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Diagnosis and treatment of catheter-related infections in paediatric oncology: an update

A. Simon[1], U. Bode[1] and K. Beutel[2]

[1]Department of Paediatric Haematology and Oncology, Children's Hospital Medical Centre, University of Bonn, Bonn and [2]Department of Paediatric Haematology and Oncology, Centre for Gynaecology, Paediatric and Adolescent Medicine, Hamburg-Eppendorf University Medical Centre, Hamburg, Germany

ABSTRACT

Otherwise unexplained clinical signs of infection in patients with long-term tunnelled or totally implanted central venous access devices (CVADs) are suspected to be CVAD-associated. Diagnostic methods include catheter swabs, blood cultures and cultures of the catheter tip or port reservoir. In the case of a suspected CVAD-related bloodstream infection in paediatric oncology patients, in-situ treatment without prompt removal of the device can be attempted. Removal of the CVAD should be considered if bacteraemia persists or relapses ≥ 72 h after the initiation of (in-vitro effective) antibacterial therapy administered through the line. Timely removal of the device is also recommended if the patient suffers from a complicated infection, or if *Staphylococcus aureus*, *Pseudomonas aeruginosa*, multiresistant *Acinetobacter baumannii* or *Candida* spp. are isolated from blood cultures. Duration of therapy depends on the immunological recovery of the patient, the pathogen isolated and the presence of related complications, such as thrombosis, pneumonia, endocarditis and osteomyelitis. Antibiotic lock techniques in addition to systemic treatment are beneficial for Gram-positive infections. Although prospectively controlled studies are lacking, the concomitant use of urokinase locks and taurolidine secondary prophylaxis seem to favour catheter salvage.

Keywords Catheter-related infection, diagnosis, intravascular catheter, paediatric oncology patients, review, therapy

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INTRODUCTION

Long-term central venous access devices (CVADs) have been used for at least 20 years in the treatment of paediatric oncology patients. Such devices are either tunnelled CVAD devices (single-lumen or multi-lumen) with a sub-cutaneous cuff adjacent to the catheter exit site, such as the Broviac (or Hickman or Groshong) model [1,2], or totally implanted port systems with sub-cutaneous reservoirs [3,4]. Routine use of long-term CVADs offers considerable advantages for both patients and the treatment team. These catheters are used as a means of straightforward and safe central venous access to administer cytotoxic agents, antimicrobial agents, analgesics and blood products. They facilitate hyper-osmolar parenteral nutrition in patients with high-grade mucositis who are unable to tolerate enteral feeding [5], and allow painless blood collection. In emergency situations, e.g., septic shock, CVADs provide immediately available large-lumen access for high-volume treatment or for catecholamine administration.

Implantation of foreign material into the vascular system enhances the risk for catheter-related infections [3,6–11]. In addition, the use of CVADs may be accompanied by mechanical problems (dislocation, catheter rupture, paravasation, chylothorax) [12–14], and also poses an increased risk for thrombotic complications for the patient [15–18]. In two recent prospective studies involving

Corresponding author and reprint requests: A. Simon, Department of Paediatric Haematology and Oncology, Children's Hospital Medical Centre, University of Bonn, Adenauerallee 119, 53113 Bonn, Germany
E-mail: asimon@ukb.uni-bonn.de

paediatric oncology patients, infectious complications were dominated by the mechanical aspects, with infections accounting for 1.3 (of 4.5) and 0.87 (of 1.7) events/1000 CVAD utilisation days (UDs), respectively [15,19].

If both inpatient and outpatient catheter days are counted as reference parameters (UDs), the reported estimates of infectious complications may be substantially biased, as most events involving catheter use and manipulation take place during an inpatient treatment period. According to a prospective study of CVAD-related infections that made a distinction between these two options, the incidence rate during hospital stay was 25-fold higher (7.4 vs. 0.3/1000 UDs) [4]. In the interim evaluation (as at 17 June 2005) of the prospective multicentre surveillance study for nosocomial infections in paediatric oncology (http://www.onkopaednki.de), the cumulative incidence densities for CVAD-related bloodstream infections are 2.21/1000 UDs (25 382 cumulative inpatient UDs) for Broviacs, and 3.73/1000 UDs (13 675 cumulative inpatient UDs) for ports. The risk of infectious complications is obviously highest during intensive use of the CVAD in the hospital.

Based on the description of a few practice-related issues concerning the aetiology and pathogenesis of CVAD-related infections, this review discusses the basic principles involved in the management of CVAD-associated infection in paediatric oncology patients. The conclusions may help to support paediatric oncologists in their individual decision-making processes [20–23]. This review refers exclusively to long-term, implanted CVADs. Non-tunnelled, central venous catheters are used in paediatric oncology only rarely for a treatment period of 2–3 weeks.

IMPORTANT PATHOGENS

In CVAD-related infections, most bacterial pathogens isolated from swabs, central-line blood cultures or explanted catheter materials are Gram-positive bacteria, particularly methicillin-resistant, coagulase-negative staphylococci (CoNS or methicillin-resistant *Staphylococcus epidermidis*; MRSE) originating from the proximal connecting end of the catheter (hub) [24,25] or from the skin at the exit site of the Broviac or the port needle [26,27]. There is some evidence that colonised gastrointestinal mucosal surfaces are a relevant source of infection with CoNS in patients receiving long-term parenteral nutrition [28,29].

CVAD-related infections with *Staphylococcus aureus* (including methicillin-resistant *S. aureus*; MRSA) are of utmost clinical relevance because of their high morbidity and an increased risk of local or systemic suppurative complications [30]. Microorganisms derived from the intestine (e.g., enterococci, including vancomycin-resistant enterococci; VRE) [31] or the oropharynx [32] (e.g., α-haemolytic streptococci: viridans streptococci and *Stomatococcus mucilaginosus* or *Leuconostoc* spp.) are less common [27,33,34] aetiological agents in catheter infections. CVAD infections caused by Gram-negative bacteria, such as *Pseudomonas aeruginosa*, *Burkholderia cepacia*, *Klebsiella* spp., *Stenotrophomonas maltophilia* [35] or *Acinetobacter baumannii* [36], are often accompanied by septic shock [37]. *Candida* spp., among which *Candida parapsilosis* seems to be particularly important in CVAD-related infections [38–44], may also cause life-threatening CVAD-related infections, such as endocarditis or septic thrombophlebitis.

Aspergillus spp. [45]. or atypical mycobacteria [46] cause rare necrotising skin infections at the exit site of a CVAD. In these cases, immediate removal of the device is required.

PATHOGENIC FACTORS RELEVANT FOR TREATMENT

Microbiological colonisation of a CVAD usually occurs within 24 h of catheter implantation. Initially, colonisation may involve the catheter lumen, originating from contamination of the catheter hub [25] or the extra-luminal surface following contamination of the Broviac exit site (port puncture site) [47]. Primary contaminated intravenous infusions [48] or haematogenous CVAD colonisation secondary to bacteraemia from a distant focus are less common events [32,49]. Bacteria capable of binding to foreign materials, cross-linked with extracellular glycopolysaccharides, fibrin and fibronectin, constitute the main problem [26]. The rapid formation of such an extracellular biofilm matrix prevents an adequate immune response against the adhering bacteria [50–53]. The biofilm also impedes the eradication of microorganisms, despite treatment with antimicrobial agents that are highly effective *in vitro* [54–57].