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Bacterial Etiology of Diarrhea in Children Admitted in Hematologic Unit in a Tertiary Care Hospital

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Abstract

Introduction: Diarrhea is a frequent complication observed in patients with hematologic cancer. The normal fecal micro flora changes in chemotherapy-induced diarrhea, which shows a higher proportion of aerobic and oxygen-tolerant bacteria. Hence the causative bacterial pathogens maybe different than the usual etiology.

Objectives: Therefore, the objective of the study was to find outthe etiology of diarrhea in children suffering from hematological malignancy and who are on chemotherapy.

Material and Methods: A retrospective study was carried out on patients in hematologic unit of pediatric ward over a period of one and half years at a tertiary care hospital in Mumbai.

A total of 55 stool samples from patients of hematological malignancy who presented with diarrhea, were included in this study. The samples were processed as per standard techniques and the bacterial pathogens were identified by standard biochemical tests.

Results: Growth of pathogenic bacteria was seen in 15 (27.27%) stool samples, of which 13 patients had acute lymphatic leukemia(ALL) and only two patients had acute myeloid leukemia (AML). Among 15 growths, 11 grew *Pseudomonas aeruginosa*, two grew *Morganella morganii* and one each grew *Aeromonas hydrophila* and *Klebsiella pneumoniae*.

Conclusion: Organisms usually considered as non pathogenic may cause disease in immunocompromised patients. Stool specimens of all leukemic patients suffering from diarrhea and on chemotherapy, should be sent routinely for culture, so as to find out the exact cause of diarrhea.

Keywords: Bacterial etiology; Diarrhea; Pediatric hematologic unit

Introduction

One of the most common complications involved in treating patients with hematologic cancer is infection. In many cases there are multiple factors that predispose these patients to infections such as neutropenia induced by therapy or bone marrow involvement, hypogammaglobulinemia, T-cell dysfunction, and mucosal damage [1]. Diarrhea is frequent complication observed which can be life threatening at times [2]. It is a usual manifestation of neutropenicenterocoltis associated with chemotherapy-induced mucosal injury, followed by a superinfection usually by Gram-negative bacteria and may lead to bacteremia [3].

It is difficult to differentiate between infectious and non-infectious causes of abdominal symptoms in these patients, but it is essential for avoidance of misinterpretation and subsequent delay of adequate treatment. The normal fecal microflora changes in chemotherapy-induced diarrhea, in many patients, which show a decreased proportion of anaerobic bacteria with a higher proportion of aerobic and oxygen-tolerant bacteria. The normally reduced nature of the lumen become oxidized following chemotherapy, inhibiting anaerobic bacteria and allowing the growth of oxygen-tolerant bacteria [4]. Hence the causative bacterial pathogens maybe different than the usual etiology. In this study we identified bacteria from 55 stool samples collected from children suffering from hematological malignancy and are on chemotherapy, to study the etiology of diarrhea in these patients.

Material and Methods

This is a retrospective study carried out on patients in hematologic unit of pediatric ward at a tertiary care hospital in Mumbai.

A total of 55 stool samples from patients of hematological malignancy were analyzed for bacterial isolates over a period of one and half years, i.e. from October 2013 to March 2015.

Pediatric patients from hematology ward who presented with diarrhea were included in this study. A brief history about the type of hematological malignancy was obtained after the sample grew pathogenic bacteria. The stool samples were collected in sterile wide mouthed containers and were sent to Microbiology Department. They were directly plated on MacConkey agar (MA) and Xylose lysine deoxycholate agar (XLD) and incubated for 24-48 hours at 37C. Bacterial pathogens were identified according to standard biochemical

tests, [5] followed by antibiotic susceptibility testing on Mueller Hinton agar by Kirby Bauer disc diffusion method, according to CLSI guidelines [6]. The turnaround time for negative result reporting was three days while that of positive reports was three to five days.

Results and Discussion

A total of 55 stool samples collected from patients admitted to hematology ward for diarrhea were taken. These patients were suffering from hematological malignancy. Growth of pathogenic bacteria was seen in 27.27% (15/55) stool samples. In remaining 40 samples, no pathogenic bacteria was grown. When analyzed for the type of leukemia these patientswere suffering, 13 patients had acute lymphatic leukemia (ALL) and only two patients had acute myeloid leukemia (AML).

Among these 15 stool samples, 11 grew *Pseudomonas aeruginosa*. Out of these,9 patients were suffering from ALL, while 2 patients had AML. Two patients with ALL grew *Morganella morganii*. Stool sample of one patient grew *Aeromonashydrophila* and one grew *Klebsiella pneumoniae*, both were suffering from ALL.

Table 1 shows the antibiotic susceptibility pattern of these 15 isolates.

Organism (No.)	Ak	Pi	Caz	Ctx	Nx	Na	Cot
*P. aeruginosa** (11)	10	8	7	-	1	-	-
M. morganii (02)	2	-	-	2	1	2	2
A. hydrophila (01)	1	-	-	0	0	0	0
K. pneumoniae (01)	1	-	-	0	0	0	0

Table 1: Antibiotic susceptibility of 15 isolates from stool samples.

