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Portal vein thrombosis (PVT): a study of 20 non-cirrhotic cases

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Summary

Background: Portal and mesenteric venous thrombosis (PVT) is an uncommon disease with serious consequences if not discovered early in order to prevent complications such as variceal bleeding and intestinal ischaemia. The objective of this study was to describe the clinical presentation and outcome of patients with PVT with a view to early diagnosis and treatment of this disease. The study was restricted to patients with PVT not caused by underlying liver cirrhosis.

Patients and methods: To analyse important clinical characteristics of this entity we performed a retrospective study of 20 non-cirrhotic patients seen in our hospital from February 1998 to March 2003.

Results: The main clinical symptom was abdominal pain (13 patients, 86%), sometimes in combination with diarrhoea and vomiting (5 patients, 33%), nausea and anorexia (3 patients). Laboratory signs were non-specific and diagnosis was usually by computed tomography (19 patients, 95%). Causative factors included prothrombotic states (9 patients, 45%) and/or local factors (5 patients, 25%). Complications must be expected from portal hypertension (15 patients, 75%), which was associated with variceal bleeding in 6 patients (30%). Bowel ischaemia (5 patients, 25%) and bowel infarction (2 patients) were less frequent. Treatment consisted of immediate anticoagulation in almost all cases (18 patients, 90%), while invasive approaches were followed in selected patients. The prognosis of PVT was good in patients without a severe underlying disease (median follow-up 21 months).

Conclusions: In agreement with other studies our results suggest that early diagnosis and treatment by immediate anticoagulation are important in preventing the serious consequences of portal and mesenteric vein occlusion. The role of more invasive approaches is less well defined. Since in 18 patients (90%) of the non-cirrhotic cases in the present series causative factors were found which may have therapeutic implications, aetiological screening seems worthwhile in every case with PVT.

Key words: portal vein thrombosis; mesenteric venous thrombosis; coagulation disorder; myeloproliferative disease; anticoagulant therapy

Introduction

Due to increased use and improvement of non-invasive imaging techniques in diagnostic evaluation of abdominal pain, acute portomesenteric venous obstruction is an increasingly recognised disorder [1]. Acute portal vein thrombosis (PVT) is distinguished from chronic PVT by the absence of collateral veins, which develop if acute portal vein thrombosis is not recognised at this stage [1–3]. Patients with acute PVT present with non-specific signs and symptoms, rendering the clinical diagnosis difficult. Diagnosis is usually either by ultrasound or CT-scan. Liver cirrhosis is an established cause of PVT and accounts for approximately 11.2% [4]–21.5% [5] of cases. Aetiological factors in non-cirrhotic PVT patients are prothrombotic states (i.e. hypercoagulability, myeloproliferative disorders) in 40–70% and local factors (i.e. intraabdominal inflammatory conditions, surgery, cancer) in 10–50% [5, 6]. Frequently more than one factor is present.

While anticoagulation was the only treatment option until recently, other more invasive therapeutic procedures, especially the use of intravenous or intraarterial catheter techniques, are increasingly used today. Overall mortality in PVT ranges from 2–3% in patients without underlying cirrhosis or malignancy [5, 7]. Age and coexisting conditions, but also time to diagnosis, are factors which appear to influence survival.

There are few published studies describing the clinical features and consequences of PVT [1, 3]. To heighten awareness of PVT we report on our experience of 20 patients with non-cirrhotic PVT seen in a general internal medicine department.

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Patients and methods

Patients were identified by a search in the computerised hospital registration system of our hospital's Department of Internal Medicine. In all of them (39 patients) portal vein thrombosis was diagnosed by either CT, ultrasound or MRI. All patients with liver cirrhosis as an underlying cause of portal vein thrombosis (19 patients, 48%) were excluded from the study. The medical records of the remaining 20 non-cirrhotic patients were reviewed to obtain the following data: *clinical presentation*, including: age at the time of diagnosis, sex, stage of thrombosis (acute or chronic [collaterals established]) and symptoms; *diagnostic procedures*, including: laboratory examinations (full blood count: thrombocytes, leukocytes and erythrocytes, blood chemistry: C-reactive protein, lactic dehydrogenase, aspartate and alanine aminotransferase, alkaline phosphatase, serum amylase and routine coagulation studies) and imaging procedures. *Aetiology:* a causative factor was searched for in the majority of cases. The thrombophilia screen included standard tests for protein C, protein S, antithrombin deficiency, activated protein C resistance (usually FV Leiden), prothrombin G20210A mutation and anti-phospholipid antibodies. Oral contraceptive use and hyperhomocysteinaemia were considered thrombotic risk factors. Myeloproliferative diseases were diagnosed by bone marrow investigation (biopsy and aspirate). *Complications* such as portal hypertension and variceal bleeding were diagnosed by endoscopy and bowel ischaemia/infarction by computed tomography. *Therapy* included anticoagulant therapy, local or systemic lytic therapy with urokinase, catheter thrombectomy or transjugular porto-systemic shunt procedures (TIPS). Variceal treatment was endoscopic (i.e. sclerotherapy or band ligation) or pharmacological (i.e. β-adrenergic blocking agents). *Outcome* was assessed either by following the patients in our clinic or by contacting their family physicians. The median follow-up was 21 (range 2–61) months.

