Catheter-related Blood Stream Infection in a Patient with Hemodialysis

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ABSTRAK

Seorang pasien pria usia 31 tahun, datang berobat jalan ke rumah sakit untuk hemodialisis (HD) rutin 2 kali dalam seminggu. Saat dilakukan tindakan HD mendadak pasien demam dan menggigil, saat itu ditegakkan diagnosis catheter-related blood stream infection (CR-BSI), dilakukan pencabutan catheter double lumen (CDL) dan pasien kemudian dirawat. Hasil kultur tip CDL dan kultur darah perifer didapatkan kuman yang sama yaitu Enterobacter cloacae. Diagnosis CR-BSI pada kasus ini ditegakkan berdasarkan kriteria Infectious Disease Society of America (IDSA) tahun 2009. Secara keseluruhan harus diperhatikan langkah pencegahan CR-BSI berupa edukasi pasien dan petugas yang memasang CDL, penerapan prosedur tindakan aseptik kulit yang benar serta perawatan exit site CDL, untuk mencegah terjadinya CR-BSI.

Kata kunci: *catheter-related blood stream infection (CR-BSI), Infectious Disease Society of America (IDSA), catheter double lumen (CDL).*

ABSTRACT

A 31-year-old patient came to visit the outpatient clinic at the hospital for his routine twice-weekly hemodialyis (HD) session. During HD, the patient suddenly developed a fever with shivering. At that time, a diagnosis of catheter-related blood stream infection (CR-BSI) was developed, HD catheter or the catheter double lumen (CDL) was uninstalled and the patient was hospitalized. Results of culture withdrawn through the tip of catheter lumen and peripheral blood revealed identical microorganism, i.e. the Enterobacter cloacae. Diagnosis of CR-BSI in the present case was made based on the 2009 Infectious Disease Society of America (IDSA) criteria. In general, prevention measures for CR-BSI should be taken into account including education for patient, awareness of the health care providers who install the CDL, implementation of procedure for appropriate skin aseptic technique and best practice for HD catheter care, particularly on the exit site of the CDL to prevent the development of CR-BSI.

Keywords: *catheter-related blood stream infection (CR-BSI), Infectious Disease Society of America (IDSA) criteria, catheter double lumen (CDL).*

INTRODUCTION

Bacteremia or the presence of bacteria in the bloodstream may occur in patients who are undergoing hemodialysis (HD) treatment and generally the source of infection includes cannula or catheter double lumen (CDL).[1] Catheter-Related Blood Stream Infection (CR-BSI) is defined when the results of cultures show that microorganism isolated from catheter tips and peripheral blood cultures are identical without another source of infection other than the catheter/CDL itself in HD patients with symptoms of systemic infection.[1-3] The term CR-BSI is determined based on accurate data of laboratory results, which identify CDL as the source of infection in the bloodstream. The term is usually used to establish diagnosis, provide treatment and study the epidemiology of bloodstream infection in patients who undergo CDL insertion.[4,5] In order to establish the diagnosis of CR-BSI, laboratory data are necessary, which include data of paired culture obtained from CVC/CDL tips and peripheral blood.[2-4]

Catheter Related Blood stream Infection (CR-BSI) is a part of the primary bloodstream infection (PBI) or laboratory confirmed bloodstream infection, in which there is an infection in the bloodstream that occurs without any suspected organ or other tissue as the source of infection. The risk factors are susceptibility to infection and intravenous (IV) catheter insertion, which is associated with type of cannula, insertion method and duration of cannula insertion.[6] Catheter insertion for HD can be done permanently or temporarily, i.e. several months prior to the permanent insertion.[5,7] Whenever the permanent insertion has not been possible, the use of temporary insertion can be extended.[7]

Permanent catheter insertion is usually carried out by performing surgical procedure of creating arteriovenous fistula (A-V fistula). The A-V fistula requires 2 to 8 weeks for recovery and maturation before it is ready and to serve a useful function for HD procedure; therefore, temporary CDL insertion can be useful as an alternative, particularly in emergency setting.[5]

