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Original Article

Frequency of portal and systemic bacteremia in acute appendicitis

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Abstract

Background: Acute appendicitis is the most common condition requiring an emergency abdominal operation in childhood. In the present study, we analyzed the frequency of portal and systemic bacteremia in 42 patients with acute appendicitis and determined the microbial agents responsible for an acute appendicitis and for portal and systemic bacteremia.

Methods: Appendectomies were performed on 50 young patients (5–18 years of age), as well as clinical and bacteriological tests. Six independent samples from each patient isolated from the peripheral vein, superior mesenteric vein, appendix and peritoneum were obtained prior to surgery, during surgery and after surgery for biochemical, immunologic and bacteriologic examination.

Results: Pathohistology confirmed the diagnosis of appendicitis in 42 patients, while in the other eight patients there were no obvious pathologic findings, so they served as a control group. Of 50 patients with a clinical appearance of acute appendicitis, in 19 patients (38%) we detected portal bacteremia in the mesenteric vein, while in only three cases (6%) did we find systemic bacteremia detected from the peripheral vein. Furthermore, bacteriologic analysis revealed that *Bacteroides* spp. and *Escherichia coli* were the predominant species isolated.

Conclusions: The results presented in this paper suggests that portal bacteremia did not influence peripheral blood reactions. Furthermore, in the present study we have found a positive correlation between the smear and bacteremia of the superior mesenteric vein, but not with the bacteremia of systemic blood.

Key words acute appendicitis, portal bacteremia, systemic bacteremia.

Acute appendicitis is the most frequent cause of acute abdomen.[1] It appears at any age, but most often occurs between the ages of 10 and 30 years and rarely before the age of 2 years. The risk of perforation is greatest in 1–4-year-old children and lowest in the adolescent age group. The first successful appendectomy was performed by Morton in 1887 and, within the next 3 years, it became the method of choice in treatment of an acute appendicitis. Because the appendix is not an immunologic organ, its removal does not influence function overall.[2]

Bacterial flora of the appendix is complex and intercomparable with colon flora,[3] where approximately 400 different bacterial species have been identified to date.[4] Usually 3.1 aerobic or facultative anaerobic species (the latter utilize oxygen to generate energy by respiration if it is present, but can use the fermentation pathway to synthesize ATP in the absence of sufficient oxygen) and 8.5 anaerobic species can be found in the average sample.[5] The distribution of bacterial species in acute appendicitis reveals that anaerobic bacteria are isolated more frequently than aerobic bacteria. However, *Escherichia coli* is the most frequent aerobic bacteria, while *Bacteroides fragilis* is the most frequent anaerobic species found in acute appendicitis. Nonetheless, *B. fragilis* is the most common isolate.[6] Furthermore, it has been demonstrated that the anaerobic species increasingly colonize the appendix and ileum in most reported cases.[7] It is evident that some bacteria may pass the intact appendiceal wall prior to perforation, while progressive infection and subsequent tissue damage with necrosis allows bacteria to move into the peritoneal cavity.[8] In the present study, we tried to determine the frequency of portal and systemic bacteremia in 42 patients with acute

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appendicitis. The aim of the present study was also to determine the microbial agent responsible for acute appendicitis and for portal and systemic bacteremia, with regard to the immunologic status of the patients.

Methods

In the present study we analyzed 50 patients who subsequently underwent appendectomy. Thirty-one were male, while 19 were female. According to age, patients were divided into three categories (under 5 years, 6–12 years and over 12 years). Two patients (one male and one female) were in the first category, 22 patients (14 male and eight female) were in the second category and 26 patients (17 male and nine female) were in the third category. Six different samples were obtained for biochemical, immunologic and bacteriologic examination from each patient analyzed. Blood samples were collected by peripheral vein puncture, 30 min preceding surgical procedure (I Sample). A second blood sample was obtained from the cubital (II Sample) and superior mesenteric veins (III Sample) during the surgical procedure. Sample III was obtained by puncturing the ileocolic vein, a tributary of the superior mesenteric vein that drains blood from the cecum and appendix. During the surgical procedure, aspiration of the appendix (IV Sample) was also performed in order to obtain material for bacteriologic and pathohistologic analysis. In addition, blood samples were drawn for biochemical and hemoculture analysis 5 h after the surgical procedure had been completed (V Sample). Peritoneal smears were analyzed for the presence of infectious species (VI Sample). To analyze the response of all patients upon acute inflammation, we examined the erythrocyte sedimentation rate (ESR), leukocyte count, differential blood count, C3 and C4 complements, IgG and IgM, aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), glutamyl transpeptidase (GGT), bilirubin, total proteins, protein electrophoresis and prothrombin time. The laboratory analyses were performed five times: 30 min prior to the surgical procedures and for 4 consecutive postoperative days.

