Dealing with immunocompromised cancer patients with infectious disease complications

Maria Chitasombat, M.D.

During my clinical rotation as infectious disease consultant, specialized in infection among immunocompromised patients, I encountered various challenging situations in this subspecialty. First of all, the patients had underlying cancer and were predisposed to various treatments such as surgery, chemotherapy and radiation. This resulted in cellular damage, loss of mucosal integrity and eventually a secondary infection due to either commensal pathogens or opportunistic pathogens. Commensal organisms in gastrointestinal flora can invade damaged tissue and can cause secondary bacteremia related to mucositis especially in the setting of neutropenia. In such patients, low virulence pathogens can become invasive. Other pathogens such as fungal infection including yeast and mould are also a concern especially in neutropenic patients as well. Newer chemotherapy regimens and immunomodulating agents have been reported with reactivation of latency of viruses and tuberculosis.

As mentioned with broad range of different diagnosis of the list of possible pathogens, in order to stratify the likelihood of pathogens in the clinical setting, individualized patient would require thorough history and physical examination. For example, in neutropenic patients, oral mucosa, dental, paranasal air sinus, skin and perirectal examination must be evaluated with special attention apart from general physical examination. Complications may have occurred from this minor mucosal damage as I recalled several cases of perianal fissures that progressed into cellulitis and abscesses later on. These were rather difficult to manage due to the frequency of recurrence and polymicrobial infection in nature or dental root infection that progressed into deep neck infection. Source of infection can be multiple sites concomitantly, such as phlebitis, mucositis, diarrhea or pneumonia. Multiple pathogens including bacteria, fungi, virus and parasites could play a role. Imaging study remains a helpful tool in the diagnosis. More importantly microbiological and tissue diagnosis remain the gold standard. However, diagnosis rarely yielded results in a timely fashion and isolating an organism was rather difficult in the setting of prior antibiotics exposure. Hospital-acquired pathogens with multidrug resistant phenotypes had become more problematic in these populations; gram-negative pathogens such as extended-spectrum beta-lactamase (ESBL) producing bacteria or carbapenem-resistant *Acinetobacter*, and *Stenotrophomonas*, and gram-positive pathogen such as methicillin-resistant *Staphylococcus aureus* (MRSA). Initial empiric antibiotics would be mostly relied on hospital epidemiology and local antibiogram.

Division of Infectious Diseases, Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand.

Reprint request: Maria Chitasombat, M.D., Division of Infectious Diseases, Department of Medicine, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand.

Email: mchitasombat@gmail.com
correlated with site of infection and possible pathogens. Frequently, I used a combination of antibimicrobial agents in neutropenic patients in setting of sepsis.

Antimicrobial management in this population is rather difficult due to comorbidity and toxicities of chemotherapeutic agents or other medication that predispose patients to hepatic and renal dysfunction. Appropriate antimicrobial treatment has to be individualized on the basis of indication, safety profile, pharmacokinetics/pharmacodynamics and drug-drug interaction. Often, I had encountered problems with drug-drug interaction such as concomitant therapy of rifampicin which is a strong enzyme inducer with azole as enzyme inhibitor in settings of treatment for tuberculosis and invasive fungal infection.

Drug allergy is also a challenging issue to differentiate whether results from chemotherapy, antibiotics commonly seen with beta-lactams or contrast agent. Various types of allergic reactions occurred, immediate or delayed types; all of those preclude the patients from such antimicrobial agents, although desensitization process can be attempted later on. Detail documentation of reaction to antibiotics must be clarified at onset including type of reaction and severity. Most of the time in clinical practice, history of penicillin allergy was mostly unreliable since history was from childhood memory.

Another dilemma lies with the diagnosis of fungal infection in these neutropenic patients, mostly dependant on biomarker and imaging study. Delay in diagnosis often occurs. Bronchoscopy and tissue diagnosis sometimes are delayed due to various conditions such as availability of personnel and blood component, and patient condition. Isolating fungal pathogens remain challenging and most of the time the diagnosis of cases were not definite; only probable and possible invasive fungal infection. Cost of treatment for invasive fungal infection remains a heavy burden especially with lengthy therapy. As response to antifungal agents depends greatly on host status and recovery of neutrophils, the duration of treatment is rather on an individual basis, and largely depends on imaging study.

Monitoring outcome of infection in these patients is also challenging since lack of effective immune system. Concurrent illness and advanced malignancy status make evaluation of outcome of success in treatment rather difficult. Delay in response and recovery from infection from immune defect would lead to prolonged antimicrobial therapy until the recovery of the immune system which also predisposes the patients to various toxicities of antimicrobial therapy such as antibiotic-associated diarrhea.

Overall infections usually get under control in patients who respond to chemotherapy and recover immune status. On the other hand in patients with relapsed refractory disease often have one type infection which lead to another and curing infection is an endless task and causes suffering for the patients.

In summary, service for immunocompromised cancer patients require multidisciplinary care and collaboration of hematologist-oncologist and infectious disease specialist. Infectious disease complications from anti-cancer treatment should be something that can be avoided or minimized from screening and preventative measures. In our institution, screening chest X-ray, dental exam, stool exam was usually done and high risk neutropenic patients would be placed in HEPA filtered unit in controlled environment in order to attempt to decrease incidence of invasive fungal infection. Close follow-up and early diagnosis and treatment could lead to prevention of morbidity and mortality.

References
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