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Stenotrophomonas Maltophilia Infection in Trauma and Orthopedic Patients: Clinical Experience and Review

Alina R. Kasimova [1,2], Ekaterina M. Gordina [1], Sergey S. Toropov [1], Svetlana A. Bozhkova [1]

[1] *Vreden National Medical Research Center of Traumatology and Orthopedics, St. Petersburg, Russia*

[2] *Pavlov University, St. Petersburg, Russia*

Background. *Stenotrophomonas maltophilia* (S. *maltophilia*) is a gram-negative non-fermenting bacillus and is a rare pathogen of orthopedic infection. Due to the relatively low virulence of *S. maltophilia*, many clinicians are still faced with the question of whether this bacterial species is simply a colonizing agent or the true cause of infection.

Aim of the study — to raise the awareness of practitioners about *S. maltophilia* as a rare pathogen of orthopedic infection.

Methods. A retrospective analysis was performed concerning the frequency of *S. maltophilia* isolation from patients treated at the Vreden Center for periprosthetic infection and/or osteomyelitis from January 1, 2009 to October 31, 2022. The literature search by keywords was carried out in the PubMed/MEDLINE, Scopus, eLIBRARY, and Cyberleninka databases. The search retrieved 587 articles published in Russian or English over the period from 2012 to November 2022.

Results. During the study period, 9 cases of orthopedic monoinfection with *S. maltophilia* were identified in 9 patients aged 36 to 83 years. At the time of admission, no leukocytosis was detected in patients, and only 2 of 9 patients had elevated C-reactive protein level. *S. maltophilia* is naturally resistant to many broad-spectrum antibiotics. Co-trimoxazole is considered the drug of choice for the treatment of *S. maltophilia* infection. The limited choice of drugs for targeted therapy, the presence of multiple determinants of antibiotic resistance, the existence of microbial associations and patient risks including implantation, chronic nature of infection, elderly age, as well as the presence of significant concomitant somatic pathology can lead to the ineffectiveness of the ongoing treatment of infections caused by *S. maltophilia*. Our experience shows that in the case of sensitivity of *S. maltophilia* strain to co-trimoxazole it is possible to prescribe this drug for a long course as monotherapy, provided that the radical surgical treatment of the focus is performed.

Keywords: periprosthetic infection, osteomyelitis, *Stenotrophomonas maltophilia*, antibacterial therapy, trimethoprim, sulfometaxazole.

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✉ *Alina R. Kasimova*; e-mail: kasi-alina@yandex.ru

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Инфекция, вызванная *Stenotrophomonas maltophilia*, у пациентов травматолого-ортопедического профиля: клинический опыт и обзор литературы

А.Р. Касимова [1,2], Е.М. Гордина [1], С.С. Торопов [1], С.А. Божкова [1]

[1] *ФГБУ «Национальный медицинский исследовательский центр травматологии и ортопедии им. Р.Р. Вредена» Минздрава России, г. Санкт-Петербург, Россия*

[2] *ФГБОУ ВО «Первый Санкт-Петербургский государственный медицинский университет им. акад. И.П. Павлова» Минздрава России, г. Санкт-Петербург, Россия*