To isolate aerobic and/or anaerobic bacteria, 10 mL blood was injected into an anaerobic or aerobic broth culture bottle (HEMOSEPT; Komed, Zagreb, Croatia) and bottles were incubated for 10 days at 37°C. Samples were directly cultured into broth optimized for aerobic growth (rate 1 + 9) in liquid nutrient media and were resuspended in solid-enriched and selective media. Antibiotic sensitivity testing was also performed. Anaerobic broths were transferred onto triptone soya blood agar (Biolife, Milano, Italy) with 5% sheep's blood enriched with vitamin K_1 and hemin. Anaerobic cultures were identified morphologically (Gram stain) and by biochemical BioMerrieux series (BioMerrieux, Milano, Italy).

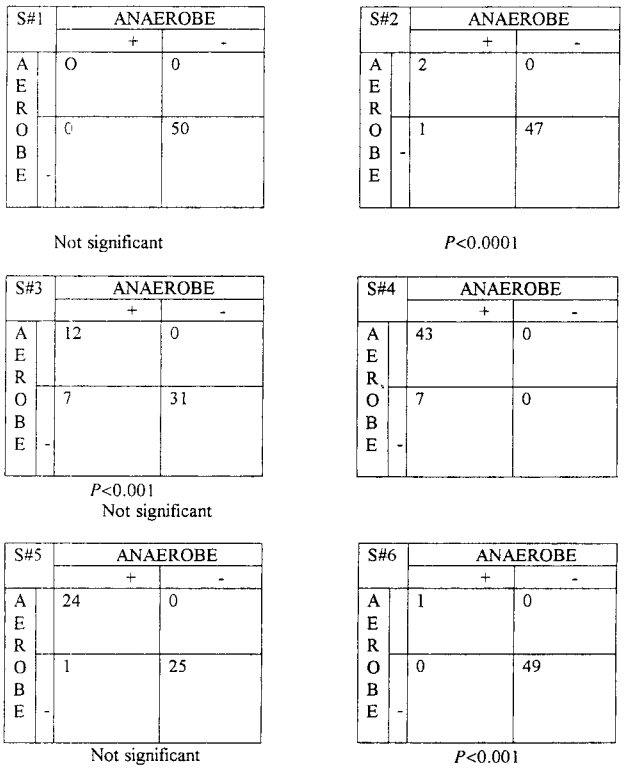

Fig. 1 Comparison between anaerobic and aerobic isolates from peripheral and mesenteric vein hemocultures, appendix aspirates and abdominal wall smears (McNemar test).

Abdominal wall smears were cultured directly onto solid media: blood agar, eosin–methylene blue (EMB) agar and sodium tioglycolate (TIO)-containing broth. Samples were cultivated aerobically and anaerobically using the procedure mentioned above. Statistical analyses were performed using the McNemar paired *t*-test, which is usually used for two related measures on the same samples. $P < 0.01$ was considered significant.

Results

Pathohistologic analysis of removed appendices confirmed the clinical diagnosis of appendicitis in 42 patients, whereas the remaining eight patients showed no pathohistologic findings. By McNemar paired *t*-test, we calculated the existence of aerobic and anaerobic samples in each particular sample. As shown in Fig. 1, the McNemar test revealed statistically significant values for Samples II, III and VI isolated from the cubital vein, superior mesenteric vein and peritoneal smears, respectively. In addition, we found that aerobic bacteria were isolated from the appendix

Table 1 Number of species and isolates from three groups of samples (only one sample per patient) in 19 patients with bacteremia in the mesenteric vein

