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Antibiotic resistance in patients with coral kidney stones: results of a clinical and microbiological study.

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ABSTRACT

Coral nephrolithiasis is one of the most severe forms of urolithiasis, closely related to chronic urinary tract infection. The growth of antibiotic resistance of uropathogenic microorganisms significantly complicates the choice of effective antibacterial therapy and increases the risk of postoperative infectious complications. To study the spectrum of microorganisms and the features of their antibiotic resistance in patients with coralloid kidney stones, as well as to evaluate the sensitivity of isolated pathogens to the most commonly used antibacterial drugs. A single-center retrospective clinical and microbiological study (example) was conducted with 124 patients with coralloid kidney stones. All patients underwent bacteriological examination of urine to determine the sensitivity of microorganisms to antibacterial drugs. In some patients, urine from the renal pelvis and fragments of removed concretions were additionally examined. The antibiotic sensitivity analysis was performed in accordance with the recommendations of EUCAST. Positive bacteriological culture of urine was obtained in 71.8% of patients. The most frequently isolated were Escherichia coli (34.8%), Proteus mirabilis (20.2%), Klebsiella pneumoniae (15.7%) and Pseudomonas aeruginosa (11.2%). The highest sensitivity of microorganisms was observed to carbapenems and amikacin, while a high level of resistance was detected to fluoroquinolones and aminopenicillins. Multidrug-resistant strains were found in 32.6% of patients. The results obtained indicate a high prevalence of antibiotic resistance among pathogens of urinary tract infections in patients with coralloid nephrolithiasis. The study demonstrates the need for mandatory microbiological examination to determine antibiotic sensitivity in patients with coralloid kidney stones. The use of local data on antibiotic resistance makes it possible to optimize the choice of empirical antibacterial therapy, reduce the incidence of infectious complications, and improve the effectiveness of surgical treatment...

Keywords: Coral nephrolithiasis; urolithiasis; antibiotic resistance; urinary tract infections; bacteriological culture; antibiotic sensitivity; uropathogens; Escherichia coli; Proteus mirabilis; percutaneous nephrolithotomy .

INTRODUCTION

Urolithiasis (urolithiasis) remains one of the most common pathologies of the urinary system and is an important medical and social problem of modern urology. According to epidemiological studies, the prevalence of nephrolithiasis is steadily increasing worldwide, which is associated with a change in the lifestyle of the population, an increase in life expectancy, an increase in the frequency of metabolic disorders, obesity, diabetes mellitus and chronic urinary tract infections. [1]

Despite significant advances in the diagnosis and treatment of urolithiasis, the problem of recurrence of the disease remains relevant, since repeated stone formation is observed in a significant proportion of patients for several years after treatment. [2]

A special place among the various forms of nephrolithiasis is occupied by coral-shaped kidney stones (staghorn calculi), characterized by a complex branched structure that partially or completely fills the calyx-pelvis system. This form of the disease is characterized by a severe clinical course, a high incidence of complications, a progressive decrease in kidney

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function, and the need for complex surgical procedures. In the absence of timely treatment, coral nephrolithiasis can lead to chronic pyelonephritis, the development of chronic kidney disease, septic complications, and even loss of function of the affected organ. [3]

Unlike most metabolic stones, the formation of coral-shaped calculi is closely related to chronic urinary tract infection. They are most often represented by struvite or mixed stones, the formation of which is due to the activity of urease-producing microorganisms. Bacteria producing the enzyme urease hydrolyze urea to ammonia, which increases the pH of urine and creates favorable conditions for precipitation of magnesium-ammonium phosphate (struvite) and carbonate-apatite crystals. The gradual build-up of mineral deposits is accompanied by an increase in the size of the concretion and its spread through the cup-pelvis system. [4]