Введение. *Stenotrophomonas maltophilia* (*S. maltophilia*) представляет собой грамотрицательную неферментирующую палочку и является редким возбудителем ортопедической инфекции. Из-за относительно низкой вирулентности *S. maltophilia* перед многими клиницистами все еще стоит вопрос, является ли этот вид бактерий просто колонизатором или истинной причиной инфекции.
Цель исследования — повысить информированность практикующих врачей о *S. maltophilia* как редком возбудителе ортопедической инфекции.
Материал и методы. Выполнен ретроспективный анализ частоты выделения *S. maltophilia* от пациентов, находившихся на лечении в Центре по поводу перипротезной инфекции и/или остеомиелита с 1 января 2009 по 31 октября 2022 г. Поиск литературы по ключевым словам осуществлялся в базах данных PubMed/MEDLINE, Scopus, eLIBRARY и КиберЛенинка. В результате поиска было найдено 587 статей за период с 2012 по ноябрь 2022 г., опубликованных на русском или английском языках.
Результаты. За изученный период установлено 9 случаев ортопедической моноинфекции *S. maltophilia* у 9 пациентов в возрасте от 36 до 83 лет. На момент поступления у пациентов не был выявлен лейкоцитоз и только у 2 из 9 регистрировали повышенный уровень С-реактивного белка. *S. maltophilia* имеет природную устойчивость ко многим антибиотикам широкого спектра действия. Ко-тримоксазол считают препаратом выбора для лечения инфекций, вызванных *S. maltophilia.* Ограниченность выбора препаратов для таргетной терапии, наличие множества детерминант устойчивости к антибиотикам, существование в составе микробных ассоциаций и риски со стороны пациентов, включающие установку имплантатов, хронический характер инфекции, пожилой возраст, а также наличие выраженной сопутствующей соматической патологии, могут приводить к неэффективности проводимого лечения инфекций, вызванных *S. maltophilia*. Наш опыт свидетельствует, что в случае чувствительности штамма *S. maltophilia* к котримоксазолу возможно назначение данного препарата длительным курсом в виде монотерапии при условии выполнения радикальной хирургической обработки очага.

Ключевые слова: перипротезная инфекция, остеомиелит, *Stenotrophomonas maltophilia*, антибактериальная терапия, триметоприм, сульфометаксазол.

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Касимова Алина Рашидовна; e-mail: kasi-alina@yandex.ru

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BACKGROUND

Implant-associated infection, including periprosthetic infection (PPI) and osteomyelitis, is currently one of the leading causes of early re-operations after primary and revision total hip or knee arthroplasty [1]. In this case, the course of the infectious process often becomes recurrent. Despite the fact that the main causative agents of bone and joint infections, including those associated with orthopedic implants, are staphylococci, the presence of Gram-negative pathogens in the etiology remains significant and represents a prognostically unfavorable sign [2]. Rare pathogens can also be etiological agents of osteomyelitis and PPI, especially in immunocompromised patients. Such pathogens may include fungi of the genus *Candida spp*. nontuberculous mycobacteria, *Treponema spp*., *Anaerococcus spp*., *Clostridium spp*., *Eubacterium spp*., *Campylobacter spp*., *Fusobacterium nucleatum*, *Prevotella spp*. and others [3, 4]. Previously, we studied the features of fungal PPI treatment based on our own clinical experience and available scientific publications [5].

One more rare causative agent of PPI may be *Stenotrophomonas maltophilia (S. maltophilia)*, which is a Gram-negative non-fermenting bacillus. Because of the relatively low virulence of *S. maltophilia*, many clinicians are still faced with the question of whether this bacterial species is simply a colonizer or the true cause of infection [6]. Infection caused by *S. maltophilia* is uncommon in immunocompetent patients, however, this species is more and more often considered an opportunistic pathogen in chronically immunocompromised patients [7].

Multiple drug resistance of the pathogen makes the treatment of infections caused by *S. maltophilia* a significant problem [8]. Clinical management of such patients is complicated by the molecular heterogeneity of the bacillus, which is reflected in the uneven distribution of antibiotic resistance determinants and virulence factors among different strains, in the lack of available antimicrobial sensitivity tests and the absence of standardized borderline values for some antibiotics with *in vitro* activity.

There are currently rather limited data on *S. maltophilia* as a causative agent of orthopedic infection. The PubMed Central database contains few studies concerning the management and treatment of orthopedic patients with *S. maltophilia* infection.

Aim of the study – to broaden the knowledge of practitioners about *S. maltophilia* as a rare causative agent of orthopedic infection.

METHODS

We performed a retrospective analysis of the incidence of *S. maltophilia* isolation from patients treated at the Russian Scientific Research Institute of Traumatology and Orthopedics named after R.R. Vreden for PPI and/or osteomyelitis from January 1, 2009 to October 31, 2022. Epidemiological analysis of results of bacteriological tests was performed using the Microbiological Monitoring System "Mikrob-2".

Laboratory and instrumental examination data were obtained from patients' medical records.

