Chapter 18
Catheter-Related Bloodstream Infection

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Case Presentation

A 16-year-old male with end-stage kidney disease (ESRD) maintained on hemodialysis (HD) by way of a tunneled HD catheter in his right femoral vein develops fever and hypotension during his dialysis treatment. He denies a history of rhinorrhea, cough, abdominal pain, nausea, emesis, or diarrhea. He is anuric. He has had no ill contacts. Physical exam reveals no obvious source of infection, and the dialysis catheter exit site is without erythema, warmth, tenderness, or purulent drainage. Blood cultures are obtained from the HD catheter, the dialysis circuit, and a peripheral vein. He receives treatment with intravenous vancomycin and a third-generation cephalosporin in addition to intravenous fluid administration, with stabilization of his blood pressure. He is admitted to the hospital where treatment with intravenous antibiotics is continued.

The patient has ESRD due to congenital nephrotic syndrome. He required a nephrectomy and treatment with peritoneal dialysis in the neonatal period, but had recurrent peritonitis with peritoneal membrane failure prompting conversion to HD by way of a tunneled catheter at 15 months of age. He received a living-related kidney transplant at age 28 months but lost graft function secondary to acute and chronic rejection at age 12 years. He has high levels of antihuman leukocyte antigen antibodies which have thus far prevented repeat kidney transplantation. He was referred for creation of an arteriovenous fistula (AVF) or placement of an arteriovenous graft (AVG) but was felt not to be a candidate given significant central venous stenoses related to numerous prior central venous catheters. He has therefore been receiving HD by way of a central venous catheter. He has had recurrent catheter

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infections and has exhausted all catheter sites except for his current site in the right femoral vein.

Within 24 h, blood cultures from both the HD catheter and dialysis circuit are positive for methicillin-resistant *Staphylococcus aureus*. Peripheral blood culture is negative. An antibiotic lock with vancomycin is initiated, in addition to ongoing treatment with intravenous vancomycin. The patient is clinically well, without fever after 36 h of antibiotic treatment, but cultures obtained from the catheter continue to grow *S. aureus*. The tunneled femoral hemodialysis catheter is exchanged over a wire and replaced with a non-tunneled catheter. Subsequent blood cultures are negative. After completion of 3 weeks of intravenous vancomycin, the non-tunneled catheter is exchanged over a wire with a tunneled hemodialysis catheter. The patient is discharged home to resume outpatient dialysis.

Clinical Questions

1. What is the definition of an HD access-related bloodstream infection (BSI) and how is it diagnosed?
2. What are the rates of HD access-related BSI in children?
3. What is the recommended treatment of an HD access-related BSI and what is the appropriate management of this child?
4. What is the most effective method to minimize the risk for HD access-related BSI?

Diagnostic Discussion

1. Although ongoing efforts seek to establish a clear and consistent definition of a catheter-related BSI, the most common definition currently used is that developed by the Centers for Disease Control and Prevention (CDC) [1]. According to the CDC, a primary BSI is a laboratory-confirmed BSI that is not secondary to an infection at another body site, and a central line-associated BSI is a laboratory-confirmed BSI where the central line was in place for >2 calendar days on the date of event [1]. The distinction between primary and catheter-associated BSI is important as the management of a positive blood culture due to an infection at another site, e.g., pneumonia, may be different than if the positive culture is reflective of infection of the catheter, particularly with regard to the management of the catheter itself [2]. Thus, diagnosis of an HD access-related BSI requires an assessment for other sites of infection, as well as careful interpretation of the blood culture results. Current guidelines from the Infectious Diseases Society of America (IDSA) suggest that if a catheter-related BSI is suspected, blood cultures should be obtained both from the catheter, after the catheter hub has been cleaned with either alcohol, tincture of iodine, or alcoholic chlorhexidine to

reduce the risk for contamination, and from a peripheral vein [2]. A definitive diagnosis of HD access-related BSI requires that the same organism grows from at least one peripheral culture and from cultures obtained from the catheter [2]. For the BSI to be attributed to the catheter, there should be a quantitative or a differential time to positivity between the cultures from the central line and peripheral vein, with at least a threefold greater colony count from blood cultures obtained from the catheter than the peripheral vein or detection of microbial growth from the catheter culture at least 2 h before the peripheral culture [2]. The IDSA guidelines recognize that there are unique aspects of managing catheters in both pediatric and HD patients, and so the guidelines specify that in HD patients in whom a peripheral venous culture cannot be obtained or is to be avoided to spare vessels for future dialysis access, a second culture may be obtained from the dialysis tubing during a dialysis session [2]. However, the IDSA guidelines recognize that it is unclear if the quantitative differential between catheter and "peripheral" cultures remains if the peripheral culture is obtained from the tubing during a dialysis session [2].