Temporary insertion of CDL is a catheter placement using vascular access through peripheral veins or large intrathoracic veins such as subclavian, internal jugular or femoral veins, which ends at the superior cava vein or right atrium. It serves a useful function in measuring central venous pressure or inserting hyperosmolar intravenous fluid during hemodialysis procedure.[4,5] There are 4 types of CDL insertion based on technique and duration of catheter insertion, which are non-tunneled CDL, tunneled CDL, peripherally inserted central catheters (PICCS) and implanted ports.[4]

CASE ILUSTRATION

Mr. A, a 31-year-old, came to outpatient clinic of HD in Fatmawati Hospital for his routine twice-weekly hemodialyis (HD) session. The patient had undergone HD within the last 2 months at Fatmawati Hospital and he had CDL insertion since the routine HD session was performed. He was on waiting list for having the Cimino arteriovenous shunt Cimino insertion in an operating room. During the HD procedure (± 4 hours after the HD had been initiated), the patient developed a fever with shivering and his doctor instructed to stop hemodyalisis and recommended the patient to be hospitalized. There was no history of fever during the previous routine HD sessions. History of having hypertension, urolithiasis or diabetes was denied. The patient worked as a casual laborer with an education level of junior high school.

His physical examination revealed that his qualitative awareness level was compos mentis (fully alert) with blood pressure of 140/90 mmHg, pulse rate of 110 beats per minute, respiratory rate of 22 beats per minute, body temperature of 380C and normal body mass index (BMI = 21.48). On his neck, a CDL was inserted on the right internal jugular vein and there was redness around the exit site of the catheter with no purulent discharge. There were no abnormal findings of his chest, abdomen and extremities. The chest radiography showed that the heart and lungs were within normal limits. A diagnosis of chronic kidney disease (CKD) on HD + suspected catheter-related bloodstream infection (CR-BSI) was made. The CDL was then removed and the patient received following treatment, i.e. intravenous fluid drip of ringer

lactate (RL) at 10 drips/minute; ceftriaxone at the dose of 2 x 1 gram by intravenous route and 3 x 500 mg paracetamol by oral route. Isolation of microorganisms, cultures and antimicrobial resistance testing were performed. Cultures were carried out with samples obtained from CDL tip and blood withdrawn from the left cubital veins.

The result of blood test revealed anemia with Hb levels of 9.9 g/dL (normal limit: 13.2-17.3 g/dL), neutrophilia with neutrophil counts of 12,000/uL (normal limit: 5000-10000/uL); while the ALT, AST, total protein and blood glucose levels were within the normal limits. There was high ureum level of 126 mg/dL (normal limit: 20-40 mg/dL) and the creatinine level was also high with 7.4 mg/dL (normal limit: 0.6-1.5 mg/dL). The estimated creatinine clearance based on the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was 9. Results of cultures through CDL tips and blood cultures as well as the antimicrobial resistance testing can be seen in **Table 1**.

Results of culture withdrawn through the tip of catheter lumen and peripheral blood revealed identical microorganism, i.e. the Enterobacter cloacae, which is one of Multiple Drug Resistant Organisms (MDRO) and the results of antimicrobial resistance testing were also identical for both cultures.

Empirical treatment using ceftriaxone was administered for 3 days and after the results of culture were received, a definitive treatment using meropenem for 3 days was provided, which was adjusted to the culture results. The patient was discharged from hospital with improvement.

