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Analysis of the microbial landscape in patients with periprosthetic infection of the hip joint

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Abstract

Introduction The concept of the pathogenesis of periprosthetic joint infection (PJI) is the ability of pathogenic microorganisms to colonize the surfaces of implants, which are infected during the surgery or by hematogenous dissemination of bacteria. It causes poor results of PJI treatment. Microbiological identification of pathogen species is the gold standard in the diagnosis of PJI.

Purpose To assess the etiology of the infectious process in patients with periprosthetic hip joint infection.

Methods The study analyzed revision interventions (n = 294) for PJI of the hip joint performed within the period from 2010 throughout 2021. A total of 147 patients were operated on: 56 % (n = 82) were men and 4 % (n = 65) were women. At the time of hospitalization, the fistula PJI type was diagnosed in 71 % (n = 105); 20 % (n = 29) had edema and hyperemia of the postoperative suture area, and 9 % (n = 13) of cases had open wounds. The object of the study was bone and soft tissue samples obtained during excision of the infected material, as well as removed implant components. Cultures were grown on dense nutrient media. Bacterial cultures were identified by generally accepted methods using TB Expression (BioMerieux, France) and Walk Away 40 (USA) bacteriological analyzers.

Results The etiology of periprosthetic infection was identified in the majority of patients (93 %), while pathogens could not be detected in the remaining cases. Bacteriological analysis revealed microbial associations in 31 % of patients, gram-positive microflora in 52 % of patients, and gram-negative microflora in 10 %.

Discussion The most common types of microorganisms are gram-positive bacteria with a tendency for resistant strains to grow. Gram-negative bacteria are isolated in joint infection, but less frequently. The results demonstrate isolated gram-negative cultures in 10 % of cases. The second most common cause of periprosthetic joint infection is polymicrobial infection, which was detected in 31 % of cases. Microbial associations occurr in 10–45 % of cases; such a clinical situation at the start of treatment complicates the empirical choice of drugs for antibacterial therapy.

Conclusions Microbiological study allowed identification of the etiology of the infectious process in 93 % of patients. In more than half of the cases (52 %), the cause of implant-associated infection is gram-positive microflora, and in 31 % of cases are microbial associations. Reinfection was noted in 41 % of cases in polymicrobial patients.

Keywords: periprosthetic infection, microflora, inflammation, arthroplasty, revision

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INTRODUCTION

The concept of the pathogenesis of periprosthetic joint infection (PJI) is based on the dynamic equilibrium of the interaction between the implant and the human immune system [1]. Implants are seeded with pathogenic microorganisms either during surgery or by hematogenous dissemination of bacteria [2–6]. Many bacteria form biofilms on metal and polyethylene surfaces of implant components [2, 7–9]. This ability of microorganisms (the so-called cecil forms) ensures their persistence and survival in the hospital environment. In addition, bacteria resistant to antimicrobial drugs are resistant to them in the biofilms. They become the least vulnerable to the action of antibiotics [10, 11]. Long-term healing of postoperative bone wounds is often associated with the penetration of pathogens and the occurrence of microabscesses in bone tissue, and the colonization of osteoblasts [12–14]. At the same time, there are difficult-to-treat types of PJI pathogens, such as staphylococcal strains resistant to antibacterial drugs of three or more classes, fluoroquinolone-resistant and carbapenem-resistant gram-negative microorganisms, and fungal microflora [2, 15, 16]. All of the above factors reveal the cause of poor results in the PJI treatment and emphasize the need to determine the etiology of the pathological process.

Microbiological diagnosis is carried out by isolating and identifying the pathogen after collecting material from several of the most contaminated affected tissues [17]. To destroy the biofilm, the removed implant components are treated with ultrasound; for the same purpose, a dithiothreitol solution can be used [18–21]. The incubation time of biofilm bacteria is 14–21 days, which leads to their higher survival rate, compared to mono infections, for which the incubation period is 5–14 days [22].