2. Given the evolving definition of an HD access-related BSI, the reported rates of these infections in children vary considerably. In addition, reports in the pediatric nephrology literature typically do not distinguish between a primary BSI and a true HD access-related BSI. Bearing this limitation in mind, previous studies have reported HD access-related BSI in pediatric patients ranging from 0.5 to 4.8 per 1,000 catheter days [3–7]. In addition, registry data have consistently demonstrated that HD access-related BSI is a leading cause of hospitalization and mortality in pediatric dialysis patients [8–10]. Gram-positive organisms account for the majority of HD access-related BSIs, with additional infections caused by gram-negative and fungal organisms [3, 6].
3. Initial management of a pediatric patient with suspected HD access-related BSI includes empiric antibiotics as well as general supportive care. Empiric antibiotic treatment should be guided by the patient's clinical status as well as the antibiogram data from the dialysis unit or hospital and should include both gram-positive and gram-negative coverage [2]. Vancomycin is recommended for empiric gram-positive coverage unless the dialysis unit has a low prevalence of methicillin-resistant *Staphylococcus aureus*, in which case cefazolin may be used [2, 11]. An aminoglycoside or third-generation cephalosporin should be used for gram-negative coverage [2, 11]. Although catheter removal is generally recommended in the setting of a catheter-associated BSI, it is recognized that in HD patients, the catheter provides access for ongoing life-sustaining dialysis, and additional vascular access sites may be limited. The potential treatment options in this setting are shown in Fig. 18.1 and include (1) intravenous antibiotics alone, (2) prompt catheter removal with placement of a new catheter after some interval of time, (3) exchange of the catheter over a guidewire, or (4) use of systemic antibiotics and an antibiotic lock [2]. Catheter removal is indicated in any clinically unstable patient and in patients who remain symptomatic for more than 36 h [2]. In patients with symptomatic improvement, catheter removal and replacement, catheter exchange, or the use of antibiotic locks should be

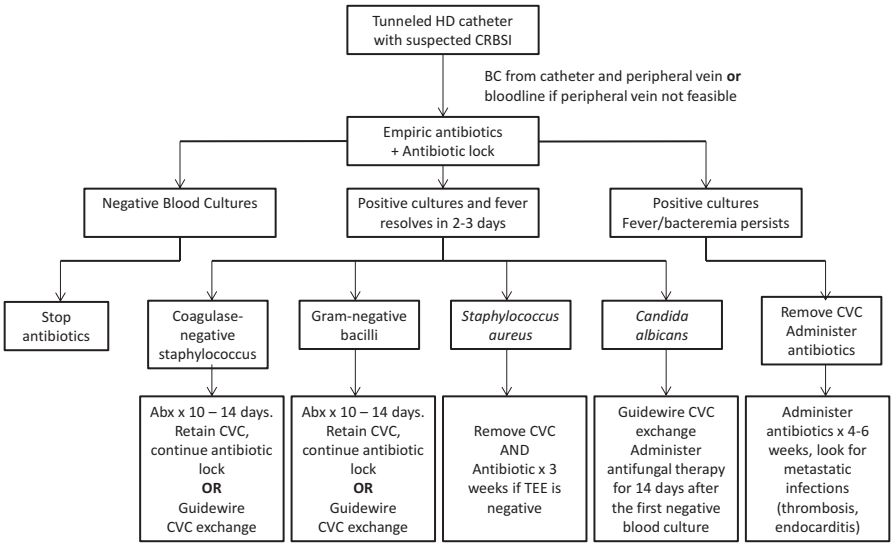

Fig. 18.1 Approach to treatment of catheter-related bloodstream infection (CRBSI) among patients who are undergoing hemodialysis (HD) with tunneled catheters. *BC* blood culture, *CVC* central venous catheter, *TEE* transesophageal echocardiograph [2] (Reprinted with permission)