DISCUSSION

Our patient is a 31-year-old male who came to outpatient clinic of HD in Fatmawati Hospital with a diagnosis of CKD + suspected CR-BSI. The whole blood count revealed normocytic normochromic anemia, neutrophilia as well as increased ureum and creatinine level, which supported a diagnosis of CKD. In this case, we found that the estimated creatinine clearance based on the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was 9, which is appropriate to the diagnosis of kidney failure or stage 5 CKD according to the 2012 KDIGO criteria and HD procedure is required. The neutrophilia indicated that there was an inflammatory process or an infection in the patient. Samples for culture and antimicrobial resistance testing from the CDL tip and blood were sent and at the same time, CDL was removed and sent for further evaluation. Results of culture withdrawn through the tip of catheter lumen and peripheral blood revealed

Table 1. Results of culture and antimicrobial resistance testing with samples obtaind from CDL tip

Isolates: *Enterobacter cloacae*			
- Amoxycillin clavulanic acid	R	Amikacin	S
- Cefuroxime	R	Gentamicin	S
- Ceftazidime	R	Ciprofloxacin	R
- Cefotaxime	R	Levofloxacin	I
- Ceftriaxone	R	Cotrimoxazole	R
- Cefepime	R	Chloramphenicol	R
- Meropenem	S	Fosfomycin	R
Results of blood culture			
- Amoxycillin clavulanic acid	R	Amikacin	S
- Cefuroxime	R	Gentamicin	S
- Ceftazidime	R	Ciprofloxacin	R
- Cefotaxime	R	Levofloxacin	I
- Ceftriaxone	R	Cotrimoxazole	R
- Cefepime	R	Chloramphenicol	R
- Meropenem	S	Fosfomycin	R

identical microorganism, i.e. the Enterobacter cloacaeand the results of antimicrobial resistance testing were also identical for both cultures that the patient was still sensitive to the following antibiotics, i.e. meropenem, amikasin and gentamicin.

There are some methods for laboratory culture evaluation with samples obtained from the catheter tip, which are qualitative and semi-quantitative methods.[4,5,8] For culture using qualitative method, the tip of catheter is aseptically removed and immersed in liquid medium and then the procedure of growing in blood agar is carried out and the culture is incubated for 24 hours at 37^{0}C. The semi-quantitative method includes rolling the tip of catheter (with ±5 cm length) on the surface of blood agar plate, the culture was incubated for 24 hours at 37^{0}C and the number of growing colonies was counted.[3-5]

According to one of criteria issued in the CDC's National Healthcare Safety Network (CDC's NHSN) for CR-BSI as quoted from the Association for Professionals in Infection Control (APIC),[4] CR-BSI is defined when the result of culture through catheter tip is semiquantitatively positive (>15 CFU/tip), which is known as positive CR-BSI. Semi-quantitative method for culture of catheter tip has been more recommended by the CDC's NHSN than the qualitative method; however, the qualitative method has also been used widely until now.[4,8] A study by Marconi[9] comparing qualitative and semi-quantitative method for cultures has found 100% sensitivity and 60% specificity for qualitative method; while 90% sensitivity and 71% specificity for semi-quantitative method. A study conducted by Safdar as quoted by Marconi has demonstrated 90% sensitivity and 72% specificity for qualitative method; while for semi-quantitative method, the study has shown 85% sensitivity and 82% specificity. Cultures using semi-quantitative method have demonstrated higher specificity than qualitative method with cut-off point of >15 CFU/tip, which can reduce the possibility of false positive result.[9]

In the present case, the patient came for routine dialysis session and during the HD procedure, he had suffered clinical symptoms of fever and shivering (pulse rate 110 beats per minute and body temperature of 38.5 ^{0}C) within several hours after having HD and he also had inflammatory signs at the site of CDL insertion. The chest radiography revealed that his heart and lungs were within normal limits. The HD procedure was stopped, double lumen catheter / CDL was removed, a diagnosis of CKD on HD + suspected CR-BSI was made and the patient was immediately hospitalized. CDL had been inserted since the patient had routine HD, i.e. within the last 2 months prior to hospitalization. The double lumen catheter (CDL) was inserted on the internal jugular vein (central vein) according to the non-tunneled CVCs technique for < 3 months insertion (short term). There was no history of fever and shivering during the previous routine HD session.

