PATTERNS OF INFECTION IN ONCOLOGY PATIENTS IN SINGAPORE

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SYNOPSIS

Infection continue to be the most frequent serious complication and chief cause of mortality in immunocompromised oncology patients. Diminished host resistant and immune defences, iatrogenic myelo-suppression secondary to chemotherapy and radiotherapy, together with poor nutritional status render them prone to nosocomial sepsis. This study of 21 cancer patients with clinical and bacteriological evidence of sepsis, illustrates their vulnerability to life-threatening, gram-negatives (especially *Pseudomonas aeruginosa*), and gram-positive (even commensal flora) infections, as well as opportunistic mycoses and parasitic infestations. Marked resistance to conventional and new antimicrobial agent was demonstrated, particularly by gram-negative enteric bacillary isolates. Ceftazidime, cefoperazone and amikacin were most active *in vitro* against these highly resistant gram-negative strains, many of which were beta-lactamase producers. Other mechanisms of antibiotic resistance are discussed. The approach to the selection of antimicrobial drugs, and other preventive and therapeutic aspects of infection control in oncology patients are reviewed.

INTRODUCTION

There is a significant incidence of sepsis and mortality in immunosuppressed patients with cancer, in particular haematological malignancies like leukaemia and lymphoma. In patients with leukemia or lymphoma there is an added problem of myelosuppression secondary to the disease process itself and/or cytotoxic chemotherapy (1, 2). This study was thus conducted, involving in-patients of a Haematology/Oncology ward in Singapore General Hospital, in order to study the prevalence pattern and microbiology of nosocomial infections in cancer patients.

Of greater importance is the need to examine the common problem of gram-negative bacterial sepsis (especially due to *Pseudomonas* species) in these patients, and these organisms' notorious reputation of multiple antibiotic resistance.

PATIENTS AND METHODS

Our study from January to April 1985, involved inpatients of the Haematology/Oncology Ward, Singapore General Hospital. Patients with malignancies particularly lymphoproliferative disorders (3, 4, 5) and who were diagnosed to be having infection in various body sites were included in the study. Infection was defined as persistence of temperature of more than 38°C for 3 hours during a 24 hour period. Antimicrobial therapeutic regimes prescribed prior to or at the time of specimen collection were noted. A total of 62 specimens were collected from 31 patients. 28 positive culture results were obtained from 21 patients and are analysed below.

All smaples were inoculated on blood agar plates (Oxoid, Basingstoke, England) and incubated aerobically at 37°C. Gram-negative bacterial isolates were identified using API 20E and API 20NE systems (API System, S.A., France). Presumptive identification of *Candida albicans* was done by the germ-tube formation test or the Reynolds-Braude phenomenon (6). API 20C strips (API System, S.A., France) were employed for the identification and confirmation of yeasts *(Candida)*.

Antimicrobial susceptibility testing was performed by the disc diffusion method of Kirby and Bauer (7) using the following antibiotic discs (Oxoid, Basingstoke, England): amikacin 30 μg, ampicillin 25 μg, cephaloridine 30 μg, chloramphenicol 30 μg, sissomicin 10 μg and trimethoprim-sulphamethoxazole 25 μg. In addition, all *Pseudomonas* and gram-negative enteric bacteria isolates were also tested against carbenicillin 100 μg, cefoperazone 30 μg, cefotaxime 30 μg, cefoxitin 30 μg, ceftazidime 30 μg and tobramycin 10 μg (Mast, Liverpool, England).

Minimum inhibitory concentrations (MIC's) were determined by the agar dilution technique (8) on Mueller-Hinton agar (Gibco, Madison, USA) using inocula of approximately 10^5 colony forming units. Antibiotic powders of known potency (Mast, Liverpool, England) were used, and doubling antibiotic dilutions from 128 mg/L to 0.25 mg/L were tested against 6 *Pseudomonas* and 5 gram-negative enteric bacillary isolates. The antibiotics and their recommended breakpoints (in mg/L) were cefotaxime (≤16), cefoxitin ≤16), ceftazidime (≤16), and tobramycin (≤4).

