

## Food-borne bacteremic illnesses in febrile neutropenic children

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### Abstract

Bacteremia following febrile neutropenia is a serious complication in children with malignancies. Preventive measures are currently targeted at antimicrobial prophylaxis, amelioration of drug-induced neutropenia, and nosocomial spread of pathogens, with little attention to community-acquired infections. A retrospective study was conducted at a pediatric oncology center during a 3-year period to identify probable cases of food-borne infections with bacteremia. Twenty-one bacteremic illnesses affecting 15 children receiving chemotherapy or hematopoietic stem cell transplantation were reviewed. Three (14%) episodes were highly suspected of a food-borne origin: a 17-year-old boy with osteosarcoma contracted *Sphingomonas paucimobilis* septicemia after consuming nasi lemak bought from a street hawker; a 2-year-old boy with acute lymphoblastic leukemia developed *Chryseobacterium meningosepticum* septicemia after a sushi dinner; a 2-year-old girl was diagnosed with acute lymphoblastic leukemia and *Lactobacillus* bacteremia suspected to be of probiotic origin. All of them were neutropenic at the time of the infections and the bacteremias were cleared with antibiotic treatment. Food-borne sepsis may be an important, but readily preventable, cause of bloodstream infections in pediatric oncology patients, especially in tropical countries with an abundance of culinary outlets.

### Introduction

Children suffering from cancer are increasingly salvageable with contemporary treatments. Acute lymphoblastic leukemia, the commonest cancer in childhood, is now curable in 80% of the cases.<sup>1</sup> The increasing success in pediatric oncology is in part related to the use of more intensive chemotherapy and high-dose chemotherapy plus hematopoietic stem cell transplantation. A multitude of factors including skin and mucosal damage, the use of indwelling central venous devices, pro-

longed or profound neutropenia, and the concurrent use of immunosuppressants make opportunistic infections a frequent and potentially life-threatening complication in this group of children.<sup>2</sup> Bloodstream bacterial infections continue to be the most significant cause of mortality and morbidity during anti-cancer treatment.<sup>3-5</sup>

Preventive measures targeting at the environment and the host have been implemented in order to reduce the morbidity and mortality associated with infectious complications in children receiving anti-cancer treatment and stem cell transplantation.<sup>6</sup> In particular, most pediatric oncology centers have strict precautions pertaining to the supply and cleanliness of food to the hospitalized children even though most of the bloodstream infections are caused by endogenous bacteria found in the flora of the skin, the oral cavity, and the intestine, and specific reports on food-borne infections are lacking. The following cases in which the bacteremic illnesses were most probably acquired from consumption of contaminated food and beverages in the community are illustrative of the importance of food precautions in children undergoing cytotoxic chemotherapy even after discharge.

### Materials and Methods

A retrospective hospital chart survey was carried out to review all cases of documented bacteremia associated with febrile neutropenia in children undergoing anti-cancer treatment or hematopoietic stem cell transplantation in the Children's Haematology and Cancer Centre from March 2007 to February 2010. Febrile neutropenia is defined as the occurrence of fever (core temperature higher than 38.5°C) with an absolute neutrophil count below  $1 \times 10^9/L$ . A case of suspected food-borne infection was diagnosed if there was a history of consuming food or beverages that were not properly cooked in the preceding 24 hours of the positive blood culture, or if the organism identified is a probable probiotic commonly used in children's food and beverages. The identified cases are to be described.

### Results

There were 21 documented bacteremic illnesses affecting 15 children during the study period. Gram-negative bacilli were responsible for 14 (67%) of the instances. Fourteen children had a central venous device at the time of infection. Three (14%) children died from infections with *Pseudomonas aeruginosa*, *Stenotrophomonas maltophilia*, and mul-

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tidrug-resistant *Acinetobacter baumannii*, respectively. Eleven episodes happened after the child was admitted to the hospital when only low-microbial diet was permitted. The infections in the other ten cases started while the children were discharged, of which three bacteremic illnesses were highly suspected of food-borne in origin.

### Case #1

A 17-year-old boy from Malaysia with localized osteosarcoma was recuperating at home after having received treatment with ifosfamide and etoposide. On day 14 after commencement of the chemotherapy, he met with some friends and consumed nasi lemak from a street hawker. This was a local delicacy made with rice soaked in coconut cream and wrapped in pandan leaves. He started to have fever and vomiting four hours later with chills and rigors. On admission, he was noted to be in compensated septic shock and was immediately resuscitated with fluids and treated with intravenous meropenem. Blood taken from both lumens of the Hickman catheter eventually grew *Sphingomonas paucimobilis* that was sensitive to the antibiotic used. The total white cell count was  $0.4 \times 10^9/L$ . He recovered from the infection and neutropenia with filgrastim and continued chemotherapy treatment without any delay.