The literature search was performed using keywords in the PubMed/MEDLINE, Scopus, eLIBRARY and CyberLeninka databases. The search request included the name of the microorganism and the words describing the course of orthopedic infections.

RESULTS

From 2009 to 2022, 9 cases of *S. maltophilia*-related orthopedic monobacterial infection were identified in 9 patients (5 men, 4 women) aged 36 to 83 years (Table 1). In 7 cases, isolated *S. maltophilia* strains showed sensitivity to trimethoprim/sulfamethoxazole (co-trimoxazole) at standard or increased medication exposure, and in two cases – resistance. All patients had a history of surgeries, including surgical interventions for an infectious process at this locus, but of a different etiology. In one case the pathogen was isolated from the components removed during revision hip arthroplasty for aseptic instability. The remaining 8 patients had an infection at the time of admission: 6 had an infection of the hip joint and 2 had an infection of the knee joint. Seven out of eight patients had chronic recurrent infection, and in one case the patient was admitted with a newly diagnosed chronic PPI caused by *S. maltophilia*. The clinical case of this patient will be discussed in detail below.

Table 1

Main characteristics of patients

Patient No	Sex	Age, y.o.	Localization	Time after the first surgery, years	Character of infection	During the hospital stay				
						ESR, mm/h/ CRP, mg/l at admission	Surgery	Focus of *S. maltophilia*	Co-trimoxazole administration	Recurrence
1	F	60	Hip	6	History of superficial SSI after arthroplasty	7 / 1.1	RA	RH	yes	yes
2	M	74	Hip	4	Chronic PPI	57 / 143	RSD, implantation of spacer	JF, TBS, RH preop and intraop	yes	No
3	M	65	Knee	15	Chronic recurrent osteomyelitis	12 / 0	RSD, implantation of spacer	JF, TBS intraop	yes	no
4	M	36	Hip	4	Chronic recurrent PPI	17 / 74.4	RA	TBS	yes	no
5	F	53	Knee	9	Chronic recurrent PPI	12 / 2.7	RA	Blood postop	no	no
6	M	68	Hip	16	Chronic recurrent PPI	5 / 1.6	RSD, reimplantation of spacer	JF preop	no	yes
7	F	63	Hip	14	Chronic recurrent PPI	8 / 0	RA	TBS	yes	yes
8	M	80	Hip	10	Chronic recurrent PPI	13 / 1.2	No surgery	Aspirate preop	no	Discharge due to comorbidity
9	f	83	Hip	6	Chronic recurrent PPI	23 / 33.4	RA	JF intraop	yes	no

RH — removed hardware; JF — joint fluid; TBS — tissue biopsy sample; RA — revision arthroplasty; RSD — radical surgical debridement; preop — preoperatively; intraop — intraoperatively; postop — postoperatively.

No leukocytosis was found on admission in all patients. The patient with newly diagnosed chronic PPI had a significantly elevated CRP and erythrocyte sedimentation rate. Only 2 of 7 patients with chronic recurrent infection had elevated CRP levels, while sedimentation rate was within normal limits. Thus, routine laboratory signs of a chronic infection were not pronounced. Only in 3 cases *S. maltophilia* was identified preoperatively, in 3 patients the microorganism was isolated from the removed hardware, in 3 cases it was isolated from the tissue biopsy samples and in one — from blood.

Average time from primary surgical intervention at this locus to the development of an infection process caused by *S. maltophilia* was 9.2 years (3.7 to 16.1). In one case, the patient was discharged without surgery in order to treat a pronounced comorbidity. Other 8 patients underwent surgery. Only in 2 cases where the pathogen was isolated from the joint fluid, etiotropic antibacterial therapy (ABT), including co-trimoxazole, was administered since the surgical debridement. In the remaining cases, the patients received empirical ABT (n = 5) or antibacterial prophylaxis (n = 1). Etiotropic antibiotic therapy was administered to the patients only after the isolation of *S. maltophilia* from the intraoperative material. Six out of nine patients received co-trimoxazole during the inpatient period. In the early postoperative period, recurrence of the infection occurred in 3 out of 8 operated patients, which required repeated surgical interventions, and the co-trimoxazole therapy was continued. The infectious process was stopped in all patients at the time of discharge.