All *Pseudomonas* and gram-negative enteric isolates were also detected for beta-lactamase production using a qualitative modified filter paper acidometric test designed by Sng et al (9).

RESULTS

The 21 patients who demonstrated clinical and bacteriological evidence of sepsis were between 15 to 65 years of age, with a male to female ratio of 4 to 3. The majority were suffering from haematological malignancies like lymphoma, leukaemia or myelodysplasia, while 2 patients had solid tumours (Table 1). 28 out of 62 specimens collected from these patients yielded positive cultures, and a total of 33 baterial and fungal isolates were obtained. The commonest site of infection was the pharynx. Septicaemia was the next most common infection with 8 positive blood cultures. The remaining sources of infection were evenly distributed, namely sputum, urine and surgical wounds. Of the 33 clinical isolates obtained, 27 were bacterial and 6 fungal (Table 2).

15 isolates (55.5%) were gram-positive bacteria recovered mainly from the respiratory tract and bloodstream. *Streptococcus pneumoniae* and other *Streptococcus* species predominated, particularly in the respiratory tract. The causative organisms of gram-positive septicaemia in this study were *Staphylococcus epidermidis, Staphylococcus aureus, Streptococcus* species and *Bacillus subtilis.*

TABLE 1
UNDERLYING MALIGNANCIES OF 21 CANCER PATIENTS WITH CLINICO-BACTERIOLOGICAL EVIDENCE OF SEPSIS

Diagnosis	No. of Patients
Acute myeloid leukaemia (AML)	8
Acute lymphoblastic leukaemia (ALL)	6
Non-Hodgkin's lymphoma*	2
Hodgkin's lymphoma	1
Testicular lymphoma	1
Myelodysplastic syndrome with CNS leukaemia	1
Carcinoma of the hypopharynx	1
Nasopharyngeal carcinoma (NPC)	1
Total	21

Gram-negative organisms constituted 12 out of 27 bacterial isolates (44.5%), *Pseudomonas* species being the most prevalent. *Pseudomonas aeruginosa* was recovered from the respiratory tract and surgical wounds, while 2 *Citrobacter fruendii* strains were isolated from mid-stream urine. Gram-negative septicaemia was secondary to *Pseudomonas putida* and *Escherichia coli* in 2 patients. One isolate each of *Klebsiella pneumoniae* and *Haemophilus influenzae* were recovered from throat swabs. Pus from a surgical wound of the patient yielded *Klebsiella pneumoniae.*

Candida albicans was isolated mainly from throat and sputum specimens, and was the aetiological agent of urinary tract infection in a diabetic cancer patient. *Candida tropicalis* event in a patient with acute myeloid leukaemia.

The antibiogram profiles of the gram-negative isolates demonstrated a remarkable degree of multiple resistance, in particular to conventional antimicrobial agents. The aminoglycosides amikacin, sissomicin and tobramycin were active *in vitro* against some gram-negative bacilli. However, two *P. aeruginosa* and two *C. fruendii* strains were resistant to these antibiotics. In addition, two *K. pneumoniae* strains were not susceptible to sissomicin and tobramycin. Ampicillin and chloramphenicol were active against gram-negative bacteria other than *Pseudomonas.* Only 3 out of the 6 *Pseudomonas* isolates were susceptible to Carbenicillin. Co-trimoxazole, ampicillin and cephaloridine (a first generation cephalosporin) demonstrated extremely poor activity against gram-negative enteric bacilli (Tables 3 and 4).

Among the newer cephalosporins tested, ceftazidime showed the highest *in vitro* activity against gram-negative bacteria, followed by cefoperazone. Gram-negative bacilli other than *Pseudomonas* were generally sensitive to cefoxitin.

