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Local Factors Favouring the Development of Portal Vein Thrombosis

Czynniki miejscowe sprzyjające rozwojowi zakrzepicy żyły wrotnej

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Abstract

Background. Recently, portal vein thrombosis (PVT) is being recognised with increasing frequency with ultrasonography, especially using Doppler ultrasonography. The local factors play an important role in development of PVT and these factors explain why in the course of a chronic and generalised state of thrombophilia, thrombosis develops suddenly in the portal vein. The local factors can be classified into four categories: local inflammatory lesions, injury of the portal system, cancer of the abdominal organs and liver cirrhosis.

Objectives. Defining the role of the local factors favouring development of PVT.

Material and Methods. Between 1996 and 2002 the authors identified 35 patients with clinical symptoms of PVT (15 males and 20 females, aged 18 to 80, mean 29.2 years). These patients were examined with duplex and color Doppler ultrasound. To ascertain a possible cause of PVT and associated local factors, the authors analyzed the clinical history for all these patients as well as previous medical records.

Results. The local factors were identified with 24 patients (68.6%) and with the remaining 11 patients (31.4%) were unknown. The local inflammatory lesions were diagnosed with 5 patients, the injury of the portal venous system with 2 patients, cancer of abdominal organs with 5 patients and liver cirrhosis with 12 patients. The HCV infection as a cause of liver cirrhosis was found with 2 patients. The toxic injury of liver was established with 3 patients. The liver cirrhosis developed on the basis of primary biliary cirrhosis with 2 patients and of primary sclerosing cholangitis with the 2 other patients as well as on the basis of autoimmune hepatitis with 3 patients. Most patients with whom the local factors were not found, have had symptoms of portal hypertension from childhood.

Conclusions. It is possible the establishment of local factors provoke PVT with most patients. Liver cirrhosis, irrespectively of its etiology, is the most frequent local factor favouring the development of PVT. Local factors are difficult for establishment with the patients who have had the portal hypertension and PVT since childhood (Adv Clin Exp Med 2005, 14, 4, 711–715).

Key words: portal vein thrombosis, local factors.

Streszczenie

Wprowadzenie. Zakrzepica żyły wrotnej jest rozpoznawana coraz częściej dzięki ultrasonografii, szczególnie dopplerowskiej. Istotną rolę w rozwoju zakrzepicy układu wrotnego odgrywają czynniki lokalne, które pozwalają wyjaśnić, dlaczego w przebiegu uogólnionej trombofilii dochodzi do zakrzepicy właśnie w układzie wrotnym. Wśród czynników lokalnych można wyróżnić cztery grupy: miejscowe stany zapalne, mechaniczne urazy układu wrotnego, nowotwory narządów jamy brzusznej i marskość wątroby.

Cel pracy. Ustalenie roli czynników lokalnych sprzyjających rozwojowi zakrzepicy żyły wrotnej.

Materiał i metody. W latach 1996–2002, posługując się ultrasonografią dopplerowską, zidentyfikowano 35 chorych z zakrzepicą żyły wrotnej (15 mężczyzn i 20 kobiet, w wieku 18–80 lat, średnio 29,2). Analizowano występowanie lokalnych czynników sprzyjających zakrzepicy żyły wrotnej na podstawie danych z dokumentacji medycznej.

Wyniki. Lokalne czynniki zidentyfikowano u 24 (68,6%) chorych z zakrzepicą żyły wrotnej. U 11 chorych (31,4%) pozostały one nieznane. U 5 chorych rozpoznano miejscowe stany zapalne narządów jamy brzusznej, u 2 chorych uszkodzenie układu wrotnego. Nowotwory narządów jamy brzusznej występowały u 5, a marskość wątroby u 12 chorych. Przyczyną marskości wątroby u 2 chorych było przewlekłe zakażenie HCV, u 3 alkoholowa choroba wątroby, u 2 pierwotne stwardniające zapalenie dróg żółciowych, u 2 pierwotna marskość żółciowa wątroby, a u kolejnych 3 autoimmunologiczne zapalenie wątroby. Większość chorych, u których nie udało się zidentyfikować czynnika lokalnego sprzyjającego zakrzepicy żyły wrotnej, miała objawy nadciśnienia wrotnego od dzieciństwa.

Wnioski. U większości chorych jest możliwe ustalenie miejscowych czynników sprzyjających zakrzepicy żyły wrotnej. Marskość wątroby, niezależnie od etiologii, jest najczęstszym czynnikiem miejscowym. Obecność czynnika miejscowego jest trudna do ustalenia u chorych z objawami zakrzepicy i nadciśnienia wrotnego występującymi od dzieciństwa (*Adv Clin Exp Med* 2005, 14, 4, 711–715).

Słowa kluczowe: zakrzepica żyły wrotnej, czynniki miejscowe.

