Research Article

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The Spectrum of Causative Agents of Complicated Abdominal Infections in Surgical Patients

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RELEVANCE Treatment of patients with complicated abdominal infections (AI) is still a difficult task, as evidenced by high mortality rates.

THE AIM OF THE STUDY is to analyze the results of microbiological investigations of patients with advanced diffuse peritonitis who were treated in the surgical department of the emergency hospital.

MATERIAL AND METHODS In this study, the main pathogens of advanced peritonitis were identified in 69 patients (the average age of patients was 64±17 years). The cause of peritonitis in the absolute majority of cases (94%) was a perforation of the gastrointestinal tract. A study of various types of clinical material was carried out: blood — 143 samples, urine — 125 samples, bronchoalveolar lavage — 119 samples and 130 samples of wound discharge. 260 strains of microorganisms were isolated.

RESULTS The predominance of the Enterobacteriacea species (K. pneumoniae and E. coli), non-fermenting bacteria (Acinetobacter spp.) as well as the increasing role of Enterococcus spp. and Staphylococcus spp. (S. aureus and CNS) were found. Multidrug-resistant strains dominated among the identified pathogens.

CONCLUSION The obtained data on the structure of pathogens of complicated abdominal infection confirm global trends. In order to develop new treatment methods for complicated AI, one of the possible solutions may be the use of human microbial ecology approaches.

Keywords: pathogens of complicated abdominal infection, Enterobacteriaceae species, Acinetobacter spp., Staphylococcus spp., multidrug-resistant strains

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AI - abdominal infection
BAL - bronchoalveolar lavage
GIT - gastrointestinal tract

The term "abdominal infection" (AI) refers to a wide range of infectious and inflammatory diseases caused by normal inhabitants of the human gastrointestinal tract (GIT), which, under stressful situations - for example, during the development of inflammatory processes as a result of necrosis and perforation of the abdominal organs, - are able to penetrate into initially sterile areas of the human body [1].

Intensive development of abdominal infectious processes leads to damage to various organs: the distal esophagus, stomach, duodenum, biliary tract, various parts of the small and large intestines, appendix, liver, spleen, pancreas, as well as pelvic organs in women.

In order to elaborate AI treatment strategies, two main subgroups have been distinguished - uncomplicated and complicated AI. Such a division is not without some convention, since it is not always possible to draw a clear line between them. However, most clinical observations can still be attributed to the first or second category [1, 2].

The main differential features underlying this division are the presence or absence of diffuse peritonitis and a systemic inflammatory response. Patients with the complicated form of AI constitute a group of severe and very severe patients who often develop septic complications, pneumonia, and abscesses in the abdominal cavity and retroperitoneal space after peritonitis. It is quite obvious that for this group of patients, the probability of death is high, and their treatment is a complex and lengthy process that requires active, effective complex therapy. Along with surgical and resuscitation methods, adequate antimicrobial therapy is an important component of the treatment process. The spectrum of causative agents of AI in patients with the complicated form is extremely wide [2], therefore, effective antimicrobial therapy should be based on the data of continuous microbiological monitoring of the main causative agents of AI and their sensitivity to antimicrobial drugs. Knowledge of the structure of causative agents of purulent-inflammatory diseases makes it possible to timely adjust the basic schemes of empirical therapy, develop therapeutic preventive measures aimed at minimizing the risk of infectious and inflammatory complications. In addition, microbiological monitoring is necessary to control the epidemiological situation in the departments of a medical hospital.

The aim of the study was to analyze the results of microbiological examination of patients with diffuse peritonitis who were treated in the surgical department of an emergency hospital.

RESULTS AND DISCUSSION

Microbiological examination was carried out in 69 patients of the Department of Emergency Surgery, Endoscopy and Intensive Care of the N.V. Sklifosovsky Research Institute for Emergency Medicine, who were diagnosed with diffuse peritonitis (for the period from July 1919 to September 2021). The cause of peritonitis in the vast majority of cases (94%) was perforation of one of the sections of the gastrointestinal tract: the colon (39.1%), the appendix, appendicitis (18.8%), the duodenum (14.5%), the small intestine (11.6%), stomach (10.1%). The mean age of patients was 64±17 years, median 65 (Q1 56; Q3 78); 29 women and 40 men. Overall mortality was 33.3% (23 out of 69).

