Journal of Turgut Ozal Medical Center 2016;23(2):167-70
ORİJİNAL MAKALE/ORIGINAL ARTICLE DOI: 10.5455/jtomc.2016.01.014

Healthcare-associated infections in patients with cancer

Kanser hastalarında sağlık Hizmeti-ilişkili enfeksiyonlar

Filiz Kizilates[1], Nefise Oztoprak[1], Alper Tahmaz[1], Armagan Aydin[2], Hande Berk[1], Derya Seyman[1], Mustafa Yildiz[2]

[1]Department of Infectious Diseases and Clinical Microbiology, Antalya Education and Research Hospital, Antalya, Turkey
[2]Department of Medical Oncology, Antalya Education and Research Hospital, Antalya, Turkey

Abstract

Objective: Infections are major causes of morbidity and mortality in patients with cancer. We aimed to determine the epidemiological features and etiologic agents in healthcare-associated infections (HCAI) in adult patients with solid tumors.

Material and Methods: Patients with solid tumors admitted to oncology unit of Antalya Education and Research Hospital between January 2012- December 2014 were evaluated retrospectively.

Results: There were 65 HCAI in 48 patients (35 with one, nine with two, and four with three episodes). In 92.3% of the episodes, the patients were neutropenic. There were 18 (27.7%) bloodstream infection (BSI), one (1.5%) central line-associated BSI, 14 (21.5%) pneumoniae, 11 (17.0%) urinary tract infection (UTI), seven (10.7%) secondary bacteremia, eight (12.3%) catheter-associated UTI and six (9.3%) soft tissue infections. Totally, 70 agents including 77.1% gram-negative, 17.1% gram-positive and 5.8% fungi were isolated. The most frequent microorganism was *Escherichia coli* (41.4%), 65.5% were producing extended spectrum beta-lactamase (ESBL). *Acinetobacter baumannii* isolates were resistant to carbepenems, coagulase negative staphylococci (CNS) isolates were resistant to methicillin. BSI rate was 40.0% and 28 microorganisms including 64.2% gram-negative, 32.1% gram-positive and 3.7% fungi were isolated. The most frequent microorganisms were *E.coli* (39.2%) and CNS (25.0%).

Conclusion: For effective empirical antimicrobial therapy, knowing the local causative agents and resistance patterns is important in immunosuppressive patients. In the light of these findings, in centers with high rate of infections caused by ESBL producing bacteria or in case of suspicion of infection with methicilin resistant gram-positive bacteria, initial antimicrobial therapy can be extended covering these agents.

Keywords: Healthcare-Associated İnfections; Oncology; Solid Tumors.

Öz

Amaç: Kanser hastalarında enfeksiyonlar önemli morbidite ve mortalite nedenleridir. Çalışmada solid tümörlü erişkin hastalarda sağlık hizmeti-ilişkili enfeksiyonların (SHİE) özellikleri ve etyolojik etkenlerin değerlendirilmesi amaçlandı.

Gereç ve Yöntemler: Solid tümörü olan ve Antalya Eğitim ve Araştırma Hastanesi onkoloji kliniğinde Ocak 2012- Aralık 2014 tarihleri arasında yatırılan hastalar retrospektif olarak incelendi.

Bulgular: Kırk sekiz hastada 65 SHİE (35 hastada bir, dokuz hastada iki ve dört hastada üç atak) saptandı. Enfeksiyon ataklarının %92.3'ünde hastalar nötropenikti. On sekiz (%27.7) kandolaşımı enfeksiyonu (KDE), bir (%1.5) santral kateter-ilişkili KDE, 14 (%21.5) pnömoni, 11 (%17.0) idrar yolu enfeksiyonu (İYE), yedi (%10.7) sekonder bakteremi, sekiz (%12.3) kateter- ilişkili İYE ve altı (%9.3) yumuşak doku enfeksiyonu tespit edildi. Elli dört (%77.1) gram-negatif, 12 (%17.1) gram- pozitif ve dört (%5.8) mantar olmak üzere toplam 70 etken izole edildi. *Escherichia coli* en sık görülen mikroorganizmaydı (%41.4) ve %65.5'i genişlemiş spektrumlu beta-laktamaz pozitifti. *Acinetobacter baumannii* izolatları karbapenemlere, koagülaz negatif stafilokoklar (KNS) metisiline dirençli idi. KDE oranı %40.0 idi ve 18 (%64.2) gram-negatif, dokuz (%32.1) gram-pozitif ve bir (%3.7) mantar olmak üzere 28 mikroorganizma izole edildi. En sık etkenler; Escherichia coli (%39.2) ve KNS (%25.0) idi.