Clinical case

A 74-year-old patient (176 cm, 85 kg) was admitted with complaints of pain, limited range of motion in the right hip and shortening of the right lower extremity. Patient had a history of coronary heart disease, atherosclerotic cardiosclerosis, grade 2 hypertension with risk of cardiovascular complication of the 3rd category, complete blockade of the right bundle branch, non-acute chronic gastritis.

In July 2016, total hybrid arthroplasty was performed in the local hospital for idiopathic right-sided hip osteoarthritis. The postoperative period was uneventful. In September 2017, the patient fell on his right side and was admitted to the hospital again. No signs of skeletal trauma were found, and he was discharged with the diagnosis of "soft tissue bruise of the right thigh". Pain syndrome was persisting, and some time later hyperemia and swelling appeared. In October 2019, the patient was consulted by a surgeon of the septic surgery department on an outpatient basis: diagnostic joint puncture was performed, *S. maltophilia* strain was isolated from the aspirate. Surgical treatment for the diagnosed chronic PPI was recommended. Diagnosis on admission: orthopedic joint implants, total arthroplasty of the right hip (2016), chronic deep surgical site infection (CDSSI), chronic osteomyelitis of the right femur and pelvis 3B (l). On admission, X-ray exa-mination showed instability of the cementless acetabular component of the right hip prosthesis with dislocation of the femoral head. Cemented femoral component was stable (Fig. 1 a). Lab tests revealed signs of an exacerbation of the infection: WBC – 8.3×10^9/l, erythrocyte sedimentation rate – 57 mm/min, CRP – 143 mg/l, and a decrease in the filtration capacity of the kidneys: blood creatinine – 118 μmol/l, estimated creatinine clearance (CC) – 71.6 ml/min.

Taking into account the patient's age and pronounced comorbidities, one-stage replacement of the prosthesis was attempted. Revision, removal of prosthetic components and bone cement and radical surgical debridement were performed. Joint fluid, 5 tissue biopsy samples and removed prosthetic components were taken intraoperatively for bacteriological examination. According to the W.G. Paprosky classification, the bone defect was IIC for the acetabulum and II for the femur. After careful cleaning of the surgical area with an antiseptic solution (polyhexanide) and washing with a large volume of a saline solution, prosthesis reimplantation (Zimmer Biomet, USA) with cemented fixation of components (6.0 g meropenem per 40 g standard DePuy CMW 3 cement package (Johnson & Johnson, USA) was performed with plastic repair of the acetabulum with augment. The wound was drained according to Redon. Intraoperative blood loss was 1100 ml. Considering the identified etiology of the infection, the patient received parenteral etiotropic ABT starting the day of the surgery: co-trimoxazole 0.96 g 2 times a day and meropenem 1.0 g 3 times a day for 10 days.