considered in addition to systemic antibiotics, as data in adult HD patients demonstrate a fivefold higher rate of treatment failure with antibiotics alone compared to catheter removal [2, 11]. In particular, catheter removal with placement of a temporary catheter in another anatomical site, or catheter exchange over a wire if no alternative sites are available, is strongly recommended for HD access-related BSI due to *Staphylococcus aureus*, *Pseudomonas* species, or *Candida* species [2]. The IDSA specifically states that the indications for catheter removal for children are similar to those for adults, but acknowledge that the difficulty in obtaining alternate vascular access sites in children often necessitates antibiotic treatment without catheter removal [2]. If the decision is made to keep the existing catheter, the addition of antibiotic locks to systemic antibiotics has been shown to improve catheter survival and decrease exposure to systemic antibiotics, with some studies showing particular success in treating gram-negative infections compared to infections with *Staphylococcus aureus* [12–14]. This approach may be particularly useful for patients with limited vascular access sites in whom preservation of the existing catheter is crucial. The ultimate choice of antibiotic and duration of therapy will be based on the causative organism, the clinical course of the patient, and adjunctive therapies including removal/replacement of the catheter (Fig. 18.1) [2].

4. National and international registry data have consistently demonstrated that use of a central venous catheter rather than an AVF or AVG is associated with a significantly increased risk for infection among pediatric HD patients [10, 15–17].

Current guidelines therefore recommend the use of an AVF/AVG for HD access in children unless the patient weighs less than 20 kg, a kidney transplant is planned within 1–2 years, or HD is serving as a bridge to PD [16, 18]. Although use of an AVF/AVG is the most effective way to minimize the risk for infection, the vast majority of children continue to receive HD by way of a central venous catheter [9, 17, 19]. Given the significant morbidity and mortality associated with HD catheter-related BSI in the United States, the CDC has launched the Dialysis Bloodstream Infection Prevention Collaborative which includes recommended practices for HD catheter care, such as cleaning the catheter exit site with an antiseptic agent, preferably chlorhexidine, and use of antimicrobial ointment at the exit site with each dressing change [20]. The CDC's core interventions also include enforcing proper hand hygiene and scrubbing of the catheter hub with an antiseptic agent when it is accessed and disconnected from the dialysis tubing [20]. Studies in adult HD patients have also shown a reduction in BSI when prophylactic antibiotic locks (such as citrate with gentamicin) are used for routine catheter maintenance compared to standard heparin locks, although there are limited data on the use of prophylactic antibiotic locks in pediatric HD patients [21, 22]. While some of the current recommendations are evidence based, others reflect expert opinion. Currently, the Children's Hospital Association's Standardizing Care to Improve Outcomes in Pediatric End Stage Renal Disease (SCOPE) Collaborative is evaluating whether increased implementation of standardized catheter practices, modeled in large part after the CDC core interventions, can reduce HD access-related BSI in children maintained on chronic dialysis at participating centers located throughout the United States [23].

Clinical Pearls

1. Hemodialysis access-related BSIs are a significant source of morbidity and mortality in children with end-stage kidney disease.
2. The most effective strategy to minimize risk for HD access-related BSI is the use of an arteriovenous fistula or graft, but the majority of children continue to receive dialysis by way of a catheter.
3. Definitive diagnosis of an HD access-related BSI requires careful examination for other sites of infection and thoughtful review of blood culture results.
4. Empiric treatment of HD access-related BSI should include both gram-positive and gram-negative coverage and should be guided by the patient's clinical status and local antibiogram data.
5. Catheter removal should be considered in clinically unstable patients or in HD access-related BSI due to *Pseudomonas* species, *Staphylococcus aureus*, and *Candida* species.

