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Case Report

Tunnelled Hemodialysis Catheter-Related Bloodstream Infection with *Ochrobactrum Anthropi*: A Report of the First Two Cases from Bulgaria and a Brief Overview

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Abstract

The use of central venous catheters for hemodialysis continues to grow worldwide, despite the efforts of many specialists. Patients with end-stage renal disease have impaired immunity, which is why infections are the most common complication seen in them. It worsens their quality of life and is a major cause of high morbidity and mortality, especially in hemodialysis patients.

We report two cases of catheter-related bloodstream infection in hemodialysis patients caused by *Ochrobactrum anthropi*, which are the first reported cases in Bulgaria and present a brief literature review of the known facts.

Keywords

catheter-related infection, hemodialysis treatment, *Ochrobactrum anthropi*

INTRODUCTION

Infections are a common complication among patients treated with hemodialysis. Patients undergoing hemodialysis with central venous catheter as a vascular access have two to three times higher risk for hospitalization due to infections in comparison with patients with arteriovenous fistula or prosthesis.[1] The frequency of catheter-related bloodstream infections (CRBSIs) has been reported to be from 1.1 to 5.5 incidents per 1000 catheter-days (CD) and they are related to increased morbidity, hospitalizations and mortality. The most common causative pathogens are gram-positive bacteria as *Staphylococcus aureus* and coagulase-negative staphylococci – 40% to 80% of CRBSIs. Gram-negative organisms cause 20% to 40% CRBSIs, whereas polymicrobial infections (10%-20%) and fungal infections (<5%) are less common.[2,3]

The changes in immunity in patients with terminal uremia are complex and not well understood. Hypercytokinemia is common in uremia and is probably associated with an increased concentration of pro-inflammatory cytokines due to both decreased renal clearance and increased production in these patients.[4,5]

Ochrobactrum anthropi is a Gram negative [G (-)], non-lactose fermenting, oxidase-positive bacillus, which used to be known as *Achromobacter*. It was defined by the Center for Disease Control and Prevention (CDC) as group Vd-1, Vd-2. [6]

