Case Report

Nosocomial infective endocarditis in a renal transplant patient: culprit central venous line

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ABSTRACT

Nosocomial infective endocarditis (IE) is a relatively uncommon but, a serious complication affecting critically ill hospitalized patients who are frequently exposed to life-saving invasive procedures. Immunosuppressive treatment in solid organ transplant recipients predisposes to infections, nevertheless, nonspecific symptoms of IE, such as fever, lassitude, weight loss, and signs of inflammation may often be misinterpreted as acute rejection episode or a common urinary tract infection. The case reported here was a recent renal transplant with methicillin-resistant Staphylococcus aureus IE. We believe the diagnoses of IE in her were missed at her first presentation due to her non-specific symptoms and lack of echocardiography and blood culture results. Septic procedure at insertion of central venous catheter (CVC) in the Intensive Care Unit with trauma to tricuspid valve (TV) at the time of CVC insertion was a possible source of infection for IE. The patient was managed effectively with intravenous antibiotics in spite of having hanging pedunculated vegetation on TV.

Keywords: Central venous catheter, Infective endocarditis, Vegetation, Solid organ transplant (SOT)

INTRODUCTION

Infective endocarditis (IE) is a rare disease reported to occur with an incidence of approximately 6/100,000 inhabitant in the general population although intensive antibiotic treatment can cure endocarditis in some instances, complications such as extension of the infection into surrounding cardiac structures, progressive valvular dysfunction, big vegetations or even septic embolism often require cardiac surgery. Prior to the introduction of echocardiography diagnosis of IE was mainly based on clinical suspicion. Therefore, most cases of IE were discovered through the appearance of secondary complications in an advanced stage when surgical treatment was associated with high perioperative mortality. Renal transplant patients with immunosuppressive therapy are predisposed to developing IE, which is associated with poor long-term survival nevertheless, nonspecific symptoms of IE, such as fever, lassitude, weight loss, and signs of inflammation may often be misinterpreted as acute rejection episode or a common urinary tract infection. Nosocomial IE in native and prosthetic valve is a relatively uncommon but nevertheless, a serious complication affecting critically ill hospitalized patients who are frequently exposed to life-saving invasive procedures such as central lines and invasive procedures. The procedure of placing a central venous catheter (CVC) is associated with known septic complications. Infection localized to the right heart valves occurs in about 5% of cases of IE and is seen mainly in drug addicts and as a complication of central venous lines or indwelling vascular catheters. Solid organ transplant (SOT) recipients, because of multiple invasive procedures, prolonged hospitalization and immunosuppressive therapy, are at high risk of developing infectious complications such as bacteremia and uncommonly IE. SOT recipients with IE vary from other patients with IE in many aspects. Their mean age is lower (46 years; range 12-67 years). Most patients have no history of valvular disease or abnormality. The clinical diagnosis of IE in these patients is surprisingly difficult.
This is due both to the inaccessibility of intra-cardiac vegetations and to the highly variable and sometimes non-specific nature of the clinical manifestations leading to a wide differential diagnosis. Prompt diagnosis and treatment are mandatory due to significant complication and poor outcome. In other words, high index of suspicion must be maintained for diagnosis of IE due to different clinical features, especially in patients with immunosuppression.

