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Case Report

A case of pediatric leukemia with multi drug resistant bacterial infections

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ABSTRACT

Infections still remain a major cause of therapy-associated morbidity and mortality in pediatric cases with acute myeloid leukemia (AML). Down syndrome (DS) children have an approximately 10-20 fold higher incidence of acute leukemia and approximately 150 fold increased risk of developing myeloid leukemia of DS (ML-DS). Multi-drug resistant (MDR-GNB) Gram-negative bacterial septicaemia is an emerging global challenge. Authors are reporting a 4 and half year old boy with diagnosis Acute Megakaryocytic Leukemia (AMKL) who developed septicaemia and diaper rash. MDR *E. coli* was isolated and he was treated with fosfomycin followed by colistin. The boy developed cardiac arrest with chest compression and expired.

Keywords: Bacterial infections, Leukemia, Multi-drug resistance

INTRODUCTION

Infections are an important cause for morbidity and mortality in pediatric acute myeloid leukemia (AML). Down syndrome (DS) children have an approximately 10-20 fold higher incidence of acute leukemia and approximately 150 fold increased risk of developing myeloid leukemia of DS (ML-DS).[1-3] In India, abandonment of care in patients with hematological malignancies is a significant challenge due to multiple and complex social issues such as poverty, living far distances from health facilities, lack of education and health information for patients, and gender inequality.[4]

Approximately, 70% of all blood stream infections (BSI) in patients with acute leukemia in India is due to Gram-negative bacteria and 30-40% of Gram-negative bacterial isolates are resistant to carbapenems.[5] There has been a change in the epidemiology of bacteremia in neutropenic patients in the past decade due to the reemergence of gram-negative infections and increased antimicrobial resistance due to overuse of antibiotics in cancer patients.

Even though various studies report that prophylaxis with antibiotics and antifungals reduce the infection rate, but the emergence of drug resistant organisms is still a main concern in the pediatric population.[6]

CASE REPORT

Here authors present a case of 4 and half year old boy with DS and Acute Megakaryocytic Leukemia (AMKL) who was diagnosed outside presented to our cancer centre by June 2018 with occasional fever and body ache and progressive abdominal distension and skin bleeding for 3 weeks. Gross motor, fine motor, social and language was delayed, and speech, hearing and vision are apparently normal. After examination and diagnosing DS with AML, the boy was evaluated for chest X-ray, USG abdomen, ECHO and the samples were sent for

biochemical and microbiological analysis. Chest X-ray was normal and USG abdomen showed thickened and edematous ascending colon, cecum and ileocecal junction, left mild hydroureteronephrosis, enlarged lymph nodes at porta hepatis.

His past history revealed Trisomy 21 at 3 and half year age. Diagnosed AML M-7. He had pyoderma in Right thigh which was managed with the following oral antibiotics namely amoxicillin-clavulanic acid and ciprofloxacin. The Immunophenotypic test revealed Acute Megakaryocytic Leukemia associated with Down syndrome with co-expression of erythroid specific antigen (CD235a). Flow cytometry showed AML (80% blasts).

Immunophenotyping test performed at our centre, by an automated hematologic analyzer (FC 500 Beckman) revealed positive for abnormal blast population- cMPO, CD 33, CD 34, CD 117, HLA-DR with aberrant expression of CD 7 which eventually proves that the boy is suffering from AML.

Blood culture revealed negative for both peripheral and central line (BD Bactec™ 9050). Fever peaked up from day 4. Swab collected from right thigh lesion which was sent to microbiology lab, showed culture positive for *Sphingomonas paucimobilis* (Gram-negative bacilli). This bacterial isolate was susceptible to all the tested antibiotics except ceftazidime. (VITEK 2 Compact system - Biomerieux, France)

The boy was on continuous monitor and on day 6 due to spike in temperature, his blood sample was sent for culture and sensitivity. *Escherichia coli* was isolated in blood culture which was resistant to multiple antibiotics namely, amoxicillin-clavulanic acid, cefuroxime, ceftriazone, cefepime, cotrimoxazole, ertapenem, gentamicin, imipenem, meropenem, levofloxacin, minocycline, piperacillin-tazobactum and showed sensitive to amikacin, tigecycline, fosfomycin, colistin. He was already on empirical treatment with levofloxacin, meropenem and fluconazole. After the culture report, the boy was treated with colistin and fosfomycin for Multi-drug resistant (MDR) *E. coli*. The boy had fresh complaints of abdominal pain, distension, multiple loose stools, perianal redness, irritability with body temperature rising to 102° F.