CASE REPORTS

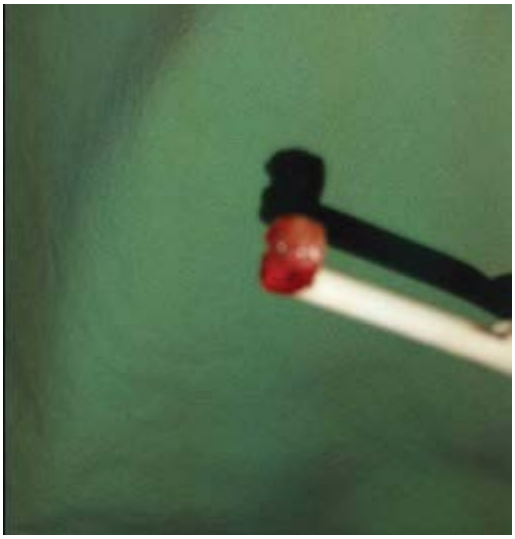
Case 1

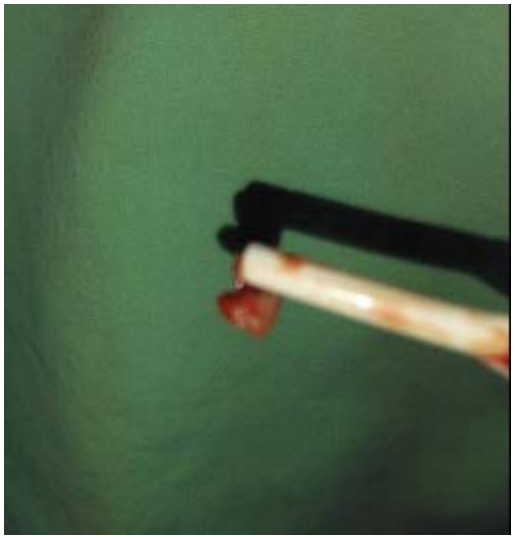
We present a 61-year-old Caucasian male, who has been treated via hemodialysis for 11 years due to chronic glomerulonephritis. His medical history shows two surgical interventions – one due to severe necrotic pancreatitis and a later one due to a bleeding gastric ulcer that could not be managed conservatively. His current vascular access is a tunnelled catheter, inserted into the right subclavian vein via supraclavicular approach two years ago, because of exhausted permanent vascular access. During this period, he had had two incidents of CRBSIs, which were caused by Acinetobacter lwoffii and Acinetobacter baumannii. The former was registered in May 2017 and was caused by Acinetobacter baumannii. Treatment was performed with levofloxacin (×500 mg/i.v.) after each dialysis session for four weeks. In August 2017, Acinetobacter lwoffii was isolated due to clinical data on CRBSI. He was then treated with ceftazidime in a dose of 1 g/daily for five weeks, and at the end of the first week, the tunnelled catheter was replaced over a metal guidewire. When the second incident happened, there was pancytopenia present, which was suspected to be myelodysplastic syndrome, but the diagnosis could not be excluded even after trepanobiopsy had been performed. In April 2018, the patient complained of cold chills during a regular hemodialysis session, with fever (38.1°C) and hypotension an hour later, with no signs of infection or cardiac causes. Blood culture tests were ordered and the isolated pathogen was Ochrobactrum anthropi. The results of the laboratory and instrumental tests were as follows: Hb: 86 g/l, Hct: 0.25, RBC: 3.21×10^{12}/l, Plt: 86×10^{9}/l, WBC: 2.2×10^{9}/l. The differential count of the white blood cells showed granulocytes: 80%, lymphocytes: 14%, monocytes: 6%. The chest X-ray, abdominal ultrasound, and echocardiography found no signs of infection metastases. There were also no signs of a local infection at the exit site and along the subcutaneous tunnel of the cuffed catheter. The infection was treated using meropenem at a dose of 1 g/daily, gentamycin: 1 mg/kg – loading dose and ×0.5 mg/kg, after each dialysis session and for the prevention of secondary candidiasis fluconazole – ×200 mg, orally, after each dialysis session from the second week of the antibiotic treatment. Treatment with meropenem, gentamycin, and fluconazole was performed over 4 weeks. The tunnelled catheter was changed over a metal guidewire 72 hours after the antibiotic treatment had been started and there were no signs of fever.

The infection was successfully treated, which was confirmed by control blood culture tests. During the year following this case, there were no reported CRBSI incidents, which were further proven by blood cultures every four months, with no bacterial growth. The last results of the blood tests showed Hb: 132 g/l, Hct: 0.39, RBC: 4.36×10^{12}/l, Plt: 56×10^{9}/l, WBC: 4.2×10^{9}/l. The differential count of the white blood cells showed granulocytes: 72%, lymphocytes: 24%, and monocytes: 4%.

Case 2

We present a 74-year-old Caucasian male, who has been treated with hemodialysis for 6 months due to hypertensive nephropathy. The vascular access from the very beginning had been a tunnelled catheter, inserted into the right subclavian vein with a supraclavicular approach. Arterio-venous anastomosis was not constructed because the patient declined. No incidents of CRBSIs have been reported so far. During a hemodialysis session the patient felt bad, had cold shivers and his temperature increased up to 39.8°C. Blood culture tests were ordered and the isolated pathogen was Ochrobactrum anthropi. The chest X-ray, abdominal ultrasound, and echocardiography found no signs of infection metastases. There were also no signs of a local infection at the exit site and along the subcutaneous tunnel of the fixed tunnelled catheter. The echocardiography showed vegetation on the top of the tunnelled catheter ***(Figs 1, 2)****.*





Figures 1, 2. Fibrin sheath on the top of the tunnelled catheter.

