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# Chronic Infection Related To Tunneled Catheter for Hemodialysis with Presence of Macroscopic Microbial Biofilm

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## 1. Abstract

Although the recommended vascular access for hemodialysis is the arteriovenous fistula, tunneled central venous catheters (CVC) are commonly used for treatment. In hemodialysis patients, infections are the most common cause of morbidity and are the second most common cause of mortality of which CVCs are common potential causes. Prevention, timely detection, and proper treatment of infections related to percutaneous vascular accesses are defining factors in the reduction of complications. The first most common pathogens that cause infections are gram-positive bacteria (S. aureus and coagulase-negative staphylococci); the second most common cause are gram-negative bacteria (Pseudomonas aeruginosa in E. coli, Klebsiella pneumoniae, and Acinetobacter baumanii); and less frequently, fungal infections (Candida Albicans). Although acute infections can be eliminated with an antimicrobial course, biofilm infections are not as easily eradicated and may cause recurrent infections that only resolve with the removal of the catheter. Strict adherence to aseptic measures before, during, and after the insertion and manipulation of Central Venous Catheters area fundamental preventive measure for catheter-related bacteremia.

## 2. Introduction

Renal replacement therapy by hemodialysis requires adequate vascular access, preferably by a native arteriovenous fistula (AVF) as opposed to a percutaneous central venous catheter in accordance with national and international guidelines. The use of a central venous catheter (CVC) versus arteriovenous fistulas or grafts is associated with increased morbidity and mortality due to the risk of both infectious and thrombotic complications. Because of this, current recommendations advise the use of AVF or grafts in 80% of patients whenever possible. However, the use of percutaneous catheters continues to be of great importance especially in emergency situations or those in whom native vascular access is not possible, such as in patients with severe vascular pathology or the elderly. Commonly, infections are due to colonies of skin flora found at the catheter insertion site. They can vary between local () to systemic (bacteremia, endocarditis, suppurative thrombophlebitis, osteomyelitis) inefction. The frequency of bacteremias due to dialysis catheter infections can range from 3-6 episodes per 1000 catheter days, which represents an incidence of approximately 1-2 episodes of bacteremia per catheter per year.

The incidence of bacteremia in patients with non-tunneled catheters is 2-3 times greater than in those with tunneled catheters while tunneled catheters have an incidence of 10-12 times greater than AV fisulas or grafts. Gram-positive microorganisms are responsible for the bulk of hemodialysis catheter-related infections. Coagu-

lase-negative Staphylococcus and Staphylococcus aureus account for more than half of the cases in most studies. Gram-negative microorganisms account for 20% to 40%, and polymicrobial infections are implicated in 10% to 20% of all episodes of bacteremia related to catheter infections. Staphylococcus aureus infections are often associated with significant morbidity and mortality. The most consequential risk factor for hemodialysis catheter infections is prolonged catheter use. Other risk factors are a history of previous infections, recent surgery, diabetes mellitus, iron overload, immunosuppression, and hypoalbuminemia.

## 3. Case Presentation

A 37-year-old male patient presents with fever and chills 30 minutes after starting the hemodialysis session. The patient has been on hemodialysis for 2 years through a right tunneled CVC. The patient is known to have type 1 diabetes with poor glycemic control and diabetic nephropathy as well as hypertension. The patient presented his first episode of bacteremia related to infection of the tunneled catheter 8 months after the catheter insertion with in blood cultures growing Pseudomonas Aeruginosa. He was treated empirically with Vancomycin and Ceftriaxone then switched to Meropenem after the culture sensitivity results came out. Six months later, the patient presented again with fever and chills during hemodialysis sessions and was initially treated with Vancomycin and Ceftazidime. Following positive blood cultures for Pseudomonas Aeruginosa, treatment was completed with Ceftazidime for 4 weeks. One month after completing the treatment, the patient had another episode of fever and chills and promptly refused treatment with intravenous antibiotics. Another blood culture was taken, which showed growth of Burkholderia cepacia. Treatment with Trimethoprim/Sulfamethoxazole orally was initiated as the patient continued to refuse intravenous therapy. The patient continued to experience bouts of fever and chills during the hemodialysis sessions, refusing removal of the tunneled catheter. A blood test was performed during this episode which showed the following: White Blood Cell 6.55X 109/L, Neutrophils 77.4%, Hemoglobin 5.92 g/dL, Platelets 107 103/uL. The patient also refused a blood transfusion and was started on iron and erythropoietin.

After finishing the antibiotic treatment, a new culture was performed which showed no bacterial growth. The patient remained asymptomatic then developed had another episode of fever during the hemodialysis and Ceftazidime was started. An additional blood culture showed new growth of Pseudomonas aeruginosa and he was started on ceftazidime based on sensitivity results the presence of a cutaneous reaction during the administration of the antibiotic, however, prompted the change to Meropenem. During the treatment period, the patient remained asymptomatic and ultimately accepted the removal of the tunneled catheter. The removal of the catheter was performed by dissection of the cuff and removal of the external tunnel tissue without complication. An echocardiogram was performed before catheter removal, and showed no valvular vegetation. After removal, a small agglomerated mass was located between the branches of the catheter (Figure 1 and 2). The catheter tip with the small mass was sent for culture and which confirmed growth of Pseudomonas aeruginosa. A right femoral catheter was inserted and antibiotics continued for 21 days with the patient remaining asymptomatic.

