Pylephlebitis: Incidence and prognosis in a tertiary hospital

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A R T I C L E  I N F O

Article history:
Received 14 January 2013
Accepted 5 September 2013
Available online 17 May 2014

Keywords:
Septic thrombophlebitis
Pylephlebitis
Intra-abdominal infection

A B S T R A C T

Objectives: Septic thrombophlebitis of the portal vein or its branches, most often secondary to intra-abdominal infection is known as pylephlebitis. The frequency and the prognosis of this complication are unknown. The aim of this study was to determine the global and relative incidence of the most frequent intra-abdominal infections and the real prognosis of this disease.

Methods: An observational retrospective study was conducted in a tertiary care hospital (University Hospital of Salamanca, Spain) from January 1999 to December 2008.

Results: A total of 7796 patients with intra-abdominal infection were evaluated, of whom 13 (0.6%) had been diagnosed with pylephlebitis. Diverticulitis was the most frequent underlying process, followed by biliary infection. Early mortality was 23%. Survivors had no recurrences, but one of them developed portal cavernomatosis.

Conclusions: Pylephlebitis is a rare complication of intra-abdominal infection, with a high early mortality, but with a good prognosis for survivors.

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Pileflebitis: incidencia y prognosis en un hospital terciario

R E S U M E N

Objetivos: La tromboflebitis séptica de la vena porta o de sus ramas se conoce como pylephlebitis. En la mayoría de ocasiones es secundaria a infecciones intraabdominales. La frecuencia y el pronóstico de esta complicación infecciosa no son conocidas. El objetivo de este estudio es describir la incidencia global, relativa y el pronóstico real de esta enfermedad respecto a las infecciones intraabdominales más frecuentes.

Métodos: Estudio observacional retrospectivo en un hospital de tercer nivel (Hospital Universitario de Salamanca) desde enero de 1999 a diciembre de 2008.

Resultados: Se evaluó a 7.796 pacientes con infecciones intraabdominales. Trece (0.6%) fueron diagnosticados de pylephlebitis. La diverticulitis fue el proceso subyacente más frecuente, seguida de la infección biliar. La mortalidad precoz fue del 23%. Los pacientes que sobrevivieron no presentaron recurrencias, pero uno de ellos desarrolló una cavernomatosis portal.

Conclusions: La pylephlebitis es una complicación poco frecuente de las infecciones intraabdominales. Presenta una elevada mortalidad precoz, pero tiene un buen pronóstico vital para los pacientes que sobreviven.

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Introduction

Pylephlebitis is septic thrombophlebitis of the portal vein or its branches.1 Although it has been described as a primary form, it normally occurs secondary to infectious intra-abdominal processes. On one hand, these are frequently accompanied by a selective bacteremia of the mesenteric or portal veins,2 which predisposes the development of thrombosis of the portal vein or its branches. On the other hand, the infection may spread to the tree from the biliary tract or superinfected pancreatic necrosis. In addition, pylephlebitis has been seen as an iatrogenic complication secondary to liver biopsy.3

Definitive diagnosis of pylephlebitis requires percutaneous drainage of purulent material from the portal tree.4 In practice, however, the diagnosis is based on a high index of suspicion of the presence of an infectious process and visualising intra-abdominal thrombosis or gas in the portal venous system, after ruling out other potential causes of portal thrombosis.5

Existing data in the literature so far is based on case reports or short case series. It is probable that the increased use of abdominal ultrasonography and CT may be responsible for the increased number of cases of pylephlebitis diagnosed.1,3–7 However, based on these studies it is difficult to estimate the incidence, relative frequency, morbidity and the presence of late complications of different intra-abdominal infections.

The aim of this paper is to describe the incidence of pylephlebitis in our environment, and more fully understand the outcome of such infections and the associated late complications.

Patients and methods

The design was an observational retrospective study. We reviewed the medical records from January 1999 to December 2008 in the University Hospital of Salamanca. A systematic search of pylephlebitis was made in the following diagnoses: (i) acute diverticulitis (CIE IX = 562.11), (ii) acute appendicitis (CIE IX = 540.9), (iii) acute cholecystitis (associated with calculi: CIE IX = 574.8; without calculi: CIE IX = 575.1), (iv) acute cholangitis (CIE IX = 576.1), and (v) bowel perforation (CIE IX = 531.9 and 532.9) only including those who had secondary peritonitis. The diagnosis of pylephlebitis was considered in the patients with the following circumstances: (i) percutaneous drainage of purulent material of portal vein or one of its branches, (ii) the existence of clinical evidence of systemic inflammatory response and radiological findings suggestive of thrombosis of the portal vein or one of its branches in the absence of other causes of portal thrombosis. We excluded patients with advanced cirrhosis, hepatoma or previous diagnosis of portal hypertension or portal thrombosis.