Results of MIC studies using ceftazidime, cefoxitin, cefotaxime, and tobramycin correlated well with the corresponding sensitivity results of the disc diffusion technique (Table 5).

TABLE 2
DISTRIBUTION OF BACTERIAL AND FUNGAL ISOLATES BY SITE OF INFECTION

Organism Group	Name of Organism	Number of isolates from source					Total number of isolates
		Blood stream	Sputum	Throat	Urine	Surgical wound	
Gram-negative							
	Pseudomonas aeruginosa	0	2	1	0	2	5
	Pseudomonas putida	1	0	0	0	0	1
	Citrobacter fruendii	0	0	0	2	0	2
	Klebsiella pneumoniae	0	0	1	0	1	2
	Escherichia coli	1	0	0	0	0	1
	Haemophilus influenzae	0	0	1	0	0	1
Gram-positive							
	Streptococcus pneumoniae	0	0	5	0	0	5
	Streptococcus spp	1	0	3	0	0	4
	Staphylococcus aureus	1	0	0	0	1	2
	Staphylococcus epidermidis	2	0	0	1	0	3
	Bacillus subtilis	1	0	0	0	0	1
Yeasts							
	Candida albicans	0	2	2	1	0	5
	Candida tropicalis	1	0	0	0	0	1
	Total	8	4	13	4	4	33

TABLE 3
ANTIBIOTIC SENSITIVITY PATTERNS OF 27 BACTERIAL ISOLATES

Organism Group	Name of Organism (No. of isolates)	Number of susceptibile isolates					
		Amikacin	Sissomicin	Chloramphenicol	Co-trimaxazole	Cephaloridine	Ampicillin
Gram-Negative							
	P. aeruginosa (5)	3	3	0	0	0	0
	P. putida (1)	1	1	0	0	0	0
	C. fruendii (2)	0	0	2	0	0	0
	K. pneumoniae (2)	2	0	1	0	0	0
	E. coli (1)	1	1	1	1	1	0
	H. influenaze (1)	1	1	1	1	0	1
Gram-Positive							
	S. pneumoniae (5)	3	4	5	2	5	5
	Streptococcus spp (4)	3	3	4	1	4	1
	S. aureus (2)	1	1	1	2	1	1
	S. epidermidis (3)	3	3	3	1	1	0
	B. subtilis (1)	1	1	1	0	0	0
	TOTAL (27)	19	18	19	8	12	8

TABLE 4
ANTIBIOGRM PROFILES AND BETA-LACTAMASE ACTIVITY OF 6 PSEUDOMONAS AND 5 GRAM-NEGATIVE ENTERIC BACTERIAL ISOLATES

Name of Organism (No. of isolates)	Number of susceptibile isolates						
	Ceftazidime	Cefoperazone	Cefoxitin	Tobramycin	Carbenicillin	Cefotaxime	B-lactamase production
P. aeruginosa (5)	5	4	1	3	3	1	2
P. putida (1)	1	1	0	1	0	0	0
C. fruendii (2)	2	0	1	0	0	0	2
K. pneumoniae (2)	2	0	2	0	0	0	1
E. coli (1)	1	1	1	1	0	1	1
TOTAL (11)	11	6	5	5	3	2	6

