

# Unusual Course of Infective Endocarditis: Acute Renal Failure Progressing to Chronic Renal Failure

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Infective endocarditis is an infection of the endocardium that usually involves the valves and adjacent structures. The classical fever of unknown origin presentation represents a minority of infective endocarditis. The presented case was a 21-year-old young lady presenting with acute renal failure and fever to the emergency room. Cardiac auscultation revealed a soft S1 and 4/6 apical holosystolic murmur extended to axilla. Echocardiography showed mobile fresh vegetation under the mitral posterior leaflet. She was diagnosed as having infective endocarditis. Hemodialysis was started with antimicrobial therapy. However, because of the presence of severe mitral regurgitation with left ventricle dilatation and large mobile vegetation, mitral prosthetic mechanical valve replacement was performed. Although treated with antibiotics combined with surgery, renal functions were deteriorated and progressed to chronic renal failure.

**Key words:** endocarditis ■ fever ■ renal failure

## INTRODUCTION

Infective endocarditis is lethal if not aggressively treated with antibiotics, combined or not with surgery. Developments in antibacterial therapy, clinical microbiology, cardiac imaging and cardiac surgery have revolutionized its diagnosis and prognosis. Despite improvements in healthcare, the incidence of disease has not changed over the past two decades.<sup>1</sup> Infective endocarditis is often classified in four categories: native-valve infective endocarditis, prosthetic-valve infective endocarditis, infective endocarditis in intravenous drug users, and nosocomial infective endocarditis. These categories delineate clinical conditions and distributions in microbial pathogens.<sup>1</sup>

Despite the decline in rheumatic heart disease worldwide and the use of antibiotic prophylaxis, there is no evidence that the incidence of infective endocarditis is decreasing. In fact, some data suggest it may be increasing. The classical fever of unknown origin presentation represents a minority of infective endocarditis cases today; thus, clinicians need to have a high index of suspicion in unusual presentations.<sup>2</sup> We present a case of infective endocarditis presenting in our emergency room as acute renal failure.

## CASE REPORT

A 21-year-old female patient was seen in the emergency room with complaints of dyspnea and lassitude. Her medical history was unremarkable except a complaint of flank pain for the last three months. She was seen in an outpatient clinic with a provisional diagnosis of nephritis 10 days prior to admission. Her biochemical investigations at that time were BUN: 20 mg/dL, Cr: 1.0 mg/dL, AST: 53 U/L, ALT: 24 U/L and T. Bil: 1.0 mg/dL. The urine analysis showed proteinuria, hematuria, and leukocyturia. Complete blood count revealed Hb: 6.9 g/dL, Htc: 21.8%, plt: 243 x 10<sup>9</sup>/L and WBC: 17 x 10<sup>9</sup>/L. Abdominal ultrasonography showed splenomegaly (145 x 65 mm). There was no renal abnormality, including the size, contour, echogenicity and parenchyma with good corticomedullary differentiation, and no sign of any

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obstructive process. Then, she was started antibiotic therapy (ciprofloxacin 500 mg bid).

On admission to emergency room of our university, the patient was dyspneic for the last three days. Epistaxis was noted a week ago that did not recur. She was also complaining of coughing, nausea, vomiting, dysuria, dizziness and sputum production for the last 10 days. At the emergency room, she had a fever of 39°C. Blood pressure was 149/79 mmHg and pulse rate was 128/min. She was pale on physical examination. Cardiac auscultation revealed a soft S1 and 4/6 apical holosystolic murmur extended to axilla. There was edema in her legs. Other physical examination findings were normal. Complete blood count revealed Hb: 2.8 g/dL, Htc: 9.1%, plt: 212 x 10<sup>9</sup>/L and WBC: 16 x 10<sup>9</sup>/L and MCV: 73.5 fL. Her biochemical investigations at that time were BUN: 119 mg/dL, Cr: 10.9 mg/dL, Na: 130 mmol/L, K: 5.8 mmol/L, Cl: 99 mmol/L, Ca: 8.7 mg/dL, uric acid: 10.2 mg/dL, AST: 16 U/L, ALT: 24 U/L, T. Bil: 1.0 mg/dL, ALP: 43 U/L, LDH: 500 U/L, T. protein: 7.4 g/dL, albumin: 2.0 g/dL, CPK: 28 U/L, and GGT: 10 U/L and erythrocyte sedimentation rate: 104 mm/h. Blood gas analysis was pH: 7.305, pO<sub>2</sub>: 101.2 mmHg, pCO<sub>2</sub>: 12.2 mmHg, HCO<sub>3</sub>: 6.1 and saturation: 96.3%.

She was hospitalized with a provisional diagnosis of acute renal failure to the internal medicine clinic. Hemodialysis was started and erythrocyte packs were given immediately. Because of fever, all of the routine cultures, including blood, urine, and sputum, were obtained. Echocardiography was planned because of the systolic murmur detected on physical examination to rule out infective endocarditis. Left atrium and left ventricle were dilated, mitral valve was thickened and fibrocalcific, and 3° mitral regurgitation was detected. Besides, a mobile fresh vegetation of 1.9 cm was observed under the mitral posterior leaflet in the atrial face. The left ventricular ejection was 56%. She received antimicrobial therapy with crystallized penicillin 3,000,000 U qid. Vancomycin 1 gm q48h and amikacin 1 x 500 mg were also added to the treatment schedule for covering both the streptococcal and staphylococcal microorganisms. Hemodialysis was performed three times a week. Blood culture revealed *Staphylococcus aureus*. Her fever subsided after appropriate treatment. However, because of the presence of severe mitral regurgitation with left ventricle dilatation and large mobile vegetation, mitral prosthetic mechanical valve replacement was performed 12 days later. There was 3-x-2 cm vegetation in the posterior leaflets of mitral valve reaching the annulus, which destroyed the mitral valve. After the operation, however, the renal impairment persisted and hemodialysis was continued.