Results

Clinical presentation: The median age at PVT diagnosis of the 20 patients enrolled in this study was 50.5 (range 17–83) years. 50% of patients were male. 15 patients had an acute portal vein occlusion (of whom two also had signs of coexisting chronic PVT) and 5 patients a chronic form. The main presenting symptoms in patients with acute disease was abdominal pain in 13 (86%), less frequent were vomiting with diarrhoea in 5 (33%) and anorexia with nausea in 3. In only one case did the patient present with fever and another with hypotension and haematemesis. In patients with chronic disease only one patient presented with abdominal pain as the sole sign of his disease; all the other 4 patients were asymptomatic (table 1).

Results of diagnostic procedures: Laboratory studies showed leucocytosis, elevated C-reactive protein and elevated lactic dehydrogenase in 10 (66%), 14 (93%) and 7 (of 11 tested, 64%) of the 15 patients with acute PVT. Acute pancreatitis was ruled out by normal amylase levels in all patients. Thrombocytosis was mainly seen in patients with myeloproliferative diseases. Four (out of 5 patients) of our cases with underlying myeloproliferative diseases had elevated thrombocytes, whereas this was seen in only one patient without this condition. Among the 15 acute cases, D-dimers were elevated in all 12 patients tested. Erythrocyte levels were slightly elevated in only two patients, but were normal in 9 (45%) or decreased in a further 9 (45%).

Diagnosis was by computed tomography in 19 (95%) of all cases and in 5 patients (25%) it was first established by ultrasound and later confirmed by computed tomography. In one patient PVT was discovered incidentally in MRI.

Aetiology: Of the twenty patients taking part in our study, 9 (45%) had a prothrombotic disorder. Six (30%) had myeloproliferative disease (diagnosed by bone marrow aspirate and biopsy): essential thrombocythaemia in 4 cases and polycythaemia vera in two. Three patients had a coagulation disorder (two cases of antiphospholipid antibodies and one case of activated-protein-C resistance). These results probably underestimate the prevalence of an underlying prothrombotic disorder, since bone-marrow aspiration and thrombophilia screening were not done in 3 patients. In addition, bone-marrow examination was not conducted in 4 patients and there was no thrombophilia screening in another 4. Prothrombotic risk factors were present in 6 patients (30%): Four were under oral contraceptives (two in combination with a prothrombotic disorder) and two had hyperhomocysteinemia. In 5 (25%) of our patients a local factor alone was the cause of PVT (screening for prothrombotic diseases was done in 3 of these 5 patients): late consequences of surgery in two cases (subtotal gastrectomy and splenectomy), septic cholangitis, chronic pancreatitis and Crohn`s disease were causal factors in 3 other cases. Only in two patients could no aetiological factor be found: in one patient with acute PVT a developing myeloproliferative disease was suspected in view of massive polyglobulia but could not be proven by bone marrow investigation. A test for spontaneous erythroid colony formation was not done.

Complications occurred in the majority of patients. 15 (75%) had signs of portal hypertension, in 6 (30%) variceal bleeding occurred at the time of presentation or during follow-up. Five patients (25%) had evidence of bowel ischaemia in CT scans and in two of them bowel infarction occurred requiring surgical resection of involved bowel. Only 4 of our patients had no complications. Two patients with chronic PVT developed acute PVT as a complication.

Table 1
Main characteristics of study population.