Bacterial group	Bacterial species	No. bacteria		
		Sample II	Sample III	Sample IV
Enterobacteria	*Escherichia coli*	2 (1)	11 (12)	13 (14)
	Citrobacter freundi		(1)	1 (1)
	Enterobacter spp.		1	(3)
	Proteus mirabilis			(1)
Gram-positive				
Aerobic and anaerobic cocci	*Enterococcus* spp.		1 (1)	1 (1)
	Streptococcus spp.		1	1
	β-Hemolytic streptococcus		1	1
Anaerobic cocci	*Peptostreptococcus*	(2)	(4)	(7)
	Peptococcus spp.	(1)	(4)	(5)
	Streptococcus spp. (AN)		(1)	(1)
Microaerophilic rods	*Lactobacillus* spp.			(5)
Gram-negative				
Non-fermentative bacilli				1
Non-spore forming rods	*Bacteroides* spp.		(8)	(9)

Numbers in parentheses indicate the number of samples. Numbers larger than number of samples indicate more than one morphologically and biochemically distinct strain was isolated from a single sample. The second number represents bacteria of the same species but cultivated by means of anaerobic cultivation procedure and, thus, calculated as part of the anaerobic count.

Sample II, hemoculture from the cubital vein; sample III, hemoculture from the mesenteric vein; sample IV, appendix aspirate; AN, anaerobic bacteria.

aspirate in 43 cases, from the peritoneal smear in 24 cases and from the mesenteric vein in 12 cases. However, anaerobic bacteria were isolated from all 50 appendix aspirates, from the 25 abdominal smears and from the 19 samples isolated from the mesenteric vein. Neither aerobic nor anaerobic bacteria were isolated from the cubital vein before or 5 h after surgical treatment. It is interesting that three hemocultures from the cubital vein were positive for anaerobic bacteria during surgical treatment.

Of 19 patients who had bacteremia in the mesenteric vein (those with anaerobic bacteria isolated), 12 also had aerobic and facultative anaerobic bacteria in their isolates. Bacteriologic analysis of aerobic and anaerobic isolates from the 19 positive mesenteric vein hemocultures obtained during surgical treatment is presented in Table 1. The frequency of isolated aerobic bacteria is greatest in the aspirate isolated from the appendix ($n = 18$), and from the mesenteric vein ($n = 15$). However, only two samples from the cubital vein hemoculture were positive for aerobic bacteria. The frequency of isolated facultative aerobic and anaerobic bacteria was very high from the appendix aspirates ($n = 47$) and from the mesenteric vein ($n = 31$), while only four samples isolated from the peripheral blood culture where positive. Only a few *Peptococcus* spp. and none of the *Bacteroides* spp. strain were isolated during surgical treatment. In contrast, many *Bacteroides* spp. were isolated from mesenteric vein blood as well as from the appendix aspirate.

Laboratory data

Of the 50 patients examined, 38 (76%) had increased ESR values, while in 28 cases (56%) the white blood cell (WBC) count was increased. Furthermore, in 42 cases (84%) we found a leftward shift of the differential blood count. In 23 and 15 cases (46 and 30%, respectively) the AST and LDH values were increased, respectively, while in 45 cases (90%) alkaline phosphatase (ALP) values were increased.

Comparative results of significant mean values between 42 patients and the control group ($n = 8$) are shown in Table 2. Mean values of for the ESR and WBC count were normal within the control group, whereas other mean values were increased. In the patient group, all mean values were above normal.

The *t*-test results for ESR, WBC count, segmented leukocyte count, AST values and ALP within patient and control groups showed that significant differences existed only for the ESR and WBC counts. For the other three values, no significant differences were found between the two groups.

The mean values for ESR, WBC count, segmented WBC count, AST values and ALP for the 19 patients who had bacteremia and the eight patients without bacteremia in the mesenteric vein are shown in Table 3.

The *t*-test revealed that the only significant difference between patients with and without bacteremia in the mesenteric vein was for ALP values.

Table 2 Statistical characteristics of basic laboratory analyses within the patient and control groups

	Appendicitis ($n = 42$)	Control ($n = 8$)
ESR (mm/h)	25.88 ± 13.44	14.13 ± 8.56
Leukocyte count ($\times 10^3$ /mm^3)	12 460 ± 4870	7650 ± 3760
Segmented leukocyte count ($\times 10^3$ /mm^3)	77.13 ± 10.35	69.69 ± 16.80
AST (U/L)	30.17 ± 17.83	27.75 ± 22.89
ALP (U/L)	352.79 ± 133.97	443.13 ± 172.82

ESR, erythrocyte sedimentation rate; AST, aspartate aminotransferase; ALP, alkaline phosphatase.