Sonuç: İmmünsupresif hastalarda etkin empirik antimikrobiyal tedavi için bölgesel etken mikrooranizmaları ve direnç paternlerini bilmek önemlidir. Bu bulgular ışığında GSBL üreten gram-negatif bakterilere bağlı enfeksiyon oranlarının yüksek olduğu merkezlerde ve gram-pozitif bakterilere bağlı enfeksiyon şüphesinde başlangıç antibiyotik tedavisi bu etkenleri de kapsayacak şekilde genişletilebilir.

Anahtar Kelimeler: Kanser Hastaları; Onkoloji Ünitesi; Sağlık Hizmeti-İlişkili Enfeksiyonlar.

Received/Başvuru: 25.01.2016
Accepted/Kabul: 04.03.2016

Correspondence/İletişim
Filiz Kizilates
Department of Infectious Diseases and Clinical Microbiology, Antalya Education and Research Hospital, Antalya, Turkey
E-mail: filizkizilates@gmail.com

For citing/Atıf için
Kizilates F, Oztoprak N, Tahmaz A, Aydin A, Berk H, Seyman D, Yildiz M. Healthcare-associated infections in patients with cancer. J Turgut Ozal Med Cent 2016;23(2):167-70.

2016;23(2):167-70
DOI:10.5455/jtomc.2016.01.014

INTRODUCTION

Infections are major causes of morbidity and mortality in patients with cancer. Due to the type of disease and type of chemotherapy used, depending on the severity and duration of immunosuppression; bacterial, viral and fungal infections are common among patients with cancer. Predisposing factors to infections are; neutropenia, splenectomy, corticosteroid therapy, disruption of anatomical and immunological protective barriers by multiple invasive devices and drugs.

Neutropenia is defined as a neutrophil count of <500 cells/mm^3 (1). Use of cytotoxic chemotherapy in patients with hematological malignancies and solid tumors has increased the probability of neutropenia (2).

Recently, healthcare-associated infections (HAIs) have been recognized as a global health problem all over the world. Subsequently, a high proportion of these infections occurs in intensive care units (ICUs) , hematology, nephrology and oncology units. These patients are prone to infection due to the reduced host defense mechanisms caused by the severity of illness, underlying diseases (diabetes, cancer, etc.) and administration of various drugs and invasive procedures. In addition, use of broad spectrum antimicrobial agents has led to the emergence of multidrug resistant (MDR) organisms (3). During this century, by the development of increased life support and immunosuppressant therapies, the need to control HAIs became apparent (3).

It is important to know regional causative agents and susceptibility patterns in order to decide the empirical antimicrobial therapy of HAIs. This study was conducted to assess epidemiological features of HAIs in adult patients with solid tumors and the species distribution and antimicrobial susceptibilities of causative pathogens in oncology unit of Antalya Education and Research Hospital (AERH).

MATERIALS and METHODS

AERH oncology unit has 26 beds and approximately 2420 patients with solid tumors are hospitalized for chemotherapy, radiotherapy and supportive therapy in a year. This study was conducted retrospectively in oncology unit of AERH with hospitalized patients who have diagnosed with solid tumors and consultated by an infectious diseases and clinical microbiology specialist between January 2012 - December 2014.

The demographic, clinical and microbiological data of patients were obtained from follow-up reports, infection control surveillance forms and microbiology laboratory reports. The following information was collected: patient's age and gender, type of the cancer, microbiology and the resistance pattern of all isolates. Infections were defined according to the Centers for Disease Control and Prevention (CDC) guidelines and National Healthcare Safety Network (NHS) surveillance as pneumoniae, laboratory-confirmed bloodstream infection (LCBI), central line-associated bloodstream infection (CLABSI), urinary tract infection (UTI) and catheter-associated urinary tract infection (CAUTI). Cultures were optained from any site where infection was suspected as blood, urine, tracheobronchial secretions and other samples. Samples were cultured using standart microbiological methods. Blood cultures were incubated at BACT/ALERT 3D otomatized blood culture system (bioMerieux, France). The identification and antimicrobial susceptibiltity of bacteria isolated from clinical samples were tested by otomatized system (Phoenix Becton Dickinson ID, Sparks, USA). Extended spectrum beta lactamase (ESBL) producing was confirmed by double disc sinergy test.

Due to the nature of this study (retrospective registry study), no written or verbal consent from patients were needed.

RESULTS

There were 65 HAIs in 48 patients (35 with one, nine with two, and four with three HAI episodes) in three years. The mean age was 61.20±11.29 years; 32 patients (66.0%) were male. Fifteen patients (31.3%) have had lung cancer, 21 patients have had gastrointestinal malignancies (43.8%), eight patients have had genitourinary system malignancies (16.6%) and four (8.3%) have had other types of malignancies. In 92.3% (60/65) of episodes, the patients were neutropenic.