The signs and symptoms of portal vein thrombosis (PVT) are relatively non-specific and include the onset or the worsening of ascites, abdominal pain or distension, gastrointestinal bleeding due to the oesophageal varices, spleen enlargement [1, 2]. Recently, PVT is being recognised with the increasing frequency with ultrasonography, especially with Doppler ultrasonography [3]. The most important findings that permit the diagnosis of PVT is absence of portal flow which is accompanied by echogenic material within the portal vein lumen [4]. If the portal vein thrombus persists without the substantial lysis, the portal vein undergoes fibrosis and may vanish from the sonographic perspective [4]. The cavernous transformation of portal vein is the principal manifestation of chronic PVT [5]. It is recanalisation of the portal venous system with development of periportal collateral channels. Cavernous transformation produces a distinctive tangle of tortuous vessels in the porta hepatis. The exact frequency of PVT remained unknown. In patients with liver cirrhosis the incidence of PVT ranges between 0.6% and 26% [6, 7] and those with hepatocellular carcinoma is about 30% [8, 9]. According to the recent reports, the venous thromboses occur when several factors coincide [10]. These factors are classified as: the inherited ones (e.g. deficiencies in protein C, in protein S and antithrombin III, factor V Leiden mutation, factor II G20210 mutation, C677T methylenetetrahydrofolate reductase gene mutation) or the acquired prothrombotic disorders and thrombophilic factors (e.g. myeloproliferative disorders, estrogen therapy) and local factors [11, 12]. The local factors play an important role in development of PVT and these factors explain why in the course of a chronic and generalised state of thrombophilia, thrombosis suddenly develops in the portal vein. The local factors can be classified into four categories: local inflammatory lesions, injury of the portal system, cancer of abdominal organs and liver cirrhosis [1, 12].

The aim of this study was to define the role of the local factors favouring the development of PVT.

Material and Methods

In the years between 1996 and 2002 the authors identified 35 patients with the clinically apparent symptoms of PVT (15 males and 20 fe-

males, aged 18 to 80, mean 29.2 years). These patients were examined with the duplex and colour Doppler ultrasound. The sonographic diagnosis of PVT was made as follows: echogenic material filled the portal trunk or its branches completely (no venous Doppler signals were detected) or partly (Doppler signals were detected around the clot) or signs of cavernous transformation of the portal vein (when the mass of tortuous vessels was found at the porta hepatis or within the liver) [4, 5]. The examinations were performed by means of Ultramark 9 (Advanced Technology Laboratories, WA) with a 3.5 MHz convex probe and a 2.5 MHz pulsed Doppler device. The Doppler settings were optimised in each case. The Doppler examination was made with the fasting patients. To ascertain the possible cause of PVT and the associated local factors, the authors analyzed the clinical history for all these patients as well as the previous medical records were available. The diagnosis of liver cirrhosis was confirmed by the histopathological examinations or only by the clinical data when a liver biopsy was impossible because of haemostatic alterations. The etiology of liver cirrhosis was ascertained according to the conventional diagnostic criteria: the presence in of ANA and ASMA in serum with the patients with autoimmune hepatitis (AIH), AMA with patients with primary biliary cirrhosis (PBC), HCV-RNA and anti-HCV with the patients infected by HCV and the characteristic image of ERCP with the patients with primary sclerosing cholangitis (PSC). All malignant lesions were confirmed by histopathological examination.

Results

The local factors were identified with 24 patients (68.6%) and with the remaining 11 patients (31.4%) were unknown. The local inflammatory lesions were diagnosed with 5 patients, the injury of the portal venous system with 2 patients, cancer of abdominal organs with 5 patients and liver cirrhosis with 12 patients. The HCV infection as a cause of liver cirrhosis was found with 2 patients. The toxic injury of liver was established with 3 patients. The liver cirrhosis developed on the basis of PBC with 2 patients and of PSC with the 2 other patients as well as on the basis of AIH

with 3 patients (Tables 1, 2). Most patients with whom the local factors were not found, have had symptoms of portal hypertension from childhood. The first episode of gastrointestinal bleeding appeared with these patients at the age of one to eight years. One patient suffered from the myeloproliferative syndrome, and 3 women were taking the estrogen therapy. The cavernous transformation of portal vein (CT) was observed with 10 patients with the identified local factors, the total portal vein thrombosis (TPVT) with 8 patients and the partial portal vein thrombosis (PPVT) with 6 patients. The history of gastrointestinal bleeding was apparent with 6 patients suffering from the liver cirrhosis and with 1 not suffering from this disorder.

