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°C or more, or the detection of two oral temperatures of 38°C 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 Haydarpasa 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...
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%, gentamyicine 64%, levofloxacin 52%. Enteric bacteria were sensitive to imipenem 90%, piperacilline tazobactam 88% and amikacine 54%.

DISCUSSION

The benefit of immediate use of appropriate antimicrobial 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).

| Bacteria               | n  | %    | Bacteria               | n  | %    |
|------------------------|----|------|------------------------|----|------|
| Gram-positive          | 23 | 42.1 | Gram-negative          | 26 | 45.6 |
| CNS                    | 13 |      | E. coli               | 14 |      |
| S. aureus              | 7  |      | Klebsiella spp.       | 7  |      |
| Streptococcus spp.     | 1  |      | Citrobacter spp       | 1  |      |
| Enterococcus spp.      | 2  |      | Stenotrophomonas      | 1  |      |
|                        |    |      | maltofilia            |    |      |
|                        |    |      | Pseudomonas spp.      | 2  |      |
|                        |    |      | Acinobacter spp.      | 1  |      |

CNS: Coagulase-negative staphylococci.
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.

REFERENCES

1. Hughes WT, Armstrong D, Bodey GP, et al. 2002 guidelines for the use of antimicrobial agents in neutropenic patients with cancer. Clin Infect Dis 2002;15;34:730-51
2. Rolston KV. New trends in patient management: risk-based therapy for febrile patients with neutropenia. Clin Infect Dis 1999;29:515-21
3. Bodey GP, Buckley M, Sathe YS, Freireich EJ. Quantitative relationships between circulating leukocytes and infection in patients with acute leukemia. Ann Intern Med 1966;64:328-40
4. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM CDC definitions for nosocomial infections, 1988. Am J Infect Control 1988;16; 128-40
5. Schimpff S, Satterlee W, Young VM, Serpick A. Empiric therapy with carbenicillin and gentamicin for febrile patients with cancer and granulocytopenia. N Engl J Med 1971;284:1061-5
6. Bille J. Laboratory diagnosis of infections in febrile neutropenic or immunocompromised patients. Int J Antimicrob Agents 2000;16:87-9
7. Schimpff SC, Young VM, Greene WH, Vermeulen GD, Moody MR, Wiernik PH. Origin of infection in acute nonlymphocytic leukemia. Significance of hospital acquisition of potential pathogens. Ann Intern Med 1972;77:707-14
8. Akan H, Koç H, Arslan Ö, et al. Febrile neutropenia in a bone marrow transplantation unit. Int J Antimicrob Agents 1997;8:127-30
9. Ketterer N, Espinouse D, Chomarat M, et al. Infections following peripheral blood progenitor cell transplantation for lymphoproliferative malignancies: etiology and potential risk factors. Am J Med 1999;106:191-7
10. Salazar R, Solá C, Maroto P, et al. Infectious complications in 128 patients treated with high-dose chemotherapy and autologous peripheral blood stem cell transplantation. Bone Marrow Transplant 1999;23:27-33
11. Engels EA, Ellis CA, Supran SE, et al. Early infection in bone marrow transplantation: quantitative study of clinical factors that affect risk. Clin Infect Dis 1999;28:256-66
12. Celebi H, Akan H, Akçağlayan E, Üstün C, Arat M. Febrile neutropenia in allogeneic and autologous peripheral blood stem cell transplantation and conventional chemotherapy for malignancies. Bone Marrow Transplant 2000;26:211-4
13. Bodey GP. Antibiotics in patients with neutropenia. Arch Intern Med 1984;144:1845-51
14. Mossad SB, Longworth DL, Goormastic M, Serkey JM, Keys TF, Bolwell BJ. Early infectious complications in autologous bone marrow transplantation: a review of 219 patients. Bone Marrow Transplant 1996;18:265-71
15. Winston DJ. Prophylaxis and treatment of infection in the bone marrow transplant recipient. Curr Clin Top Infect Dis 1993;13:293-321
16. Klastersky J. Empirical antibiotic therapy in neutropenic cancer patients. Eur J Cancer 1993;29A Suppl 1:6-10
17. Akova M, Akan H, Kortlen V, et al. Comparison of meropenem with amikacin plus ceftazidime in the empirical treatment of febrile neutropenia: a prospective randomised multicentre trial in patients without previous prophylactic antibiotics. Meropenem Study Group of Turkey. Int J Antimicrob Agents 1999;13:15-9
18. Erman M, Akova M, Akan H, et al. Febrile Neutropenia Study Group of Turkey. Comparison of cefepime and ceftazidime in combination with amikacin in the empirical treatment of high-risk patients with febrile neutropenia: a prospective, randomized, multicenter study. Scand J Infect Dis 2001;33:827-31
19. Demiraslan H, Yildiz O, Kaynar L, Altuntaş F,
Eser B, Aygen B. Isolated microorganisms from febrile neutropenic patients and their antimicrobial susceptibility: A data of 2005. Erciyes Med J 2007;29:376-80

20. Baysallar M, Güçlü AÜ, Şenses Z, Kaptan K, Ataergin S, Baştcaoğlu AC. Bacterial spectrum and antimicrobial susceptibility profile in hemocultures of patients with febrile neutropenia. Gulhane Med J 2007; 49: 168-72

21. Gram-positive bacteraemia in granulocytopenic cancer patients. EORTC International Antimicrobial Therapy Cooperative Group. Eur J Cancer 1990;26: 569-74