CASE OF THE MONTH

An Interesting Case of Recurrent Pyelonephritis

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Abstract

A 35-year-old male presented with repeated episodes of fever and abdominal pain of 3-month duration. He had been hospitalized twice with similar complaints in the past 3-month. He was diagnosed as pyelonephritis and managed with intravenous antibiotics. However, fever recurred after ten days of discharge from the hospital. With these complaints, he was referred to the Department of Medicine, AIIMS, New Delhi.

After evaluation, he was diagnosed as pyelonephritis with right sided consolidation and was started on broad spectrum antibiotics. After a transient initial improvement, his dyspnea worsened, fever recurred and he developed a tender submandibular abscess. Further evaluation for the actual focus of infection, revealed a small mass attached to the right coronary aortic cusp on transthoracic ECHO. Diagnosis of native Aortic valve endocarditis was made and suitably treated. The patient became afebrile on the 8th day of therapy and was discharged after 20-day. He is doing well on subsequent follow-up.

Introduction

There are myriad ways through which any disease can present itself. This ever-expanding conundrum of clinical presentations when further complicated by iatrogenic addendums and previous inadequate therapies further confound the diagnosis. Such perplexing case scenarios are not only intriguing but also highly informative and sharpen clinical acumen for early detection of similar conditions in the future. We describe the elusive case of a young male presenting with recurrent fever with dysuria and shortness of breath.

Case Presentation

A 35-year-old male shopkeeper without any co-morbidities presented with complaints of high-grade fever with associated chills and rigor since the last 3-month. It was associated with burning in micturition along with urgency and frequency and abdominal pain. The pain was constant and dull aching in the left middle and lower abdomen and had increased acutely in the last 5-day. He had noticed painless, gradually progressive swelling over both the lower limbs over the last one month. Over the past 2-day, he had developed acute onset shortness of breath, present even at rest and had difficulty in completing full sentences. He had also noticed decreased frequency of micturition and had not passed urine over the last 12-hour. For similar complaints, he had been evaluated at a local hospital near his hometown about 2-month back. He was diagnosed with bilateral pyelonephritis based on urine analysis and radiological investigations. He received 1-week of intravenous antibiotics (IV). After discharge, he was prescribed oral antibiotics for 5-day. Though compliant with medications, the fever spikes recurred after 2-week of discharge along with similar complaints of dysuria. He was readmitted to the hospital and was started on IV antibiotics. Ureteral stents were inserted (double-J stents) on the suspicion of ureteral obstruction (Figure 1). After 2-week of in-hospital care and medications, the patient became afebrile and asymptomatic. Ureteral stents were removed before discharge. However, after about 10-day of discharge, the patient developed fever again. This was also associated with pedal edema. The patient used over the counter medications for fever but due to worsening of symptoms presented to Medicine out-patient department (OPD) at All India Institute of Medical Sciences (AIIMS) New Delhi. There was no history of evening rise of fever, jaundice, insect bite, recent travel, visit to a forest or scrub, skin rash or photosensitivity, oral ulcers, alopecia, arthralgia, recurrent urinary tract infections or respiratory tract infections in childhood.

On examination, the patient was febrile (101°F), tachycardic (110/minute) and tachypnoeic (24/minute). There was pallor...
and bilateral pitting pedal edema extending up to the knees but no signs of icterus, clubbing or lymphadenopathy or elevated jugular venous pressure. He had bilaterally decreased breath sounds in the infra-axillary and infra-scapular regions. It was associated with diffuse coarse crackles more on the right side than the left. The abdomen was distended with flank fullness. Shifting dullness was present and left renal angle was tender. Rest of his systemic examination was unremarkable.

Laboratory investigations (Table 1) revealed leucocytosis with neutrophil predominant along with mild anaemia. erythrocyte sedimentation rate (ESR) was elevated. Renal functions were deranged and associated severe hypoalbuminemia was also present. Urinalysis (Table 2) showed pyuria with proteinuria along with white blood cell (WBC) casts. Pleural fluid analysis revealed exudative effusion with leucocyte count of 300 cells/mm³ with neutrophilic predominance and a pH of 7.25, adenosine deaminase (ADA) was 4 International Unit (IU)/Litre (L) and Xpert Mtb Rif test was negative. Ascitic fluid was transudate. Ultrasound revealed normal sized kidneys with raised echogenicity and maintained cortico-medullary differentiation. Blood and urine cultures were sent. His blood glucose was normal and HbA1c levels was 5.5%. Vasculitis and immunodeficiency workup including HIV and Hepatitis B infections was negative. Fundus was normal and he had associated anaemia of chronic disease. Emergency room bedside echocardiography revealed moderate pericardial effusion with normal left ventricular function. Chest X-ray (Figure 2) and computerised tomography (CT) scan revealed a right sided lobar consolidation with associated parapneumonic effusion and right subdiaphragmatic fluid collection.
Our likely diagnosis was complicated urinary tract infection i.e. complicated pyelonephritis with urosepsis with septic embolism leading to pneumonia and sepsis-related acute kidney injury (AKI). Disseminated tuberculosis (TB) was our second differential, however, response to antibiotics, low ADA levels in pleural fluid made TB less likely. Infective endocarditis (IE) leading to septic embolization and bacteremia was our third differential. However, lack of any underlying predisposing condition, no other embolic phenomenon and only pericardial effusion on bedside echocardiography were against it.

