LEADING ARTICLE

UNUSUAL BUGS IN IMMUNO-COMPROMISED HOSTS

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Within the last several years, a number of microbes have been newly recognized as causing infections in the immuno-compromised host. Immune defects and multiple environmental exposures during the course of work, hobbies and hospitalisation, may be responsible for opportunistic infections with common and unusual pathogens. The underlying immune defects, the unusual organisms encountered and current therapy will be reviewed.

Immune defects

The infecting organisms can be anticipated in the presence of particular immune defects. Neutropenia is most commonly due to acute leukaemia or cytotoxic chemotherapy. Sepsis due to multi-resistant S. epidermis, P. aeruginosa and enterococci have emerged in neutropenic hosts. Fungi such as Aspergillus, Candida and Mucor and less commonly Pseudoallescheria boydii and Trichosporon species have emerged as pathogens in neutropenic hosts.

T-cell dysfunction are exemplified by those with Hodgkin's disease, organ transplants or AIDS and any patient on long-term corticosteroid therapy. Cellular immunity with activation of monocytes and macrophages by T. lymphocytes secreted lymphokines is the main mechanism against intra-cellular pathogens namely some viruses (eg cytomegalovirus and herpes simplex virus), mycobacterium species (eg Mycobacterium kansasii and Mycobacterium avium intracellulare) and Pneumocystis carinii.

Interrupted integument due to indwelling urinary catheters, intravenous catheters and needles can give rise to infections. A resistant corynebacterium JK has caused severe infections in transplant and cancer patients. Fungi such as Fusarium species colonize intravenous catheters and hence become invasive.

People with splenic dysfunction, C3 complement deficiency and γ globulin dysfunction develop severe infections due to S. pneumoniae, H. influenzae and N. meningitidis. Late phase complement deficiency is associated with recurrent or disseminated infections with Neisseria species.

Unusual bacteria

Rhodococcus equi (formerly corynebacterium equi), a soil organism, is a well known animal pathogen but rare human pathogen. It is an aerobic, non-spore forming, non-motile, gram-positive rod to coccus. It is a facultative intracellular pathogen, surviving inside macrophages to cause granulomatous inflammation. R. equi may be regarded as a component of the normal flora or contaminant and may be ignored as a "diphtheroid" or "micrococcus". Of the 32 reported cases, 88% were associated with immunosuppression following the development of AIDS, treatment for hemolymphatic tumours or prevention of rejection following renal transplantation[1]. Pneumonia is the commonest manifestation in humans. Parapneumonic effusions or empyema is common. ß-lactam antibiotics should be avoided as ß-lactam resistance may develop during therapy. Successful treatment depends on the use of lipophilic antibiotics such as clindamycin, rifampicin or trimethoprim - sulfamethoxazole.

Stomatococcus mucilaginosus is an organism of low virulence which appears to be an emerging pathogen especially in immuno-compromised hosts[2]. This encapsulated gram-positive coccus is a normal inhabitant of the human mouth and upper respiratory tract and can be easily misidentified as Staphylococcus or Streptococcus. To date, 19 cases of S. mucilaginosus bacteremia have been reported. Risk factors shared by the infected patients were foreign bodies (particularly indwelling vascular catheters), cancer, cardiac valve disease, intravenous drug abuse and severe neutropenia. Isolates were susceptible to penicillin, oxacillin, cefazolin, clindamycin, vancomycin and ciprofloxacin.

In this issue, the article on "*Leuconostoc* Bacteremia" highlights the importance of this gram-positive cocci as a potential pathogen in the immuno-compromised host. The natural habitat of *Leuconostoc* is foodstuff which suggests that the gastrointestinal tract is a potential reservoir from which it may cause infection. In a recent review, *Leuconostoc* bacteremia was noted to be associated with fever, leukocytosis and gastrointestinal complaints[3]. Clinical isolates of *Leuconostoc* were frequently misindentified as viridans streptococci and may also be confused with enterococci and lactobacilli. All clinical isolates to date demonstrate a high level of resistance to vancomycin. The mechanism of vancomycin resistance is unknown. Successful treatment regimens include high dose penicillins, clindamycin and where appropriate, removal of infected intravascular catheters.

Chryseomonas luteola and Flavimonas oryzihabitans are phenotypically similar aerobic, oxidase-negative, catalase positive, yellow-pigmented gram-negative bacilli.They are also referred to as CDC groups Ve-1 and Ve-2 respectively. They should be added to an expanding list of nosocomial pathogens with a propensity to infect critically ill or immuno-compromised patients who have undergone surgery or had indwelling catheters or other foreign bodies placed[4]. Both groups of Ve organisms are uniformly sensitive to aminoglycosides and third-generation cephalosporins except moxalactam. Limited data suggest that both are sensitive to the quinolones.

Bordetella bronchiseptica is an aerobic gram-negative non-fermentative bacilli causing respiratory tract disease in many mild and domestic animals. The human infections associated with B. bronchiseptica encountered in the literature included pneumonia, tracheobronchitis and sinusitis[5]. Most patients had a severely compromised clinical status. The most effective agents for this pathogen appear to be aminoglycosides, anti-pseudomonal penicillins, broad spectrum cephalosporins, tetracyclines and chloramphenicol.