Purpose: to assess the etiology of the microbial landscape in patients with periprosthetic hip joint infection

MATERIAL AND METHODS

The study was conducted on the material obtained from 147 patients (56 % men, 44 % women) after revision surgeries for periprosthetic hip joint infection. The age of the patients was (54.7 ± 12.7) years. The number of study samples was 294. Fistulous PJI type was observed in 105 (71 %) patients, hyperemia and edema in the area of the postoperative suture were noted in 29 (20 %), and open wounds were present in 13 (9 %) cases. In 28 patients (19 %), an acute course of the infectious process duration was on average 21.8 days (Me — 22; 95 % CI from 19.7 to 24.0) and in 119 (81 %) chronic infection continued on average 26.3 months (Me — 13; 95 % CI from 20.5 to 32.3).

In 114 (78 %) cases, purulent inflammatory complications developed after primary arthroplasty and only in 33 (22 %) cases after revision. The treatment process was significantly complicated by severe comorbid conditions of patients according to the ASA (American Society of Anesthesiology) scale, diagnosed in 82 (56 %) patients.

The objects of the study were samples of bone and soft tissues obtained during resection of the infected tissues as well as removed implant components of the patients with hip PJI. Based on the recommended methods, seeding was performed on solid nutrient media (bile-salt agar, Sabouraud agar, Levin medium, Columbia agar and nutrient agar with 5 % sheep blood). The samples were placed in a thermostat and incubated at 37 °C for 24–48 hours. The number of colonies in Petri dishes was calculated; the obtained result was converted to a decimal logarithm, expressed in CFU/ml. To create anaerobic conditions, gas generator bags "Anaerogas" were used, growing fungal flora for 5 days at 30 °C.

Bacterial cultures were studied with conventional methods, as well as using bacteriological analyzers TB Expression (BioMerieux, France) and Walk Away 40 (USA).

Statistical data processing was performed using the Statistica for Windows, v. 13.0 (Stat Soft Inc., USA) and Microsoft Excel (Microsoft, USA) software package. Percentage calculations were performed to characterize the microbiological spectrum. Descriptive statistical results were the mean ± standard error (SE) for quantitative data. Data distribution was analyzed using the Shapiro – Wilk and Kolmogorov – Smirnov normality tests. Comparisons between unrelated samples were performed using the Mann – Whitney test. Differences were considered significant at $p < 0.05$.

RESULTS

In the intra-operatively harvested biological material, 196 strains of pathogenic microorganisms were isolated, the spectrum of which is presented in Figure 1. *Staphylococcus aureus* family was dominant in 64 % of cases, a significant part of the isolated strains also included *Enterobacteria ceae* (10 %), *Enterococcus aureus* (9 %) and Pseudomonas *aureus* (9 %).

MRSA and MRSE were detected in 39 cases (20 %), and in 17 (9 %) cases it was *P. aeruginosa* (Fig. 1).

Identification of microorganisms to verify the taxonomic affiliation of pathogenic bacteria showed that among the isolated and identified bacteria, the main part of the microflora was made up by *Staphylococcaceae* and the dominance of strains *Staphylococcus aureus, Staphylococcus epidermidis* and *Staphylococcus saprophyticus*.

Microflora was identified in 137 patients (93 %), but in 10 patients, pathogens could not be identified. In 76 patients (52 %), isolates of gram-positive microflora were detected, in 15 patients (10 %) it was gram-negative microflora in monoculture. In 46 patients (31 %), the presence of microbial associations was revealed (Fig. 2).