On day 11, his serum, blood and stool samples were again sent for laboratory investigation. His CRP was elevated to 260mg/dl. Blood culture was negative. There was a heavy growth of *Enterococcus faecium* in his stool sample. The organism showed sensitive to linezolid, vancomycin and teicoplanin. *Clostridium difficile* toxin (CD-Toxin) testing was found to be negative. Fosfomycin was stopped when the blood culture was found to be negative. The boy was afebrile for two days. He developed fever on day 21 with symptoms of diaper rash which started to increase with infected lesions. Fosfomycin was restarted in combination with amikacin and teicoplanin. Swab taken from the rashes revealed again MDR *E. coli* which was sensitive only to colistin. His general condition worsened with refractory hypotension with tachycardia. Chest X ray showed pneumoniae with pericardial effusion. Pericardial fluid culture was negative. Pericardiocentesis done and ventilator support was given. Fosfomycin was stopped and colistin was administered.

On day 27, his general conditions deteriorated, and heart rate gradually declined from 130 to 60 rates per minute. The boy developed cardiac arrest with chest compression. Atropine was administered, and immediate resuscitation was given but the boy expired.

DISCUSSION

Acute leukemia patients are immunocompromised. Patients given chemotherapy for neutropenia are much more prone for various bacterial and fungal infections as they are immunocompromised.[6] Children with DS and AML have been reported to achieve significantly lower rates of remission, with higher mortality and a poor overall survival. Treatment of AML in children with DS is associated with a higher incidence of life-threatening infections compared to the overall pediatric population.[7,8]

In pediatric AML patients, BSIs are the most important infection complications and could lead to high mortality during the course of treatment. Studies reported that 10-30% hematologic malignant patients who had fever with neutropenia during chemotherapy found to be complicated with sepsis.[7-9] A bigger challenge is the increased incidence of MDR bacteria in this pediatric population. The current situation of MDR bacteria also limits the options of intensifying chemotherapy as a strategy to reduce the risk of relapse and improve long-term survival.

Suppola et al documented that *E. faecium* very often out numbers other enterococci in fecal samples from patients with hematologic malignancies. The author also pointed out that, treatment with third-generation cephalosporins is strongly associated with *E. faecium* overgrowth. In our study, *E. faecium* was isolated from the stool sample. To our surprise this *E. faecium* isolate was also resistant to much of the antibiotics.[10,11]

Sepsis increases mortality in pediatric population with multiple organ dysfunction syndrome. There are wide regional variations in the incidence of each resistant pathogen, and these epidemiologic factors must be considered when making decisions about empiric antibiotics. Infections related to MDR Gram-negative bacteria (GNB) in patients with cancer are increasing globally. Evaluation of underlying disease, the severity and the duration of immune-deficiency, severity of clinical presentations, and the presence of additional predisposing factors to infections are the initial approach

to hematological patients with suspected drug resistant infections. Treatment options for drug-resistant infections are often limited. Carbapenems are the drug of choice for infections caused by extended-spectrum ß-lactamase (ESBL) producing microorganisms. Colistin is the last drug of choice for treating MDR gram negative organisms. Excessive use of this colistin antibiotic for these microorganisms has resulted in colistin resistance too.

There are very few new antimicrobial agents available for the treatment of MDR-GNB. Owing to the lack of novel agents to treat resistant infections, clinicians must use antibiotics judiciously and appropriately to limit the development of resistance.

CONCLUSION

In conclusion, antimicrobial resistance is recognized as a major complex problem and addressing it requires various countries to make joint effort across various disciplines.

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