TABLE 5
MINIMUM INHIBITORY CONCENTRATIONS OF 11 GRAM-NEGATIVE ISOLATES

Patient	Organism	MIC (mg/L)			
		Ceftazidime	Tobramycin	Cefoxitin	Cefotaxime
RBD	P. aeruginosa	4 (S)	1 (S)	> 128 (R)	> 128 (R)
NPC	P. aeruginosa	0.25 (S)	8 (R)	2 (S)	0.25 (S)
ALL	P. aeruginosa	4 (S)	0.5 (S)	> 128 (R)	64 (R)
LSF	P. aeruginosa	8 (S)	> 128 (R)	> 128 (R)	128 (R)
GBA	P. aeruginosa	16 (S)	1 (S)	> 128 (R)	> 128 (R)
LGH	C. fruendii	8 (S)	> 128 (R)	> 128 (R)	> 128 (R)
VSV	C. fruendii	16 (S)	> 128 (R)	> 128 (R)	> 128 (R)
MBY	K. pneumoniae	16 (S)	> 128 (R)	8 (R)	128 (R)
LSF	K. pneumoniae	16 (S)	> 128 (R)	2 (R)	128 (R)
MBY	E. coli	0.25 (S)	4 (S)	2 (S)	0.25 (S)
TKC	P. putida	2 (S)	0.5 (S)	> 128 (R)	128 (R)
Control	E. coli ATCC 25922	0.25 (S)	0.25 (S)	0.25 (S)	0.25 (S)
Total Number of susceptible isolates		11	5	4	2

(S) = sensitive (R) = resistant

6 out of 11 gram-negative bacterial isolates were beta-lactamase producers and revealed highly resistant antibiogram profiles.

CASE REPORTS

Five interesting case reports in which varied infections are encountered are presented below:

1. MBY, a moribund middle-aged Malay man was diagnosed to have myelodysplastic syndrome (MDS) with central nervous system (CNS) leukaemia. A swab from a surgical wound taken on 15.2.85 yielded a highly resistant strain of *Klebsiella pneumonieae.* Three days later, he was septicaemic and blood culture grew *E. coli.* In addition, he had profuse diarrhoea, and numerous *Strongyloides stercoralis* helminths were detected in his stools, which were however negative for *Cryptosporidia.*
2. VSV. This 60 year old Indian man was a case of Hodgkin's lymphoma on the Mustine Hydrochloride, Vincristine, Procarbazine, Prednisolone (MVPP) chemotherapeutic regime who developed pyrexia. Bacteriological investigations were undertaken, and parenteral ampicillin and amikacin therapy was commenced. Urine culture grew *Citrobacter fruendii* sensitive only to chloramphenicol, ceftazidime and cefoxitin. *Candida albicans* was also recovered from his sputum.
3. LHS, an elderly Chinese man with acute myeloid leukaemia (AML) on the Daunorubicin, Cytosine, Arabinoside, and 6 Thioguanine (DAT) drug regime demonstrated clinical evidence of septicaemia. A pure culture of *B. subtilis* was isolated from his bloodstream. This isolate was sensitive to chloramphenicol, amikacin and sissomicin but resistant to ampicillin, cephaloridine and co-trimoxazole.
4. CAE was a cachetic 30 year old Chinese lady diagnosed as AML with pulmonary tuberculosis, who was treated with the DAT protocol and anti-tuberculosis chemotherapy. In the ward, she developed *K. pneumoniae* septicaemia which failed to respond to parenteral antibiotic treatment. Subsequent sputum culture yielded *Candida albicans.* She ultimately succumbed to *Candida tropicalis* septicaemia which was the terminal event.
5. HUS, a middle aged Indian man was an amputee with diabetes mellitus and AML also on the DAT regimen. He had a positive urine culture which yielded *Candida albicans.*

DISCUSSION

Nosocomial infection in the immunocompromised host with malignancy, especially of haematological origin, is a well-documented and mounting problem (10, 11). Of the 21 cancer patients studied, two-thirds (14 patients) had leukaemia namely acute myeloid leukaemia and acute lymphoblastic leukaemia. These patients have altered host immune responsiveness and quantitative or qualitative defects in granulocytes (particularly polymorphonuclear leucocyte counts of 500/ul). In addition they have impaired lymphocytic function, which may be secondary to the underlying haematological disorder or to myelosuppression following cytotoxic chemotherapy.

Granulocytic functions including chemotaxis, phagocytosis and intraleucocytic killing may be impaired (12). Humoral or B-cell and cellular or T-cell mediated immunity may be defective particularly in Hodgkin's and non-Hodgkin's lymphoma, and solid tumours like Nasopharyngeal carcinoma and hypopharyngeal carcinoma in our study. The underlying malignancy and the associated therapeutic modalities of chemotherapy and radiotherapy are predisposing factors in the pathogenesis of bone marrow depression.