CASE REPORT

The patient presented is a 34-year-old married, Yemeni female who was suffering from end stage renal failure of unknown etiology. She was on maintenance Hemodialysis over 2 years via left radio cephalic arterio venous fistula (AVF). She had a live-related renal transplant done in December 2013 and was put on tacrolimus, mycophenolate, and prednisolone; she developed drug-induced post transplant diabetes mellitus and was managed with mixtard insulin. 1 month post transplant she presented to the renal clinic with low grade fever, lethargy, malaise, and anorexia. She was evaluated and was documented to have pyuria and hematuria and sterile urine cultures, her complete blood count, X-ray chest, kidney functions, and ultrasound of the graft kidney were normal. Her urine showed alb+, pus cells 40-50, red blood cells (RBCs) 8-12, and no casts. Urine culture was sterile. She was diagnosed as lower urinary tract infection and was advised intravenous (IV) ciprofloxacin for a period of 10 days. Her symptoms improved and treatment was stopped and discharged on oral ciprofloxacin for a period of 5 days more. She again presented to the outdoor clinic with same symptoms and investigations again revealed the pyuria and hematuria. Her kidney functions and chest X-ray were normal and urine culture was sterile. She was once again treated with a course of ciprofloxacin and discharged with improvement. 4 months post transplant, she was referred to our hospital with anorexia, low grade fever, sweating, weight loss, and easy fatigability. On examination, she was ill-looking, lean thin. She had moderate pallor, no lymphadenopathy, left arm radio cephalic AVF was working with a thrill and bruit, and there were no stigmata of IE in the form of finger clubbing, olsers nodes, petechi, erythema, and roth spots. Abdomen examination revealed mild splenomegly and no hepatomegly. Cardiovascular examination apex was in 5th ICS, there was no thrill or heave. Both heart sounds were normal and well heard. There was no murmur or pericardial rub. Chest and central nervous system examination were normal. Investigation revealed hemoglobin 8.8, white blood cell 5.7, polymorph 67%, lymph 28%, eos 3%, baso 1.6% urine examination showed Alb+, pus cells 50-60/HPF, RBCs 20-30/HPF, no casts. Her urea was 8.0 m mol/L, cretinine 78 mica mol/L, Na 145 Me/l, K 4.5 Me/l. Normal liver functions. X-ray chest computed tomography ratio was 0.5, normal lung parenchyma and no pleural effusion. Ultrasonography of the graft kidney was normal with no change in size, echogenicity or hydronephrosis no local collection seen. Three simultaneous blood samples from different sites AVF vein and other arm vein were sent for cultures. She was empirically started with vancomycin 1 g IV twice a day. 3 days later, echocardiography documented moderate sized pedunculated vegetation on the posterior leaflet of tricuspid valve (TV) with no regurgitation of TV (Figures 1 and 2) and on 5th day, the blood cultures documented as growth positive for methicillin-resistant Staphylococcus aureus (MRSA). She was continued with IV vancomycin 1 g twice daily and clindamycin 600 mg 6 hrs was added to treatment. She was a febrile 3 days after start of therapy and had a stable course. In hospital, she was monitored for graft functions which remained within normal range her cyclosporine and vancomycin levels were also monitored regularly. Follow-up blood cultures were negative at 2 weeks and echocardiography revealed a tremendous decrease in the size of the TV vegetation (Figures 2 and 3), urine was free of pyuria and hematuria. The double antibiotic was continued for a period of

high morbidity and mortality. We report on a patient with TV endocarditis believed to be due to direct damage, inoculation, and sepsis onto the valve surface by the central line catheter tip inserted in Intensive Care Unit (ICU) during the post renal transplant period and was kept for 1 month post renal transplantation. SOT recipients, because of multiple invasive procedures, prolonged hospitalization, and immunosuppressive therapy, are at high risk of developing infectious complications such as bacteremia and uncommonly IE. Although immunosuppression predisposes to systemic infection, reports regarding IE after SOT are sparse. IE in SOTs is a unique entity due to its rare occurrence, multiple confounding symptoms and signs. Hence, the diagnosis can be difficult. TV injury associated with CVC is rarely reported and poses significant clinical and diagnostic challenge due to a normal structural heart and no predisposing conditions. Catheter-related bacteremia and sepsis is a typical and serious complication of implantable venous access devices, caused mainly by staphylococci. This varies considerably by type of catheter, frequency of catheter manipulation, time period, and patient-related factors (e.g. underlying disease and acuity of illness). The majority of serious catheter-related infections are associated with CVCs placed in patients in ICUs than in the operation theater and less acute inpatients. In the ICU setting, the catheters are needed for extended periods of time and are manipulated multiple times for administration of fluids, drugs, blood and blood products, for hemodynamic measurements or to obtain samples for laboratory analysis. These make the patients prone for colonization with hospital-acquired organisms and augment the potential for contamination and clinical infection. There is no consensus about the safe length of guide wire required to secure vascular access, but 18 cm has been concluded to be safe in most adult patients from right internal jugular venous entry point to cavoatrial junction. This guideline may reduce or eliminate the risk of entrapment and valve injury, but has not been practiced widely as evident from our case report. The incidence of IE associated with central line infections is increasing, and an incidence of 7-29% is reported in the literature. One to 16% of patients with S. aureus bacteremia and a removable focus of infection (mostly central venous lines) have manifest endocarditis with a poor prognosis due to rapid destruction of the affected valves if untreated. The optimal position of the CVC tip remains the subject of debate. And the right tracheobronchial angle and carina are considered common radiological marker for insertion depth, which can be reflected practically to the sternal angle as a surface marker while cumulating the right internal jugular vein. This avoids entering the right ventricle and injury to the TV. This is practical, easy to follow, and is relatively safe. Fully inserted CVCs, although placed uneventfully, tend to lie close to the tricuspid leaflets and can cause abrasive injury of the leaflets and endocardium secondary to forceful and rapid injection of volume or drugs. This, along with guide wire injury, especially when the firm straight end is used by the operator instead of the “J” tip, may contribute to endocarditis of the tricuspid leaflet in patients with adequate substrates, and we believe

