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Severity in biliary peritonitis

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SUMMARY: **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 42 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: **Valutazione prognostica di gravità nelle peritoniti biliari.**

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Obiettivo. *Analizzare i risultati clinici e di laboratorio in modo da identificare variabili predittive della gravità delle peritoniti biliari (PB).*

Pazienti e metodi. *Sono stati valutati 42 pazienti con PB analizzando dati clinici, decorso della malattia, dati diagnostici strumentali e di laboratorio per stimare statisticamente il loro valore prognostico.*

Risultati. *Malattia grave e prognosi peggiore erano associati a: età ≥ 60 anni (P=0.025), ritardato trattamento (P = 0.025), febbre ≥ 38°C (P=0.009), conta dei globuli bianchi ≥ 17.000 cell/mm³ (P=0.043), diffuso dolore addominale (P=0.034), e bile infetta (P=0.048).*

Conclusioni. *La maggior parte dei malati sono peggiorati per sopravvenuta infezione, mentre il drenaggio precoce della bile evita gravi complicanze. Inoltre, il dolore addominale, la febbre e la conta dei globuli bianchi risultano essere predittivi di gravità della PB.*

KEY WORDS: Biliary peritonitis - Severity - Prognosis.
Peritonite biliare - Gravità - Prognosi.

Introduction

The term "Biliary Peritonitis" (BP) includes a huge spectrum of different clinical conditions.

Clinical experience and previous researches in literature 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 addition, a number of patients who become severely ill never shows any obvious abdominal sign(s) (3). Peritoneal signs alone cold not be 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). Objective of the present study was to retrospectively perform a statistical analysis of demographic, clinical, and laboratory findings in a cohort of patients with BP, in order to identify any possible factors predictive of severity and of a worse prognosis.

Patients and methods

One thousand two hundred and forty four patients with acute peritonitis were admitted to the "P. Valdoni" Department of Surgery, "Sapienza" University of Rome Medical School, Rome, Italy,

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between January 2000 and December 2012. Of these, 42 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 US evidence of abdominal fluid collection.

The reviewed variables included demography, pre- and post-operative physical signs and symptoms, laboratory results (hematology), imaging, pathology and microbiology. In addition, we considered: age; gender; time between onset of symptoms and drainage; abdominal pain (diffuse or localized); occurrence of nausea, vomiting and jaundice; peritoneal signs (abdominal tenderness and rebound pain); 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. Then we evaluated treatment strategies, length of hospital stay, morbidity and mortality rates.

All patients received intravenous fluids, analgesics and antibiotics; nasogastric decompression was routinely employed. Drainage of abdominal bile collection was the first step in these patients. Subsequently, the underlying cause for bile leakage was sought in each case and tailored different therapeutic measures. Surgery was performed on 37 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 favorable outcome), group B (patients with BP, who had a severe progression of the condition and eventually died).

Statistical analysis

Variables were submitted to univariate analysis to evaluate the prognostic relevance of collated data. Data in the records regarding laboratory findings, age and fever were compiled using continue and class values. The results are presented as means with standard deviation (SD) for normally distributed data, or medians with percentiles for non-normal distributions. Differences between groups were assessed by two-sided unpaired and paired t-test as appropriate for continuous data, and by analysis of frequency distribution (c^2 statistics) for categorical data. Statistical analysis was performed using SPSS 9 statistical software and a probability value of less than 0.05 was considered significant.

Results

Thirty-seven 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 22 cases (54.5%), hepatobiliary surgery in 14 cases (31.8%), and abdominal trauma in 6 cases (13.6%).

Mean overall age of the studied population was 62 years (range 19/82 years); 20 of these were males and 22 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 16/37 cases (47.1%) of group A and in 5/5 cases (100%) of group B (P=0.034); 9/37 cases of group A (52.9%) *vs* no patients of group B reported abdominal pain localized to the right upper quadrant (RUQ) (P = n.s.). Nausea and vomiting were present in 7 (41.2%) and in 6 (35.3%) patients of group A, and in 4 (80.0%) and 3 (60.0%) patients 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= 4/37 or 23.5% patients *vs* group B=2/5 or 40.0%; P = n.s.). Jaundice was recorded in 29.4 % in group A (5/37 patients), and in 40.0% of group B (2/5) (P = n.s.) (Table 2). 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 (3/37 patients) and in 80% of patients of group B (4/5 patients)(P=0.009).

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 cells/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 cells/mm^3 was found in 29.4% of group A and 80% of group B (P=0.043) (Table 3).

Bile volume recovered at laparotomy in the 37 operated patients ranged between 500 and 3,000 ml (mean = 1,200 ml). Microbiology analysis of bile col-

TABLE 1 - DEMOGRAPHIC CHARACTERISTICS IN THE TWO STUDY GROUPS.

	Group A (No. = 37)	Group B (No. = 5)	P
Age, mean ± SD, years	58 ± 20	74 ± 8	n.s.
Age ≥ 60 years, %	47.1	100	0.034
Gender			
Male, %	35.3	80.0	n.s.
Female, %	64.7	20.0	n.s
Time between onset of symptoms and drainage ± SD (days)	4 ± 2	12 ± 5	0.025

TABLE 2 - CLINICAL FINDINGS IN THE TWO STUDY GROUPS.

	Group A (No. = 37)	Group B (No. = 5)	P
Abdominal pain, %			
diffuse	47.1	100	0.034
localized in RUQ	52.9	0.0	n.s.
Nausea, %	41.2	80.0	n.s.
Vomiting, %	35.3	60.0	n.s.
Peritoneal signs, %	23.5	40.0	n.s.
Jaundice, %	29.4	40.0	n.s.
Fever > 38 °C, %	17.6	80.0	0.009

TABLE 3 - LABORATORY IN THE TWO STUDY GROUPS.

	Group A (No. = 37)	Group B (No. = 5)	P
WBC, mean ± SD x10³ cells/mm³	15.2 ± 6.2	20.3 ± 5.1	n.s.
WBC > 17,000 cells/mm³, %	29.4	80.0	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, %	52.9	100	0.048

lection 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 9/37 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 1).

Discussion

Collection of bile in the peritoneal cavity is unusual, representing only 2% of all peritonitis (7-9) reported in literature, 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). 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). Other authors define as BP all abdominal bile collections, as even sterile bile causes an inflammatory reaction on the peritoneal lining, with damage of the mesothelium and of the capillary endothelium (4,20). 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. 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. 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 (20-25) showed that morbidity and mortality increase in patients with diffuse abdominal pain, fever >38 °C and WBC count >18,000 cells/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 shown 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. 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). Therefore, patients who initially do not show infected bile should nonetheless be promptly treated, as they would ultimately develop a time-related septic process.

Conclusion

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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