In this patient, we found identical results between culture withdrawn through the tip of catheter lumen and peripheral blood as well as identical results of antimicrobial resistance testing, which is in consistent with the IDSA criteria guideline for CR-BSI diagnosis. According to the guideline, diagnosis of CR-BSI is made when there are no bacteria in blood, there is clinical and laboratory indication of infection, no clear source of infection other than the CDL and positive culture reveal identical microorganism between blood culture and culture through CDL. Definitive diagnosis of CR-BSI is established when during the CVC/ CDL insertion there is signs of infection on the insertion site, there is clinical symptoms of bacteremia or sepsis, the clinical signs resolved and diminished following the removal of CVC/ CDL, results on type of microorganism between culture withdrawn through the tip of catheter lumen and peripheral blood are identical, no other source of infection has been found to cause bacteriemia other than the CVC/CDL (primary bacteremia).3, I0 Among those criteria, the most important gold standard for establishing the diagnosis of CR-BSI is when results between culture withdrawn through the tip of catheter lumen and peripheral blood at the same time are identical.[2-4,8]

In the present case, we found several evidences which pointed out to the possibility

that CR-BSI has occurred, i.e. on history taking, the patient had fever and shivering during HD procedure, which diminished immediately after the catheter was removed. On physical examination, there were signs of phlebitis on the exit site of the CDL, no other source of infection was found other than catheter and the results between culture withdrawn through the tip of catheter lumen and peripheral blood were identical, which is the diagnostic gold standard for CR-BSI. Therefore, the data of our patient has fulfilled the diagnosis criteria for CR-BSI. Accurate diagnosis of CR-BSI is extremely important and needed for effective and prompt management such as removing catheter as it may serve the source of infection and therefore, more serious complications can be avoided for the patient's sake.[2,10]

CDL insertion must consider some issues, i.e. catheter must be inserted using aseptic technique and must be removed immediately when it is no longer necessary or if it is suspected leading to sepsis. Catheter that has been inserted through jugular and subclavian veins must not be removed on a routine base and when it must be continued for longer use, gauze dressing for catheter must be checked and replaced every 48-72 hours.[6] When performing CVC/CDL insertion, in addition to aseptic procedure, a good and appropriate hand hygiene must be carried out as well as using gloves and mask to prevent and reduce the incidence of infection. The use of skin antiseptic such as povidone iodine or 2% chlorhexidine gluconate prior to CVC/CDL insertion may reduce the incidence of CR-BSI. Overall, the strategy of preventing CR-BSI includes measures of providing education for patients and health care providers who perform CVC/CDL insertion, the use of antibiotic lock or heparin lock on CVC/CDL insertion, applying the procedure of appropriate aseptic technique, the use 2% chlorhexidine gluconate for skin antiseptic when performing CVC insertion as well as checking and replacing dressing for CVC/CDL once in every three days before and after HD procedure has been carried out.[3,9,11]

The incidence of CR-BSI, as quoted by Fletcher,[3] varies between 3 and 16 % depending on risk factors and types of the inserted catheter. The rate of CR-BSI incidence depends on different site and duration of catheter placement, types of catheter material that has been used, potency of contamination at the exit site or hub, CVC/CDL insertion technique and risk factors for infection in the patients themselves.[7]

The lowest incidence of infection has been found when CVC/CDL is inserted through subclavian vein followed by internal jugular vein as the insertion site and the highest incidence of CR-BSI is found when the femoral vein is used as the insertion site. Regarding the catheter material, polyurethane or silicone catheters are good enough; however, further studies need to be done on selecting the best catheter material to prevent the development of CR-BSI.[3]