Table 3 Laboratory values for erythrocyte sedimentation rate, leukocyte count, segmented leukocyte count, aspartate aminotransferase and alkaline phosphatase in patients with and without bacteremia in the mesenteric vein

	Bacteremia in SMV ($n = 19$)	Without bacteremia ($n = 8$)
ESR (mm/h)	24.22 ± 11.84	27.89 ± 15.24
Leukocyte count ($\times 10^3$ /mm^3)	12 660 ± 4790	12 220 ± 5070
Segmented leukocyte count ($\times 10^3$ /mm^3)	74.92 ± 10.65	79.80 ± 9.56
AST (U/L)	30.35 ± 15.89	29.95 ± 20.37
ALP (U/L)	391.74 ± 134.55	305.63 ± 120.29

SMV, superior mesenteric vein; ESR, erythrocyte sedimentation rate; AST, aspartate aminotransferase; ALP, alkaline phosphatase.

Discussion

In this paper we present data that suggest a significant relationship between the number and type of isolated bacteria in the mesenteric vein branch hemocultures and the appendix aspirate isolates. This leads us to postulate that a significant percentage of bacteria (45%) within acute appendicitis penetrate into the mesenteric vein and reach the liver tissue through the portal vein. Because we did not have a significant number of positive isolates from the peripheral vein hemocultures, we suppose that the liver acts as a very efficient barrier in preventing bacteria from entering the peripheral blood circulation.

Moreover, our results suggest that there is a significant relationship between the number and type of bacteria isolated from the hemoculture of the mesenteric vein (Sample III), the aspirate from the appendix lumen (Sample IV) and the peritoneal smear (Sample VI). Our data are consistent with similar work performed by others.[1-3,7-11] From the results presented in Table 1, it is clear that enterobacteria (especially *E. coli*) and Gram-positive cocci are the most frequent isolates that penetrate into peripheral circulation. *Escherichia coli* is a mobile bacteria capable of penetrating through the intestinal wall and capillaries to reach the blood flow of the mesenteric vein, after penetration of the immunologic barrier. However, streptococci, as non-mobile microorganisms, have a different penetration strategy. By multiplying themselves they passively penetrate an active defense and enter the mesenteric vein.

We have also found that in three of 19 patients with bacteremia in the mesenteric vein, pathogenic agents, such as enterobacteria and Gram-positive anaerobic cocci groups (*E. coli*, *Peptococcus* spp. and *Peptostreptococcus*) have penetrated into the peripheral circulation. Furthermore, we have also found that the same group of bacteria, as well as Gram-negative non-sporogenic anaerobic rods (*Bacteroides* spp.), are the predominant microorganisms in mesenteric vein hemocultures. This finding is similar to that for appendix aspirates. These data confirm the results published by Pieper *et al.*[12]

We have found that, even in complicated cases of acute appendicitis, the liver is still effective in hindering bacterial agents from entering the systemic circulation. The data we have obtained by different laboratory tests can be explained as a consequence of the reaction to acute inflammation.

Higher AST and ALP values, as well as a lower prothrombin time, can be explained as a result of consequent liver reaction[10] and possible liver damage. We noted that there is some difference in the ALP level between patients with and without portal bacteremia. Work performed by Bennion *et al.*[5] describes the presence of 3.1 aerobes and facultative anaerobes as well as 8.5 anaerobic species on average from every analyzed sample. They also found *Bacteroides* spp. to be the predominant bacteria within the Gram-negative anaerobes and *E. coli* to be the predominant bacteria from the aerobes. Similar results have been published by Itagaki *et al.*,[13] where 14 bacterial species were isolated from purulent ascites where *E. coli* was predominant.

Bennion *et al.* noted that, in patients with gangrenous and perforated appendices, 223 anaerobic and 82 aerobic bacterial species were recovered (an average of 10.2 different organisms per specimen).[6] However, *B. fragilis* group and *E. coli* were isolated from almost all specimens.

These results were supported by those of Roberts,[14] who also found that *Bacteroides* spp., *E. coli* and *Streptococcus* spp. are the most frequent isolates in acute appendicitis.

Results presented in this paper suggest that portal bacteremia does not influence peripheral blood reactions. Furthermore, our data indicate that there is no statistically significant relationship between bacteremia of the superior mesenteric vein and liver dysfunction.

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