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Analysis of variables predictive of severity in biliary peritonitis

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SUMMARY: **Analysis of variables predictive of severity in biliary peritonitis.**

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Objective. *To analyze clinical and laboratory findings in order to find variables predictive of severity of Biliary Peritonitis (BP).*

Patients and methods. *Physical findings, course of illness, imaging and laboratory data were evaluated in 22 patients with BP, and statistically analysed to assess their prognostic significance.*

Results. *Serious illness and worse outcome were associated with: age > 60 years (P=0.034), long time between onset of symptoms and treatment (P=0.025), fever > 38°C (P=0.009), WBC count > 17.000 cell/mm³ (P=0.043), diffuse abdominal pain (P=0.034), and infected bile (P=0.048).*

Conclusions. *Most patients become severely ill due to supervening infection, while early bile drainage avoids serious complications. In addition, abdominal pain, fever and WBC count are also predictive of severity of BP.*

RIASSUNTO: **Analisi dei fattori prognostici nelle peritoniti biliari.**

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Obiettivo. *Analizzare le caratteristiche cliniche ed i dati di laboratorio al fine di individuare i fattori prognostici negativi nelle peritoniti biliari (PB).*

Pazienti e metodi. *Analisi delle caratteristiche cliniche, decorso della malattia, dati di laboratorio e radiologici di 22 pazienti affetti da PB e successiva analisi statistica per valutarne il loro significato prognostico.*

Risultati. *Un decorso grave con prognosi infausta e associato a: età maggiore di 60 anni (P=0.034), maggior tempo intercorso tra inizio della sintomatologia e trattamento (P=0.025), febbre > 38°C (P=0.034), conta dei globuli bianchi maggiore di 17,000 cell/mm³ (P=0.043), dolore addominale diffuso (P=0.034) e presenza di bile infetta (P=0.048).*

Conclusioni. *Il decorso clinico di molti pazienti peggiora in seguito al verificarsi di una infezione; pertanto un rapido drenaggio della bile diminuisce la comparsa di serie complicanze. Inoltre, dolore addominale diffuso, febbre alta e marcata leucocitosi sono predittivi di una prognosi peggiore.*

KEY WORDS: Biliary peritonitis - Bile drainage.
Peritoniti biliari - Drenaggio biliare.

Introduction

The term biliary peritonitis (BP) includes a wide spectrum of different clinical situations. Clinical experience and previous researches have not shown any relationship between early onset of clinical findings and prognosis, therefore it is difficult to identify clinical signs predictive of the severity of prognosis of BP (1, 2). In fact, a number of patients who become severely ill never show any obvious abdominal sign(s) (3). Peritoneal signs alone are not reliable to predict severity and outcome of BP due to delay of their onset, which contributes to increase both mortality (8-40%) and morbidity (20-30%) (4-6).

Purpose of the present study was to retrospectively perform a statistical analysis of demographic, clinical, and laboratory data in a cohort of patients with BP, in order to identify any possible factors predictive of severity and of a poor prognosis.

Patients and methods

One thousand two hundred and forty four patients with acute peritonitis were admitted to the Department of Surgery "P. Valdo-

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ni", "Sapienza" University of Rome Medical School, Rome, Italy, between January 2000 and December 2007. Of these, 22 patients (1.8%) had BP and their medical records were reviewed. All cases of bile collection in the abdominal cavity were classified as BP. Diagnosis was based on medical history and clinical findings supported by ultrasonographic evidence of abdominal fluid collection.

The reviewed variables included demography, pre- and post-operative physical signs and symptoms, and laboratory results (hematology, diagnostic imaging, pathology and microbiology). Therefore, we considered: age; gender; time between onset of symptoms and drainage; abdominal pain (diffuse or localized); occurrence of nausea, vomiting, jaundice; peritoneal signs (abdominal tenderness and rebound); fever; WBC count; serum level of bilirubin (total and conjugated), ALP; volume of bile collection, and bile microbiology analysis. Data recorded were evaluated at the admission of patients to the hospital. Treatment strategies, length of hospital stay, morbidity and mortality rates were also evaluated.

