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Bacterial isolates in neutropenic febrile patients

M Karim
Aga Khan University

W Khan
Aga Khan University

B Farooqi
Aga Khan University

I Malik
Aga Khan University

BACTERIAL ISOLATES IN NEUTROPENIC FEBRILE PATIENTS

Pages with reference to book, From 35 To 37

Michelle Karim, Waheed Khan, Imtiaz Malik (Departments of Medicine, Faculty of Health Sciences, The Aga Khan University, Karachi-74800.)
Badar Farooqi (Departments of Microbiology, Faculty of Health Sciences, The Aga Khan University, Karachi-74800.)

ABSTRACT

One hundred consecutive patients with documented bactéremia and neutrophil count of 0.5x109 /L or below were retrospectively studied to determine the pattern of infection at the Aga Khan University Hospital in Karachi. These included patients with primary haematologic malignancies presenting with low counts, and those patients with cancer who developed neutropenia as a result of chemotherapy. The gram negative organism pseudomonas aeruginosa was the most common bacterial organism isolated constituting 31% of all positive blood cultures. Gram positive organisms were frequently isolated comprising 24% of all isolates of which 15% were Staph.aureus. Staph. epidermidis was not isolated in this series. Salmonella species were isolated in 9 patients. The other gram negative rods included non-lactose fermenting organisms frequently isolated in a nosocomial setting including Serratia and Acinetobacter. Four patients had positive fungal blood cultures. A single positive anaerobic culture was obtained. Sensitivities of the Pseudomonas aeruginosa reflected the high frequency of resistance seen in nosocomial isolates and those from the community. More than half (54.8%) of the isolates were resistant to carbenicillin and 9.6% resistant to gentamicin. Although 3.2% were resistant to cefotaxime, none were resistant to ofloxacin or ceftazidime reflecting the relatively recent arrival of the latter. In contrast, 23% of Staph: aureus were still sensitive to penicillin. Methicillin (cloxacillin) resistant Staph. aureus did not occur. However 26.6% of the Staph. aureus were resistantto erythromycin. Knowledge of the prevailing pattern of infection permits the development of investigative and therapeutic approaches of optimal efficacy (JPMA 41: 35, 1991).

INTRODUCTION

Patients with haematologic and other malignancies are susceptible to infections. Many factors predispose this patient population to infection including tumor specific deficiencies in host defence mechanisms due to malignant processes and cytotoxic chemotherapy. Neutropenic patients are most susceptible to infections caused by gram negative bacilli and gram positive cocci. Candida and aspergillus[1]. The spectrum of infection may be further altered by changes in medical practices (use of indwelling catheters, etc), changes in the ecology of infective agents, demography of patients at risk or by prevailing community infections[2]. Hence to achieve the highest percentage of survival, it is necessary to determine the pattern of infection in these patients, so that the most effective empiric therapy maybe used at the earliest sign of infection. In the present paper we retrospectively analyze, 100 positive blood cultures in patients with neutropenia. The data presented here show the similarity in patterns of infection[3] and emerging bacterial resistance at a tertiary referral center in a developing country.

PATIENTS AND METHODS

Patients

This study included 100 consecutively bacteremic patients with neutropenia defmed as a neutrophil count of $0.5x10^9$ /L or less, who developed a sustained temperature of 38 C or above. Patients who became febrile in proximity to having received blood products were excluded. Patients were included regardless of whether they had primary neutropenia related to their underlying haematologic malignancies and were therefore new admissions from the community or they were neutropenic secondary to cytotoxic therapy while in the hospital.

Microbiologic evaluation

Two sets of blood cultures were obtained. Brain heart infusion broth was used for aerobic cultures and thioglycolate broth for anaerobic cultures. Cultures were incubated for 7 days. Blind sub- cultures of medium and gram stains were done daily on blood agar plates and after 48 hours additionallyon Sabouraud Dextrose Agar for betteryleld of fungus. On the 5th day both anaerobic and aerobic cultures were plated on chocolate and blood agar plates.

RESULTS

Analysis of 100 positive blood cultures in neutropenic patients with both haematologic and other malignancies (Table I)

TABLE I. Underlying Disorders.

Underlying Disease		Number	n = 100
1.	Acute myeloid leukemia	=	42
2.	Acute lymphoblastic leukemia	=	12
3.	Non-Hodgkins lymphoma	=	8
4.	Hodgkins lymphoma	=	9
5.	T. Cell lymphoma	=	3
6.	Aplastic anaemia	=	5
7.	Myelodysplastic syndrome	=	3
8.	Chronic myeloid leukemia with acute blast crises	=	4
9.	Multiple myeloma	=	1
10.	Carcinoma cervix	=	1
11.	Rhabdomyosarcoma	=	1
12.	Osteogenic sarcoma	=	1
13.	Ewings sarcoma	=	2
14.	Carcinoma ovary	=	1
15.	Carcinoma breast	=	1
16.	Carcinoma tongue	=	1
17.	Chorio-carcinoma	=	1
18.	Angio-immunoblastic lymphadenopathy	=	1
19.	Astrocytoma	=	1
20.	Carcinoma urinary bladder	=	1
21.	Teratoma	=	1

Majority of these patients had leukemia (54%) and had prolonged neutropenia.

revealed Pseudomonas aeruginosa as the most common organism. Majority of the patients had underlying leukemia and remained neutropenic for prolonged time periods. The different types of organisms and the numbers cultured are shown, in Table II.