The results of the laboratory and instrumental tests showed Hb: 73 g/l, Hct: 0.21, RBC: 6.3×10^{12}/l, Plt: 218×10^{9}/l, WBC: 2.2×10^{9}/l. The WBC differential count showed granulocytes: 89%, lymphocytes: 8%, and monocytes: 3%. The patient was treated with meropenem, gentamycin, and fluconazole for 4 weeks with the same doses as described in Case 1. The tunnelled catheter was changed with metal guidewire. The infection was successfully treated which was confirmed by control blood culture tests. After the end of treatment of the described infection, we constructed latero-terminal brachiocephalic anastomosis of the non-dominant arm, which is the current vascular access for this patient.

DISCUSSION

The changes in the immunity of patients with ESRD affect both innate and adaptive immunity.[7] Congenital immune detection of pathogens is characterized by the speed of its action and the presence of pathogen-related molecular models (PAMPs). These cells have receptors contained on their surface or in the cell called pattern recognition receptors (PRRs). They recognize molecules that are widely shared by pathogens but are different from host molecules, collectively referred to as pathogen-related molecular models.[8] These receptors are expressed in many cells, such as dendritic antigen-presenting cells (APCs). Coordinated cellular interaction is associated with dendritic cells (DC), natural killer (NK) and T-helper cells (Th) may be affected by different pathogen-associated molecular models and possibly different responses.[7,8] PAMPs of the secretory class support the cell's ability to recognize the complement system. The mannose-binding lectin family represents them. Patients with ESRD often have an increased level of mannose binding lectin. On the other hand, there are reports that patients undergoing hemodialysis with low levels of these opsonins have increased mortality due to infections.[9] Anding K, et al.[10] report that bactericidal capacity of neutrophils declines in patients treated with HD in comparison with healthy controls. As this capacity can be improved by the HD procedure, it is suggested that the eliminated by the HD procedure hemodialysis toxic substances could impair neutrophil function.[10] This damage could also be the result of the effect of the uremic state on the fragile balance of neutrophils apoptosis and necrosis.[11] These factors include different glycation end products, TNF-α, oxidized low-density lipoproteins (oxLDL) and others.[7] ESRD is a condition of hypercytokinemia, including various pro-inflammatory cytokines such as IL-10, TNF-α[12], and IL-6[13]. Impaired renal function enhances production and decreases the elimination of cytokines, which is the main cause of their elevated levels in patients with ESRD.[12] In addition to uremia, membrane biocompatibility and the ability to "leak" cytokines through reverse filtration leads to activation of complement and leukocytes during HD session.[14] The high incidence of bacterial infections in ESRD patients is indicative of their weakened adaptive immunity.[15] In laboratory conditions, decreased proliferation of T cells has been observed in these patients.[7,16] Hemodialysis patients also often have B-cell lymphopenia. The likely cause of this phenomenon is the decreased survival of these lymphocytes due to marked apoptosis.[17] *Ochrobactrum* spp. belongs to the family *Brucellaceae*.[18] It is named after the Greek word '*ochros',* which means light yellow. This is the typical color of the colonies of *Ochrobactrum*. This microorganism has the potential of colonizing extremely various habitats.[18-20] The genus of *Ochrobactrum* presently consists of 9 species, but currently only 3 of them – *O. anthropi*, *O. intermedium*, and *O. pseudointermedium* can be isolated in clinical samples.[21] *O. anthropi*, from the clinically significant species, is increasingly often reported as potentially problematic, opportunistic, and nosocomial pathogen.[17,18,21] *Ochrobactrum anthropi* is an aerobic, oxidase-positive, urease-positive, Gram-negative, mobile, non-lactose fermenting bacillus, which used to be known as "*Achromobacter*", group Vd.[22] Most cases of human infections caused by this pathogen have been reported in connection with a central venous catheter but their number is still quite small.[17,18,23] This microorganism has been established as a causative agent of infectious endocarditis, pancreatic abscess, osteochondritis, endo-ophtalmitis, urine infection, meningitis, pelvic abscess, and osteomyelitis.[17,18] Infections with this pathogen are most common in immunocompromised patients.[18,24,25] It has been proven that most isolates of *O. anthropi* are widely resistant to chloramphenicol and all β-lactams (apart from imipenem) via production of AmpC β-lactamase OCH-1. This β-lactamase is chromosomal, inducible, and resistant to inhibition by clavulanic acid.[26] Overall, the microorganism is considered sensitive to gentamycin, fluoroquinolones, sulfamethoxazole-trimethoprim, and colistin.[18,27-29]

