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Blood culture time to positivity in oncology pediatric patients

Tiempo de positividad en hemocultivos de pacientes oncológicos pediátricos

Dear Editor:

Bloodstream infections (BSI) are common and severe in patients with oncologic and hematologic diseases, mainly accounting for chemotherapy-induced neutropenia alongside with invasive procedures.[1] In these patients, microorganisms of the saprophytic microbiota are frequently considered clinically significant, as they often colonize intravascular devices (IVD).[2] In our pediatric hospital, we inoculate blood from the IVD[3] only in one blood culture (BC) bottle and we do not usually obtain a peripheral BC, making it more complex to discriminate contamination from infection.[4] We aimed to assess the usefulness of time to blood culture positivity (TTP) to predict significant bacteriemia.

This is an observational prospective study in a cohort of oncology and hematology pediatric patients (<18 years at inclusion) that presented with fever during treatment, in most cases during neutropenia periods, at Hospital Sant Joan de Dèc)u (Barcelona, Spain) from January to December 2016. Blood samples were obtained from IVD, usually a one-lumen tunneled central venous catheter (Port-A-Cath), and inoculated into one pediatric aerobic BacT/Alert PF bottle, to be later processed using BacT/Alert (BioMèc)rieux, Durham, NC, USA) automatic incubation system. As per local protocols, BC were performed at onset of each febrile episode, and consecutively every 24•48 h if fever persisted despite antibiotics.

For isolates belonging to saprophytic microbiota to be considered clinically significant, at least one of the following criteria had to be fulfilled: (a) fever coincided with the use of the IVD; (b) the same strain was isolated in at least 2 consecutive BC; (c) the same strain was isolated from BC and the device exit site; and (d) the same strain was isolated from BC and the device culture after its removal. Clinical and microbiological data were collected and assessed together with the physician in charge of the patient.

During the study period, 1923 BC from pediatric hematology and oncology patients with fever were processed in the microbiology laboratory. Overall, bacterial growth was detected in 151 BC (7.9%, 95%CI: 6.7•9.1%) from 74 patients, of which 86 (4.5%), belonging to 47 episodes of bacteraemia from 37 patients, were considered clinically significant and 65 (3.4%), from 50 patients, were deemed contaminants.

Underlying diseases of patients with a clinically significant positive BC included solid tumors ($n = 39$), acute leukemia ($n = 30$), lymphoma ($n = 1$) and other hematologic diseases ($n = 4$). Primary pathogens included the following (number of isolates/episodes of bacteremia): 17/14 *Enterobacteriaceae*, 11/3 *Staphylococcus aureus*, 4/3 *Pseudomonas aeruginosa*, 2/2 *Streptococcus pneumoniae*, 1/1 *Haemophilus influenzae*, 1/1 *Enterococcus faecium*, 1/1 *Campylobacter jejuni* and 2/1 *Candida parapsilosis*. Microorganisms from the saprophytic microbiota that were considered clinically significant were: 35/14 *Staphylococcus epidermidis*, 5/2 *Staphylococcus hominis*, 3/2 *Micrococcus* spp., 3/2 *Bacillus cereus* and 1/1 *Streptococcus mitis*.

Finally, 42 coagulase-negative staphylococci, 9 *Micrococcus* spp., 2 *Bacillus* spp. and 12 isolates of other species were considered contaminants. Median (IQR) TTP of contaminants (25.2 h [18.0•34.3]) was significantly longer than that of all clinically significant BC (15.1 h [10.3•24.0]; $p < 0.0001$), but not enough to set up a useful TTP cut-off to discriminate both groups.

However, when only the first BC of each episode was considered, the TTP differences (13.2 h [8.9•18.0]) with contaminant BCs increased ($p < 0.0001$); 93.6% of clinically significant isolates (including all those from the saprophytic microbiota) were detected in less than 24 h, *versus* 43.1% of contaminants and 53.8% of significant isolates from non-first BCs ($p < 0.0001$). TTP exceeded 24 h in only 3 first clinically significant BCs (*C. parapsilosis*, *H .influenzae* and *C. jejuni*, which grew after 48, 57 and 91 h, respectively) that are known to usually show a slow growth.[5] Sensitivity, specificity, positive and negative predictive value for a clinically significant first BC to grow within 24 h after inoculation were 0.94, 0.57, 0.61 and 0.93, respectively.