The BACTEC 9240 blood-culture system (Becton Dickinson Diagnostic Instrument Systems, Sparks, MD) with a standard aerobic and anaerobic medium was used in all blood samples.

In the study of thrombophilia, activity antithrombin, protein C and protein S were measured by chromogenic substrate assays (HemosIL, MA, USA). FV Leiden, prothrombin 20210G>A and C677T MTHFR mutations (heterozygous mutation in the methylenetetrahydrofolate reductase gene) were demonstrated by polymerase chain reactions.3,9 Lupus anticoagulant (LA) was detected using diluted Russell’s viper venom time (LAC screen, Instrumentation Laboratory). LA-positive samples were identified by mixing studies and a confirmation test (LAC confirm, HemosIL, MA, USA). An enzyme-linked immunosorbent assay (ELISA, Diamedix Diagnostics, Inc-Florida) was used to assess aCL (IgG and IgM antibody isotypes) and anti-β2GPI. Levels of homocysteine were measured by high-performance liquid chromatography.10

We estimated the incidence of pylephlebitis in the Salamanca province out of the total population on the 1st of January 1999

(351,128 inhabitants). Statistical tests were carried out using the SPSS Statistical Package 20 (SPSS Inc., Chicago, IL). The results are expressed as means and SDs or medians, ranges and percentages.

Results

During the study period a total of 7796 patients with diagnoses of intra-abdominal infection were admitted (Table 1): 3305 (42.3%) patients with acute infectious disease of the biliary tract (1890 lithiasis with acute cholecystitis, acalculous acute cholecystitis 536, 879 with acute cholangitis), 3088 (39.6%) with acute appendicitis, 569 (7.2%) with abdominal perforation and 834 (10.6%) with acute diverticulitis.

Among these patients, 0.16% of total population met the diagnostic criteria of pylephlebitis. The detected cases of pylephlebitis are summarised in Table 2. The average age of these patients was 64.7 years, with a range of 17–90 years; nine patients were male (69.2%). Pylephlebitis occurred in all the states studied, although the most frequent was in patients with diverticulitis with three cases, followed by infections of the biliary duct (cholangitis and/or cholecystitis) in six cases. Pylephlebitis only complicated three (0.09%) cases of appendicitis, although only CT imaging was only performed in 5% of patients diagnosed with appendicitis. The cumulative incidence was 0.37 cases per 100,000 inhabitants/year.

The median time between the initial abdominal infection and hospital admission was three days (range 1–60) and the time between the final diagnosis of pylephlebitis was eight days post-admission (range 1–15). The diagnosis was made in eight patients due to the persistence of SIRS after abdominal surgery and the remaining 10 because the septic symptoms continued after conservative management with antibiotic treatment of intra-abdominal infectious process.

The radiological findings on CT of portal vein thrombosis were seen in thirteen cases and in two of these, gas was also visualised. Thrombosis affecting the superior mesenteric vein was seen in seven (53.8%) cases and in five in the splenic vein (38.4%). Ten patients diagnosed of pylephlebitis had previously ultrasound but this only detected evidence of thrombosis in four (40%).

Blood cultures were positive in eight (61.5%) patients. Microbiological agents most frequently detected were Escherichia coli in six cases (46.1%), Streptococcus viridans in three (23.0%) cases and one case of each of Bacteroides sp., Enterococcus faecium, Enterococcus faecalis and Enterobacter cloaceae (7.6%). Only three (23.0%) of our patients had mixed bacteremia. Thrombophilia screening was performed in seven (53.8%) of the thirteen patients included in the study. In three (23.0%) thrombophilia was detected: one patient was heterozygous for factor V Leiden, hyperhomocysteinemia and other two patients had heterozygous mutations for MTHFR. Other prothrombic factors predisposing to thrombosis included one case of intestinal lymphoma and one of non-cirrhotic alcoholic liver disease.