All patients received intravenous fluids, analgesics and antibiotics; nasogastric decompression was routinely employed. Drainage of abdominal bile collection was the first step in the management of these patients. Subsequently, the underlying cause for bile leakage was sought in each case and tailored different therapeutic measures. Surgery was performed on 17 patients (77.3%), and interventional radiology techniques in 5 (22.7%). Patients were divided in two groups: **group A** (patients with BP, but no serious complications and a benign outcome), **group B** (patients with BP, who had a severe progression of the condition and eventually died).

Results

Seventeen patients were assigned to group A, 5 to group B. Overall mortality was 5 patients (22.7%) and morbidity 6 (27.3%).

In our experience, BP followed acute cholecystitis in 12 cases (54.5%), hepatobiliary surgery in 7 cases (31.8%), and abdominal trauma in 3 cases (13.6%).

Mean overall age of the studied population was 62 years (range 19/82 years); 10 of these were males and 12 females. Thirteen patients (59.1%) were over 60 years. Time between onset of symptoms and drainage ranged from 2 to 17 days (mean 7 days); length of hospital stay ranged between 7-70 days (mean 24 days). Statistical relevance and differences by groups for these variables are reported in Table 1.

Diffuse abdominal pain was present in 8/17 cases (47.1%) of group A and in 5/5 cases (100%) of group B (P=0.034); 9/17 cases of group A (52.9%) *vs* no patients of group B reported abdominal pain localized to the right upper quadrant (RUQ) (P=not significant, n. s.). Nausea and vomiting were detected in 7 (41.2%) and in 6 (35.3%) patients of group A, and in 4 (80.0%) and 3 (60.0%) individuals of group B (P=n. s.). No statistical differences in peritoneal signs (e.g., abdominal tenderness, rebound, etc.) were noted in group A compared to group B (group A = 4/17 or 23.5% patients *vs* group B = 2/5 or 40.0%; P=n.s.). Jaundice was recorded in 29.4 % of group A (5/17 patients), and in 40.0% of group B (2/5) (P=n. s.). Fever, ranging from 37 to 39.5°C (mean 37.8°C), was overall recorded in 77.3%, and a temperature >38°C was detected in 17.6% of patients of group A (3/17 patients) and in 80% of patients of group B (4/5 patients) (P=0.009).

TABLE 1 - DEMOGRAPHIC CHARACTERISTICS IN THE TWO STUDY GROUPS.

	Group A (no. = 17)	Group B (no. = 5)	P
Age, mean ± SD (years)	58±20	74±8	n.s.
Age > 60 years, % (no.)	47.1 (8)	100 (5)	0.034
Gender Male, % (no.)	35.3 (6)	80.0 (4)	n.s.
Female, % (no.)	64.7 (11)	20.0 (1)	n.s.
Time between onset of symptoms and drainage, mean±SD (days)	4±2	12±5	0.025

Mean serum levels of ALP was 272 U/L, bilirubin (total, tot. and conjugated, conj.) 2.05 mg/dl and 1.10 mg/dl respectively. Mean overall WBC count was 16.420 cells/mm^3 (range 8,520–34,200 cells/mm^3); WBC>17,000 cell/mm^3 was found in 9 cases belonging to both groups. No statistical differences were observed with regard to ALP and bilirubin levels (P=n.s.), while WBC count >17.000 cell/mm^3 was found in 29.4% of group A and 80% of group B (P=0.043) (Table 2).

Bile volume ricovered at laparotomy in the 17 patients who received surgery ranged between 500 and 3.000 ml (mean 1,200 ml). Microbiology analysis of bile collection drained showed an overall infection rate of 63.6%. *Enterococcus Faecalis* (33%) and *Escherichia Coli* (29%) were the bacteria most frequently detected. Infected bile was observed in 9/17 cases of group A and in 5/5 cases of group B (P=0.048); no significant differences of bile volumes were found in the two groups (P=n. s.) (Table 2).

TABLE 2 - LABORATORY VALUES IN THE TWO STUDY GROUPS.