There were 18 (27.7%) LCBI, one (1.5%) CLABSI, 14 (21.5%) pneumoniae, 11 (17.0%) UTI, seven (10.7%) secondary bacteremia, eight (12.3%) CAUTI and six (9.3%) soft tissue infections (STI). Of all HAIs, 64 (98.5%) were culture-confirmed and one (1.5%) was clinically defined as culture-negative infection. There were 70 microorganisms isolated, of which 54 (77.1%) gram negative, 12 (17.1%) gram positive and four (5.8%) fungi. The most frequent microorganism was *Escherichia coli* (29/70, 41.4%) and 19 (65.5%) of them were ESBL-producing.

The rate of ESBL-producing was 42.6% (23/54) in gram negative isolates and 32.8% (23/70) in all isolates. All *Acinetobacter baumannii* (3/3, 100.0%) isolates were resistant to carbepenems and all coagulase negative *Staphylococci* (CNS) isolates (7/7, 100.0%) were resistant to methicillin (Table 1).

Bloodstream infection (BSI) rate was 40.0% (26/65) and 28 microorganisms were isolated: 64.2% (18/28) gram negative, 32.1% (9/28) gram positive and 3.7% (1/28) fungi. The most frequent microorganisms were *Escherichia coli* (39.2%, 11/28) and CNS (25.0%, 7/28). The 63.6% (7/11) of *Escherichia coli* isolates were ESBL-producing and all CNS isolates were resistant to methicillin. The mortality rate of these patients was 41.6% (20/48) and mortality rate attributed to infection was 33.3% (16/48).

2016;23(2):167-70
DOI:10.5455/jtomc.2016.01.014

Table 1. Healthcare Associated Infections and Microorganisms Isolated in Patients with Cancer

Microorganism	Pneumonia	UTI	CAUTI	LCBI	CLABSI	STI	Secondary Bacteremia	Total
Escherichia coli								
ESBL	3	4	3	6	-	2	1	19
Non-ESBL	-	2	2	1	-	2	3	10
Klebsiella pneumoniae								-
ESBL	1	1	-	1	-	1	-	4
Non-ESBL	2	-	1	-	-	1	1	5
Pseudomonas aeruginosa	3	2	1	-	1	2	2	11
Acinetobacter baumannii	2	-	1	-	-	-	-	3
Other Gram-negative	1	-	-	1	-	-	-	2
Staphyloccoccus aureus								
MRSA	2	-	-	-	-	-	-	2
MSSA	-	-	-	2	-	1	-	3
Other Gram-positive	-	-	-	7	-	-	-	7
Candida albicans	-	3	-	1	-	-	-	4
Total	14	12	8	19	1	9	7	70

UTI: Urinary tract infection, CAUTI: Catheter associated urinary tract infection, LCBI: Laboratory -confirmed bloodstream infection, CLABSI: Central line-associated bloodstream infection, STI: Soft tissue infection, ESBL: Extended spectrum beta lactamase

DISCUSSIONS

Cancer is a leading cause of death worldwide, accounting for 13% of all deaths in the year (4). As well the high incidence of cancer, more cancer patients receive multimodal treatment with chemotherapy, radiation therapy, surgery, and/or molecular targeted therapies, with increased rates of remission and cure (5).

The rate of HAIs is much higher in ICUs, hematology, nephrology and oncology units depending on the patients' underlying diseases, comorbidities, severity of illness, length of stay, grade of immunosupression and use of invasive devices (6). And frequently the causative agents of infections were MDR. Because of higher morbidity and mortality of infection in these patients, antimicrobial therapy should be started as soon as possible. Beside increasing morbidity and mortality, the intrusive infections prolong the day of hospitalization, increase patient costs and delay the therapy of underlying disease.

The local data of common pathogens is important to initiate the appropriate empirical antibiotic therapy (7). In a study, the causative agents of nosocomial infections were 67.0% gram negative, 29.8% gram positive in neutropenic patients and the most observed microorganism was *Escherichia coli* in the gram negative group (8). In our study with a rate of 77.1%, gram negative bacteria were dominant in HAIs and 42.5% of them were producing ESBL.