Kluyvera, a new genus in the family Enterobactericeae, are infrequent but potentially dangerous pathogens in humans. Kluyvera are motile gram-negative bacilli. There are 3 species: K ascorbata, K cryocrescens and K species 3. The potential of this bacteria to cause diarrhoea was reported by Fainstein

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et al[6]. Majority of the patients were elderly, neutropenic and febrile.

Leptotrichia buccalis is an anaerobic gram-negative bacillus that is part of the normal flora. Its identification requires carbohydrate fermentation studies and the identification of lactic acid as the end-product from PYG broth (gas-liquid chromatographic analysis). L buccalis should be considered as a potential pathogen in neutropenic patients who often suffer from disruption of gastrointestinal mucosal integrity as a result of cytotoxic therapy and infection. To date, there have been 8 cases of L buccalis bacteremia in cancer patients[7]. ß-lactam antibiotics provides adequate coverage for this organism.

Capnocytophaga are facultatively anaerobic or microaerophilic, capnophilic (carbon dioxide-loving) gram-negative bacilli. They are found as normal oral flora in humans. The genus has 3 species: C. ochracea, C. sputigena and C. gingivalis. Capnocytophaga is a cause of severe life-threatening sepsis in immuno-compromised patients, especially granulocytopenic patients with oral ulceration[8]. It is also associated with juvenile periodontitis. Bactericidal activity has been shown for penicillin, anti-pseudomonal penicillins, imipenem, newer cephalosporins, newer quinolones and metronidazole. All strains are resistant to trimethoprim and aminoglycoside.

Unusual Fungi

Phaeohyphomycosis is a subcutaneous tissue infection caused by several species of dermatiaceous black fungi (ie moulds having dark-walled hyphae). The most frequently recovered species are Exophiala jeanselmei and Wangiella dermatitidis. Lesions are usually subcutaneous nodules with central cysts and little tendency to extensively involve the epidermis. Several cases of phaeohyphomycosis have been reported in immuno-compromised hosts. Chromohlastomycosis should be considered in the differential diagnosis and can be differentiated by more marked epidermal changes[9]. Infections with such fungi do not respond well to chemotherapy and should be excised when possible.

Tricosporon biegelii colonizes human skin as well as respiratory, gastrointestinal and urinary tracts and is thought to gain entry into deep tissues of immuno-compromised hosts through pulmonary and gastrointestinal lesions. Most infections have complicated acute leukaemia and bone marrow aplasia. T. biegelli is reported to be susceptible to amphotericin B, but the outcome for patients who receive any form of antifungal therapy is generally poor[10].

Blastoschizomyces capitatus (formerly named Trichosporon capitatum or Geotrichum capitatum) is an emerging agent of disseminated fungal disease in severely immunocompromised hosts particularly among those with hematologic malignancies and neutropenia[11]. It is a yeastlike fungi characterized by production of anelloconidia rather than arthroconidia. Patients with B. capitatus infection may present with syndromes suggestive of hepatosplenic candidiasis or pulmonary aspergillosis. Early therapy with amphotericin B and 5-flucytosine in addition to recovery of the immune defence mechanism with remission of the underlying malignancy help to achieve a clinical cure.

Pseudoallescheria boydii is a saprophyte that has been isolated from soil and manure. The fungus enters the body by the airborne route or by penetrating injury. It produces either a chronic suppurative infection called mycetoma or colonization of paranasal sinus, pulmonary cavities or ectatic bronchi. Invasive infection occurs in immuno-compromised patients producing hematogenous endophthalmitis and invasive sinusitis[12]. Histopathologic findings reveal masses of septate hyphae showing conidia or clumped groups of hyphae in parallel array. Intravenous amphotericin B plus surgical drainage appears to be the treatment of choice.

Unusual Virus

JC virus is a new human papovavirus of the polyomavirus sub-group. It is associated with the vast majority of cases of progressive multifocal leukoencephalopathy (PML)[13].

Most cases of PML have occurred in patients with myeloproliferative and lymphoproliferative neoplasms. It accounts for up to 4% of neurologic disease in AIDS patients[14]. Recovery of JC virus requires inoculation of infectious material onto primary human fetal glial cell cultures containing a preponderance of spongioblasts. There is no effective therapy at present.

Conclusion

The appearance of new microbes parallels advances in medical technology, laboratory diagnosis and anti-microbial therapy. The intense therapeutic and prophylactic use of new therapeutic compounds is likely to increase the risk of colonization and clinical diseases due to unusual microbes.

The status of the host will continue to be an important determinant of when colonization changes to superinfection.

There is an increasing number of bacteria, fungi and viruses recognized as new pathogens in immuno-compromised hosts. Many of these micro-organisms were previously thought to be non-pathogenic and discounted as contaminants but now recognized as true pathogens.

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