Neutropaenia increases the risk of bacterial infection, predominantly by gram-negative bacilli and *Staphylococci.* B-cell deficiency and/or dysfunction leads to infection with *Pneumococci, Streptococci* and *Haemophilus influenzae.* Patients with T-cell deficiency or impairment succumb to chronic bacterial, fungal, viral and parasitic infections (12).

In this survey, gram-positive organisms predominated, with *Pneumococci* and other *Streptococcus* species colonising mainly the pharynx. Two strains of *S. epidermidis,* one each of *S. aureus* and *B. subtilis* were isolated from blood of septicaemic patients. Although these organisms are usually considered endogenous microbial flora, they should not be dismissed as specimen contaminants, but be regarded as opportunistic pathogens in immunocompromised cancer patients (13, 14, 15). *S. epidermidis,* has been reported to invade intravenous infusion sites with resultant bacteraemia (1). The difficulty in interpretation may be resolved by repeating multiple blood cultures obtained from separate venepunctures (16, 17).

Gram-negative organisms belonging to the families *Pseudomonadaceae* and *Enterobacteriaceae* were almost equally distributed in the infection sites studied, that is, the respiratory tract, bloodstream, surgical wounds, and urinary traot. *P. aeruginosa* was the commonest gram-negative organism isolated, and its association with patients with blood dyscrasias and solid tumours is widely documented (18). 3 out of the 5 isolates were from the respiratory tract, which is also the major source of infection in other studies (18, 19, 20). *P. putida* septicaemia was seen in a leucopaenic patient with large cell lymphoma who was on chemotherapy. Two patients developed urinary tract infection from *C. fruendii* strains which were highly resistant to multiple antimicrobial agents.

Patient MBY, a case of MDS with the unusual association of CNS leukaemia was severely immunosuppressed with marked leucopaenia, lymphopaenia ($<1500/\mu l$) and reduction of T-helper cell subset. He developed *Klebsiella* wound infection and *E. coli* septicaemia. Investigations of his profuse diarrhoea revealed no AIDS (acquired immune deficiency syndrome) — related *Cryptosporidia* (21). Stool examination, however, was strongly positive for *Strongyloides stercoralis.* This is often a dormant helminthic infestation but which may be reactivated in an immunosuppressed patient years after being acquired (15, 22). HTLV III antibodies was negative in this patient.

K. pneumoniae and *H. influezae* were isolated from the pharynx of an AML patient on two separate occasions, indicating the immuno-compromised host's susceptibility to a multiplicity of pathogens.

Mycotic infections in the immunosuppressed attributed to *Candida albicans* are well-known e.g. mucocutaneous candidiasis and oral thrush. Four isolates of *C. albicans* were recovered from respiratory tract specimens. A sputum isolate of *C. albicans* in a febrile patient with pulmonary infiltrates in the CXR may suggest pulmonary candidiasis (15). *C. albicans* was also recovered from a urine specimen of an AML patient who was an insulin-dependent diabetic. Even

though the culture yielded less than 10^5 colonies per ml urine, it was considered significant, as the underlying diseases could well predispose him to the risk of *Candida* urinary tract infection.

C. tropicalis septicaemia was the terminal event in a female patient with AML and pulmonary tuberculosis. *K. pneumoniae* was also previously isolated from her bloodstream. These infections may reflect severe impairment of T-lymphocyte and neutrophil functions. Moreover, the administration of broad-spectrum antimicrobials to treat bacterial sepsis could also render the immunocompromised host prone to fulminating opportunistic mycoses due to the decolonisation of the commensal microbiota. Underdiagnosis of systemic mycoses in cancer patients is not uncommon, and there is an unwarranted concern about the toxicity of antifungal agents like amphotericin B(23, 24). Tragically lethal fungal infections may be prevented by the parenteral administration of this potentially life-saving drug or other broad-spectrum antimycotic agents like the new generation imidazoles, whilst closely monitoring potential adverse side-effects like nephro-hepatotoxicity.

