies, sorafenib, selective or supra-selective chemoembolization, and selective internal yttrium-90 radioembolization, may be management options. [22]. In our series, all patients with HCC received symptomatic treatment.

In developed countries, etiological investigation in cases of PT identifies one or more systemic prothrombotic factors in approximately 60% of patients [10].

The frequent finding of multiple prothrombotic disorders in the same individual justifies the need for comprehensive thrombophilia screening, even in the presence of known underlying predisposing factors or obvious abdominal causes.

The frequent finding of multiple prothrombotic disorders in the same individual justifies the need for complete screening for thrombophilia, even in the presence of known underlying predisposing factors or obvious abdominal caus-

es. Conversely, a local factor should be sought even when one or more systemic prothrombotic factors have been identified. This is relevant because it involves important decisions regarding long-term anticoagulation. On the other hand, currently available investigations fail to identify a causative factor in approximately 20% of patients. This suggests the existence of other, yet unidentified, prothrombotic risk factors. In our region, the high cost of investigations limits the search for general factors. In our study, the thrombophilia work-up was performed in 2 patients and allowed the diagnosis of a combined protein C and S deficiency. The etiology was undetermined in 7 patients because the thrombophilia work-up could not be performed. In the West, myeloproliferative syndromes constitute about 30% of the etiologies of PT. Only a few of these patients meet the conventional hematological diagnostic criteria. In most cases, the blood cell count is normal due to hemodilution and hypersplenism. The JAK2 mutation is present in approximately 40% of patients with PT [10]. JAK2 mutation testing has not been performed because of its high cost.

The aim of treatment in the acute phase is to permeabilize the thrombosed vessels and avoid the passage to chronicity. It combines treatment of the local cause and anticoagulants for six months in the absence of underlying disease and for life in the case of a proven or strongly suspected disease that promotes thrombosis. At the portal cavernoma stage, the aim of anticoagulant treatment is to prevent recurrence and extension of the thrombosis to the intestinal venous arches. In our series, anticoagulant therapy was only administered in the patient with protein C and S deficiency. The morbidity of PT is mainly related to bleeding, recurrence of thrombosis, symptomatic portal biliopathy and hypersplenism. Mortality in patients with chronic PT is low (5% - 10% at 5 years) and is mainly related to the age, etiology of PT [10].

In our patients, the evolution was marked by a significant number of deaths with a mortality rate of 74.6%. The circumstances of death were related to the underlying pathology in all patients.

Our study has some limitations. The study was retrospective, and the number of patients was small.

5. Conclusion

PT has a prevalence of 1.9% in the Hepato-Gastroenterology Department of Aristide Le Dantec Hospital in Dakar. The chronic form is very dominant, and cirrhosis complicated by HCC is the primary etiology.

Conflicts of Interest

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

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