

Department of Infection Control

Seiji Hori, *Professor*
Hiroshi Takeda, *Assistant Professor*
Yasushi Nakazawa, *Assistant Professor*

Masaki Yoshida, *Associate Professor*
Koji Yoshikawa, *Assistant Professor*
Tetsuya Horino, *Assistant Professor*

General Summary

Rapid diagnosis and appropriate antimicrobial treatment are required for a good prognosis in cases of bacterial infection. Because an antibiotic must be administered as an empiric therapy before a pathogen has been detected, we should know bacterial epidemiology and antibiograms. Our investigations have shown that extended-spectrum β -lactamase (ESBL)-producing *Escherichia coli* should be considered, even for a community-acquired bacteremia. In addition, we have shown that methicillin-resistant *Staphylococcus aureus* (MRSA) derived from bacteremia in our hospital was susceptible to vancomycin, teicoplanin, linezolid, daptomycin, and arbekacin. Although both studies included small numbers of patients, they demonstrated important results.

To prevent the spread of pathogens, all medical staff should understand and carry out infection control. The “cross monitoring and feedback” is an extremely important tool for these practices. In addition, the infection control team (ICT) will promote an appropriate antimicrobial treatment and may prevent emerging antibiotic resistance.

Research Activities

Clinical studies of patients with bacteremia due to ESBL-producing E. coli

We investigated the clinical features and outcome of 19 patients with bacteremia due to ESBL-producing *E. coli*. The patients' median age was 61 years. Sixteen (84.2%) of the 19 patients had a community-acquired infection, and 15 (93.8%) of these 16 patients had been admitted from a nursing home or other hospital. The source of infection was the urogenital tract in 13 patients (68.4%). Severe sepsis or septic shock was present in 6 patients (31.6%). The efficacy rate of initial treatment was 100% with a carbapenem (meropenem, doripenem), 85.7% with tazobactam/piperacillin, 75.0% with cefmetazole, and 0% with other antimicrobials. Crude mortality was 10.5%. All patients who died had been treated with other antimicrobials. These results indicate that the most adequate agents of empiric therapy for bacteremia due to ESBL-producing *E. coli* are carbapenems. Further study is needed of the efficacy of tazobactam/piperacillin and cefmetazole.

Nontechnical skill has been successfully applied to hospital infection control

We have attempted to educate healthcare workers by means of TeamSTEPPS (Team Strategies and Tools to Enhance Performance and Patient Safety), which is one of the most popular educational tools for nontechnical skills. The “cross monitoring and feedback” tool was applied to develop the hand hygiene compliance in each hospital unit. After these efforts, the total amount of alcohol hand rub consumption was 23 ml/patient-days

(ptd) in 2013 and 32 ml/ptd in 2014. The incidence index of newly nosocomial MRSA carriers was 0.21/1000 ptd in 2013 and 0.12/1000 ptd in 2014. The TeamSTEPPS is useful for developing infection control practice in our hospital.

Human immunodeficiency virus testing: Relationship between reasons for testing and late diagnosis

We attempted to clarify the rate of late diagnosis of human immunodeficiency virus (HIV) infection and identify the relationship between the reasons for HIV testing and a late diagnosis. Our retrospective cohort study among HIV-positive patients at The Jikei University Hospital was performed from 2001 through 2014. Patient characteristics from medical records, including age, sex, sexuality, reason for HIV testing, and the number of CD4-positive lymphocytes, when HIV was diagnosed were assessed. A total of 459 patients (men, $n = 437$; 95.2%) were included in this study, and their median age at HIV diagnosis was 36 years (range, 18–84 years). The rate of late diagnosis (CD4 cell counts $< 350/\text{mm}^3$) was 61.4% (282 of 459 patients), and the rate of very late diagnosis (CD4 cell counts $< 200/\text{mm}^3$) was 36.6% (168 of 459 patients). The most common reason for HIV diagnosis was voluntary testing (38.6%, 177 of 459 patients) and was followed by acquired immunodeficiency syndrome (AIDS)-defining illness (18.3%, 84 of 459 patients). Multivariate analysis revealed a significant association of voluntary HIV testing with non-late and non-very late diagnoses and also revealed that the late and very late diagnosis groups had higher proportions of AIDS-defining illness than did other groups. MSM (Men who have sex with men) was a factor for non-late diagnosis, whereas non-specific abnormal results of blood tests, such as hypergammaglobulinemia and thrombocytopenia, were risk factors for very late diagnosis. Voluntary HIV testing should be encouraged, and physicians should screen all patients who have signs or symptoms, particularly hypergammaglobulinemia and thrombocytopenia, which may nonspecifically indicate HIV infection.

Infection Control Team Ward Rounds for Gram-negative bacilli bacteremia

We analyzed the Infection Control Team ward rounds (ICT round) result for Gram-negative bacilli bacteremia. The 36 cases (23 in men and 13 in women) of Gram-negative bacilli were detected in blood collected in March through May 2015, the median age of patients was 71.6 years, and 18 of the cases were in patients with malignancy. Of the 36 cases, 22 were of community onset and 14 cases were of hospital onset. The portals of entry were the biliary tract in 16 cases (44.4%), the gastrointestinal tract in 11 cases (30.6%), and the urinary tract in 8 cases (22.2%). The most common bacteria, including 3 cases in which 2 species had been detected at the same time, were *E. coli* (50%, 19 cases) and *Klebsiella pneumoniae* (32%, 12 cases). Initial antibiotics were sulbactam/cefoperazone in 12 cases (33.3%), tazobactam/piperacillin in 6 cases (16.7%), and meropenem in 5 cases (13.9%). According to susceptibility, the appropriate antimicrobial agent was changed in 15 cases (42%, including 2 cases of escalation against ESBL) and de-escalation was not properly performed in 8 cases (22%). Deaths within 30 days occurred in 2 cases. Antimicrobial stewardship can be promoted by the ICT round for Gram-negative bacilli bacteremia. More accurate ICT intervention is a future challenge.