The aminoglycosides amikacin, sissomicin and tobramycin were active *in vitro* against some gram-negative organisms. However, a significant number of these, including *P aeruginosa* and *C. fruendii* strains, showed resistance to this group of antibiotics, which is increasingly being reported elsewhere (20, 25, 26). Falkiner et al (27) have reported an outbreak of amikacin, gentamicin and tobramycin resistant *P. aeruginosa* in a leukaemic ward mediated by a plasmid which determined aminoglycoside adenylyltransferase activitiy.

Gram-negative bacilli other than *Pseudomonas* were susceptible to chloramphenicol, which unfortunately has the undesirable potential adverse side effect of marrow suppression.

Other conventional agents including ampicillin, co-trimoxazole and cephaloridine (a first generation cephalosporin) demonstrated poor activity against gram-negative organisms.

The antipseudomonal penicillin, carbenicillin, was active against *Pseudomonas* species, albeit only 50% of the strains. Carbenicillin resistance is well-known (20, 28) and is often due to the production of TEM beta-lactamase commonly determined by plasmids as described by Jacoby (29). Williams et al (30) have also reported novel mechanisms of beta-lactam resistance of *P. aeruginosa* associated with the chromosomally-determined Sabath and Abrahams' beta-lactamase. Yet another major mechanism of resistance of *P. aeruginosa* to new beta-lactamase resistance beta-lactams like carbenicillin, moxalactam and cefsulodin, is reduced outer membrane permeability as investigated by Godfrey and Bryan (31). In our study, 6 out of 11 gram-negative isolates were beta-lactamase producers.

Gram-positive organisms especially *Streptococcus* species were generally sensitive to amikacin, sissomicin, chloramphenicol and cephaloridine. However, ampicillin and co-trimoxazole were not generally active against gram-positive clinical isolates, particularly *Staphylococcus* species, many strains of which are well-documented penicillinase producers.

Of the newer cephalosporins, ceftazidime, a third generation cephalosporin, was the most active, with relatively low MIC values, in agreement with similar studies by other investigators (26, 32). Another third generation cephalosporin, cefoperazone also demonstrated some antipseudomonal activity. Gram-negative enteric bacteria other than *Pseudomonas* were susceptible to cefoxitin, a cephamycin and second generation cephalosporin. The majority of gram-negative organisms were resistant to another third-generation cephalosporin, cefotaxime, tested singly *in vitro*, and showed high MIC values. Two strains of *C. fruendii* isolated from urine were resistant to virtually all antimicrobials tested except ceftazidime and cefoxitin (one strain). Together with other gram-negative microbes especially *P. aeruginosa*, and even *Staphylococcus* species, they exemplify the notoriety and ever-increasing emergence of antibiotic resistant strains in the hospital setting.

The degree and multiplicity of antimicrobial resistance of nosocomial pathogens may be due in part to the selective pressures of the rather extensive use of potent antibiotics on microbial ecology especially in an oncology ward (24).

The empirical selection of appropriate antimicrobial agents in immunocompromised cancer patients with suspected life-threatening septicaemia, especially of gram-negative origin, should be instituted following the prompt collection of blood and other suitable cultures (15, 33, 34). Many regimens are in current use, but most authorities (15, 35) recommend a two-drug combination therapy, whose synergistic effects have been demonstrated by good *in vitro* experiments (36) and *in vivo* clinical trials (19). Examples of such useful combinations include (15):

1. An antipseudomonal penicillin (such as carbenicillin, ticarcillin, mezlocillin, piperacillin or azlocillin) *plus* a new generation cephalosporin (such as ceftazidime, cefoperazone, cefotaxime or cefoxitin).
2. An antipseudomonal penicillin *plus* an aminoglycoside (such as gentamicin, tobramycin or amikacin). A continuous infusion of tobramycin combined with carbenicillin has been advocated by Issell et al (19) who showed this regimen's therapeutic efficacy for infections in cancer patients.
3. A new generation cephalosporin *plus* an aminoglycoside.