References

1. O'Grady NP, Alexander M Burns LA, Dellinger EP, Garland J, Heard SO, Lipsett PA, Masur H, Mermel LA, Pearson ML, Raad II, Randolph AG, Rupp ME, Saint S. Healthcare Infection Control Practices Advisory Committee. Guidelines for the prevention of intravascular catheter-related infections. 2011. http://www.cdc.gov/hicpac/pdf/guidelines/bsi-guidelines-2011.pdf. Accessed 18 Apr 2016.
2. Mermel LA, Allon M, Bouza E, Craven DE, Flynn P, O'Grady NP, et al. Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis. 2009;49(1):1–45.
3. Araya CE, Fennell RS, Neiberger RE, Dharnidharka VR. Hemodialysis catheter-related bacteremia in children: increasing antibiotic resistance and changing bacteriological profile. Am J Kidney Dis. 2007;50(1):119–23.
4. Eisenstein I, Tarabeih M, Magen D, Pollack S, Kassis I, Ofer A, et al. Low infection rates and prolonged survival times of hemodialysis catheters in infants and children. Clin J Am Soc Nephrol. 2011;6(4):793–8.
5. Kovalski Y, Cleper R, Krause I, Davidovits M. Hemodialysis in children weighing less than 15 kg: a single-center experience. Pediatr Nephrol. 2007;22(12):2105–10.
6. Onder AM, Chandar J, Coakley S, Abitbol C, Montane B, Zilleruelo G. Predictors and outcome of catheter-related bacteremia in children on chronic hemodialysis. Pediatr Nephrol. 2006;21(10):1452–8.
7. Paglialonga F, Esposito S, Edefonti A, Principi N. Catheter-related infections in children treated with hemodialysis. Pediatr Nephrol. 2004;19(12):1324–33.
8. Lofaro D, Vogelzang JL, van Stralen KJ, Jager KJ, Groothoff JW. Infection-related hospitalizations over 30 years of follow-up in patients starting renal replacement therapy at pediatric age. Pediatr Nephrol. 2016;31(2):315–23.
9. NAPRTCS. 2011 annual dialysis report. http:www.emmes.com/study/ped/. Accessed 18 Apr 2016.
10. United States Renal Data System. 2015 USRDS annual data report: epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, 2015.
11. Allon M. Treatment guidelines for dialysis catheter-related bacteremia: an update. Am J Kidney Dis. 2009;54(1):13–7.
12. Krishnasami Z, Carlton D, Bimbo L, Taylor ME, Balkovetz DF, Barker J, et al. Management of hemodialysis catheter-related bacteremia with an adjunctive antibiotic lock solution. Kidney Int. 2002;61(3):1136–42.
13. Onder AM, Billings AA, Chandar J, Nield L, Francoeur D, Simon N, et al. Antibiotic lock solutions allow less systemic antibiotic exposure and less catheter malfunction without adversely affecting antimicrobial resistance patterns. Hemodial Int. 2013;17(1):75–85.
14. Poole CV, Carlton D, Bimbo L, Allon M. Treatment of catheter-related bacteraemia with an antibiotic lock protocol: effect of bacterial pathogen. Nephrol Dial Transplant. 2004;19(5):1237–44.
15. Fadrowski JJ, Hwang W, Frankenfield DL, Fivush BA, Neu AM, Furth SL. Clinical course associated with vascular access type in a national cohort of adolescents who receive hemodialysis: findings from the clinical performance measures and US renal data system projects. Clin J Am Soc Nephrol. 2006;1(5):987–92.
16. National Kidney Foundation. KDOQI clinical practice guidelines and clinical practice recommendations for 2006 updates: hemodialysis adequacy, peritoneal dialysis adequacy and vascular access. Am J Kidney Dis. 2006;48(Suppl1):S1–S322.
17. Hayes WN, Watson AR, Callaghan N, Wright E, Stefanidis CJ, European Pediatric Dialysis Working G. Vascular access: choice and complications in European paediatric haemodialysis units. Pediatr Nephrol. 2012;27(6):999–1004.

18. Fischbach M, Edefonti A, Schroder C, Watson A, European Pediatric Dialysis Working G. Hemodialysis in children: general practical guidelines. Pediatr Nephrol. 2005;20(8):1054–66.
19. Fadrowski JJ, Hwang W, Neu AM, Fivush BA, Furth SL. Patterns of use of vascular catheters for hemodialysis in children in the United States. Am J Kidney Dis. 2009;53(1):91–8.
20. Centers for Disease Control and Prevention Dialysis Bloodstream Infection (BSI) Prevention Collaborative. http://www.cdc.gov/dialysis/collaborative. Accessed 18 Apr 2016.
21. Moore CL, Besarab A, Ajluni M, Soi V, Peterson EL, Johnson LE, et al. Comparative effectiveness of two catheter locking solutions to reduce catheter-related bloodstream infection in hemodialysis patients. Clin J Am Soc Nephrol. 2014;9(7):1232–9.
22. Moran J, Sun S, Khababa I, Pedan A, Doss S, Schiller B. A randomized trial comparing gentamicin/citrate and heparin locks for central venous catheters in maintenance hemodialysis patients. Am J Kidney Dis. 2012;59(1):102–7.
23. Children's Hospital Associations Standardizing Care to Improve Outcomes in Pediatric ESRD (SCOPE) Collaborative. https://www.childrenshospitals.org/Programs-and-Services/Quality-Improvement-and-Measurement/Collaboratives/SCOPE. Accessed 18 Apr 2016.