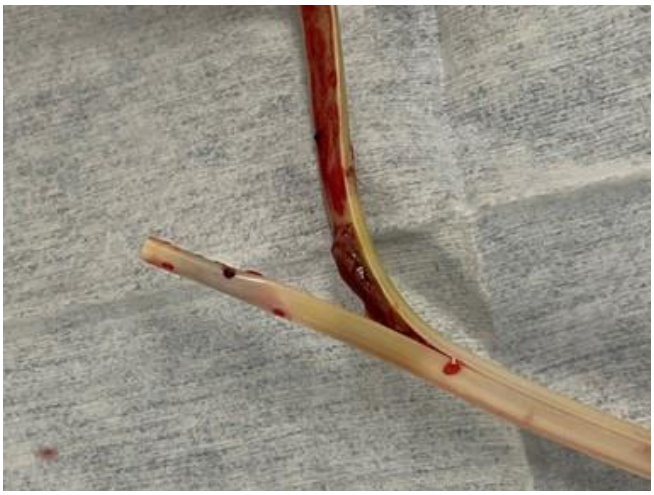

**Figure 1**: After removal, a small agglomerated mass was located between the branches of the catheter.

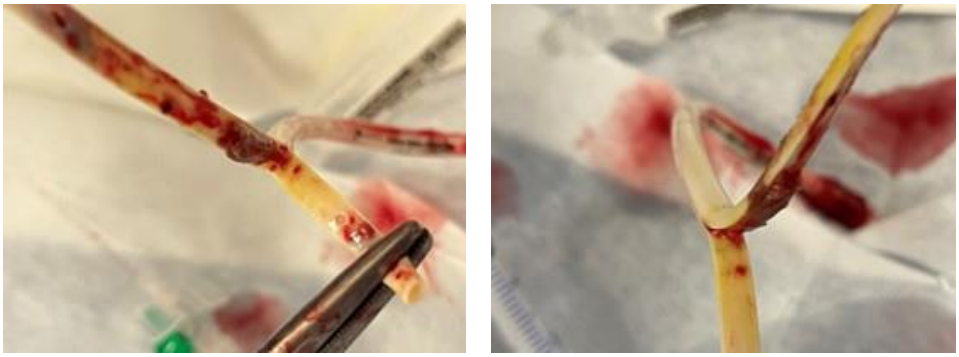

**Figure 2**: After removal, a small agglomerated mass was located between the branches of the catheter.

## 4. Discussion

In this case the patient had a history of chronic infection of the hemodialysis catheter which resulted in recurrent episodes of bacteremia. As seen in the images of the catheter tip, a biofilm had formed and adhered to the catheter near the arterial branch; presenting a reservoir of bacteria and a constant source of infection. Although the patient responded temporarily to antibiotic treatment, the source of the infection remained given the creation of a biofilm.

The most probable main source of the contamination was the bacterial flora of the patient's skin or during the accessing of the catheter. Contamination occurs mainly due to suboptimal aseptic measures and can lead to intra- or extra luminal colonization. Subsequent to contamination, adhesion occurs on intravascular catheter surfaces, which can then lead to colonization and biofilm formation. The best preventative approach is hand hygiene and skin antiseptic methods for catheter insertion and manipulation. The most active and superior disinfectant has been proven to be Chlorhexidine-alcohol. Biofilms are communities of microorganisms that grow aggregated and protected by an extracellular matrix that they produce themselves. The extracellular matrix is composed of proteins, extracellular deoxyribonucleic acid and exopolysaccharides. The study of biofilms has become very important in recent decades since their presence favors the development of other infections such as wound infections, osteomyelitis, otitis, infections of intravascular catheters, urinary catheters, and joint prostheses. Moreover, the presence of biofilms favors antimicrobial tolerance and increases the development of resistance. Microorganisms that grow in a biofilm develop a high tolerance to antimicrobial agents which can be thousand times higher compared to those that grow in free form. Several studies have concluded that the physicochemical characteristics of the extracellular matrix that protects microorganisms also have the ability to repel and retard the penetration of most antimicrobial agents. In addition, biofilms have also been observed to maintain the presence of persistent microbial cells that present an inactive metabolic state and have morphological changes that allow them to resist antimicrobial treatments. Once secreted, these are activated again favoring new foci of infection and formation of new biofilms. An important approach to the treatment and prevention of biofilm formation is the catheters lock with antimicrobial agents, which are instilled at high concentrations inside the catheter for long dwell times. Several solutions have been sought to prevent the colonization of hemodialysis catheters, the combination of broad-spectrum antibiotics (Vancomycin, Gentamicin) and anticoagulants such as heparin or Trisodium citrate and chelators such as EDTA have shown in vitro efficacy in preventing the formation of biofilms. Taurolidine is a broad-spectrum anticoagulant and antimicrobial agent effective in infection prophylaxis.

Locking central catheters with antiseptics such as Taurolidine, ethanol, the combination of citrate with methylenoparabens blue, or Taurolidine and heparin have shown efficacy against bacterial biofilm and in the prophylaxis of bacteremia in relation to vascular catheters. The clinical experience in the use of these substances is still limited to be able to make recommendations. In addition, some adverse effects observed with the use of some substances also limit their use, for example, complications associated with the passage of ethanol to peripheral blood have been described. Some of these complications include cardiovascular collapse, pulmonary embolism, ethyl intoxication, and, in the case of Trisodium citrate, hypocalcemia and ventricular arrhythmias.

## 5. Conclusion

Following sterile technique during central line insertion and maximum asepsis during frequent handling of vascular accesses is of great importance for the prevention of infections related to central venous catheters. Educating hemodialysis patients as to the importance of a more permanent access in those who are eligible is important. In those in whom central lines ore studies are needed to more effectively prevent infection in those who require catheters, including developing catheter lock. This would help reduce both vascular access failure as well as the development of systemic infections that may lead to increased morbidity and mortality.

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