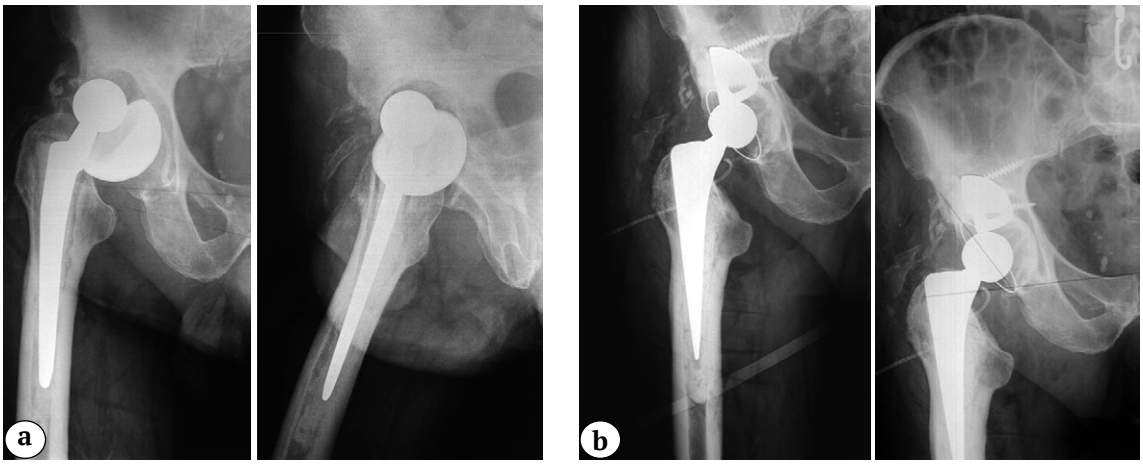

Fig. 1. X-rays of the right hip:
a — on admission with signs of acetabular component instability and prosthetic head dislocation;
b — after one-stage revision arthroplasty

Control X-ray the first day after the surgery showed the replacement of the right hip with a total prosthesis with cemented fixation of the components in the correct stable position. Postoperative period was uneventful (Fig. 1b). The drains were removed on the 5th day. The wound healed with primary intension. *S. maltophilia* strain was isolated from all intraoperatively sampled materials, which did not require ABT correction. The sutures were removed on the 14th day. The patient was discharged in satisfactory condition with the recommendation to take co-trimoxazole tablets 0.96 g 2 times a day for 8 weeks and to monitor the clinical blood count, creatinine, transaminases once every 2 weeks to detect possible adverse reactions.

The patient experienced closed dislocation of the prosthesis later the day of discharge being at home in his sleep. He was admitted to the on-call hospital, where an unsuccessful attempt of closed reduction of the prosthesis led to the instability of the femoral component. One week later, the patient was readmitted to the department of septic osteology for surgical treatment. According to the patient, he had been taking the recommended ABT. X-ray showed total right hip replacement with unstable position of cemented prosthetic components with dislocation of the head of the femoral component (Fig. 2 a). No microbial growth was observed in the preoperative punctate.

From the day of the patient's readmission to the hospital, oral form of antibiotics was substituted for parenteral: co-trimoxazole and meropenem in the same dose until the discharge of the patient. He received analgesic treatment and symptomatic therapy to correct anemia as part of preparation for revision surgery.

Revision surgery with reinstallation of the acetabular and femoral components was performed 5 days after admission (27 days after one-stage revision arthroplasty). Double-mobility acetabular component and cemented (6.0 g meronem per 40 g standard package of DePuy CMW 3 cement (Johnson & Johnson, USA)) femoral component (Zimmer Biomet, USA) were implanted. Given the stable position of the augments, they were not replaced to prevent an increase of the bone defect.

Early postoperative period was uneventful. Control X-ray on the first day after the surgery showed right hip replacement with correct and stable position of the total prosthesis with cemented fixation of the components (Fig. 2b). On the 14th day after the surgery the patient was discharged from the hospital. At the outpatient stage, the patient was recommended to continue taking co-trimoxazole 0.96 g 2 times a day for 8 weeks.

The patient had a total ABT course of 97 days. He did not complain of adverse reactions related to treatment with antibiotics. Two years later, on admission for elective total left hip replacement, there were no signs of infection and inflamma-

tion in the right hip area. Given the absence of recurrence of the infection, we can retrospectively affirm the complete eradication.

Thus, in the vast majority of the analyzed clinical cases, *S. maltophilia* was isolated as the only etiological agent in patients with long-term chronic recurrent infection, indicating the presence of secondary immunodeficiency. There were no typical changes in the laboratory markers of the infection and inflammation. In 3 out of 8 cases recurrences of infection were diagnosed in the early postoperative period, which required reoperations while continuing co-trimoxazole therapy as the only etiotropic antibiotic.

