

## *Bacillus cereus* Catheter-Related Infection in Acute Lymphoblastic Leukemia (ALL) Patient: A Case Report and Review of Literature

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### Abstract

*Bacillus cereus* is an aerobic Gram-positive spore forming rod that is ubiquitous in the environment. A case of severe infection due to *Bacillus cereus* isolated on the tip of central venous catheter (CVC) of a patient with acute lymphoblastic leukemia (ALL) is reported here. We point out the role played by a rapid diagnosis of *Bacillus cereus* sepsis and early therapeutic intervention in the control of this life-threatening infection

**Keywords:** Lymphoblastic; Hemoglobin; Microorganism

### Introduction

*Bacillus cereus* (*B. cereus*) is an aerobic Gram-positive spore forming rod that is ubiquitous in the environment. This microorganism is widely distributed in the air, water, soil and feces with some species being a part of the normal flora particularly in patients with prolonged hospitalization [1,2]. The most commonly reported systemic infection is bacteremia. Importantly *B. cereus* is a growing concern as cause of life-threatening infection in patients suffering from hematologic malignancies [3]. We report here a patient with acute lymphoblastic leukemia (ALL) who developed a *B. cereus* catheter related infection during the remission induction treatment.

### Case Report

A 60-year old man was firstly admitted at our institution because of fatigue, abdominal pain and fever dating from about a month. The white blood count was  $1.4 \times 10^9/L$ , the hemoglobin concentration 7.1 g/dl and the platelet count  $57 \times 10^9/L$ . A small enlargement of spleen (115 mm) was detected by ultrasonography.

The evaluation of bone marrow aspirate smears revealed an increased number (i.e., 80%) of moderate size blasts with soft fine chromatin and a scant amount of basophilic cytoplasm. Flow cytometry findings were consistent with a diagnosis of pre-B ALL (i.e., positivity for CD34, CD10, CD19, TdT, intacytoplasmatic  $\mu$ -chain). Reverse transcriptase polymerase chain reaction (RT-PCR) did not reveal the presence of bcr/abl transcript. Finally, no central nervous system (CNS) or meningeal leukemic involvement could be found.

After positioning a peripherally inserted central catheter (PICC), induction chemotherapy according to Hyper-CVAD regimen was started [4]. Treatment was generally well tolerated and clinical conditions of patients were constantly good. However, 11 days after the starting of chemotherapy a continuous-remittent fever was observed. At that time white blood count was  $0.0 \times 10^9/L$ . The diagnostic work-up of our patient with febrile neutropenia included blood sample culture collections from either PICC or peripheral vein, high

resolution computed tomography (HRCT) of chest, quali-quantitative assay for cytomegalovirus (CMV) antigenemia and blood D-galattomannan. Meanwhile, an empiric antibiotic therapy consisting of intravenous tazobactam and piperacillin (i.e., 4,5 gr IV every 8 hours) was given. The persistence of fever along with negativity of all previous mentioned tests led us, after four days from the starting of therapy with tazobactam and piperacillin to switch to an antibiotic association consisting of meropenem (i.e., 1 gr IV every 8 hours) plus gentamicin (i.e., 1 gr IV every 8 hours) and tigecycline (i.e. 50 mg IV every 12 hours) after five days cause persistent fever.

Seven days from the beginning of fever, the patient condition worsened. He complained of abdominal pains and fever tended to become continuous. However, patient was hemodynamically stable and no central nervous system (CNS) manifestations were observed. The suspicion of catheter-related bacteremia led us, after 18 days from the PICC insertion, to remove the device and to send the catheter tip for culture. The BD Phoenix™ PMIC/ID-88 panel which is currently used in our laboratory for the rapid identification of most aerobic and anaerobic gram-positive bacteria of human origin allowed to isolate a *B. cereus* on the catheter tip culture. According to the information provided by antibiotic susceptibility tests, we switched to an association of clindamycin (i.e. 600 mg IV every 8 hours) and imipenem 500 mg-cilastatin 500 mg (i.e., every 8 hours IV) and vancomycin (i.e., 500 mg IV every 6 hours). The patient obtained a complete resolution of fever in couple of days. At that time the white blood count was  $0.7 \times 10^9/L$ ; the hemoglobin concentration 9.1 g/dl; the platelet count  $16 \times 10^9/L$ . A complete haematological response was obtained in the next days.

### Discussion

*B. cereus* septicemia is a relatively rare event which accounts for about 2% of all cases of bacteremia or fungemia [5]. The few reports of septicemia due to *B. cereus* deal with patients with severe neutropenia who were receiving chemotherapy for hematologic malignancies [2,6-15]. In these patients the clinical course was generally fulminant and death was rapid.

A systematic and comprehensive search of the literature was performed using MEDLINE databases from October 1996 to

September 2016. We used the following Medical Subject Headings (MESH) to identify potential studies: ‘*B. cereus*’ (hits 5132 ), “*B. cereus*” and “Acute Leukemia” (hits 33). An additional search

performed by combining the MESH terms “*B. cereus*” and “Acute Lymphoblastic Leukemia” yielded 14 citations. Table 1 provides an overview of these studies.

Author	Reference	N. pts.	Diagnosis	Intravenous central catheter	Outcome	Abdominal symptoms	SNC
				(Yes/No)	(Dead/Alive)	(Yes/No)	symptoms
Arnaout et al.	[6]	2	ALL	2/0	2/0	2/0	NA
Chou et al.	[7]	11	ALL	NA	04-Jul	NA	NA
Gurler et al.	[8]	10	ALL	06-Apr	04-Jun	07-Mar	NA
Dabscheck	[9]	1	ALL	NA	Alive	NA	Yes
Hansford	[10]	1	ALL	NA	NA	NA	Yes
Hirabayashi	[11]	1	ALL	NA	Alive	NA	Yes
Nishikawa	[12]	1	ALL	NA	Alive	NA	Yes
Cone	[13]	1	ALL	NA	Dead	No	Yes
Frankard	[14]	1	ALL	NA	NA	NA	NA
Sakai	[15]	1	ALL	NA	Alive	NA	Yes
Present case		1	ALL	Yes	Alive	Yes	No
TOTAL		31	ALL	09-Apr	11/18	10-Apr	Yes 6/1

**Table 1:** Characteristics and clinical outcome of patients with acute lymphoblastic leukemia who developed *B. cereus* infection.

Since *B. cereus* is frequently described as a contaminant, a relevant question raised by our case report is represented by the possibility that catheter tip infected by *B. cereus* might be expression of contamination. *B. cereus* produces biofilms which enhance its attachment to catheters and from a clinical standpoint the association between *B. cereus* infection and the presence of central intravenous catheter was reported in 9 out of 13 reported cases [6,8].

Finally, our case report indicates how relevant is the CVC removal in patients with persistent bacteremia unresponsive to appropriate antimicrobial treatment in the absence of other obvious sites or sources of infection [16].

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