Patients with malignancies and neutropenia are at high risk for the development of nosocomial BSI. The attack rate of BSI in neutropenic patients is 11%–38% (9-11). In our study, BSI rate was 40.0% and 64.2% of the isolates was gram negative bacteria, 32.1% was gram positive bacteria and 3.7% was *Candida albicans*. And the most frequent microorganisms were *Escherichia coli* (39.2%; 63.6% of them were producing ESBL) and CNS (25.0%; all of them were resistant to methicillin). In a study with a group of patients who had nosocomial fever and neutropenia, gram positive microorganisms were seen in 71.7% of cultures, which CNS being the most prominent (12). In another study, 61.0% of all BSIs were caused by gram positive organisms, and 27% were caused by gram negative organisms and methicillin resistance was detected in 29% of *Staphylococcus aureus* isolates and in 77% of CNS isolates (13). But in recent years studies conducted with neutropenic patients report a predominace toward gram negative microorganisms (13-15). HAIs are important causes of mortality in this group of patients. In our study mortality rate attributed to infection was 33.3%. In a study, the mortality rate of the patients was 18% and 23% of were associated with HAIs (5). Our hospital is a tertiary healthcare centre and because of this fact especially patients with terminal oncological diseases are referred and high mortality rate of patients could be associated with their underlying disease status.

As a result, it's important to keep in mind the regional causative agents and susceptibility patterns of hospitals in order to decide the empirical antimicrobial therapy.In centers with high rate of infections caused by ESBL-producing bacteria, initial antimicrobial therapy can be extended including these agents. In the suspicion of gram positive bacteria related BSIs, effective antimicrobial agents to methicillin resistant of *Staphylococci* can be added to the initial therapy.

REFERENCES

1. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions of nosocomial infections. Am J Infect Control 1988;16(3):128-40.
2. Pizzo PA. management of fever in patients with cancer and treatment-induced neutropenia. N Engl J Med 1993;328(18):1323-32.
3. Padoveze MC, Fortaleza CM. Healthcare-associated infections: challenges to public health in Brazil. Rev Saude Publica 2014;48(6):995-1001.
4. World Health Organization. Global Health Observatory. Cancer mortality and morbidity :http://www.who.int/gho/ncd/mortalitymorbidity/cancer/en/index.html access date: 02,10.2013

2016;23(2):167-70
DOI:10.5455/jtomc.2016.01.014

5. Cornejo-Juarez P, Vilar-Complete D, Perez-Jimenez C, Namendys-Silva SA, Sandoval-Hernandez S, Volkow-Fernandez P. The impact of hospital-acquired infections with multidrug-resistant bacteria in an oncology intensive care unit. Int J Infect Dis 2015;31:31–4.
6. Erbay H, Yalcin AN, Serin S, Turgut H, Tomatir E, Cetin B, et al. Nosocomial infections in intensive care unit in a Turkish university hospital: a 2-year survey. Intensive Care Med 2003;29(9):1482–8.
7. Inweregbu K, Dave J, Pittard A. Nosocomial infections. Crit Care Pain 2005;5:14–7.
8. Latif S, Anwar MS, Ahmad I. Bacterial pathogens responsible for blood stream infection (BSI) and pattern of drug resistance in a tertiary care hospital of lahore. Biomedica 2009;25:101-5.
9. Yadegarynia D, Fatemi A, Mahdizadeh M, Movahhed RK, Alizadeh MA. Current spectrum of bacterial infections in patients with nosocomial fever and neutropenia. Caspian J Intern Med 2013;4(3):698-701.
10. Madani TA. Clinical infections and bloodstream isolates associated with fever in patients undergoing chemotherapy for acute myeloid leucemia. Infection 2000;28(6):367–73.
11. Gaytan-Martinez J, Mateos-Garcia E, Sanchez-Cortes E, Gonzales-Llaven J, Casanova-Cardiel LJ, Fuentes-Allen JL. Microbiological findings in febrile neutropenia. Arch Med Res 2000;31(4):388–94.
12. Serody JS. Fever in immunocompromised patients. N Engl J Med 2000;20;342(3):217–8.
13. Syrjala H, Ohtonen P, Kinnunen U, Raty R, Elonen E, Nousiainen T. et al. Blood stream Infections during Chemotherapy-induced Neutropenia in Adult Patients with Acute myeloid leukemia: treatment cycle matters. Eur J Clin Microbiol Infect Dis 2010;29:(10)1211-8.
14. Ghosh I, Raina V, Kumar L, Sharma A, Bakhshi S, Thulkar S. et al. Profile of infections and outcome in high-risk febrile neutropenia: experience from a tertiary care cancer center in India. Med Oncol 2012;29(2):1354-60.
15. Roongpoovapatr P, Suankratay C. Causative pathogens of fever in neutropenic patients at King Chulalongkorn Memorial Hospital. J Med Assoc Thai 2010;93(7):776-83.
16. Swati M, Gita N, Sujata B, Farah J, Preeti M. Microbial etiology of febrile neutropenia. Indian J Hematol Blood Transfus 2010;26(2):49-55.