DISCUSSION

Recent advances in the diagnostic methods and therapeutic procedures have changed the spectrum of patients with IE. Infection localized to the right heart valves occurs in about 5-10% of cases of IE and is seen mainly in drug addicts, central lines or indwelling vascular catheters. A CVC is inserted for measurement of hemodynamic variables, delivery of nutritional supplements, drugs and access for hemodialysis and hemofiltration. CVC is a common practice and there is more to the technique than routine placement as evident when a procedure-related complication occurs. More than 15% of the patients who receive CVC placement have some complications and infectious endocarditis involving the TV is a rare and serious complication with
this as the possible source of infection in our patient as reported by others,\textsuperscript{15,16} moreover, some catheters are inserted in urgent situations, during which optimal attention to aseptic technique might not be feasible. Although recently ultrasound guided CVC has helped to achieve safe venous puncture at the first stage of CVC. Complications still occur at other stages of the procedure, including the guide wire, the dilator or the catheter insertion. Prompt diagnosis and treatment of complication are mandatory due to significant complication and high mortality. In other words, high index of suspicion must be maintained for diagnosis of IE due to different clinical features, especially in patients with immunosuppression. The case presented here has echocardiography documented big pedunculated vegetation on TV and blood culture positive for MRSA. Inspite of immunosuppression and large pedunculated TV vegetation, it was decided to adopt a conservative approach with IV antibiotics. This was based on patient’s clinical stability and laboratory results with no pulmonary symptoms or cardiac complications. She was closely monitored for response to therapy and any evident complication. But Patient definitely showed a good and quick clinical response and follow-up echocardiography revealed a considerable decrease in the size of TV vegetation. Therefore, surgical therapy was deferred. Current indications for surgical treatment are refractory heart failure directly related to valve dysfunction, uncontrolled infection; and prevention of embolic phenomena.\textsuperscript{17} The risk of embolism is high (20-50\%) in patients with IE, though it decreases rapidly following institution of directed antibiotic therapy, particularly after 2 weeks.\textsuperscript{18} The embolic risk of vegetations is closely linked to their size and mobility, and surgery is recommended for those measuring $>10$ mm in diameter after one or more embolic events, for those associated with predictors of unfavorable evolution such as heart failure or persistent infection, and especially for those measuring $>15$ mm, the latter being a class IIb recommendation, level of evidence.\textsuperscript{19}

Although the source of infection for IE was not evident, but we believe the patient acquired TV trauma and infection at insertion of central venous line in the ICU. Retrospectively considering, there was a definite delay in the diagnosis of IE in this patient due to her vague symptoms and simultaneously an early echocardiography was not requested upon her.

**CONCLUSION**

The present case illustrates an unusual evolution of IE in renal transplant recipient and highlights the need for a carefully considered approach to septic procedure at central line insertion. Prompt diagnosis and treatment are mandatory due to significant complication and high mortality. In other words, high index of suspicion must be maintained for diagnosis of IE due to different clinical features, especially in patients with immunosuppression. Assessment of patient’s characteristics, clinical course, laboratory results, imaging studies risks, and benefits of surgical intervention should be considered in order to decide the best therapeutic option.

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