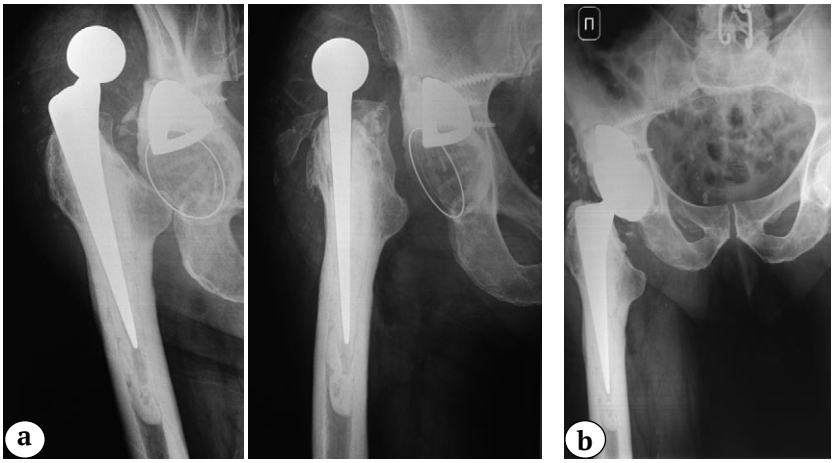

Fig. 2. X-rays of the right hip on re-admission:
a — on admission with signs of femoral component instability and prosthetic head dislocation;
b — after repeated revision arthroplasty

DISCUSSION

S. maltophilia can colonize the surface of medical devices and therapeutic equipment, causing infections of various localizations [9]. Bacteria of this species possess various virulence and persistence factors, including elastase, hyaluronidase, protease, lipase, DNase, RNase and mucinase, providing invasion into the tissues of the macroorganism and protecting against the host immune system [10]. *S. maltophilia* is characterized by its ability to form biofilms consisting of polymeric matrix of polysaccharides, proteins, lipids, nucleic acids and minimally active bacteria, which can disseminate by colonizing new surfaces in less than 24 hours [10].

S. maltophilia has natural resistance to many broad-spectrum antibiotics [8]. Resistance to most beta-lactams is realized via two produced enzymes: L1 — class B zinc-dependent penicillinase and L2 — class A serine-cephalosporinase, which makes *S. maltophilia* resistant to ceftriaxone, piperacillin-tazobactam and carbapenems [8]. Clavulanic acid demonstrated activity only against L2 beta-lactamase [9]. Besides, acetyltransferase synthesis provides resistance to aminoglycosides. Resistance to a number of other antimicrobial drugs is achieved by a system of efflux pumps (e.g., SmeDEF and SmeABC) acting on fluoroquinolones, aminoglycosides, macrolides and tetracyclines. Resistance to co-trimoxazole is regulated by the *sul1* and *dfrA* target modification genes via class 1 integrons [10].

S. maltophilia is often one of the causative agents of polymicrobial infections. The frequency of identification of representatives of this species as a component of microbial associations ranges from 33% to 70% [11, 12]. The presence of *S. maltophilia* in polymicrobial biofilms even with low virulence of their strains increases the risk of horizontal transmission of antibiotic resistance genes to other bacterial species [13]. It has been shown that the transfer of genetic material between sessile forms of bacteria occurs at a higher speed than between planktonic cells. This is due to the enhancement of interbacterial interaction by limiting the mobility of bacteria in biofilms, which allows the biofilms to be considered as reservoirs of genetic diversity [14]. In addition, a number of studies have shown that in case of polymicrobial types of infection, the intermicrobial interaction can influence the prognosis of the infectious disease outcome [11].

Our study revealed low incidence of orthopedic infections caused by *S. maltophilia* (9 cases

over 14 years of follow-up). This fact may be explained by the limited virulence of the strains of this species, its existence in microbial associations where other species are considered the leading pathogens, as well as the difficulties in bacteriological diagnostics associated with the biochemical identification of this bacterial species.

There is an extremely limited number of publications on bone and joint infections, including implant-associated infections caused by *S. maltophilia*. M.E. Hantes et al. successfully managed PPI caused by *S. maltophilia* that developed after total shoulder arthroplasty. The authors note that the infection markers were poorly expressed (white blood cell count — 12.7×10^9/l, CRP — 9.1 mg/l, erythrocyte sedimentation rate — 55 mm/h). Basing on the results of bacteriological examination of intraoperative tissue biopsy samples, levofloxacin and co-trimoxazole were prescribed. In addition, the patient underwent complete immunological examination within the course of treatment, since *S. maltophilia* is more often detected in patients with immunosuppression. However, no possible concomitant pathologies affecting the immune system were detected. This clinical case showed that *S. maltophilia* strains could also cause orthopedic infection in non-immunocompromised patients [15].