*One isolate of *P. aeruginosa*, which was resistant to all first line antibiotics, was susceptible to imipenem. Ak = Amikacin; Pi = Piperacillin; Caz = Ceftazidime; Ctx = Cefotaxime; Nx = Norfloxacin; Na = Nalidixic acid; Cot = Trimethoprim-Sulphamethoxazole

Diarrhea is a common and frequently unclear symptom in patients with acute leukemia after intensive chemotherapy. However, no systematic study is available concerning the proportion of infectious causes. In this study, we observed total 55 patients suffering from hematological malignancy on treatment, with diarrhea. All patients were neutropenic and were on chemotherapy. Out of these, only 15 (27.3%) patients' stool culture grew pathogenic bacteria. Remaining 30 stool culture did not grow any pathogenic bacteria. This observation suggests that only one third of the patients presenting with symptoms suggestive of diarrhea, suffer from bacterial diarrhea. Rests of the patients have other etiology. This percentage is higher than that was reported by Gorschlu¨ter et al. (17.7%) [7]. This difference may have resulted, as this study enrolled only neutropenic patients with acute leukemia and observed for symptoms of abdominal infection. Acute myeloid leukemia was more common than other hematological malignancy in patients with bacterial diarrea [1]. Similar results were observed in study by Aksoy et al. who observed patients with neutropenic enterocolitis having diarrhea as one of the symptom [2]. But in this study, there were only two patients with AML and maximum number of cases was of ALL (13), as this might vary according to different geographic locations.

Organisms isolated were *Pseudomonas aeruginosa* (11), *M. morganii* (02), *A. hydrophila* (01) and *K. pneumoniae* (01). Routine enteric pathogens were not observed in these patients. Similar results were observed in a study by Gorschluter et al. done on patients with acute leukemia, where only one C. jejuniiwas isolated [7]. *Pseudomonas aeruginosa* was isolated in maximum number of cases (73.33%). *Pseudomonas* was isolated in over 60% of the leukemic patients who developed a bacterial infection [8,9]. It is possible that the chemotherapeutic drugs used in these patients may be partially responsible for the selection of infecting organisms as is the type of neoplasm per se [10]. *Pseudomonas* can not only survive but can also dominate a mixed population by virtue of a high degree of drug resistance,both to most antibiotics and also to several of chemotherapeutic agents [11]. Another study also reported that a substantial number of patients with leukemia became carriers of *Pseudomona*s after 2 to 4 weeks of hospitalization and chemotherapy [8]. The normal fecal microflora changes in chemotherapy-induced diarrhea. Many patients show decreased proportion of anaerobic bacteria with a higher proportion of aerobic and oxygen-tolerant bacteria [12]. In a study by Adlard et al., it was observed that P. *aeruginosa* can be an etiological agent of diarrhea, particularly in immunodeficient or antibiotic-treated individuals [13]. These results are in conformity with this study.

In this study, it was observed that one of these isolates was resistant to all baseline drugs. When tested for higher antibiotics, it was sensitive to imipenem. In a study by Goldschmidt and Bodey also, it was seen that *Pseudomonas* strains were by far the most resistant of all the organisms studied [11].

Morganella morganii is an opportunistic secondary invader that was originally thought to be the cause of summer diarrea [14]. In a study done in 1986, *M. morganii* was isolated significantly more in numbers from patients with gastrointestinal disease than from healthy controls [15]. Infections are more common in immunocompromised patients. In this study, two cases of diarrhea showed growth of *Morganella morganii* in stool sample. Both the cases were of AML.

Klebsiella pneumoniae has been studied as cause of diarrhea in HIV infected patients. These isolates are shown to have HEp 2 adherence as pathogenic property. These specific isolates are isolated more frequently in immunocompromised patients [16]. One study have reported *E.coli* and *Klebsiella* from the stool culture of a leukemic child, who developed necrotizing enterocolitis [17]. In the present study, one *Klebsiella pneumonia* was isolated in a patient with AML.

In this study, one *Aeromonas hydrophila* was also isolated. Though the pathogenic role of *Aeromonas* species is controversial in healthy individuals but it has been isolated in patients withsome associated immunocompromised status. There is accumulating evidence that these bacteria are capable of causing usually mild, self-limited diarrheal disease [18].

All organisms were sensitive to baseline drugs. All isolates except one was sensitive to amikacin. The one isolate resistant to amikacin was *Pseudomonas aeruginosa*. It was also resistant to other baseline drugs and put up for higher antibiotic susceptibility. It was sensitive to imipenem. *Klebsiella pneumonia* and *Aeromonas hydrophila* were sensitive to only amikacin. Similar finding was observed in a study in Dakar, where *Klebsiella pneumonia* was resistant to many of the antibiotics used routinely to treat diarrea [16]. Timely and appropriate treatment will help to avoid delay in treatment in these patients.

The normal fecal microflora changes in chemotherapy-induced diarrhea in many patients, showing a higher proportion of aerobic and oxygen-tolerant bacteria [12]. Organisms usually considered as non-pathogenic may cause disease in immunocompromised patients. Therefore, stool specimens of all leukemic patients suffering from diarrhea and on chemotherapy, should be sent routinely for culture, so as to find out the exact cause of diarrhea. Reporting of pathogens causing diarrhea will help the clinicians to start the appropriate antibiotics and limit the morbidity and mortality in these cases.

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