12 patients received antibiotic treatment (92.3%). Empirical antibiotics were used: (in order of frequency) five had piperacillin and tazobactam (38.4%), three were prescribed carbapenems (23.0%), two had piperacillin, tazobactam and an aminoglycoside (15.2%), or the combination of cephalosporin-metronidazole

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>Cases (no.)</th>
<th>CT available (no.)</th>
<th>Pylephlebitis (no./%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diverticulitis</td>
<td>834</td>
<td>463</td>
<td>3(0.34)</td>
</tr>
<tr>
<td>Appendicitis</td>
<td>3088</td>
<td>176</td>
<td>3(0.09)</td>
</tr>
<tr>
<td>Biliary infection</td>
<td>3305</td>
<td>808</td>
<td>6(0.18)</td>
</tr>
<tr>
<td>Intestinal perforation</td>
<td>569</td>
<td>97</td>
<td>1(0.17)</td>
</tr>
<tr>
<td>Total</td>
<td>7796</td>
<td>1544</td>
<td>13</td>
</tr>
</tbody>
</table>
Table 2
Cases of pylephlebitis studied. Main clinical characteristics and evolution.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age/sex</th>
<th>Underlying infection</th>
<th>Underlying thrombophylic</th>
<th>Delay (days)</th>
<th>Blood isolated</th>
<th>Diagnosis method</th>
<th>Vein affected</th>
<th>Complication</th>
<th>Anticoagulation</th>
<th>Outcome (m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20/M</td>
<td>Operated appendicitis Factor V Leiden</td>
<td>Operated appendicitis Factor V Leiden</td>
<td>8</td>
<td>E. coli S. faecium S. group viridans Bacteroides sp.</td>
<td>CT scanning</td>
<td>PVT, SMVT, SVT</td>
<td>Portal hypertension Splenomegaly</td>
<td>LMWH/acenocoumarol 6 m</td>
<td>Cured Permeation (3 m)</td>
</tr>
<tr>
<td>2</td>
<td>73/M</td>
<td>Operated appendicitis Lymphoma</td>
<td>Operated appendicitis Lymphoma</td>
<td>7</td>
<td>E. coli</td>
<td>CT scanning</td>
<td>PVT, SMVT</td>
<td>Splenic ischaemia Shock Portal hypertension Portal cavernomatosis Esophageal varices</td>
<td>LMWH/acenocoumarol 12 m</td>
<td>Died</td>
</tr>
<tr>
<td>3</td>
<td>65/M</td>
<td>Cholecystitis MTHFR mutation</td>
<td>MTHFR mutation</td>
<td>12</td>
<td>E. cloacae E. faecalis</td>
<td>CT scanning</td>
<td>PVT, SMVT</td>
<td>Portal hypertension Portal cavernomatosis</td>
<td>LMWH/acenocoumarol 12 m</td>
<td>Cured Permeation (8 m)</td>
</tr>
<tr>
<td>4</td>
<td>81/M</td>
<td>Cholecystitis N/A</td>
<td>Cholecystitis N/A</td>
<td>11</td>
<td>E. coli</td>
<td>CT scanning</td>
<td>PVT, SMVT</td>
<td>No</td>
<td>LMWH/acenocoumarol treatment for life LMWH 10 days</td>
<td>Cured Permeation (3 m)</td>
</tr>
<tr>
<td>5</td>
<td>88/F</td>
<td>Diverticulitis N/A</td>
<td>Diverticulitis N/A</td>
<td>8</td>
<td>Negative</td>
<td>CT scanning</td>
<td>PVT, SVT</td>
<td>Portal hypertension Splenomegaly Multiple abscesses</td>
<td>LMWH/acenocoumarol 12 m</td>
<td>Cured Permeation (1 m)</td>
</tr>
<tr>
<td>6</td>
<td>52/M</td>
<td>Cholangitis Negative</td>
<td>Cholangitis Negative</td>
<td>8</td>
<td>E. coli</td>
<td>CT scanning</td>
<td>PVT</td>
<td>No</td>
<td>LMWH/acenocoumarol 12 m</td>
<td>Cured Permeation (4 m)</td>
</tr>
<tr>
<td>7</td>
<td>71/M 17/M</td>
<td>Cholecystitis/cholangitis Operated appendicitis</td>
<td>Operated appendicitis MTHFR mutation</td>
<td>8</td>
<td>Negative</td>
<td>CT scanning</td>
<td>PVT, SMVT, SVT</td>
<td>Multiple abscesses Portal cavernomatosis</td>
<td>LMWH/acenocoumarol 6 m</td>
<td>Cured Permeation (8 m)</td>
</tr>
<tr>
<td>8</td>
<td>85/F</td>
<td>Perforation N/A</td>
<td>Perforation N/A</td>
<td>1</td>
<td>Negative</td>
<td>CT scanning</td>
<td>Aeroportia, PVT, SMVT, SVT</td>
<td>Intestinal ischaemia Shock No</td>
<td>LMWH/acenocoumarol 6 m</td>
<td>Cured Permeation (&lt;1 m)</td>
</tr>
<tr>
<td>9</td>
<td>69/F</td>
<td>Cholangitis Negative</td>
<td>Cholangitis Negative</td>
<td>6</td>
<td>Negative</td>
<td>CT scanning</td>
<td>PVT</td>
<td>No Abscesses</td>
<td>LMWH 10 days LMWH/acenocoumarol 6 m</td>
<td>Not monitored Cured Cured Permeation (3 m) Not monitored &gt; 3 m</td>
</tr>
<tr>
<td>10</td>
<td>61/M</td>
<td>Diverticulitis Negative</td>
<td>Diverticulitis Negative</td>
<td>13</td>
<td>S. group viridans E. coli</td>
<td>CT scanning</td>
<td>PVT</td>
<td>No</td>
<td>LMWH 10 days LMWH/acenocoumarol 6 m</td>
<td>Not monitored Cured Cured Permeation (3 m) Not monitored &gt; 3 m</td>
</tr>
<tr>
<td>11</td>
<td>90/F</td>
<td>Cholangitis N/A</td>
<td>Cholangitis N/A</td>
<td>1</td>
<td>S. group viridans E. coli</td>
<td>CT scanning</td>
<td>Aeroportia, PVT</td>
<td>Intestinal ischaemia Shock No</td>
<td>LMWH/acenocoumarol 6 m</td>
<td>Cured Permeation (1 m)</td>
</tr>
<tr>
<td>12</td>
<td>70/M</td>
<td>Diverticulitis N/A</td>
<td>Diverticulitis N/A</td>
<td>10</td>
<td>Negative</td>
<td>CT scanning</td>
<td>PVT</td>
<td>No</td>
<td>LMWH/acenocoumarol 6 m</td>
<td>Cured Permeation (1 m)</td>
</tr>
</tbody>
</table>