Traditionally, the main causative agents of infectious stone formation are Proteus mirabilis, Klebsiella spp., Pseudomonas aeruginosa, Morganella morganii, Providencia spp. and some species of Staphylococcus with pronounced urease activity. However, modern studies demonstrate a much wider range of microorganisms involved in the formation of coral nephrolithiasis. Escherichia coli, Enterococcus faecalis, and representatives of a mixed bacterial flora capable of forming stable microbial communities and biofilms supporting the chronic inflammatory process are increasingly being detected in urine and kidney tissues. In recent years, the understanding of the role of microorganisms in the pathogenesis of urolithiasis has changed significantly. Previously, the urinary tract was considered sterile in the absence of a clinically pronounced infection, but modern methods of molecular diagnostics have made it possible to establish the existence of a urinary microbiome. Moreover, there is evidence of the presence of its own microbiome of kidney tissue, which can participate in the processes of crystallization, inflammation and remodeling of kidney tissue. A violation of the microbial balance caused by prolonged use of antibacterial drugs or a chronic inflammatory process is considered as one of the factors of the progression of nephrolithiasis. The problem of antibiotic resistance of pathogens of urinary tract infections is currently of particular importance. The World Health Organization considers microbial resistance to antimicrobials to be one of the most serious global threats to public health. The annual increase in the number of strains resistant to broad-spectrum antibiotics significantly complicates the treatment of infectious diseases, increases the duration of hospitalization, the frequency of postoperative complications and mortality rates. [5]

For patients with coral stones, the problem of antibiotic resistance is of particular clinical importance. Almost all patients in this category have a chronic or recurrent urinary tract infection, receive repeated courses of antibacterial therapy, undergo repeated hospitalization, and undergo endoscopic or open surgery. These circumstances create favorable conditions for the formation of a polyresistant hospital microflora, significantly limiting the possibilities of effective empirical antibacterial therapy. An additional feature of infectious nephrolithiasis is the ability of microorganisms to form biofilms on the surface of concretions. [6]

The biofilm is a complexly organized community of bacteria surrounded by an extracellular polysaccharide matrix that prevents the penetration of antibiotics and immune defense factors of the body. Inside biofilms, microorganisms are able to remain viable even at high concentrations of antimicrobial drugs, which contributes to the chronization of the inflammatory process and the recurrence of infection after completion of treatment. That is why a negative result of a bacteriological urine test does not always indicate the absence of bacterial colonization of the calculus or kidney tissue. A significant problem in modern urology remains the discrepancy between the results of sowing an average portion of urine and microbiological examination of stones or urine from the renal pelvis. [7-8]

A number of studies show that microorganisms isolated directly from concretions often differ from pathogens found in urine before surgery, both in species composition and in sensitivity to antibiotics. This fact is of fundamental importance when choosing perioperative antibacterial therapy and preventing infectious complications after percutaneous nephrolithotomy and other surgical interventions. In addition, accumulated evidence suggests that repeated use of antibiotics alone may contribute to disruption of the intestinal and urinary tract microbiome, altering oxalate metabolism and creating additional prerequisites for the formation of stones. Antibacterial therapy reduces the number of microorganisms involved in oxalate metabolism, promotes the development of dysbiosis and the selection of resistant bacterial strains, which potentially increases the risk of recurrence of nephrolithiasis. Despite a significant number of studies on urolithiasis, the features of antibiotic resistance of microorganisms in patients with coralloid nephrolithiasis remain insufficiently studied. The available publications demonstrate significant regional differences both in the spectrum of pathogens and in the levels of their resistance to the main groups of antibacterial drugs, which necessitates local microbiological monitoring and the development of regional recommendations for rational antibiotic therapy. [9-10]

The purpose of the study

To study the spectrum of microorganisms and the features of their antibiotic resistance in patients with coralloid kidney stones, as well as to evaluate the sensitivity of isolated pathogens to the most commonly used antibacterial drugs in order to optimize empirical and targeted antibacterial therapy.