Discussion

The local factors are found with about 25 to 75 percent of patients with PVT [12]. In the study by Denninger et al. [12], the local factors were identified with 10 of the 36 patients with PVT. There were splenectomy, *Bacteroides pylephlebitis* infection, cholecystectomy (each of those factors apparent with 2 patients), whereas umbilical cannulation, abdominal trauma, colon adenocarcinoma and intestinal obstruction (each of those factors apparent with 1 patient). In this study, the patients with the liver cirrhosis and liver, pancreas and bile ducts cancers were excluded [12]. Małkowski et al. [13] observed the liver cirrhosis in 33 percent, liver neoplasm in 4 percent, chronic pancreatitis in

Table 1. Characterization of patients with portal vein thrombosis

Tabela 1. Charakterystyka pacjentów z zakrzepicą żyły wrotnej

Local factors (Miejscowe czynniki)	Age/Gender (Wiek/płeć)	US Doppler Image (Ultrasonografia dopplerowska)	Gastrointestinal bleeding (Krwawienie z przewodu pokarmowego)	Esophageal varices/grade (Żylaki przełyku/ stopień)
Local inflammatory lesions (Miejscowe stany zapalne)				
Acute pancreatitis	27/F	CT	Y	Y/I
Chronic pancreatitis	45/M	CT	N	N
Inflammatory tumour (colon)	23/F	CT	N	Y/II
Chronic pancreatitis	52/M	CT	N	N
Liver abscess	47/M	TT	N	Y/I
Injury of the portal venous system (Uszkodzenie układu wrotnego)				
Abdomen trauma	47/F	CT	N	Y/II
Pancreatectomy	33/F	CT	N	Y/I
Cancer of abdominal organs (Nowotwory narządów jamy brzusznej)				
Neurofibrosarcoma	54/F	CT	N	Y/I
Pancreas cancer	52/M	TT	N	N (SV)
Stomach cancer	62/M	CT	N	N
Bile ducts cancer	65/M	TT	N	N
Hepatoma	40/F	PT	N	N
Liver cirrhosis (Ch-P score) (Marskość wątroby)				
Toxic (A)	40/M	CT	Y	Y/III
PSC (A)	21/M	TT	Y	Y/II
PBC (B)	47/F	TT	Y	Y/I
PBC (C)	47/F	TT	N	Y/II
AIH (C)	61/F	TT	N	Y/I
Toxic (A)	30/F	PT	N	N
PSC (A)	21/M	CT	Y	Y/I
AIH (B)	40/M	TT	N	Y/I
HCV (A)	80/M	PT	N	Y/I
Toxic (A)	36/F	PT	N	Y/I
AIH (A)	32/M	PT	Y	Y/II
HCV (A)	19/F	PT	Y	Y/I

PT – partial thrombosis, TT – total thrombosis, CT – cavernous transformation, SV – stomach varices, Y – yes, N – no.

PT – częściowa zakrzepica, TT – całkowita zakrzepica, CT – przekształcenie jamiste, SV – żylaki żołądka, Y – tak, N – nie.

Table 2. Local factors in patients with portal vein thrombosis**Tabela 2.** Czynniki miejscowe u chorych z zakrzepicą żyły wrotnej

Local factors (Miejscowe czynniki)	No of pts – men (Liczba punktów – mężczyźni)	No of pts – women (Liczba punktów – kobiety)	%
Local inflammatory lesions (Miejscowe stany zapalne)	3	2	14.3
Injury of the portal venous system (Uszkodzenie układu wrotnego)	–	2	5.7
Cancer of abdominal organs (Nowotwory narządów jamy brzusznej)	3	2	14.3
Liver cirrhosis (Marskość wątroby)	6	6	34.3
Toxic	(1)	(2)	
AIH	(2)	(1)	
PBC	–	(2)	
PSC	(2)	–	
HCV infection	(1)	(1)	
Other (unknown local factors) Inne (nieznane czynniki lokalne)	3	8	31.4
Portal hypertension from childhood	(3)	(4)	
Estrogen therapy		(3)	
Myeloproliferative syndrome		(1)	

1.3 percent out of 225 patients with PVT. In this study, 1.3 percent of patients with PVT underwent surgical operations. In the study by Ścieszka [14] who analyzed 35 patients with PVT, the liver cirrhosis was diagnosed with 48 percent, the injury to the portal venous system with 8 percent, the local inflammatory lesions with 11 percent and the cancer of abdominal organs with 8 percent. In present study, the authors identified the local factors with about 70 percent of patients with PVT. According to the studies by Małkowski and Ścieszka [13, 14], the liver cirrhosis was the most frequent local factor contributory to the development of PVT, but in these studies, the etiology of liver cirrhosis were not analyzed. In present study, the liver cirrhosis developed on the basis of HCV infection, autoimmune alterations (PBC, PSC, AIH) and alcohol abuse. It seems that etiology of liver cirrhosis and the degree of alteration of liver function (according to Child-Plough scale) does not influence the frequency of PVT, but the further re-

search is required. The cavernous transformation was less observed with the patients with the liver cirrhosis than the other patients. This is probably connected with the “double block” in the portal system (prehepatic and intrahepatic).

Most patients with the unknown local factors manifested the signs of portal hypertension since childhood [15]. With those patients, the first most frequent symptom was gastrointestinal bleeding due to the oesophageal varices. The establishment of local factors was impossible despite the accurate analysis of clinical histories and the previous medical records.

PVT should be suspected with the patients with the contributory local factors whose clinical status deteriorates, especially when apparent are ascites, abdominal pain, splenomegaly and gastrointestinal bleeding. The early diagnosis of PVT and the adequate anticoagulant therapy results benefits to those patients [16].

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