Our study revealed that all patients with *S. maltophilia* as an etiological factor of PPI had a history of debridement surgery, i.e., the infection was recurrent. Significant number of surgical interventions, in their turn, may contribute to low immune status and increase the susceptibility of patients to this pathogen.

E.J. Chesnutis 3rd et al. described a case of the secondary *S. maltophilia* osteomyelitis that developed after an open fracture of the distal tibia, and despite daily infusions of ticarcillin/clavulanate and levofloxacin, amputation of the limb at the level of the upper third of the tibia was required [16].

Co-trimoxazole is considered the drug of choice for the treatment of infections caused by *S. maltophilia*, and has been widely used for many years [17]. A number of adverse effects of this drug are known, including renal and hepatic dysfunction, water-electrolyte imbalance, inhibition of bone marrow function and hypersensitivity reactions [18]. The patient in our clinical case did not complain of any adverse reactions after long-term (97 days) treatment with co-trimoxazole.

In recent years, *S. maltophilia* isolates resistant to co-trimoxazole have been increasingly reported [17, 19, 20]. The existing regulatory documents determining the antibacterial sensitivity criteria specify the epidemiological cut-offs for co-trimoxazole. However, in 2020 the susceptibility range of *S. maltophilia* strains has been changed, and the vast majority of isolated cultures will be evaluated as sensitive only with increased drug exposure or resistant. These changes may significantly limit the eligibility of co-trimoxazole administration in case of infections caused by *S. maltophilia*, despite many years of successful experience of its use.

Fluoroquinolones are used as an alternative for treating infections caused by co-trimoxazole-resistant *S. maltophilia* or in patients with its intolerance [8]. However, levofloxacin also has adverse effects, including cardiac conduction disorders, tendopathy, gastrointestinal disturbances and the high risk of *Clostridioides difficile* infection [8, 20]. A large study showed that levofloxacin was an effective alternative to co-trimoxazole in case of *S. maltophilia* infection [20]. Despite this, there are no criteria for assessing the sensitivity of *S. maltophilia* to fluoroquinolones in the international guidelines for determining the antimicrobial activity of drugs against different types of pathogens (EUCAST, CLSI).

M.L. Landrum et al. report on successful treatment of a case of osteomyelitis after L5-S1 rediscectomy caused by *S. maltophilia*. During the treatment process, etiotropic therapy including levofloxacin for 6 weeks was administered. However, 2 months later, the patient returned to the hospital with increasing low back pain. MRI scans showed recurrence of osteomyelitis, and *S. maltophilia*, sensitive to co-trimoxazole and resistant to levofloxacin, was identified again in the disc aspirate. The patient received co-trimoxazole for 18 months, and the infection was stopped [21].

Tetracyclines (tigecycline, doxycycline, minocycline) are other antibiotics showing efficacy against *S. maltophilia* [22]. In five review studies, the sensitivity rate of *S. maltophilia* to minocycline was 99.5% [12]. In the Russian Federation, minocycline has been registered since May 2022 as an indication for infectious and inflammatory

diseases caused by the pathogens sensitive to this drug (including purulent soft tissue infections, osteomyelitis). In addition to the high level of sensitivity of *S. maltophilia* to minocycline, it is characterized by minimal drug-drug interaction and is relatively well tolerated by patients. This antibiotic can be prescribed in combination with co-trimoxazole in case of ineffectiveness of alternative treatment regimens [8].