Total sample		**N = 20**	**(100%)**
Median age (years)		50.5	
Males		10	(50%)
Stage of thrombosis			
Acute		13	(65%)
Chronic		5	(25%)
Chronic plus acute		2	(10%)
Manifestation of acute thrombosis			
Abdominal pain		13	(86%)
Vomiting and diarrhoea		5	(33%)
Nausea and anorexia		3	(20%)
Laboratory: elevated parameters	WBC	10	(66%)
	CRP	14	(93%)
11 patients tested	LDH	7	(64%)
12 patients tested	D-dimers	12	(100%)
Diagnostic method (primary diagnosis)			
Computed tomography		14	(70%)
Ultrasound		5	(25%)
Magnetic resonance imaging		1	(5%)
Causal factors of PVT			
Prothrombotic disorder		9	(45%)
Myeloproliferative disease		6	(30%)
Coagulation disorder		3	(15%)
Local factor		5	(25%)
Prothrombotic risk factor only		4	(20%)
Idiopathic		2	(10%)
Complications			
Portal hypertension		15	(75%)
Variceal bleeding		6	(30%)
Bowel ischaemia		5	(25%)
Bowel infarction		2	(10%)
Therapy			
Anticoagulation		18	(90%)
Additional antiplatelet agent		8	(40%)
Conservative (medication only)		11	(55%)
Pharmacomechanical treatment		7	(35%)
Surgery		3	(15%)
Outcome			
Anticoagulation		17	(85%)
Deaths due to PVT		0	0

Therapy: 18 (90%) of all PVT patients received immediate anticoagulation with heparin (one of the two non-anticoagulated patients presented with hypovolaemic shock due to gastrointestinal haemorrhage and the other patient had chronic asymptomatic PVT and no prothrombotic risk factors). Pharmacomechanical management and surgery were additionally performed in 10 patients (50%). Pharmacomechanical treatment in 7 cases (35%) included transjugular porto-systemic shunting, catheter thrombectomy and thrombolytic therapy with transcatheter delivery of a thrombolytic agent (urokinase), administered directly into the superior mesenteric vein or intra-arterially. TIPS was attempted in 6 patients (30%) followed by local thrombolysis and thrombectomy in 3 of them due to shunt-rethrombosis. One patient underwent arterial thrombolysis followed by venous thrombolysis and thrombectomy for insufficient venous return. Band ligation of bleeding varices was necessary in 3, resection of infarcted bowel in two other cases and liver transplantation due to fulminant liver failure in a further patient with simultaneous Budd-Chiari syndrome. In addition, two patients received folic acid to treat hyperhomocysteinaemia and a further two were treated with a β-adrenergic blocking agent as prophylaxis for variceal bleeding.

Outcome: Transjugular porto-systemic shunting was performed successfully in one patient, while in 3 others venous thrombolytic therapy and catheter thrombectomy had to be performed after TIPS due to shunt rethrombosis; in all 3 patients this procedure was ultimately successful. In two patients TIPS was not possible at all because a large portal vein was not accessible. 17 (85%) of our patients stayed on oral anticoagulation at the end of follow-up. Only 3 patients received no anticoagulation, in view of contraindications or absence of thrombotic risk factors. All patients with acute PVT due to myeloproliferative disease also received an antiplatelet agent (aspirin in 5 patients or clopidogrel in one). Three patients died as a consequence of their underlying diseases. Patient 1 died at age 50 from a brain tumour (glioblastoma multiforme) and patient 2 died at age 71 as a consequence of a metastatic stomach carcinoma. The myeloproliferative disease of patient 3 progressed to acute myeloid leukaemia and this patient died from a septic embolisation to the brain during induction therapy at age 40.

Discussion

We analysed a cohort of 20 noncirrhotic patients with portal vein thrombosis (PVT) seen in a general internal medicine setting. Median age at the time of diagnosis was 50.5 years, with ages ranging from 17–83 years.

Clinical presentation: Acute PVT usually presents with abdominal pain that is typically not explained by physical or laboratory findings. About one third of our cases additionally presented with vomiting and diarrhoea. The laboratory results were also non-specific in our study, although leucocytosis, elevated C-reactive protein and lactic dehydrogenase were usually present. D-dimer levels were elevated in all cases tested, and thus appear to be a sensitive but probably not very specific indicator of acute thrombosis in the portal vein also. Nevertheless, the combination of acute abdominal pain and elevated D-dimer levels should arouse suspicion of thrombosis in the portal and/or mesenteric veins.

Diagnosis: In agreement with other studies, computed tomography is the diagnostic tool of choice. As well as serving to diagnose mesenteric venous thrombosis and visualise the thrombus, CT allows complete examination of the structure of the bowel, the detection of potential complications such as bowel ischaemia and perforation, and identification of potential precipitating causes of the thrombosis (e.g. pancreatic pathology).