	Group A (no. = 17)	Group B (no. = 5)	P
WBC, mean ± SD (x10^3 cells/mm^3)	15.2±6.2	20.3±5.1	n.s.
WBC > 17000 cells/mm^3, % (no.)	29.4% (5)	80.0% (4)	0.043
Tot. Bilirubin, mean ± SD (mg/dl)	2.14±2.06	1.71±0.60	n.s.
Conj. Bilirubin, mean ± SD (mg/dl)	1.17±1.64	0.90±0.037	n.s.
ALP, mean ± SD (U/L)	231.8±111.7	435.5±150.6	n.s.
Bile volume, mean ± SD (ml)	1680±899	785±500	n.s.
Infected bile, % (no.)	52.9% (9)	100% (5)	0.048

Discussion and conclusions

Collection of bile in the peritoneal cavity is unusual, representing only 2% of all peritonitis (7-9), and it can be related to a number of causes, such as acute cholecystitis (33-65%), abdominal trauma (16-33%), complications of abdominal surgery (23-41%) (cholecystectomy 60-79%, hepatic resections, 3.5-12%, liver transplantations, 7-13%) (5, 10-17). With regard to acute cholecystitis, free perforation is found only in 1-2% of patients, quite commonly early in the condition when gangrene develops before adhesions seal the gallbladder. Preoperative diagnosis is achieved in less than 50% of such cases (18).

The above reported inconsistent rates mainly depend on different definitions of BP given by different authors. Some consider BP only those cases with collection of infected bile in the abdomen, and severe peritoneal signs and symptoms (3, 5, 19), defining "bile ascites" the presence of bile in the abdomen. Other authors define as BP all abdominal bile collections, regardless of whether this is infected or not, or if there are peritoneal signs, as even sterile bile causes an inflammatory reaction on the peritoneal lining, with damage of the mesothelium and of the capillary endothelium (4, 20). Therefore, in the present study, we defined as BP all bile collections in the abdominal cavity.

In our series, peritoneal signs could be found only in 27.3% of cases, while abdominal pain, nausea and vomiting were common occurrences. As suggested by previous researches (2, 21, 22), we noted that the presence of bile does not necessarily produce a clear clinical picture, and most patients with BP initially complain only of mild, vague, and non-specific abdominal symptoms. In these instances, bile collection remains unsuspected with delay in diagnosis, failure of treatment, and poor outcome. In contrast, only few patients with signs of peritonitis become critically ill and develop serious complications. Therefore, it is difficult to reliably predict the course of BP and to establish the outcome of these patients. Our research confirmed that advanced age (> 60 years) is one of the main risk factors. Tokunaga (23) reported that advanced age is related to septic complications, gangrenous changes and positive bile cultures. Medical conditions (e.g. diabetes mellitus, vascular or renal failure and immunodeficiency) common in elderly people contribute to promote sepsis.

Other studies (20, 24, 25) showed that morbidity and mortality increase in patients with diffuse abdominal pain, fever >38°C and WBC count >18,000 cell/mm^3. Even if these figures do not permit to achieve early diagnosis of BP, our study suggests that they are useful indexes to evaluate step by step the course of disease more than other laboratory findings, such as bilirubine and ALP (24, 25). Evidence shows that most patients become severely ill due to supervening infection, and length of time that bile remains in the abdomen is associated to a poorer prognosis. In our research, delayed drainage of bile was associated with higher incidence of severe illness, as normally sterile bile in the abdominal cavity eventually becomes infected with positive cultures (26). Researches carried out on animals have shown: 1) bile salts constitute the toxic component of bile, 2) large amounts of bile in the abdomen can be rapidly lethal, and 3) mortality is greater if the bile is infected (27). Therefore, patients who initially do not show infected bile should be promptly treated, as they would ultimately develop a time-related septic process.

In conclusion, we recommended high index of suspicion for all patients in whom a BP could be justified, especially with advanced age (>60 years), and even in presence of mild clinical signs, as absence of peritonitis is common but does not imply a less severe disease. Early use of diagnostic imaging is recommended, and as soon as collection of bile is ascertained, this should immediately be drained in order to avoid serious complications. Besides, abdominal pain, fever and WBC count represent useful indexes to follow the course of the disease and to prevent ominous complications.

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