EUCAST v. 12 (https://www.eucast.org/clinical_breakpoints) indicates the criteria for evaluating the sensitivity of *S. maltophilia* to the new antibacterial drug cefiderocol, which was approved in the United States and the EU in 2019, but has not been registered in the Russian Federation yet. Five cases of pneumonia caused by *S. maltophilia* treated with this antibiotic were registered within the study of cefiderocol activity against Gram-negative carbapenem-resistant bacteria (CREDIBLE-CR). At the same time, despite the high *in vitro* activity of cefiderocol, the response to treatment in all five cases was considered undetermined, and all-cause mortality was 80% (4 of 5) at the end of the study [23]. This, in our opinion, does not allow to consider the drug as promising for the treatment of patients with PPI.

Due to the wide range of mechanisms of *S. maltophilia* resistance to antimicrobial drugs and the difficulty of achieving target antibiotic concentrations in some body tissues (bone, central nervous system, pulmonary), the combinations of antimicrobial drugs to overcome *S. maltophilia* resistance or to achieve drug synergism were studied. Experimental studies have shown that in case of confirmed sensitivity of *S. maltophilia* to co-trimoxazole, ceftazidime, ticarcillin/clavulanate and aminoglycosides their double or triple combinations have a synergistic effect [8]. Combinations of co-trimoxazole or inhibitor-protected beta-lactams with antibiotics such as tigecycline, fluoroquinolones, televancin [24], rifampicin [25] or colistin in aerosol have also been studied. These drugs have demonstrated various degrees of synergism, including the ability to maintain efficacy in the microbial biofilm.

In clinical practice, the combination of co-trimoxazole, ceftazidime and levofloxacin has been shown to be effective against *S. maltophilia*-induced meningitis [26], while intravenous colistin infusion plus parenteral administration of phosphomycin with tigecycline have resulted effective against complicated biliary tract infection [27]. These groups of drugs are widely used for treating PPI of various etiology and, probably, can be used in case of PPI caused by *S. maltophilia*.

When determining the prospects of clinical use of various antibiotic combinations for the treatment of *S. maltophilia* infection, it is important to understand that *in vitro* synergism must correlate with clinical outcomes, and comparative studies of clinical outcomes are absent due to the rare occurrence of the pathogen. In addition, evaluation of *S. maltophilia* sensitivity is limited by the lack of susceptibility checkpoints for the vast majority of drugs used in clinical practice.

CONCLUSION

Thus, the limited choice of drugs for targeted therapy, the presence of multiple determinants of antibiotic resistance, the existence of microbial associations and patient risks, including implantation, chronic character of infection, advanced age, as well as the presence of pronounced concomitant somatic pathology, can lead to the ineffectiveness of the ongoing treatment of infections caused by *S. maltophilia*. Despite the fact that the representatives of this bacterial species are not obligate pathogens, the described clinical case demonstrates the necessity to consider S. *maltophilia* as a possible etiological agent capable of causing severe chronic infections, including orthopedic ones. At the same time, our study demonstrates that in case of sensitivity of *S. maltophilia* strain to co-trimoxazole, it is possible to administer this drug for a long course as a monotherapy provided that the radical surgical debridement of the focus is performed.

DISCLAIMERS

Author contribution

Kasimova A.R. — literature review, analysis of data, writing the draft, editing.

Gordina E.M. — literature review, analysis of data, writing the draft, editing.

Toropov S.S. — dada collection and writing the draft.

Bozhkova S.A. — idea and concept of the study, text editing.

All authors have read and approved the final version of the manuscript of the article. All authors agree to bear responsibility for all aspects of the

study to ensure proper consideration and resolution of all possible issues related to the correctness and reliability of any part of the work.

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Authors' information

✉ *Alina R. Kasimova* — Cand. Sci. (Med.)
Address: 8, Akademika Baykova st., St. Petersburg, 195427, Russia
https://orcid.org/0000-0001-6284-7133
e-mail: kasi-alina@yandex.ru

Ekaterina M. Gordina — Cand. Sci. (Med.)
http://orcid.org/0000-0003-2326-7413
e-mail: emgordina@win.rniito.ru

Sergey S. Toropov
https://orcid.org/0000-0002-9451-1834
e-mail: doctoropovss@yandex.ru

Svetlana A. Bozhkova — Dr. Sci. (Med.)
http://orcid.org/0000-0002-2083-2424
e-mail: clinpharm-rniito@yandex.ru