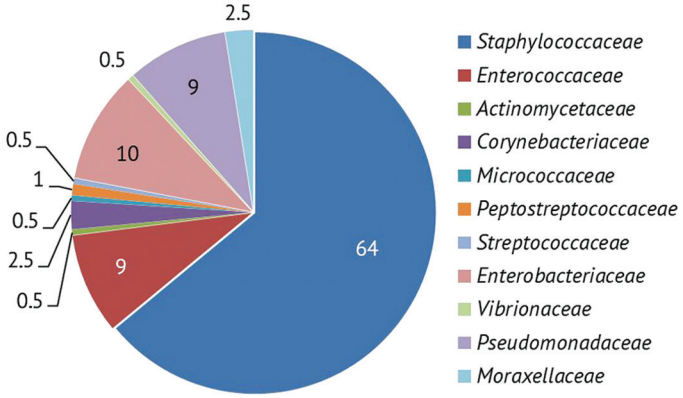

Fig. 1 Spectrum of pathogens causing hip PJI

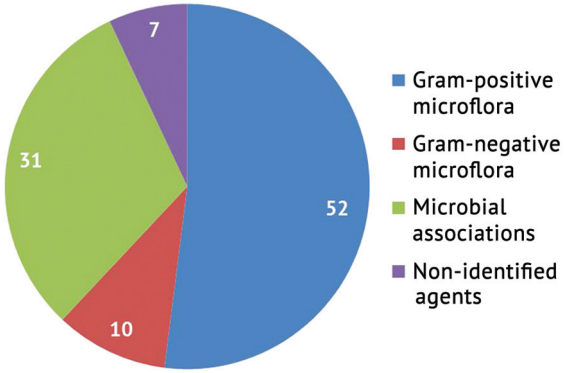

Fig. 2 Identified microflora

It should be noted that in 22 % of cases, or in 17 of 76 patients with isolated gram-positive microflora (dominant strain of *Staphylococcus aureus*, as well as *epidermal Staphylococcus*), recurrence of infection occurred. Repeated suppuration in 15 patients with gram-negative microflora (represented mainly by the strains of *Pseudomonas aeruginosa*) was noted only in two cases (13 %). The most frequently isolated families in the polymicrobial infection were *Staphylococcaceae* (78 %), *Enterobacteriaceae* (28 %), *Enterococcaceae* (26 %), *Pseudomonadaceae* (15 %) and *Moraxellaceae* (6.5 %).

Apparently due to previous therapy with antibacterial drugs, polymicrobial associations are quite common in patients with PJI and occupy the second place after gram-positive microflora. Microbial association of two agents was detected in 34 patients (74 %), of three agents in 11 (24 %). The growth of four microorganisms was revealed in one patient.

The total number of patients with recurrent infection in the presence of microbial associations was 19 (41 %) which was the highest number of complications. In order to stop the inflammatory process, six patients with recurrent infection underwent repeated surgical debridement; eight patients underwent spacer change, and the rest underwent resection arthroplasty.

With an unidentified composition of microflora, two out of 10 patients experienced repeated suppuration during their hospital stay. These patients underwent a two-stage revision intervention.

A comparative assessment of the results of an intraoperative study of the microbiological spectrum of pathogens in patients with acute and chronic forms of implant-associated infection is presented in Fig. 3.

In the structure of surgical interventions for PJI, the manifestation of infection was 22 days (ICI-17 — 27.5 days) in 28 (19 %) patients, and in 119 patients the duration of the purulent process averaged 26 months (8–35 months).

In the structure of the microbial landscape of patients with acute and chronic infection, the contribution of isolated gram-positive (44 % and 55 %) and gram-negative (7 % and 10 %) microflora was comparable (Fig. 3). However, it was noted that microbial associations and MRSE strains were significantly ($p < 0.05$) more common in patients with acute infection. Methicillin-resistant strains of epidermal staphylococcus were the cause of acute infectious process in almost every third case (29 %). In general, re-infection occurred in 7 (25 %) patients with acute and in 39 (33 %) patients with chronic PJI.

