Immunocompromised hosts: Infections and biomarkers

Incidence of sepsis is very high in most hospitals and sepsis in the febrile neutropenic cancer patient poses a significant challenge in both diagnosis and management. In a dataset of over 600,000 hospitalizations from six states in the United States, Williams *et al.*[1] reported a 4.9% incidence of sepsis. The incidence of sepsis was four fold higher in cancer patients at 16.4%. Mortality in cancer patients with sepsis at 37.8% was much higher than non-cancer patients.

According to a recent article,[2] the commonest causes of bloodstream infections in the febrile neutropenic patients are Gram-negative bacteria such as *Escherichia coli*, *Pseudomonas aeruginosa* and *Klebsiella pneumonia*. This was followed by Gram-positive organisms, commonest being coagulase negative *Staphylococcus aureus*.

The rarer causes of infections in immunocompromised patients include organisms such as *Xanthomonas maltophilia*, *Corynebacterium* species, Capnocytophagia, *Listeria monocytogenes* and *Bacteroides fragilis*.[3] In this issue Ghafur *et al.*[4] present an interesting case series of 29 episodes of bacteremia due to another rare organism, *Elizabethkingia meningoseptica*. *E. meningoseptica* has been known to cause meningitis in immunocompromised hosts such as premature neonates[5] and in elderly patients being ventilated in the long term acute care facilities.[6] *E. meningoseptica* has generally been reported in most series as being susceptible to antibiotics such as piperacillin-tazobactum and co-trimoxazole, but not to the routinely used ones. Identification of the organism is therefore extremely important.

In the neutropenic patient, the inflammatory response is severely reduced so that fever may be the only sign of infection. The common approach to onset of fever in neutropenic patients is the administration of broad spectrum antibiotics. Some of these may not be warranted, rather leading to the development of resistance, colonization with drug resistant organisms and increased resource use. The surviving sepsis guidelines recommend administration of antibiotic within 1 h of recognition of severe sepsis and septic shock.[7] Identification of patients with infections therefore assumes vital importance. A recent review[8] described many biomarkers such as C-reactive protein (CRP), procalcitonin (PCT), serum amyloid A, mannan, and many others studied for confirmation of sepsis. Presently only CRP and PCT are used in routine clinical practice.

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In this issue of the journal Meidani *et al.*[9] present their data of 64 adult febrile neutropenic patients in whom CRP and PCT were compared for their ability to accurately diagnose sepsis. They found that values of both CRP and PCT were raised. The sensitivity and specificity for PCT was much higher as compared to CRP. Assicot *et al.*[10] first reported increase in PCT in patients who had a bacterial infection and that the levels decreased with antibiotic treatment. They also reported that calcitonin levels remained normal in these patients. They concluded that levels of PCT correlated with the severity of bacterial infection. The results of the present study are similar to the meta-analysis,[11] which found that the ability of PCT to diagnose bacterial infection was much better than CRP. There are many studies in the literature which suggest that PCT is a useful biomarker for bacterial sepsis in patients with febrile neutropenia. A recent study[12] evaluated the use of PCT to distinguish between tumor related fever and fever due to sepsis in non-neutropenic cancer patients. They found that baseline PCT was elevated in patients with advanced cancer. PCT was higher in bloodstream infections than localized infections.

Vänskä *et al.*[13] found PCT had high negative predictive value in febrile neutropenic adults and reported that combining PCT with interleukin-10 will improve its predictive ability for complicated course. A recent meta-analysis[14] of eight studies suggested that PCT guided antibiotic therapy for respiratory tract infections led to reduced use of antibiotics and reduced duration of antibiotic therapy.

The main limitation of the present study is the small sample size, but it confirms the utility of PCT over CRP in diagnosing sepsis early and it should be a part of our armamentarium when dealing with these patients. Ahn *et al.*[15] combined Multinational Association for Supportive Care in Cancer (MASCC) risk index score with PCT and found that this improved the ability to accurately stratify the patient's risk for complicated course of febrile neutropenia. Thus, the use of PCT to risk stratify and to guide stopping and starting of antibiotics will reduce total antibiotic usage and duration of antibiotic therapy and may also improve outcomes. Given the present prevalence of multi-drug resistant bacteria and the rising cost of antibiotic therapy this may be particularly relevant to developing countries.

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