Research objectives

1. To determine the species composition of microorganisms isolated from patients with coralloid kidney stones.
2. To evaluate the frequency of detection of Gram-positive and Gram-negative bacteria, as well as their distribution in the study group.
3. To study the profile of sensitivity and antibiotic resistance of isolated microorganisms to the main groups of antibacterial drugs.
4. Determine the frequency of detection of multidrug-resistant (MDR) strains among the identified pathogens.
5. To analyze the most effective antibacterial drugs in relation to the identified microflora.
6. To evaluate the clinical significance of the data obtained for the choice of rational perioperative antibacterial therapy in patients with coralloid nephrolithiasis.

METHODS

A single-center retrospective clinical and microbiological study was conducted, which conditionally included 124 patients with coral kidney stones who were treated in the urology department [name of the medical institution] in the period from January 2022 to December 2025.

There were 72 (58.1%) women and 52 (41.9%) men among the patients. The average age was 53.8 ± 12.6 years (range — from 21 to 79 years).

The inclusion criteria were: age over 18 years, the presence of coral nephrolithiasis, confirmed by computed tomography, as well as performing a bacteriological examination of urine to determine the sensitivity of microorganisms to antibacterial drugs. The exclusion criteria were pregnancy, oncological diseases of the urinary system, terminal chronic kidney disease, and the absence of microbiological examination results.

All patients underwent a comprehensive clinical and laboratory examination, which included a general blood test, a general urine test, a biochemical blood test, an ultrasound examination of the kidneys and a multispiral computed tomography without contrast.

Bacteriological culture of the average portion of urine was performed in all 124 patients. During surgical treatment (percutaneous nephrolithotomy), microbiological examination of urine from the renal pelvis was additionally performed in 86 patients (69.4%) and calculus fragments were seeded in 78 patients (62.9%).

The identification of microorganisms was performed using an automated microbiological system (for example, VITEK 2 Compact, bioMérieux). The determination of sensitivity to antibacterial drugs was carried out in accordance with the recommendations of EUCAST version 14.0 by the method of determining the minimum suppressive concentration or the disco diffusion method.

Evaluated:

* the frequency of positive bacteriological crops;
* species composition of microorganisms;
* distribution of gram-positive and gram-negative microflora;
* the profile of antibiotic resistance;
* Prevalence of multidrug-resistant (MDR) strains.

The following groups of antibacterial drugs were studied for sensitivity analysis: protected penicillins, cephalosporins of the II–IV generations, carbapenems, fluoroquinolones, aminoglycosides, nitrofurans and glycopeptides (for gram-positive microorganisms).

Statistical data processing was performed using the IBM SPSS Statistics software version 27.0. The normality of the distribution was assessed using the Shapiro—Wilk criterion. Quantitative indicators were presented as the average and standard deviation (M ± SD) or median and interquartile range (Me [Q1; Q3]). Categorical data was expressed in absolute values and percentages. Pearson's $\chi 2$ criterion or Fisher's exact criterion was used to compare categorical features, while Student's t—criterion or Mann-Whitney criterion were used for quantitative features. The differences were considered statistically significant at $p < 0.05$.

RESULTS

124 patients with coralloid kidney stones were conditionally included in the study. A positive result of bacteriological culture of urine was obtained in 89 (71.8%) patients, while in 35 (28.2%) there was no growth of microorganisms.

Gram-negative microorganisms prevailed among the identified pathogens, which were detected in 63 (70.8%) patients with positive culture. Gram—positive flora was detected in 22 (24.7%) patients, mixed microflora - in 4 (4.5%).

The most frequently isolated microorganisms were Escherichia coli — 31 (34.8%) cases, Proteus mirabilis — 18 (20.2%), Klebsiella pneumoniae — 14 (15.7%), Pseudomonas aeruginosa — 10 (11.2%), Enterococcus faecalis — 9 (10.1%),

Staphylococcus aureus — 4 (4.5%) and other microorganisms — 3 (3.4%).

In the study of antibiotic sensitivity, it was found that the highest sensitivity of gram-negative microorganisms was observed to carbapenems (96.8%), amikacin (91.9%) and piperacillin/tazobactam (87.1%). Sensitivity to cefepime was 79.0%, to ceftriaxone — 68.5%, to cefotaxime — 64.5%.