Aetiology: In most of our cases one or more known causative factors were identified. Their relative frequency was in agreement with the results of previous studies investigating the causes of PVT [5, 6, 8]. These causative factors are divisible into two main groups: prothrombotic disorders (including prothrombotic risk factors) and local factors, with a prevalence of 65% and 25% respectively in our study. In only two cases could no cause be identified, although screening was done in both patients. The group of prothrombotic disorders includes myeloproliferative diseases, coagulation disorders and prothrombotic risk factors, with a contribution of 46%, 23% and 31% respectively. While risk factors such as oestrogen-containing oral contraceptives are reported to account for 4%–9% of the episodes of mesenteric venous thrombosis in women [9], the role of hyperhomocysteinemia is still controversial [10, 11].

The group of local causes leading to PVT consists of various factors such as inflammatory diseases (i.e. cholangitis, pylephlebitis [12], pancreatitis [1], inflammatory bowel disease [13]), injuries due to trauma (i.e. blunt abdominal trauma [14]) or surgery (i.e. intra-abdominal operations, especially splenectomy [15]) and malignancies compressing and/or invading the portal vein (in particular hepatocellular, pancreatic or gastric carcinoma).

Therapy: Spontaneous repermeation of a PVT is possible but uncommon. On the other hand, complete or extensive repermeation can be achieved with anticoagulant therapy. The effect of anticoagulant therapy is to prevent not only rethrombosis but also extension of thrombosis into the portal venous system, thereby preventing an increase in portal pressure [2, 7]. Initial treatment of PVT should therefore be anticoagulation with heparin if there is no evident risk of bleeding. This recommendation is supported by a recent study showing a favourable benefit-risk ratio for anticoagulant therapy in patients with acute portal vein thrombosis. Anticoagulation should be maintained for at least six months and continued depending on the cause of thrombosis [2, 7]. Although our patient number is small, in our experience the addition of an antiplatelet agent in patients with a myeloproliferative disease appears not to increase the risk of bleeding. Other more invasive modes of treatment are transjugular catheterisation of occluded veins, local thrombolytic infusions directly into the thrombus or into the superior mesenteric artery, the creation of a transjugular portosystemic shunt, stent implantation and mechanical thrombectomy [16–18]. Only small studies have been reported and the benefit of these procedures remains unclear at present. Measures to prevent variceal bleeding should be taken according to recommendations derived from the management of cirrhotic patients [19, 20].

Outcome: In agreement with other studies, the prognosis of non-cirrhotic PVT is generally good. Outcome is primarily determined by the under-

lying disease leading to portal vein occlusion and not by PVT and its consequences [5, 7].

Our series suggests that PVT is an important differential diagnosis in patients presenting with abdominal pain out of proportion to the physical findings and with a negative workup for the common causes of abdominal pain. Raised D-dimer levels may be a diagnostic hint. Once PVT is diagnosed by CT, patients should be anticoagulated and examined for any prothrombotic tendency or local pathology possibly affecting the portal venous system.

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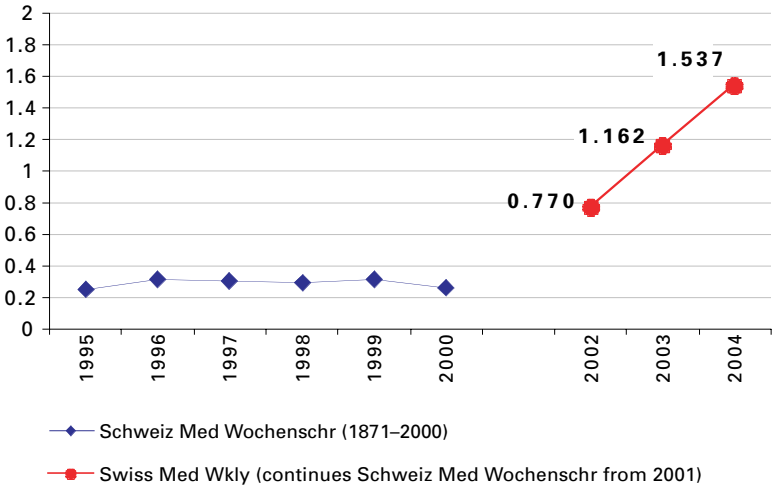

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