With the most likely diagnosis of pyelonephritis with urosepsis, the patient was started on intravenous (I.V.) Piperacillin and Tazobactam and oral linezolid. The patient became afebrile after 3-day and his renal function tests also improved. His blood culture was sterile. On the third day of admission, his urine culture revealed Enterococcus fecalis infection resistant to linezolid and sensitive to vancomycin and teicoplanin. He was started on Teicoplanin and other antibiotics were discontinued.

3-day later the patient developed sudden onset dyspnoea with associated orthopnea. He had spikes of fever and a tender swelling in the submandibular region. There were associated diffuse fine crepitations in bilateral lower lung field. The patient was started on diuretic therapy and continuous positive airway pressure ventilation. Urgent CT pulmonary angiography revealed no evidence suggestive of pulmonary embolism. Ultrasound imaging of the submandibular swelling was suggestive of an abscess. Appearance of a new onset abscess lead us to relook foci of actual infection. So, keeping in mind a strong suspicion of IE Trans-oesophageal echocardiography was ordered which demonstrated a firm mobile mass attached to the right aortic leaflet (Figure 3). There was a resolution in the pericardial effusion. With the diagnosis of infective endocarditis likely due to enterococci, the patient was started on IV gentamicin with vancomycin and ceftriaxone. His fever responded in about one week. His general condition along with laboratory investigations improved after a week of therapy. He also showed radiological resolution (Figure 4). He was discharged after 2-week of IV antibiotics as he wished to complete the remaining course from his regional clinic. He is in medicine OPD follow-up over the past one year and has been symptom-free.

**Discussion**

The patient presented with recurrent episodes of pyelonephritis since 3-month. This time it was associated with acute kidney injury and pneumonia. On presentation, there was associated acute kidney injury which was likely related to sepsis or pyelonephritis. Proteinuria is uncommonly seen with pyelonephritis. Though all the organs involved could be due to separate entities as per the Hickam’s dictum, however following Occam’s razor we tried to make the least assumptions for the underlying cause of ailments. One of the disease with such disparate manifestations is infective endocarditis. The therapeutic response of the patient after starting combination therapy for enterococcal endocarditis further supports the diagnosis.

The echocardiographic presence of mass lesion along with fever, the initial blood culture positive for enterococci and the manifestations suggestive of associated glomerulonephritis fulfill one major and three minor criteria of the Duke’s criteria. These criteria are highly specific and sensitive for the diagnosis of Infective endocarditis. Though the association of IE and pyelonephritis is not very well known, increasing number of case reports have shown correlation. In report by Loulergue et al. Recurrent episodes of pyelonephritis was found to be associated with underlying prosthetic valve infective endocarditis by Hafnia Alvei. The combined antibiotic therapy for six weeks was effective in treating the condition and there was no further relapse. These findings were further underscored by Micol et al whose study found E.coli bacteremia to be significantly associated with native valve endocarditis. The initial episode of pyelonephritis and the resultant enterococcal bacteremia is the most likely cause of the patient’s subacute IE. This led to recurrent episodes of pyelonephritis in the patient. The history of previous hospitalizations, the invasive
procedure (DJ stenting) also makes hospital acquired infection a likely possibility. The exact indication for DJ stenting was not clear from previous records, however this invasive procedure could have led to the enterococci bacteremia and subsequent IE.

Enterococcal IE is a leading cause of infective endocarditis specially in hospital acquired infective endocarditis. In a recent study by Francischetto et al, *E. faecalis* was responsible for 19% of hospital-acquired IE, and 57% of all hospital-acquired IE were in the native valve. Similar results were found in a study by Damasco et al, where *E. faecalis* attributed for 27.2% of hospital-acquired IE cases seconded only by *S. aureus* (32.5%). In this study, intravascular catheter was found to be the most likely source of infection. In a recent study by Dahl et al, similar values were seen. However, univariate analysis revealed that male sex, community-acquired bacteremia, unknown site of origin of infection and mono bacterial bacteremia were significantly associated with risk of IE. β- lactam antibiotics in combination with gentamicin are the cornerstone of therapy of enterococcal IE. In native valve endocarditis, 4-week of therapy is advised, however in the case of suspected penicillin resistance or long-standing IE (> 3 months) treatment is extended up to 6-week. Recent studies have advocated the short term (2- week) use of gentamicin to be as effective as prolonged therapy. Vancomycin based therapy is used only in cases of ampicillin intolerance. As our case had previously received penicillin group of antibiotics we started him on the vancomycin based regimen. Dramatic response to therapy in our case is likely attributable to the synergistic action of the vancomycin and gentamicin. The prolonged course of therapy led to the successful treatment of the patient.

Despite being a colonizer in the respiratory system, pneumonia is an infrequent manifestation of enterococcal bacteremia. Though the reason is not well understood, decreased isolation of the bacteria due to the widespread use of β-lactam antibiotics may be the reason. Bacteremia is the most likely cause of bilateral pneumonia in our case. Right sided infective endocarditis was not seen despite repeated investigations. The prompt response to therapy supports infection with similar bacteria.

To conclude, we had an atypical presentation of recurrent pyelonephritis with significant proteinuria and bilateral pneumonia. These resulted from native valve subacute enterococcal endocarditis. Upon initiation of therapy, the myriad manifestations resolved in almost 1-week and the patient is asymptomatic since. A high index of suspicion and knowledge of such conditions can guide reach a prompt clinical diagnosis. Importance of avoiding unnecessary medical interventions cannot be over emphasized. It also paves way for future research to assess the role of bacteria and association of these two distinct clinical diseases.

References