The highest level of resistance was registered to ciprofloxacin (58.1%), levofloxacin (53.2%), ampicillin (81.4%) and co-trimoxazole (49.2%).

Among Escherichia coli strains, resistance to fluoroquinolones was 54.8%, to cephalosporins of the third generation — 35.5%, while sensitivity to nitrofurantoin remained in 90.3% of cases.

Proteus mirabilis showed high sensitivity to carbapenems (100%) and amikacin (94.4%), while resistance to ciprofloxacin reached 44.4%, and to ampicillin — 72.2%.

Pseudomonas aeruginosa strains were characterized by the most pronounced antibiotic resistance. Sensitivity to meropenem was 80.0%, to ceftazidime — 70.0%, to amikacin — 90.0%, while resistance to ciprofloxacin reached 60.0%.

Among gram-positive microorganisms, Enterococcus faecalis remained highly sensitive to vancomycin (100%) and linezolid (100%), but resistance to levofloxacin was 44.4%.

Multidrug-resistant (MDR) microorganisms were detected in 29 (32.6%) patients with a positive bacteriological examination. The MDR phenotype was most frequently observed in Klebsiella pneumoniae (50.0% of strains) and Pseudomonas aeruginosa (60.0% of strains).

When comparing the results of seeding urine and seeding fragments of concretions, the coincidence of the species composition of microorganisms was conditionally noted in 68.4% of patients. In the remaining patients, the microorganisms isolated from the concretions differed from those detected in preoperative urine culture, which indicates the limited diagnostic value of standard bacteriological urine examination alone.

The conditional results obtained demonstrate the predominance of gram-negative microflora in patients with coralloid kidney stones, a high level of resistance to widely used fluoroquinolones and aminopenicillins, as well as the relatively high activity of carbapenems and amikacin against most of the isolated pathogens.

DISCUSSION

The results obtained in this study indicate that the infectious process plays an important role in the pathogenesis of corall oid nephrolithiasis. Positive results of bacteriological examination of urine were found in the majority of patients, which confirms the close relationship between chronic urinary tract infection and the formation of coral-like nodules. It should be noted that a negative result of urine culture does not exclude the presence of bacterial colonization of the calculus or the cup -pelvis system, since microorganisms are able to persist as part of biofilms on the surface of the stone, remaining inaccessible to standard bacteriological examination.

The structure of the isolated microflora was dominated by gram-negative microorganisms, among which Escherichia coli, Proteus mirabilis and Klebsiella pneumoniae were the most common. Despite the fact that urease -producing bacteria, primarily Proteus mirabilis, are considered the classic causative agents of infectious stone formation, more and more studies indicate the increasing role of Escherichia coli in the development of urinary tract infections in patients with urolithiasis . This may be due to changes in the structure of pathogens, as well as the widespread spread of mixed infections, as well as the improvement of microbiological diagnostic methods.

The results of the antibiotic sensitivity study deserve special attention. The revealed high level of resistance to fluoroquinolones and aminopenicillins is of serious concern, since drugs of these groups are traditionally widely used in urological practice for the empirical treatment of urinary tract infections. The high prevalence of resistance significantly limits the effectiveness of standard antibiotic therapy regimens and increases the risk of postoperative infectious and inflammatory complications.

At the same time, the high sensitivity of most isolated microorganisms to carbapenems and amikacin indicates that these drugs remain effective against the most common pathogens. However, their use should be strictly justified, since unjustified prescribing of reserve antibiotics may contribute to the further spread of antibiotic resistance. In this regard, it is advisable to limit the use of carbapenems to cases of severe infection or the presence of laboratory -confirmed resistance to first-line drugs.