According to the 2012 Kidney Disease Improving Global Outcomes (KDIGO) criteria,[12] CKD patients with creatinine clearance of <15 are categorized into patients with renal failure or End State Renal Disease who require HD procedure. In CKD patients who are on HD with insertion of CVC/CDL, there is a risk of developing CR-BSI.[12] In addition to CVC/CDL insertion, catheter caring and duration of CVC/CDL insertion may also have a risk for developing infection. Some other risk factors that may have roles on the development of CR-BSI in patients with hemodialysis are elderly age, comorbidities of CKD such as diabetes mellitus, malignancy, hypoalbuminemia and anemia. In patients with diabetes mellitus and CKD, there can be some abnormalities of immune system, which can be aggravated by uremia that may facilitate the development of infection. Hypoalbuminemia may also exacerbate immune defect in CKD patients.[1,13]

Actually, the most common cause and microorganism that allows colonization or phlebitis on the site is *Staphylococcus sp*. such as *S. epidermidis* or *S.aureus*. The most common bacteria causing CR-BSI in HD patients are Gram-positive cocci (52 to 70%) such as S.aureus and S.epidermidis. Gram-negative bacteria are found as etiologies in about 24 to 26.7% cases.[13] (**Table 2**)

Microorganism causing CR-BSI can enter bloodstream thorugh several mechanisms and the first is through direct migration from skin

Table 3. Profile of bacteria causing CR-BSI[13]

Gram positive cocci	52-70%
S. aureus	21.9-60%
S. epidermidis	8.8-12.6%
MRSA**	6.0-8.0%
Enterococcus faecalis	2.4-8.0%
Gram negative bacilli	24-26.7%
Pseudomonas aeruginosa	2.3-15.2%
Escherichia coli	10.4%
Acinetobacter spp.	12.8%
Serratia marcesens	1.2-2.3%
Klebsiella pneumoniae	6.4%
Enterobacter doacae	8.8%
Polymicrobial	16.2-20%

surface, i.e. from the outer surface of catheter to catheter tip at the location of catheter insertion (extraluminal), which is usually associated with bacteria colonization on the skin surface.

The second mechanism is through catheter hub, which is contaminated during HD procedure is performed; while the third mechanism is through contamination of dialysis fluid (intraluminal). Bacteria on skin surface near the location of catheter insertion can migrate through catheter reaching the catheter tip and finally entering bloodstream and spread through catheter lumen.[3,13] When the catheter is inserted, the exit site of the catheter will be immediately covered by serum protein such as fibrinogen, fibronectin, laminin and collagen that cover the outer surface of intravenous catheter. The protein layers along with glycocalix (slime) produced by the bacteria will develop a biofilm, which become the site of bacterial attachment, replication and colonization.[3]

In the present case, we found a different type of microorganism, i.e. the *E. cloacae*, which is a Gram-negative rod bacteria and it is included in the Enterobacteriaceae family. The free-living bacteria are found in gastrointestinal tract, septic tank, river water and plants. They have optimum growth at 37^0C and they are facultative anaerobs, oxidase negative and katalase positive. The bacteria can cause nosocomial infection in the hospital and resulting in bacteremia, skin and soft tissue infection and urinary tract infection.

Moreover, the bacteria can also produce beta laktamase and they easily become resistant to the third and fourth generation of cephalosporin or become Multiple Drug Resistant Organism (MDRO). Transmission of infection or outbreaks may occur through contaminated hands of the health-care workers, contaminated medical equipment or water. *E. cloacae* found in the present case was probably caught by the patient when he had a bath/cleaned himself in the public toilet at the HD department in the hospital and used water contained in water basin (tile tub) next to the toilet that might have been contaminated, which subsequently caused phlebitis at the exit site of CDL and then the bacteria entered the bloodstream when the HD procedure was performed.

In the present case, although the wound dressing at the exit site has been checked and replaced each time the patient had a controlled visit for HD session twice a week, but waterproof occlusive dressing had not been used and therefore, it had a high potency for contamination. There are some ways for microorganism entering bloodstream, which are through contaminated dialysis fluid or through contaminated hub or through colonization at the exit site and the microorganism enters bloodstream during the HD procedure.