While these regimes may have favourable therapeutic efficacy, the seum levels and adverse reactions of the drugs must be constantly monitored closely (37) e.g. serum urea and creatinine levels to detect aminoglycoside nephrotoxicity (19).

The mechanism of synergy of drug combinations is not only superior to single-drug regimens, but also reduces the high possibility of anti-microbial resistance when either drug is used alone (36, 38). This point is further illustrated by the report of King et al, who have demonstrated a decrease in sensitivity to beta-lactam antibiotics during treatment of *P. aeruginosa* infections with ceftazidime, attributed to chromosomally-mediated cephalosporinase production (39). Furthermore, Preheim et al (40) have reported the emergence of increased resistance to aminoglycosides and cross-resistance to antipseudomonal beta-lactams during moxalactam therapy of *P. aeruginosa* infections, which did not involve plasmid-mediated enzymatic antibiotic degradation.

Despite the deveopment of newer and more potent antibiotics, some septicaemic infections remain uncontrollably fatal, thus emphasising that antimicrobial chemotherapy is not the mainstay in the overall management of septicaemia in the immuno-compromised host (18). Other equally important preventive

and therapeutic measures against nosocomial infection often overlooked but can contribute favourably in influencing the prognosis of these patients include:

1. Minimising environmental reservoirs of microbes and protective isolation (41, 42). Reverse barrier units and the sterile kitchen are pertinent examples.
2. Tce role of the nurse in the observance of strict aseptic techniques in patient care and management of equipment cannot be overemphasised (1, 2).
3. Provision of good oral hygiene and skin care (2).
4. Avoidance of instrumentation and invasive procedures if possible. If not, proper care of intravenous cannula sites, for example, is mandatory to prevent septic thrombophlebitis which may serve as a portal of entry for invading skin commensal flora including *S. epidermidis* and diphtheroids (43, 44).
5. Better control of the patients' underlying malignancy (18).
6. Drainage of abscesses.
7. Granulocyte transfusion therapy particularly for neutropaenic septicaemic patients with failure to respond to antimicrobials (15). In the local setting, leucocyte platelet rich red cell concentrate (LPRC) is an acceptable alternative, especially in patients who are pancytopaenic from severe myelodepression. Granulocytes are given to febrile septicaemic patients with an absolute polymorph count of 500 or less.
8. Antifungal prophylaxis. This is indicated in febrile neutropaenic patients who do not respond to antibiotics. Drugs of choice include amphotericin B and imidazoles like miconazole and ketoconazole.
9. The recognition of other serious infections including anaerobic, parasitic and viral sepses are essential since some are amenable to treatment. For example, *Bacteroides fragilis* septicaemia by metronidazole theapy, *Pneumocystis carinii* pneumonia by co-trimoxazole or pentamidine, and disseminated *Herpes simplex* or *Varicella zoster* by acyclovir (15).
10. Epidemiological surveillance, analysis of plasmids mediating notorious multiple antimicrobial resistance, implementation of and adherence to antibiotic policies and infection control guidelines have vital roles in the overall approach against nosocomial infection in general, and sepsis in the immunocompromised host in particular (24).

CONCLUSION

A better understanding of the pattern of common bacterial infections in immunocomprised cancer patients in Singapore is required. This offers the clinician a more rHtional and effective selection of antimicrobial agents in suspected cases of gram-negative sepsis occurring in an oncolgy patient. Guidelines for antibiotic selection against nosocomial gram-negative sepsis in other immunocompromised individuals may be applied in other disciplines e.g. primary or acquired immunodeficiency states, organ transplant recipients, prolonged corticosteriod therapy and intensive care unit patients.

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