Collection and transportation of samples of clinical material was carried out in accordance with the Methodical Guidelines MU 4.2.203905 [3]. Blood sampling, contents of abdominal cavity drainages and bronchoalveolar lavage (BAL) were taken during 10–12 days after the main celiac surgery. 517 culture tests of various types of clinical material were performed: blood - 143 samples, urine - 125 samples, BAL - 119 samples and 130 samples of wound discharge. 260 strains of microorganisms were isolated. Primary inoculation was carried out in a microbiological laboratory in accordance with generally accepted standards for 5% blood, chocolate, mannitol salt agar; Endo, Saburo, thioglycolic media. The set of culture media depended on the type of clinical material under study.

Microorganisms were identified using a WalkAway-40 automatic microbiological analyzer (Siemens, USA) or by conventional microbiological methods [3]; blood was analyzed using a BACTEC 9050 analyzer (BD, USA). Antibiotic susceptibility was determined using a WalkAway-40 automatic microbiological analyzer or by the disk diffusion method on Mueller-Hinton agar using paper disks (BD, USA). When analyzing data on the susceptibility of the isolated microorganisms, only strains falling into the category of "susceptible" were selected.

When isolating several microorganisms from one sample of clinical material for subsequent analysis, all etiologically significant pathogens were taken into account. The determination of etiologically significant pathogens was carried out in accordance with generally accepted standards [4]. For the purposes of this research, the results of repeated microbiological tests from one patient in the case of isolation of the same pathogens were not considered. A single detection of coagulase-negative staphylococcus was interpreted as contamination of a blood sample during collection [5]. If in several blood samples of a patient one type of microorganism with the same sensitivity to antibiotics was isolated, only the first result was taken into account for subsequent analysis..

РЕЗУЛЬТАТЫ И ОБСУЖДЕНИЕ

The main causative agents of purulent-inflammatory diseases in patients with diffuse peritonitis are shown in Figure 1.

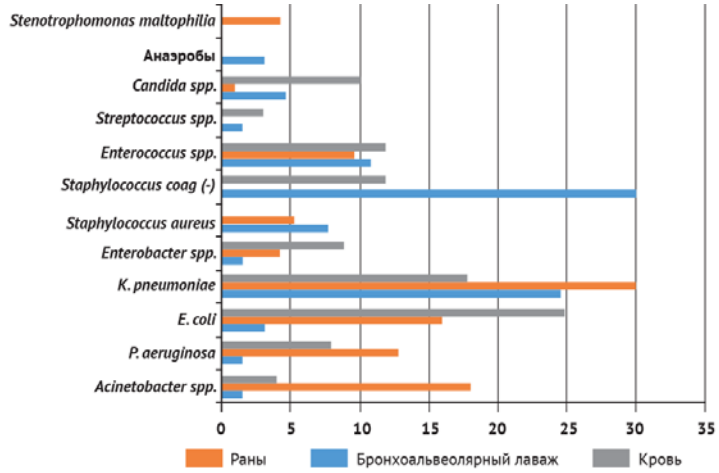

Fig. 1. Leading causative agents of pyoinflammatory complications in surgical patients with advanced diffuse peritonitis (percentage of each strain, in % of the total)

Out of 143 blood samples obtained in the course of microbiological studies, the growth of microorganisms was detected in 46.4% of the samples, 65 strains of microorganisms were isolated. The leading causative agents of bacteremia were gram-positive cocci (50.1% of strains), among which coagulase-negative staphylococci (30.1%) and Staphylococcus aureus (7.7%) prevailed. Enterococcus spp. (10.8%) and Streptococcus spp. (1.5%) were also isolated. The share of representatives of gram-negative rods accounted for a little less than a third of the pathogens of bacteremia (32.2% of strains). Among gram-negative rods, Klebsiella pneumoniae strains (24.6%) were the absolute leader, with a long lag followed by strains of Escherichia coli (3.1%), bacteria of the genus Acinetobacter (1.5%) and Enterobacter spp. (1.5%). In addition, yeast-like fungi of the genus Candida (4.6%), as well as anaerobic bacteria of the genus Bacteroides (1.5%) and Clostridium (1.5%) were isolated.

Growth of etiologically significant microorganisms was found in 78.3% of BAL samples. Among the causative agents of purulent-inflammatory diseases of the lower respiratory tract (total number of strains - 94), K. pneumoniae (30.0% of strains), non-fermenting bacteria of the genus Acinetobacter (18.1%), E. coli (16.0%) and P. aeruginosa (12.8%) prevailed. Gram-positive cocci were isolated much less frequently, while the proportion of Enterococcus spp. was 9.6%, and strains of S. aureus barely broke the bar of 5%. Yeast-like fungi of the genus Candida were isolated rarely - only 1 strain of C. albicans.