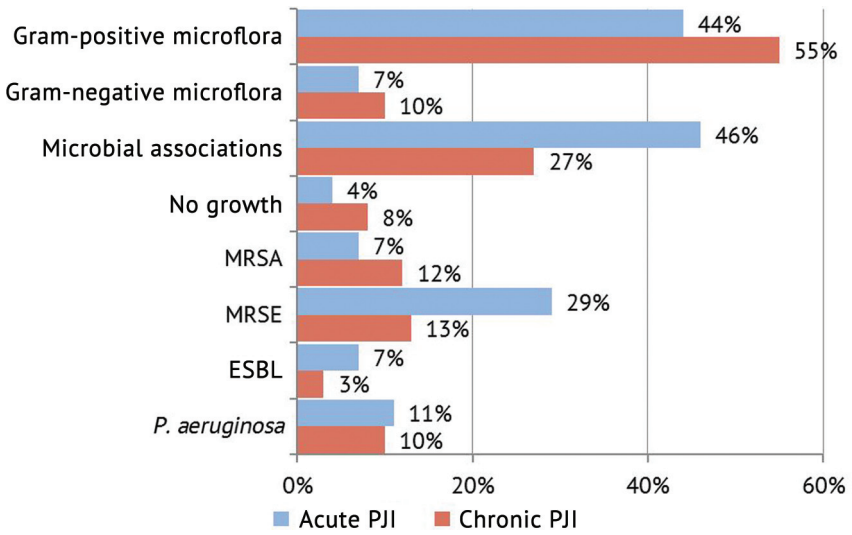

Fig. 3 Microbiological characteristics of the inoculation material of patients with acute and chronic hip joint PJI

DISCUSSION

Assessing the microbial landscape of patients with implant-associated infection, it should be noted that microbial cells, especially in biofilm conditions, acquire increasingly pronounced resistance to antimicrobial drugs. This, in turn, requires new approaches to risk assessment and treatment of the infectious process that developed after hip arthroplasty. The risk of PJI remains during the entire period of presence of an orthopedic implant in the body. The main pathogens are gram-positive bacteria (most often *Staphylococcus aureus* and *Staphylococcus epidermidis*), characterized by the growth of resistant strains [23–26]. The lack of targets for the manifestation of the action of antimicrobial therapy in many gram-positive microorganisms leads to the lack of control over resistant strains, causing legitimate concern among treating physicians, which is reflected in both domestic and foreign publications [27–30].

The second most significant etiologic cause of implant suppuration is polymicrobial infection. The incidence of polymicrobial infection tends to increase; we observed it in 31 % of cases. Polymicrobial infection in our patients is represented by a predictable spectrum: *Staphylococcaceae* — 78 %, *Enterobacteriaceae* — 28 %, *Enterococcaceae* — 26 %, *Pseudomonadaceae* — 15 %, and *Moraxellaceae* — 6.5 %. Such a clinical situation complicates the choice of an adequate antibiotic therapy and often leads to poorer outcomes compared to PJI due to monomicrobial microflora, what has also been stressed in the literature [31, 32]. A number of researchers point out the need to consider the expression of pathogenicity of microorganisms, as well as their ability to form biofilms [33–37]. In this regard, the identification of the spectrum of PJI pathogens is of great importance.

Fungal microflora was not detected in the patients in our study, but foreign literatures reports fungal infections, which occur in 1–4 % of cases. The overwhelming majority (80 %) are *Candida* fungi [38, 39]. This problem is typical for immunocompromised patients [40, 41].

The microbiological study of periprosthetic tissues revealed the etiology of the infection in the overwhelming majority (93 %) of the cases studied. The most common reason for non-identification of the pathogen was obviously the use of antibacterial drugs before the pathogen was detected.

CONCLUSION

The dominant cause of PJI development is gram-positive microflora and microbial associations. Reliable differences in patients with acute and chronic PJI were noted in the level of microbial associations and the presence of MRSE strains with a trend toward dominance in the group with an acute nature of infection.

Conflict of interests *Authors declare no conflicts of interests.*

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Ethical approval *The study was approved by the Ethics Board of the Federal State Budgetary Institution Ilizarov National Medical Research Center of Traumatology and Orthopedics of the Ministry of Health of the Russian Federation (protocol dated 04/28/2022 No. 1(71)).*

Informed consent *Not applicable.*

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