In the oncologic child, the primary focus of bacteraemia is frequently the colonization of IVD,[6] and often the causative agent is part of the saprophytic microbiota. This fact would explain the differences among first and following BC TTP in clinically significant isolates. Despite adequate antibiotic therapy, some microorganisms remain in the inert structure of the IVD, out of reach of antibiotics, and are still detected in subsequent BC. In the latter, lower concentrations of the microorganism in the blood sample would lengthen the BC TTP. *S. epidermidis* was the most frequently isolated microorganism in our study, making it critical to discriminate between true infection and IVD contamination. At present, *S.*

epidermidis has been associated with persistent and recurrent bacteriemia, and also with the need for IVD replacement,[1] which has an important impact in the management of patients.

Although there is not a single study that has specifically assessed BC TTP in oncology children, our data are consistent with prior reports in general pediatric[5,7,8] and adult patients,[4,9,10] in which most pathogens grew within the first 24 h of incubation. These data, together with patient clinical status, can be useful for taking management decisions, such as the need for ongoing antibiotic treatments or delays in chemotherapy schedules.

Our study had several limitations. We cannot assure that the time between collection of BC and placement in the incubator system was homogeneous (our protocol suggests less than one hour); therefore, we may have underestimated TTP in some cases. Depending on the age of the patient and other blood tests requested, the amount of blood available for each BC ranged from 1 to 4 ml, which does impact in TTP and also hinders comparisons.[4] Nevertheless, both these facts reflect usual working conditions.

In conclusion, in pediatric oncology patients with IVD presenting with fever, clinically significant isolates almost universally grew within 24 h of first BC inoculation, as did 43% of contaminants. Since in our study, a first BC growth beyond 24 h mostly represented contamination, this 24-h cut-off promises to be a useful tool in the management of fever in this specific and difficult-to-manage population.

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Conflict of interests

The authors of this study have no conflict of interest in relation to their content.

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The use of co-trimoxazole in catheter lock therapy. A report on a difficult case☆

Uso de cotrimoxazol en sellado de catéter. A propósito de un caso en una situación difícil

Dear Editor,

Today, the use of long-term catheters to administer therapeutic agents (chemotherapy, antibiotic therapy, or blood or plasma derivatives), as well as the extraction of blood samples, is becoming increasingly common.[1,2] Such devices avoid the need for repeated venipunctures, which are associated with discomfort for patients and derived complications (e.g. phlebitis, etc.). However, it is not uncommon that they lead to infections (bacterial or fungal).[1] The management of catheter-related infections is complex, as, on the one hand, removing the catheter decreases the options for vascular access (which are often limited), while keeping it in place is associated with maintaining the focus of the infection. In some cases, an alternative option is used, consisting of both systemic treatment of the bacteraemia and the local administration of antimicrobial agents, known as "locks".[3] The examples of vancomycin (gram-positive cocci) and amikacin (gram-negative bacilli) are well established,[2] and there are efficacy data for other antimicrobial agents (e.g. amoxicillin-clavulanic acid or ciprofloxacin).[2,4] Nevertheless, there are some circumstances in which the options are more limited due to the characteristics of the patient or the type of microorganism.

We report the case of a 51-year-old woman diagnosed with seronegative myasthenia gravis (MG) who underwent a thymectomy in February 2003. She subsequently required various hospital admissions due to myasthenic crises, including on one occasion to the ICU. She attended the Accident and Emergency Department due to presenting a fever of 40 °C, primarily in the evenings, accompanied by tremors for one month prior to admission. The patient had had a Port-a-Cath® (BARD) since 2005 for the administration of immunoglobulins, but did not report other signs of local involvement, such as the existence of pain, erythema or purulent discharge at the insertion site. On admission, and after taking blood cultures peripherally and from the catheter for study

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