Despite the availability of novel and highly effective broad-spectrum antimicrobial chemotherapeutic agents, intravascular catheter-related bloodstream infections (CRBSI) continue to be associated with an attributable mortality rate of 25% in critically ill patients. Because of their complexity, the management of such infections is often a challenge to the physician caring for seriously ill hospitalized patients. In approaching a patient with a central venous catheter (CVC) and fever or a positive blood culture the physician should be able to answer the following questions related to management: (i) Is the positive blood culture related to contamination from skin microorganisms, colonization of the internal surface of the catheter or bloodstream infection? (ii) What is the source of the bloodstream infection? The catheter or elsewhere? (iii) Should the catheter be removed? (iv) What is the choice and duration of antimicrobial therapy?

Colonization versus infection

Febrile patients with a CVC are often managed by drawing blood cultures simultaneously through the CVC and a peripheral vein. A single positive blood culture with a skin organism (such as coagulase-negative staphylococci, diphtheroids, Bacillus spp., or Propionobacterium spp.) could be the result of skin contamination rather than a true infection, particularly if the positive blood culture was drawn from the peripheral vein. Electron microscopy studies have shown that the catheter lumen usually becomes highly colonized with Gram-positive cocci embedded in biofilm soon after the insertion of the catheter. Therefore, a positive blood culture drawn through the CVC could reflect intraluminal catheter or hub colonization rather than true bacteraemia. A false positive blood culture resulting from contamination or catheter colonization might result in the unnecessary use of antimicrobial agents, hence increasing the risk of emergence of antibiotic-resistant microorganisms and the cost of health care. In addition, a false positive blood culture might divert the clinician’s attention from the true underlying cause of the fever. Laboratory findings suggestive of true bloodstream infection include the following: multiple positive blood cultures with the same organism (at least two blood cultures for coagulase-negative staphylococci); the isolation of more than 30 cfu/mL by quantitative blood culture; the blood culture becomes positive within 24–48 h of being drawn; catheter insertion site inflammation; the isolation of >15 cfu by semiquantitative culture of a catheter tip segment obtained after the exchange of a catheter over a guide wire.

The source of bacteraemia

If the evidence suggests a true bloodstream infection rather than contamination or colonization, the clinician should then determine whether the catheter is the source of the bloodstream infection. There are a number of clinical and microbiological factors that suggest that the catheter is the source of the bloodstream infection and, hence, that it is a CRBSI. Firstly, catheter exit site or tunnel infection, manifesting in the form of erythema, tenderness, warmth and swelling at the insertion site or tunnel. Secondly, the absence of evidence of other sources for the bloodstream infection, e.g. pneumonia, urinary tract infection, surgical wound infection and intra-abdominal abscess. Thirdly, the blood culture being positive for an organism recognized as a common cause of catheter-related infection, e.g. Staphylococcus epidermidis, Staphylococcus aureus, Candida parapsilosis, Bacillus spp. or Stenotrophomonas maltophilia. Fourthly, simultaneous quantitative blood cultures drawn through the CVC and peripheral vein showing that the number of colonies isolated from a blood culture obtained through the catheter is at least five-fold greater than that...
quantitated from a concurrent peripheral blood culture. Bilot and colleagues have recently suggested that if the time difference between non-quantitative blood cultures drawn simultaneously from a central catheter and a peripheral vein becoming positive is in excess of 2 h, then this also suggests CRBSI. The explanation is that, if the blood cultures drawn through the CVC become positive at least 2 h earlier than simultaneous blood cultures drawn from a peripheral vein, then this reflects a significantly higher inoculum, suggesting that the CVC is the source. Finally, if the catheter has been removed or exchanged over a guide wire, then a catheter tip yielding > 15 cfu per segment with the roll plate semiquantitative culture technique, or > $10^3$/mL by the sonication or the vortex techniques, providing that the same microorganism (with the same antibiotic susceptibility pattern) is isolated from the catheter tip and the blood drawn from the peripheral vein, suggests CRBSI.

Catheter removal

Determining whether the catheter should be removed or remain in place in patients with CRBSI should take into consideration at least three factors: the type of CVC (whether the catheter is a short-term non-tunnelled catheter or a long-term surgically implantable catheter); the type and microbiology of the infection; and the status of the underlying host.