The neutropenia we found could be interpreted as such in conditions of sepsis caused by gram-negative bacteria.[30,31] Given the pancytopenia described in Case 1, which was established even before the development of this infection, we refrain from theorizing in this direction.

The final diagnosis of CRBSI requires growth of the same organism from at least one percutaneous blood sample and from the top of the catheter (A-I) or two blood culture tests (one from the catheter insert and one from a peripheral vein) complying with the requirements of quantitative blood culture tests or DTP (A-II).

Quantitative blood culture is the most accurate test for diagnosing CRBSI of patients with tunnelled catheter, but differential time of positivity (DTP) is also highly reliable. None of the methods requires catheter removal. If the blood sample cannot be taken from a peripheral vein, more than 2 blood samples, from the catheter, must be taken from both lumens.[32]

In our practice, we use culture medium BD BACTECR Plus Aerobic/F (Bacton, Dickinson and Company, Sparks, MD 21152). For determination of antibiotic sensitivity of the isolated bacteria, we use the disk-diffusion method of Bauer-Kurby or via determination of the minimal inhibito-

ry concentration (MIC) by using the automatic system VITEK 2.

The described clinical cases were 7 months apart in time, which excludes the possibility of a nosocomial infection with the same strain at the same time.

According to G. Beathhard[33], patients with tunnelled catheters and signs of CRBSI together with positive blood culture can be treated in several ways:

- by removing the catheter;
- by changing the catheter with the help of a metal guidewire;
- by changing the catheter with the help of a metal guidewire and making a new exit site and a new tunnel;
- by leaving catheter in place until the infection is managed.

Tunnelled catheters must be removed from patients with CRBSI due to some of the following states: severe sepsis, purulent thrombophlebitis, endocarditis, continuing bloodstream infection despite more than 72 hours of antibiotic therapy that the microorganism is sensitive to, infections caused by *S. aureus*, *P. aeruginosa*, fungi or mycobacterium.[32]

We made a decision to change the catheter with the help of a metal guidewire based on two considerations: there was catheter sepsis, caused by potentially problematic, opportunistic organism and there were no signs of exit-site infection and/or infection of the subcutaneous tunnel of the catheter.

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Инфекция кровотока, связанная с катетером при туннельном гемодиализе, вызванная *Ochrobactrum Anthropi*: отчёт о первых двух случаях из Болгарии и краткий обзор

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Резюме

Несмотря на усилия многих специалистов, использование центральных венозных катетеров для гемодиализа продолжает расти во всём мире. У пациентов с терминальной почечной недостаточностью нарушен иммунитет, поэтому инфекции являются наиболее частым осложнением, наблюдаемым у них. Это ухудшает их образ жизни и является основной причиной высокой заболеваемости и смертности, особенно у пациентов, находящихся на гемодиализе.

Мы сообщаем о двух случаях катетер-ассоциированной инфекции крови у пациентов, находящихся на гемодиализе, вызванной *Ochrobactrum anthropi*, которые являются первыми зарегистрированными случаями в Болгарии, и даём краткий обзор литературы по установленным фактам.

Ключевые слова

катетерная инфекция, лечение гемодиализом, *Ochrobactrum anthropi*