

FEBRIL NEUTROPENIA ETIOLOGY IN A HEMATOLOGY DEPARTMENT

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Aim: Chemotherapy-induced febrile neutropenia (FN) predisposes patients to life-threatening infections and typically requires hospitalization. Patients with profound neutropenia have increased risk of septicemia associated with significant morbidity. To provide the appropriate broad-spectrum antimicrobial cover, documentation of causative agents and their antimicrobial susceptibilities should be established in each hospital.

Methods: The goal of the present study was to investigate the causative microorganisms in 27 febrile neutropenic patients between January 2006 and December 2007.

Results: In our hematology unit, among 122 febrile neutropenic episodes 57 isolates from cultures of febrile neutropenic patients, gram-negative bacteria was prevalent (45.6%). Among the gram-positives (%42.1% of isolates) coagulase-negative staphylococci (CNS) were the predominant bacteria (13/23) followed by *Staphylococcus aureus* (7/23). *Escherichia coli* (14/26) and *Klebsiella* spp. (7/26) were the most common species among 26 gram-negative bacteria.

Conclusion: The most important issue in febrile neutropenia is still a mortal situation in immunocompromised patients. So documentation of the flora in each unit would help to decide appropriate empirical therapy which is life saving.

Key words: Febrile neutropenia, hematological malignancies, antibiotic treatment.

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INTRODUCTION

Febrile neutropenia is a common complication in the practice of hematology. Absolute granulocyte count of 500/mm³ or less should be considered neutropenia. Single oral temperature of 38,5 0C or more, or the detection of two oral temperatures of 38 0C or more within a 12-hour period should be defined febrile neutropenia (1).

Standard management of febrile neutropenia requires prompt administration of empirical, broad-spectrum, parenteral antibiotic therapy, since febrile neutropenia is associated with a significant risk of infectious complications and mortality (2,3). Infections in the neutropenic patient can be rapidly fatal if not managed properly. Mortality rate in the 1960's was 50%. This rate is less than 5% with proper management today. Due to mortality, the agents causing infection should be known and appropriate antibiotic therapy

should be started immediately. The etiological agents and their antibiotic susceptibilities differ by time and by hospitals as a result of therapeutic and medical manipulations. As immediate administration of antibiotic therapy is crucial for successful management of infections, at least yearly documentation of causative microorganisms is mandatory in each center (3).

In this study we report the microorganisms isolated from cultures of neutropenic patients in GATA Haydarpaşa Hospital department of hematology between January 2006 and December 2007.

MATERIAL AND METHODS

The selected patients were adults hospitalized in the hematology department, whose cultures were obtained at the time they had fever and neutropenia

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Table 1. The types of microorganisms from positive cultures

Bacteria	n	%		n	%		n	%
Gram-positive	23	42.1	Gram-negative	26	45.6	Candida spp.	7	12.3
CNS	13		E. coli	14		C. albicans	7	
S. aureus	7		Klebsiella spp.	7		Other		
Streptococcus spp.	1		Citrobacter spp.	1		Aspergillus spp.	1	0.3
Enterococcus spp.	2		Stenotrophomonas maltophilia	1				
			Pseudomonas spp.	2				
			Acinobacter spp.	1				

CNS: Coagulase-negative staphylococci.

(PMNL<500/mm³ or expected neutropenia within few days due to chemotherapy). Twenty seven patients (five of them with catheter) were included in this study. All the patients in this retrospective study were with hematological malignancies and had neutropenia duration of average 16±2 days.

At least one set of cultures were taken before the initiation of antibiotic therapy. Cultures were observed by BACTEC 9240 continuous monitoring system (BD Biosciences). Microbiological investigation of positive cultures were performed by classical microbiological methods and by miniAPI identification system. For commensal skin flora members at least two consequent isolates either from peripheral vein or one from catheter was considered to be positive. If catheter site was positive, the clinical sign and symptoms of septicemia were sought for significant positivity (4).

RESULTS

During the two year period, twenty seven febrile neutropenic cases were hospitalized. One hundred twenty two febrile neutropenic episodes were observed. In 57 episodes positive cultures were obtained. Thirty eight (67%) isolates were from hemocultures, 12 (20.8%) were from urine cultures and 7 (12.2%) were from catheter, abscess and wound. Twenty six (45.6%) isolates were gram negative bacteria, whereas 23 (42.1%) isolates were gram positive bacteria. The predominant bacteria were E.coli and coagulase-negative staphylococci. The isolated microorganisms are shown in Table 1.

Gram positive bacteria were sensitive to vancomycine 100%, trimethoprim

sulfomethosazole 43%, gentamycine 64%, levofloxacin 52%. Enteric bacteria were sensitive to imipenem 90%, piperacilline tazobactam 88% and amikacine 54%.

DISCUSSION

The benefit of immediate use of appropriate antimicrobiological therapy has been implied years ago (5). It is easier to define the infection and to take cultures in cases with apparent site of infection. It is not usually possible in cases with febrile neutropenia due to difficult localization of infection (6). Approximately in 80% of cases the causative microorganism is from the endogenous flora (7).

In previous reports, microbiologically documented infections varied between 32.5% and 48% (8-12). In our study documented infections are 47% which is comparable to the results of mentioned studies.

Early studies show that gram-negative microorganisms were the most frequently isolated pathogens during the neutropenic episodes (13). After transplantation procedures and use of long term intravascular catheters in clinical practice, gram-positive isolates have become more frequent in febrile neutropenic patients (9,14-16).

In our country, in two large studies by the year 1996 blood isolates were gram-positive microorganisms, whereas in 1998 both gram-positive and gram-negative bacteria were found to be equal (17,18). However in the study of Demiraslan et al gram negative bacteria were detected in 74.2% of the positive cultures whereas 25.8% were gram positive bacteria (19). Recently Baysallar et al reported cultures with gram positive bacteria of 69% and gram negative bacteria of 31% (20).

There are different reports from different centers in all around the world. The difference may be due to used chemotherapy protocols or due to antimicrobial therapy. Among gram-negative microorganisms, the most common isolate is *E.coli* whereas in gram-positive microorganisms the most common one is coagulase-negative staphylococci (6,21). In our report we detected similar results.

In this study we report the data of isolated microorganisms in our unit. Forty six percent of isolates were gram negative bacteria, whereas 42% of isolates were gram positive bacteria. There is a slight predominance of gram-negative microorganisms in our unit which can be explained by lack of transplantation and no long term use of intravascular catheters.

The most important issue in febrile neutropenia is still a mortal situation in immunocompromised patients. So documentation of the flora in each unit would help to decide appropriate empirical therapy which is life saving.

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