## Case #2

A 2-year-old boy from Indonesia with acute lymphoblastic leukemia was discharged after treatment with cyclophosphamide during the second part of the induction chemotherapy. While taking oral 6-mercaptopurine, he went with his family to enjoy a sushi dinner in a Japanese restaurant. He was noted to be cyanotic with chills 10 hours later and was immediately admitted to the hospital. He was resuscitated with intravenous fluid for septic shock in the Accident and Emergency Department followed by the commencement of intravenous meropenem and amikacin. The absolute neutrophil count was  $0.48 \times 10^9/L$ . *Chryseobacterium meningosepticum* was found in the blood cultures. He recovered after antibiotic treatment.

## Case #3

A 2-year-old girl from France was admitted for investigation of fever with no obvious source. The initial full blood counts showed mild anemia (10.2 g/dL), leucopenia ( $4.2 \times 10^9/L$ ), profound neutropenia ( $0.08 \times 10^9/L$ ) and normal platelet counts. Acute lymphoblastic leukemia was diagnosed on bone marrow aspiration while the blood culture taken on admission grew *Lactobacillus* species that was sensitive to penicillin and ceftriaxone but resistant to ciprofloxacin and erythromycin. The infection was cleared with intravenous ceftriaxone treatment.

## Discussion

Febrile neutropenia is a common complication in children with leukemia, bone marrow failure syndromes, and those receiving cytotoxic chemotherapy or undergoing hematopoietic stem cell transplantation. Bacteremia is seen in 10-30% of cases and is associated with serious complications and death, with case fatality rates ranging from 9-24% in the recent series.<sup>2-5</sup>

Mucosal damage as a result of intense chemotherapy and the use of central venous devices are commonly identified as the predisposing factors for bloodstream infections in the neutropenic hosts. As a result, the causative organisms are usually part of the normal flora found in the oral cavity, the gut, and on the skin. *Klebsiella pneumoniae*, *Escherichia coli*, and *Pseudomonas aeruginosa* from the gastrointestinal tract are still the most common pathogens in our experience, accounting for nine of the 14 episodes of Gram-negative bacteremia. *Staphylococcus aureus*, coagulase-negative *Staphylococcus*, and *Bacillus* species, commonly found on the skin, constitute five of the seven episodes of

Gram-positive bacteremia.

Recent studies on the epidemiology of bacteremia in febrile neutropenic children have reported remarkably similar spectrum of organisms.<sup>3-5</sup> The use of central venous catheters, prolonged neutropenia (>14 days), profound neutropenia ( $<0.1 \times 10^9/L$ ), and comorbid conditions are strongly associated with bloodstream infections. Paul *et al.*<sup>5</sup> have also emphasized the duration of hospital stay as another predisposing factor, suggesting that nosocomial transmission of bacterial pathogens as an important causative factor. However, none of the studies has looked into the possibility of out-of-hospital acquisition of infection by the oral route. Food hygiene has long been regarded as an important aspect of infection control in the neutropenic host. It is a common practice that children undergoing cytotoxic chemotherapy and stem cell transplantation in the hospital are to receive the low-microbial diet. Once the patient is discharged, however, meticulous respect to food hygiene may not be followed. The present case reports illustrate the potentially dire consequences of the lapses in food precautions among the pediatric oncology population. The three cases represent 14% of the bacteremic illnesses complicating febrile neutropenia during the study period. The tropical climate, the popularity of local delicacies sold by hawkers and Japanese cuisine with raw seafood could have contributed to such a high incidence of food-borne infections among the susceptible children. In Cases #1 and #2, the infecting organisms, which are not found in the normal skin or gut flora, were most likely acquired from the improperly handled or uncooked food. The origin of the *Lactobacillus* in Case #3 was uncertain and molecular test to prove a genuine dietary source from probiotic strains is not available.<sup>7</sup> However, concerns about potential pathogenicity and transfer of acquired drug resistance to resident flora have led to recommendations against their use in hospitalized and immunocompromised patients.<sup>8</sup>

Various attempts at reducing the risk of bacteremia have been attempted or implemented in pediatric oncology. The effectiveness and adverse effects of antibiotic prophylaxis are still controversial in pediatric oncology.<sup>9</sup> Hematopoietic growth factors to ameliorate the severity and duration of neutropenia have been widely used with a consensus that infectious complications following chemotherapy and duration of hospital stay are reduced.<sup>10</sup> The treatment is, however, expensive. The exclusion of unclean food and attention to food hygiene is often part of patient education and can be easily followed without much cost.

In summary, food-borne bacteremic infections in febrile neutropenic children may be more prevalent in tropic regions where the warm climate and the abundant supply of

improperly handled delicacies can predispose the children to the opportunistic pathogens. The relatively small patient sample and the multi-national composition of the patient population may limit the generalization of the observation. Nevertheless, compared with other risk factors, food-borne bacteremic illnesses in febrile neutropenic children can be readily prevented by diligent observation of the proper food handling.

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