TABLE. II. Organism isolated from blood.

Name Of Organism	Number n = 100
Pseudomonas aeruginosa	31
Staphylococcus aureus	15
E. Coli	9
Salmonella	
typhi	6
paratyphi A	1
paratyphi B	2
Enterobacter species	5
Acinetobacter species	4
Klebsiella species	6
Candida species	4
Serratia liquificans	3
Streptococcus group D	5
Streptococcus viridans	2
Neisseria sicca	1
Streptococcus pneumonia	1
Bacteroids species	1
Proteus species	1
Aeromonas hydrophilia	1
Streptococcus-not group D	1
Bacillus species	1

Pseudomonas aeruginosa was the commonest isolate.
Surprisingly Staphylococcus epidermidis was encountered.
Candida species were isolated from four patients.

Pseudomonas aeruginosa was isolated from 31% of the cases, followed by Staph. aureus in 15%. Salmonella species isolated in 9% of cases is much higher than reported elsewhere. These isolates have not been separated according to the type of malignancy or the time of positivity i.e.on admission or afterwards.

TABLE. III. Antibiotic Resistance Patterns

Antibiotics	Percent Resistance
Pseudomonas aeroginosa	n = 31
Carbenicillin	54.8
Gentamycin	9.6
Ceftazidime	nil
Cefotaxime	3.2
Azactam	6.4
Ofloxacin	nil
Staphylococcus aureus	n = 15
Penicillin	73.3
Cloxacillin	nil
Erythromycin	26.6
Gentamycin	6.6
Clindamycin	6.6
Ofloxacin	nil

Pseudomonas had high resistance to Carbenicillin and some resistance to gentamycin. Staphylococcus aureus was uniformly sensitive to cloxacillin but highly resistant to penicillin and erythromycin.

Table III indicates sensitivity patterns of pseudomonas aeruginosa and Staph. aureus. Pseudomonas was highly (54.8%) resistant to carbenicillin and 9.6% isolates were resistant to gentamycin whereas, 73% of Staphylococcus aureus were resistant to penicillin and 26% to Erythromycin.

DISCUSSION

Malignancies, as well as their treatment, are associated with potentially serious and even life-threatening complications. One of the commonest of these is the development of infections, caused by a wide variety of pathogenic organisms. Although many reasons exist for the enhanced susceptibility to infections, neutropenia is the single most important factor. These patients require prompt empiric antibiotic therapy, if they become febrile, as delay often results in fatality[4]. Selection of the antibiotic regimen should take into consideration the organisms that are prevalent in the hospital and their usual pattern of antibiotic susceptibility. The spectrum of organisms causing infections in neutropenic patients changes according to the duration of neutropenia[5]. The concept of empiric antibiotic therapy was in itiated for febrile leukemic patients in the 1960's because of the exceptionally high mortality rate in neutropenic patients if antibiotic administration was delayed until the organism was identified[6] . Since neutropenic patients are unable to mount an adequate inflammatory responses, they are mostly dependent on antibiotics to control infections. Results of clinical studies have clearly demonstrated that

synergistic antibiotics with high serum bactericidal activity are critical in the management of gram negative bacillary infections[7]. There has been a shift in the microbial flora at many oncology centers during the last 10 years. Increasing number of gram positive organisms specifically Staph. epidermidis, Staph. aureus, Streptococcus and Bacillus species are being encountered[8]. However, although these infections produce moderate morbidity (e.g.fever), mortality is fairly low. Therefore empiric treatment is mostly directed at the gram-negative organisms. Most clinical studies suggest that empiric therapy using combinations of two bactericidal antibiotics is necessary[9-12]. Effective antibiotic combinations have usually included an aminoglycoside plus an extended spectrum penicillin (e.g. ticarcillin or carbenicillin) or a broad spectrum antipseudomonal cephalosporin (e.g. ceftazidime, cefotaxime). Double beta-lactam combinations have also been used but some concern has been expressed that these combinations may interact in an antagonistic fashion[13,14]. Inmost studies, however, the double beta-lactam regimen has been as effective as the beta-lactam plus aminoglycoside[15,16]. In the patients with prolonged neutropenia, on multiple antibiotics, the likelihood of fungal infections, e.g., Candida and Aspergillus increase tremendously[17]. In these cases empiric amphotericin therapy may have to be considered. This study demonstrates that in our hospital setting Pseudomonas aeruginosa is the commonest bacterial isolate, followed by Staph. aureus. We have routinely used cloxacillin and amikacin as the empiric antibiotic therapy. Besides covering the two most likely organisms, it also covers against gentamycin-resistant Pseudomonas. In those responding poorly, we add cefotaxime or azactam to enhance gram negative coverage. Growth of fungus in four patients indicates that it may not be an uncommon problem in Pakistan and empiric amphotericin therapy is indicated in those who continue to befebrile and neutropenicwithout any evident infection We conclude that gram negatives are the commonest bacterial isolates in neutropenic febrile patients, followed by Staph. aureus. Choice of empiric antibiotic therapy should be tailored towards these organisms. Similar studies need to be repeated at regular intervals to evaluate any changes in bacteriologic spectrum or their antibiotic susceptibility.

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