Drug resistance in HIV infection

The recent evolution of antiretroviral agents, such as those with more activity, higher genetic barrier, fewer side effects, and less drug burdens, has achieved highly successful rates of HIV treatment. However, the resistance of HIV to drugs is an occasional problem. Drug-resistant HIV has several causes, but the most important factor is patient adherence. The treatment for drug-resistant HIV infection requires active antiretroviral agents and greater patient adherence. Furthermore, it is necessary to consider drug-drug interaction and side effects of antiviral agents that restrict the treatment options in clinical practice. Because drug-resistant HIV infection has no typical management, accurate consideration is needed for each case.

Surgical site infection due to Clostridium difficile

The bacterium *Clostridium difficile* colonizes healthy persons as a standard bacterial flora of the intestinal tract but can induce colitis after an antibiotic has been used. However, extraintestinal manifestation due to *C. difficile* is rare. A 71-year-old woman was hospitalized for suturation of the left Achilles tendon, which had ruptured because of an accident. The antibiotic cefmetazole was administered for 4 days during the perioperative period. After 2 weeks, the surgical site was opened with effusion, and *C. difficile* was isolated from the culture of this site. The *C. difficile* was not isolated from the patient's diarrhea or stool, and *C. difficile*-related colitis was not diagnosed in any other patients of the ward. Therefore, we could not identify an earlier patient with *C. difficile* infection. Thus, physicians should be more aware of extracolonic manifestations of *C. difficile*. Furthermore, we will investigate the risk factors for extracolonic manifestations of *C. difficile*.

Analysis of pathogenic factors of MRSA isolated from blood culture

In cases of bloodstream infection caused by *S. aureus*, severe metastatic infections, such as infective endocarditis, septic pulmonary embolism, and iliopsoas abscess, may occur and lead to a patient's death. This trend is more common in MRSA bacteremia than in methicillin-sensitive *S. aureus* (MSSA) bacteremia. Previously we revealed that in MSSA bacteremia, predictive factors for metastatic infection were a delay in appropriate antimicrobial treatment of > 48 hours, persistent fever for > 72 hours after starting antibiotic treatment, and lowest C-reactive protein levels of > 3 mg/dL for 2 weeks after the onset of bacteremia. To analyze the predictive factors for metastatic infection due to MRSA bacteremia, we performed a broth microdilution method for the antibiotic susceptibility testing of 10 isolates that were clinically isolated during 2013. All 10 isolates were susceptible to vancomycin, teicoplanin, linezolid, daptomycin, and arbekacin according to the Clinical Laboratory and Standards Institute criteria, which indicated that the appropriate antibiotics were selected. We are now investigating the host-related predictive factors and MRSA-related pathogenic factors.

Publications

Hori S, Uchino K, Matsumoto T, Yamaguchi H, Takahashi M, Hamajima S, Nukui K, Eda H,

Shiina A, Takita A, Yamanouchi N, Mizuno M, Okutani Y. Study on the safety and efficacy of

sitaflloxacin at a dose of 100 mg once a day — results of the use—results survey (in Japanese). *Jpn J Antibiot.* 2014; **67**: 175-91.

Hori, S, Uchino K, Yamaguchi H, Yokomizo A, Takahashi M, Hamajima S, Nukui K, Eda H, Shiina A, Kobayashi F, Yamanouchi N, Mizuno M, Okutani Y. Safety and efficacy of intravenous levofloxacin 500 mg once a day (in Japanese). *Nihon Kagaku Ryoho Gakkai Zasshi.* 2014; **62**: 687-702.

Yoshikawa K, Sato F, Takeda H, Yoshida M, Kojima A, Hori S. Three cases of active tuberculosis in patients receiving anti-TNF (tumor necrosis factor) agents despite treatment for latent tuberculosis infection (in Japanese). *Nihon Kagaku Ryoho Gakkai Zasshi.* 2014; **62**: 681-6.

Horino T, Sato F, Hosaka Y, Hoshina T, Tamura K, Nakaharai K, Kato T, Nakazawa Y, Yoshida M, Hori S. Predictive factors for metastatic infec-

tion in patients with bacteremia caused by methicillin-sensitive *Staphylococcus aureus*. *Am J Med Sci.* 2015; **349**: 24-8.

Okino S, Nakamura K, Ono K, Nakayama K, Horino T, Yoshida M, Hori S. Clinical study of mental illness and psychological stress among HIV-infected patients (in Japanese). *Shinshin Igaku.* 2015; **55**: 156-62.

Maezawa K, Terajima T, Kuroda Y, Hori S, Kizu J. Changes in infection control in medical facilities after the revision of medical fees (in Japanese). *Nihon Kankyo Kansen Gakkaishi.* 2014; **29**: 429-36.

Kizu J, Takagi K, Kuroda Y, Maezawa K, Matsumoto K, Hori S. Stability and color degradation in solutions of complex-type chlorine-based disinfectant cleaner (in Japanese). *Nihon Kankyo Kansen Gakkaishi.* 2014; **29**: 411-6.