Situations that do not require the removal of the catheter include: a definite non-catheter source for the infection and the absence of microbiological and clinical data suggesting the catheter as the source of the bacteremia; and catheter-related coagulase-negative staphylococcal bacteremia. Studies have shown that at least 80% of such infections respond to antibiotic therapy without the removal of the catheter. However, the persistence or recurrence of fever and bacteraemia should lead to catheter removal. On the other hand, situations in which it would be prudent to remove the catheter would include the following: CRBSI associated with hypotension or organ hypoperfusion; persistence of the fever and positive blood cultures while on antimicrobial therapy; CRBSI associated with septic thrombosis of a great vein (as determined by a doppler flow study) or septic emboli in the lungs; and long-term CRBSI associated with long-term catheters and a tunnel or port-pocket infection. Retention of the catheter in patients with CRBSI caused by S. aureus has been shown to be associated with persistence of the candidaemia and increased risk of relapse, as well as a high mortality rate. Therefore, for short-term non-tunnelled central catheters, it is prudent to remove the CVC in CRBSI caused by either S. aureus or Candida spp. In long-term CVC with CRBSI caused by S. aureus, the use of antibiotics has been shown to help treat the infection without the removal of the catheter.

'A nontoxic lock therapy' involves the use of antibiotics after a flush solution of anticoagulant through the catheter. This 'locks' a high concentration of the antibiotics in the lumen of the catheter at least once daily. Various antimicrobial agents such as vancomycin, cefazolin and clindamycin have been used. Occasionally, fluconazole and amphotericin B have been used as antimicrobial lock solutions for Candida spp. infections. Therefore, for long-term catheters that are difficult and expensive to remove, a consideration should be given to the use of antimicrobial lock solutions, together with systemic antimicrobial therapy, for the treatment of S. aureus and Candida spp. catheter-related bloodstream infections. Persistence of the bloodstream infection, persistence of the fever or relapse should lead to the removal of the catheter. A new catheter flush solution containing low concentrations of minocycline and EDTA has been developed recently. The combination of minocycline and EDTA has been shown to be synergic and to have broad-spectrum activity against staphylococci, Gram-negative bacilli and Candida spp. This flush solution has been shown, in association with systemic therapy, to assist in the prevention of complicated catheter-related staphylococcal bacteraemia.

The persistence of fever or bloodstream infection after the removal of the catheter should lead the clinician to investigate the possibility of deep-seated infection, particularly endocarditis or septic phlebitis. A thorough physical examination that includes a cardiac evaluation for a new murmur and fundoscopic evaluation for possible retinitis or Roth spots is necessary, particularly for patients with persisting CRBSI caused by S. aureus and Candida spp. In addition, a flow study (venogram or doppler ultrasound) is necessary to determine whether the patient has septic phlebitis of the vena cava. R ecent data suggest that transesophageal echocardiography is highly sensitive in determining whether the patient has S. aureus bacteremia has endocarditis. A transesophageal echocardiogram is unnecessary for patients with CRBSI whose catheters are removed and who respond (afebrile with negative blood cultures) within 48 to 72 h of the initiation of antimicrobial therapy.

Antimicrobial therapy

Vancomycin is the drug of choice for the treatment of CRBSI caused by methicillin-resistant staphylococci. The treatment duration is not well defined. However, seven days of treatment should be sufficient for CRBSI caused by coagulase-negative staphylococci. For S. aureus infections, vancomycin is the drug of choice if the patient is allergic to penicillin or the organism is resistant to methicillin. For patients with S. aureus infection susceptible to methicillin,
a semi-synthetic antistaphylococcal antibiotic such as nafcillin, oxacillin (flu)cloxacillin or a first-generation cephalosporin could be used. The treatment duration for uncomplicated CRBSI caused by S. aureus should be at least 10 (and possibly 14) days. However, patients with catheter-related septic phlebitis caused by any organism, especially S. aureus, should be treated for at least 4 weeks with appropriate antimicrobial agents.

CRBSI caused by Candida spp. may be treated with fluconazole if the organism is Candida albicans or C. parapsilosis. However, for organisms such as Candida glabrata or Candida krusei, amphotericin B is the drug of choice. A prospective randomized study of 206 non-neutropenic patients with candidaemia (three-quarters of whom were considered to have vascular catheter-associated candidaemia) showed that fluconazole given for at least 14 days was as efficacious as amphotericin B.

References

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