Of the 130 samples of wound discharge taken from the drains, 77.7% of the samples contained microorganisms. E. coli (24.8%), K. pneumoniae (17.8%), and Enterobacter spp. (8.9%) prevailed in the structure of pathogens of wound infection. Gram-positive coccal flora accounted for 26.8% of strains: 11.9% - Enterococcus spp., 11.9% - coagulase-negative staphylococci and 3.0% - Streptococcus spp. Yeast-like fungi C. albicans were isolated from wound discharge more often than from blood and BAL — 10.0% of strains.

In general, the main causative agents of infectious complications isolated from blood, BAL, and drainage contents in patients with peritonitis were gram-negative pathogens - Kl. pneumoniae (23.8% strains), E. coli (16.1%) and Acinetobacter spp. (8.5%).

Analysis of data on the sensitivity of the main pathogens of AI to antibacterial drugs showed the predominance of multidrug-resistant strains. As an example, Figure 2 shows antimicrobial susceptibility of E. coli and K. pneumoniae.

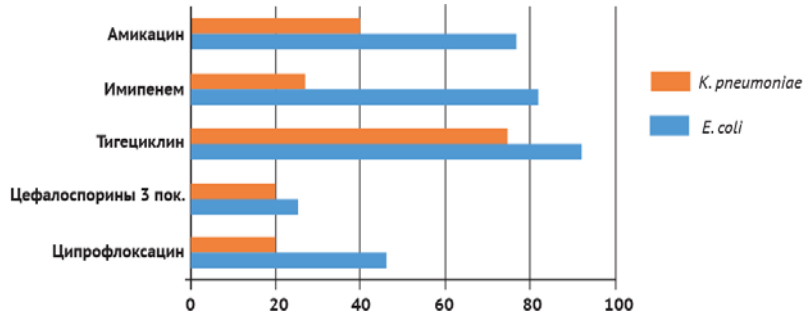

Fig. 2. Sensitivity to antibiotics of the leading causative agents of pyoinflammatory complications — K. pneumoniae and E. coli (% of sensitive strains)

Most strains of K. pneumoniae were multidrug-resistant, while 40.0% of strains remained sensitive to amikacin, 27.3% to imipenem, and 74.5% to tigecycline. A slightly better picture was observed in E. coli: 25.3% and 46.1% of strains, respectively, were sensitive to 3rd generation cephalosporins and ciprofloxacin, while only 20% of K. pneumoniae strains remained sensitive to these antibacterial drugs. Strains of non-fermenting bacteria of the genus Acinetobacter were resistant to almost all drugs. Among staphylococci, methicillin-resistant strains prevailed: the proportion of methicillin-resistant coagulase-negative staphylococci was 80.0%, the proportion of MRSA among strains of Staphylococcus aureus was 67.3%. All isolated strains of staphylococci were sensitive to vancomycin and linezolid. Among Enterococcus spp. 82% of the strains retained sensitivity to ampicillin. All isolated strains of enterococci remained sensitive to vancomycin and linezolid.

The results obtained coincide with the data of global practice [2]. Representatives of the Enterobacteriacea family — K. pneumoniae and E. coli, non-fermenting bacteria of the genus Acinetobacter and P. aeruginosa are invariably leading among pathogens of complicated forms of AI. In contrast to patients with uncomplicated AI, enterococci and staphylococci (strains of Staphylococcus aureus and coagulase-negative staphylococci) are increasingly isolated in the peritoneal fluid of patients with diffuse peritonitis. In addition, in the development of severe infectious complications in patients with diffuse peritonitis, yeast-like fungi of the genus Candida begin to play an increasingly important etiological role, which is a consequence of prolonged therapy with broad-spectrum antibiotics. In the present work, obligate anaerobes (bacteroides) were isolated only from blood (3.7% of strains). A possible explanation for the infrequent detection of bacteroides may be the fact that in medical practice the polymicrobial nature of infection sources is always taken into account, therefore drugs with an antianaerobic spectrum of action are administered intraoperatively. Besides, many species of obligate anaerobes slowly develop resistance to antibacterial drugs.