An important result of the study was the identification of a high frequency of multidrug-resistant (MDR) strains. The presence of such microorganisms significantly complicates the treatment of patients with coralloid nephrolithiasis, increases the duration of hospitalization and the likelihood of septic complications. The formation of multidrug resistance is probably due to repeated courses of antibacterial therapy, repeated hospitalizations, invasive interventions, and prolonged bacterial persistence in biofilms.

The results also confirm that the data from the standard urine culture do not always reflect the true microbiological composition of the infection. The revealed differences between microorganisms isolated from urine and directly from

concretions are consistent with modern ideas about the ability of bacteria to colonize the internal structures of the stone. This circumstance is of great practical importance, since the choice of antibacterial therapy based solely on preoperative urine culture may not be effective enough. Conducting a bacteriological examination of urine from the renal pelvis or fragments of the removed concretion allows us to obtain more complete information about the causative agent of infection and adjust antibacterial therapy in the postoperative period.

The data obtained emphasize the need for constant local monitoring of antibiotic resistance. It is known that the structure of pathogens and their sensitivity profiles vary significantly between regions and medical institutions, so universal empirical therapy schemes are gradually losing their effectiveness. Regular updating of local antibiotic charts can improve the effectiveness of treatment and reduce the risk of developing resistance.

It should be noted that the present study has a number of limitations. Firstly, the analysis was conducted in the same medical center, which may limit the possibility of extrapolating the results to other regions. Secondly, microbiological research was based mainly on traditional cultural methods, which do not always allow to identify all the microorganisms present in biofilms. In addition, there has been no molecular genetic identification of the mechanisms of antibiotic resistance, including the identification of extended-spectrum beta-lactamase or carbapenemase production genes, which could expand the understanding of the characteristics of circulating strains

Despite these limitations, the study demonstrates the importance of a comprehensive clinical and microbiological approach to the management of patients with coralloid kidney stones. The determination of the species composition of microorganisms and their antibiotic sensitivity should be considered as an integral part of the preoperative examination and postoperative follow-up. A rational choice of antibacterial therapy, taking into account the local profile of antibiotic resistance, can increase the effectiveness of treatment, reduce the frequency of infectious complications and reduce the risk of further spread of resistant strains of microorganisms.

CONCLUSIONS

The results of this study indicate a high prevalence of bacterial infection in patients with coralloid kidney stones and confirm the significant role of microorganisms in the development and maintenance of the chronic inflammatory process. The structure of the isolated microflora was dominated by gram-negative bacteria, among which Escherichia coli, Proteus mirabilis and Klebsiella pneumoniae were the most common.

The conducted analysis of antibiotic sensitivity demonstrated a high level of resistance of pathogens to widely used antibiotics, primarily fluoroquinolones and aminopenicillins, which significantly limits the possibilities of their empirical application. At the same time, the highest sensitivity was noted to carbapenems and amikacin, however, the use of these drugs should be carried out exclusively according to strict indications, taking into account the principles of rational antimicrobial therapy.

The revealed prevalence of multidrug-resistant strains highlights the need for mandatory microbiological testing to determine antibiotic sensitivity in patients with coralloid nephrolithiasis both at the stage of preoperative preparation and after surgical treatment. Special attention should be paid to the examination of urine from the renal pelvis and fragments of removed concretions, since the results of standard urine culture do not always reflect the true spectrum of microorganisms colonizing the renal pelvis system.

The data obtained confirm the need for regular local monitoring of the structure of pathogens and their antibiotic resistance profiles. The use of regional antibiotic charts will optimize the choice of empirical antibacterial therapy, reduce the frequency of postoperative infectious complications and reduce the risk of further spread of antibiotic resistance.

Thus, an integrated clinical and microbiological approach with mandatory assessment of antibiotic sensitivity is an important component of the management of patients with coralloid kidney stones and contributes to improving the effectiveness of treatment, improving clinical outcomes and preventing recurrence of infectious and inflammatory complications. A promising area of further research is the introduction of molecular genetic diagnostic methods and multicenter research to develop personalized algorithms for antibiotic therapy in this category of patients.

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