Unfortunately, no culture had been done based on samples from dialysis fluid in the present case; however, the most recent data on culture of dialysis fluid, which is performed every 3 months, shows that the dialysis fluid is still useable and there was no other case of CR-BSI found in other patients who also had used the dialysis fluid. Based on findings of phlebitis signs and the development of fever within 4 hours following the HD procedure, there is a great possibility that the microorganism was caught through the exit site of CDL, which might have formed colonization at the exit site and entered the bloodstream during the HD procedure. Education for patient is also necessary, particularly on CDL care when the catheter has been removed and replaced by a new CDL so that the catheter is always in a clean and dry condition without any contamination to avoid colonization or infection at the exit site of CDL. Providing antibiotics such as i cefazolin, gentamicin (antibiotic lock), heparin (heparin

lock) into catheter lumen and skin antiseptics (chlorhexidine) will reduce the migration of microorganism from the intracutaneous to intravascular segment of the catheter.[10,12,13] Heparin lock was administered at the dose of 1.5 mL/ 7500 U heparin into the catheter lumen following the HD procedure, which has a role to prevent blood clot that may develop into septic thrombophlebitis. The heparin lock can be administered simultaneously with antibiotic lock. The antibiotic lock is usually given for long-term CDL for 7-14 days and it should not be given on a routine basis as may induce antimicrobial resistance. If bacteremia or sepsis has developed, clinical symptoms such as shivering, fever or even hypotension and shock may occur.[14]

Antibiotics that are quite effective for the bacteria are aminoglycosides, cefotaxime and cefoperazone.[15] Antibiotic treatment should be based on results of culture and antimicrobial resistance test.[3,11] Empiric treatment for Gram-negative bacteria depends on pattern of microorganism and the severity of disease. Usually, the fourth generation of cephalosporin, carbapenem, combined treatment of beta lactam and aminoglycosides are administered. Vancomycin can be given as empiric treatment whenever the presence of Methicillin Resistant Staphylococcus Aureus (MRSA) is suspected. Definitive antibiotic treatment for CR-BSI is usually given for 7 to 10 days; while for CR-BSI cases with complications, the antibiotic can be given up to 2 weeks.[11,14,16]