To date, there have been no generally accepted schemes for the treatment of patients with complicated forms of AI, since the microbiological landscape in the conditions of each particular clinic varies significantly [2]. The severity of the condition, the multiplicity of sources of infections, the presence of concomitant pathology - this is not a complete list of reasons. To this we must add the global trend of continuous growth in the number of multidrug-resistant strains of microorganisms, not only inside medical hospitals, but also in outpatients [6–10]. This “multidrug-resistance epidemic” makes it difficult to develop initial empiric antimicrobial therapy. This is evidenced by the high figures of its inefficiency, often exceeding 20% [11–16].

However, the existence of basic principles of antimicrobial therapy for complicated forms of AI cannot be denied. Initially, standard empirical antimicrobial therapy should be complex and include broad-spectrum antimicrobials active against Enterobacteriaceae, enterococci, streptococci, staphylococci, and obligate anaerobic bacilli that are inhabitants of the gastrointestinal tract. In addition, in the case of a particularly severe course of AI, when mechanical lung ventilation and other therapeutic and diagnostic invasive manipulations are necessary, generalized infections, the occurrence of septic complications and joining of polyresistant strains of non-fermenting bacteria (acinetobacter and Pseudomonas aeruginosa) should be concidered.

In the case of bronchopulmonary complications, K. pneumoniae strains - with a high proportion of poly- and even pan-resistant strains - inevitably become the leading pathogens. This approach to starting empiric antibiotic therapy has underlain the development of treatment strategy over the past 20 years [2]. A specific implementation of the postulated principles for the treatment of severe forms of AI does not have tight restrictions and includes the use of monotherapy or combination therapy. With regard to less common

microflora, for which the presence of resistant strains is also not a rarity, there are currently no recommendations on the use of antibiotic therapy [2, 17]. But even for them, apparently, a de-escalation option of therapy is supposed - a transition from antibiotics with a wide spectrum of action to narrowly targeted drugs.

In recent decades, more and more attention has been paid to the development of new approaches to the prevention of the development of severe forms of AI, and, above all, to the improvement of methods for early diagnosis and initial treatment strategy for patients with AI [13]. Timely diagnosis, assessment of the severity of patient condition, detection of the focus (or foci) of infection are still the most vulnerable links in the treatment of patients with AI. This is evidenced by the disappointing mortality statistics, which can reach 67.8% with the development of severe septic complications in the postoperative period [16]. From a microbiological point of view, preventive measures should be aimed primarily at combating hospital strains, the basis of which is inevitably the reasonable use of antibacterial drugs. Modern clinical guidelines increasingly propose to use a minimum course of antibiotics (up to the abandonment of antibacterial drugs in uncomplicated forms of AI).

CONCLUSION

The results of this study confirm what is declared in the medical literature: among the causative agents of abdominal infection, the leading position belongs to the representatives of the Enterobacteriacea family (K. pneumoniae and E. coli), non-fermenting bacteria (Acinetobacter spp.); the increasing role of gram-positive coccal microflora - Enterococcus spp. and Staphylococcus spp. Among the main causative agents of infectious and inflammatory complications, the prevalence of multidrug resistant strains (K. pneumonia, E. coli, Acinetobacter spp.), as well as methicillin-resistant strains of staphylococci, was also revealed.

To date, the starting empirical antimicrobial therapy of complicated forms of abdominal infection is based on broad-spectrum antimicrobials that are active against the widest possible number of representatives of the luminal microflora of the gastrointestinal tract, including obligate anaerobes. It should also take into account the possible growth of gram-positive microflora and yeast-like fungi.

In bronchopulmonary complications, in addition to the threat from K. pneumonia, non-fermenting bacteria (acinetobacter and Pseudomonas aeruginosa) remain a constant problem. The only reasonable and effective option so far is the de-escalation option of antibiotic therapy, but it contains a "delayed-action mine" - the use of broad-spectrum antibiotics leads to the selection of multi-resistant strains, which deprives medical practice of the last reserve of antibacterial drugs.

To combat antibiotic resistance in recent decades, the refusal to use excessive antibacterial drugs has been increasingly declared, which inevitably contradicts the “comprehensiveness” of starting antibiotic therapy. In parallel, a search is underway for new ways of "microbiological prevention" of infectious and inflammatory diseases, including abdominal infections. In this regard, attempts to use pro- and prebiotics, enterosorbents, as well as bacteriophages are of constant interest. But these directions still remain more in the field of research (the effect is sometimes present, sometimes absent; the mechanism is not completely clear), and would benefit from further study.

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