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CASE REPORT

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Fulminant septicemia of *Bacillus cereus* resistant to carbapenem in a patient with biphenotypic acute leukemia

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Abstract We report a case of fulminant septicemia with *Bacillus cereus* resistant to carbapenem. A 33-year-old man was suffering from febrile neutropenia (FN) on day 15 after the start of remission-induction therapy for biphenotypic acute leukemia under gut decontamination with polymyxin B and nystatin. Meropenem, a carbapenem, was administered according to the guideline for FN. Two days later (on day 17), he complained of severe abdominal pain, lost consciousness, went into sudden cardiopulmonary arrest, and died. Autopsy showed multiple spots of hemorrhage and necrosis caused by bacterial plaque in the brain, lungs, and liver. *B. cereus* was isolated from a blood sample obtained in the morning on day 17 and it was after his death that the isolated *B. cereus* was revealed to be resistant to carbapenem. *B. cereus* obtained from blood samples has been reported to be usually sensitive to carbapenem and also to vancomycin, new quinolones, and clindamycin. If *B. cereus* resistant to carbapem increases, our method of gut decontamination with polymyxin B and nystatin may have to be changed to one containing a new quinolone for the prevention of septicemia. Careful watching to determine whether *B. cereus* resistant to carbapem increases may be also important for empiric therapy, because carbapenem is often selected as the initial therapy for FN in patients with severe neutropenia.

Key words *Bacillus cereus* · Carbapenem · Febrile neutropenia

Introduction

Members of the genus *Bacillus* are aerobic Gram-positive spore-forming rods that are ubiquitous in the environment. *Bacillus cereus* isolated from blood samples may be a contaminant or it may be the causative pathogen of opportunistic infections. *B. cereus* may form abscesses in the brain, lungs, liver, and digestive tract in an immunocompromised host, and may induce a rapidly fatal course. This type of opportunistic infection has been reported as fulminant *B. cereus* septicemia.[1–8] In 1993, we reported two patients with acute leukemia with fulminant *B. cereus* septicemia.[9] Here we report a patient with biphenotypic acute leukemia who died of fulminant septicemia with *B cereus* that was resistant to carbapenem. We discuss the drug sensitivity of the isolated bacteria, the gut decontamination regimen during chemotherapy for acute leukemia, and the present guideline for the treatment of febrile neutropenia (FN).[10]

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Case report

A 33-year-old man suffering from biphenotypic acute leukemia was admitted to our center in August 2006. On admission, his leukocyte count was 5400/μl with 13.5% blasts, hemoglobin concentration was 11.2 g/dl, and platelet count was 130 000/μl. Bone marrow examination revealed hyperplastic marrow with an increase in blasts to 87.4%. The blasts were positive for CD22, CD10, CD19, HLA-DR, CD34, KOR-SA, CD13, and CD33, and negative for cytoplasmic MPO by a flow cytometric method, suggesting the leukemia was biphenotypic. Karyotypic analysis revealed 46, XY. At age 6 years he had suffered from rhabdomyosarcoma in the right elbow, and had undergone operation and irradiation. He had a relapse in the right humerus at age 9 years and underwent irradiation and chemotherapy. No further relapse was seen.

He received remission-induction therapy, which consisted of cyclophosphamide 1200 mg/m^2 administered intravenously on day 1; vincristine 2 mg administered intravenously on days 1, 8, 15, and 22; doxorubicin 60 mg/m^2 administered intravenously on days 1 to 3; L-asparaginase 3000 ku/m^2 administered intravenously on days 9, 11, 13,

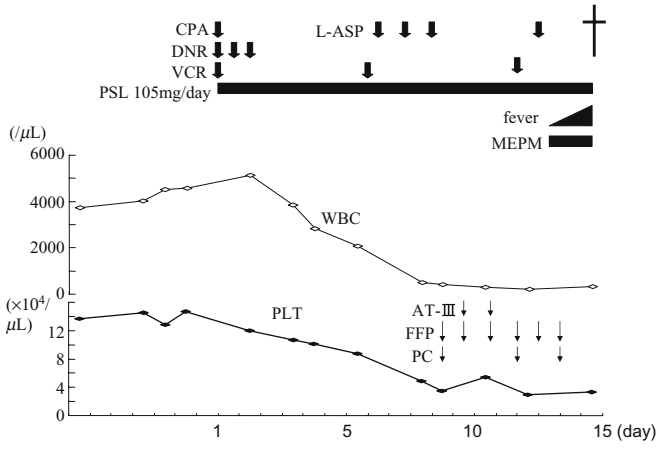

Fig. 1. Patient's clinical course. *CPA*, Cyclophosphamide; *DNR*, doxorubicin; *VCR*, vincristine; *L-ASP*, L-asparaginase; *PSL*, prednisolone; *MEPM*, meropenem; *PLT*, platelets; *AT-III*, antithrombin III; *FFP*, Fresh Frozen Plasma; *PC*, platelet count