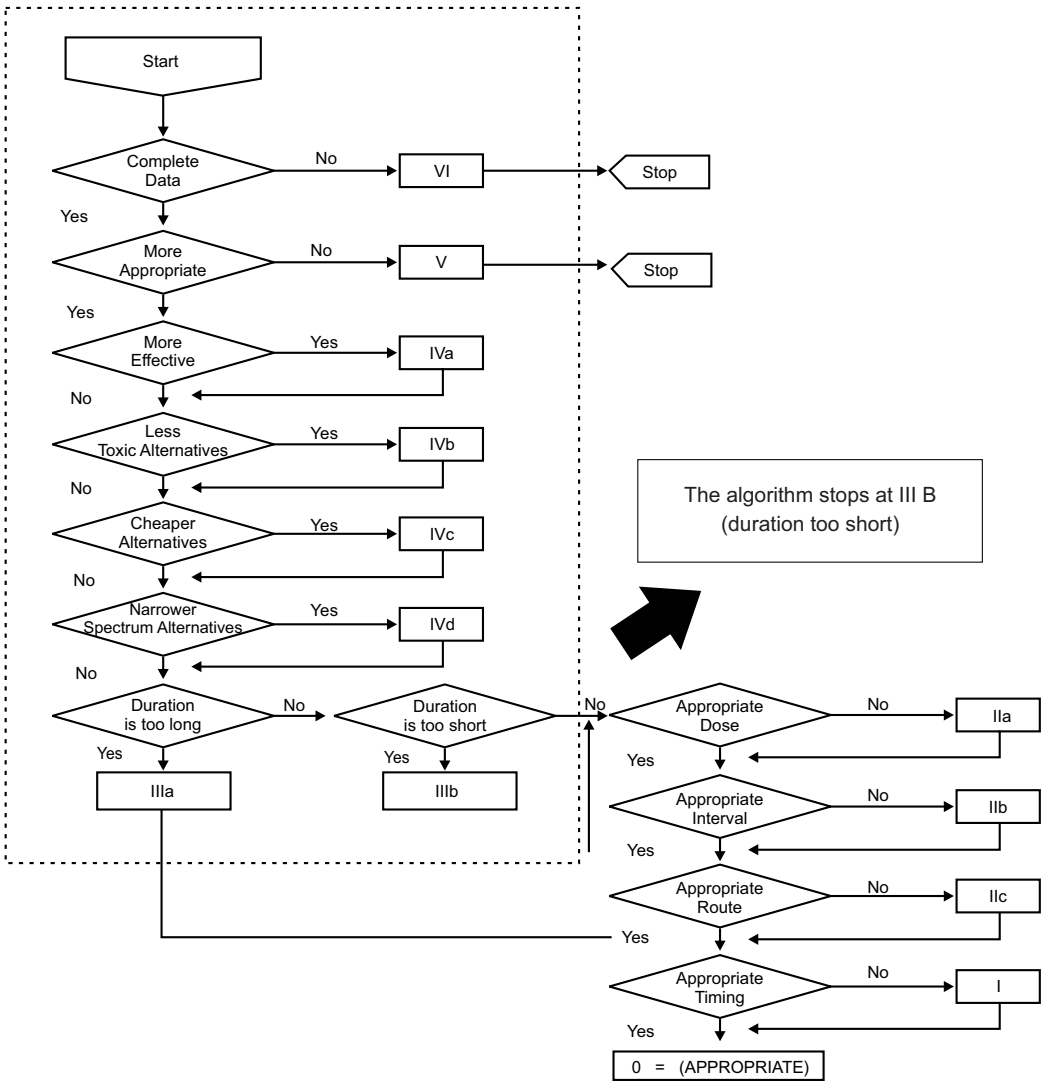

Figure 1. Gyssens algorithm for evaluating the use of meropenem

Empiric treatment using ceftriaxone for 3 days in the present case obviously did not bring any significant clinical improvement as the patient was still having fever and the leukocyte count was increasing. After receiving the result of blood culture and culture of the CDL tip, we knew that the microorganism was indeed resistant to ceftriaxone.

Based on the results of antimicrobial resistance testing, blood culture and culture of the CDL tip, the antibiotic treatment was then replaced by meropenem. The meropenem treatment was provided after the result of blood culture and CDL tip had been known and it was obvious that there was identical microorganism between both cultures, which is consistent with the diagnosis criteria of CR-BSI. Afterwards, there was clinical improvement and the patient was discharged from the hospital without any oral antibiotics.

When evaluating the use of meropenem with Gyssen algorithm (**Figure 1**), we found that the data of medical records was complete, the indication for definitive treatment was appropriate, the antibiotic given had a narrow spectrum, inexpensive, safe and the most effective against *E. cloacae*; however, the duration of treatment was too short (less than 5 days); in contrast, the recommended duration of antibiotic treatment for CR-BSI should be at least 7 days; therefore, the evaluation for the used Meropenem using Gyssen algorithm stopped at the III B, i.e. in the category of duration of treatment was too short.

CONCLUSION

Whenever there is a sudden fever during hemodialysis procedure, the possibility of developing Catheter Related Blood Stream Infections (CR-BSI) should be considered. We found that results of culture withdrawn through the tip of catheter lumen and peripheral blood revealed identical microorganism, i.e. Enterobacter cloacae, which supports the diagnosis of CR-BSI. Overall, prevention measures for CR-BSI should be taken into account including education for patient, awareness of the health care providers who install the CDL, implementation of procedure for appropriate skin aseptic technique and best practice for HD catheter care, particularly on the exit site of the CDL to prevent the development of CR-BSI.

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