N/A: Not available.
Delay: time between the beginning of symptoms of pylephlebitis and diagnosis.
Vein affected: PVT, portal vein thrombosis; SMVT, superior mesenteric vein thrombosis; SVT, splenic vein thrombosis.
In our series, we found an association between anticoagulation and mortality (100% non-anticoagulated mortality vs 0% in the anticoagulated). This association is due to an obvious selection bias, due to the catastrophic deterioration in these patients with shock and multiorgan failure that did not allow time for early initiation of anticoagulant therapy before the patient died. The small number of patients determines the conclusions of our work. Indeed, death may be due to other causes.

A recent retrospective study also showed a lower mortality among patients who received anticoagulant therapy, although the information in the study did not exclude obvious selection bias of patients. No patients received percutaneous drainage of the portal vein, a technique that has proven effective in the diagnosis and treatment of this pathology.

Follow-up after discharge of survivors occurred for seven of the ten surviving patients with a median time of twelve weeks. No patients had evidence of recurrence of infection and in all those in whom reperfusion was detected, none displayed clinical signs of portal hypertension. Reperfusion was detected in 14% of non-anticoagulated and 25% of the anticoagulated. This high degree of reperfusion detected in our series compared with previous series justifies the exclusion of patients with chronic portal vein thrombosis and favours an early diagnosis and treatment of our patients.

In conclusion, pylephlebitis remains an uncommon disease in intra-abdominal infections with high morbidity and early mortality; nevertheless, prolonged treatment with antibiotics and anticoagulants is associated with a low recurrence rate and a high probability of reperfusion of the portal system.
Conflict of interest

The authors declare no conflict of interest.

Acknowledgment

We are grateful to Elisabeth Kane for their help with the translation.

References