16, 18, and 20; and prednisolone 60 mg/m^2 administered orally on days 1 to 21, after a central venous catheter was inserted (Fig. 1). During the chemotherapy, he stayed in an aseptic management room and received polymyxin B and nystatin for gut decontamination. On the night of day 15 after the start of chemotherapy, his temperature rose to 38.1°C, without complaints. He received meropenem, a carbapenem, according to the guideline for febrile neutropenia (FN), but the high temperature continued. In the early morning on day 17, he developed severe abdominal pain which gradually increased. Laboratory tests in the morning had the following results: leukocyte count was 330/μl with 44.7% neutrophils; hemoglobin concentration, 8.0 g/dl; platelet count, 33 000/μl; total bilirubin, 2.3 mg/dl; indirect bilirubin, 1.3 mg/dl; aspartate aminotransferase, 62 IU/l; alanine aminotransferase, 117 IU/l; alkaline phosphatase, 330 IU/l; γ-glutamyl transpeptidase, 108 IU/l; lactate dehydrogenase, 176 IU/l; amylase, 32 IU/l; blood urea nitrogen, 19 mg/dl; creatinine, 0.6 mg/dl; and C-reactive protein, 1.8 mg/dl. His abdominal computed tomography and ultrasound images showed no abnormality. In the evening on day 17, he suddenly lost consciousness. He underwent evaluation via urgent computed tomography of the head. Just after the computed tomography was completed, he went into cardiopulmonary arrest and died in spite of cardiopulmonary resuscitation. The computed tomography scan of the head revealed hemorrhagic infarction in the brainstem (Fig. 2). Autopsy showed multiple lesions of hemorrhage and necrosis caused by bacterial plaque in the brain, lungs, and liver (Fig. 3). *B. cereus* was isolated from a blood sample obtained in the morning on day 17, and it was after the patient's death that the isolated *B. cereus* was revealed to be resistant to carbapenem (imipenem and meropenem). It was sensitive to ofloxacin; a sensitivity test to vancomycin was not performed (Table 1).

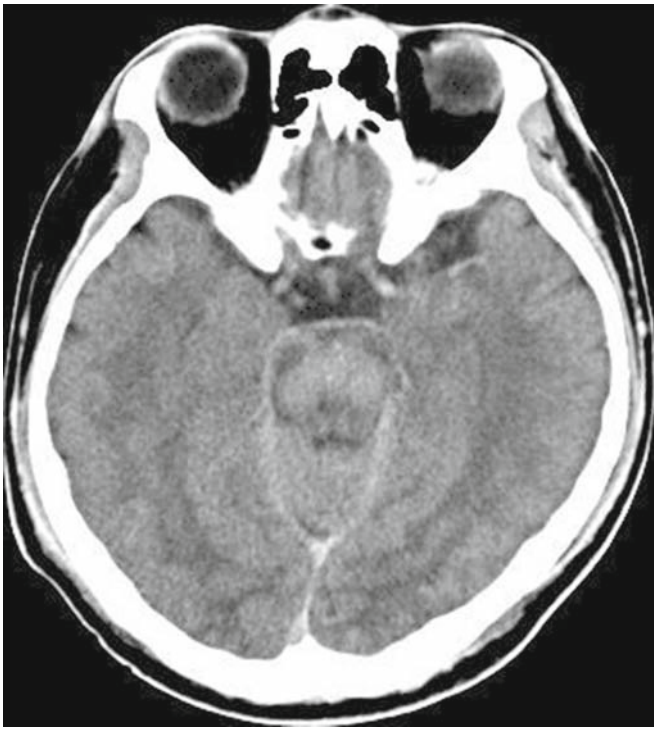

Fig. 2. Computed tomography scan of the head on day 17. The brainstem was swollen and its density was high for the most part and low in a small portion; revealing hemorrhagic infarction in the brainstem

Discussion

B. cereus isolated from blood samples has been reported to be resistant to penicillins and cephems and usually susceptible to carbapenems, new quinolones, vancomycin, and clindamycin.[11,12] We have reported here fulminant septicemia with *B. cereus* resistant to carbapenem in a patient with biphenotypic acute leukemia. To our knowledge, this is the first report of fulminant septicemia with *B. cereus* resistant to carbapenem.

In 1993, we reported two cases of fulminant septicemia with *B. cereus* which occurred during remission-induction chemotherapy for acute leukemia under the same gut decontamination regimen with polymixin B and nystatin as in the present patient.[9] We had thought that the reason we lost these two patients was because, at that time, carbapenems, new quinolones, and vancomycin were not available. Since then we have had no case of *B. cereus* fulminant septicemia even though we have been using the same gut decontamination with polymyxin B plus nystatin in remission-induction chemotherapy in acute leukemia. We treated the FN in the present patient with carbapenem according to the guideline for FN,[10] which recommends the use of a third- or fourth-generation cephem or carbapenem with or without aminoglycoside as the initial therapy. Soon after the patient's death the *B. cereus* isolated from the blood sample was revealed to be resistant to carbapenem. The reason that we lost the present patient was thought to