She was discharged from the hospital in good health with coumadin treatment and hemodialysis three times a week. Two months later, she was seen in the outpatient clinic. Abdominal ultrasonography revealed that the sizes of both kidneys were decreased (right kidney: 75 x 25 mm and left kidney: 65 x 25 mm) with grade-2 echogenicity consistent with chronic renal failure. Control echocardiography revealed normal mitral valve functions, diffuse global hypokinesia, left ventricular ejection of 45%. Complete blood count revealed (normal reference ranges are given in parenthesis): Hb: 8.3 g/dL (11–18 g/dL), Htc: 0.23 (0.35–0.60), plt: 179 x 10<sup>9</sup>/L (150–450 x 10<sup>9</sup>/L), WBC: 7.5 x 10<sup>9</sup>/L (4.3–10.3 x 10<sup>9</sup>/L) and MCV: 93.6 fL (80.7–95.5 fL). Her biochemical investigations at that time were: BUN: 62 mg/dL (10–50 mg/dL), Cr: 4.8 mg/dL (0.4–1.2 mg/dL), AST: 38 U/L (8–38 U/L), ALT: 86 U/L (8–41 U/L), T. Bil: 1.2 mg/dL (0.3–1.1 mg/dL), LDH: 727 U/L (240–480 U/L), T. protein: 9.6 g/dL (6.2–8.7 g/dL), albumin: 3.5 g/dL (3.4–5.5 g/dL) and erythrocyte sedimentation rate: 38 mm/h (1–18 mm/h).

## DISCUSSION

In infective endocarditis, the primary event is the bacterial adherence to heart valves, which is completed within minutes during transient bacteremia, and involves valve tissue and bacterial factors. The second step involves persistence and growth of bacteria within the cardiac lesions, usually associated with local extension and tissue damage. Dissemination of septic emboli to distant organs—e.g., kidney, spleen and brain—then takes place.<sup>1</sup> Despite advances in diagnosis and treatment, infective endocarditis still carries a high morbidity and mortality rate.<sup>3</sup> In the presented case, delayed diagnosis and treatment of infective endocarditis resulted in chronic renal failure, which is rarely observed. Therefore, an acute renal failure presentation in the initial diagnosis of infective endocarditis may be the sole manifestation of an iceberg.

The organisms most frequently responsible for infective endocarditis are those that have the greatest ability to adhere to damaged valves, especially in the setting of rheumatic valve disease. Together, *S. aureus*, *Streptococcus* spp and *enterococci* are responsible for >80% of all instances of disease.<sup>1</sup> *S. aureus* is one of the major cause of infective endocarditis in all population groups. *S. aureus* infective endocarditis is characterized by highly toxic febrile illness, frequent focal metastatic infection and a 30–50% rate of congestive heart failure and systemic embolization. In excess of 90% of *S. aureus* cases, whether acquired in the hospital or community, produce beta-lactamase and thus are resistant to penicillin and ampicillin.<sup>4</sup>

Surgery is necessary in 25–30% of cases during

acute infection and in 20–40% in later phases. The main indications for surgery comprise refractory cardiac failure caused by valvular insufficiency, persistent sepsis caused by a surgically removable focus or a valvular ring or myocardial abscess, presence of >1-cm mobile vegetation and persistent life-threatening embolization.<sup>1</sup> Prognosis is better if surgery is performed before cardiac pathology develops and the general condition of the patient severely deteriorates. In the presented case, the indication for surgery is the severe mitral regurgitation with left ventricular impairment and the persisted mobile large vegetation despite treatment.

The underlying etiology, leading to a rapidly progressive renal impairment, might be due to an immune complex glomerulonephritis since a bilateral renal involvement might hardly be due to renal emboli. The use of nephrotoxic agents and cardiac surgery may also contribute to the progression of acute renal failure. The absence of a nephrotoxic drug usage and contrast agent or a medical history related to a possible renal impairment previously makes the diagnosis more clear. The indication for a renal biopsy was quite evident to understand the cause of renal impairment and to guide the treatment in the presented case. However, the findings in the abdominal ultrasonography after intensive antibiotic treatment and surgery were consistent with chronic renal failure. In patients with chronic renal failure, the biopsy is contraindicated for cases where the thickness of the cortical section of the kidney is lower than 8–10 mm because of possible technical difficulties and lower diagnostic information due to sclerosis and higher risk of complications.

Not a definitive but a possible diagnosis of infective endocarditis can be made with three minor criteria at the initial presentation. In the presented case, those criteria were possible glomerulonephritis, cardiac murmur and fever. However, any patient suspected of having native valve endocarditis by clinical criteria should be screened by echocardiography as in the presented case.

There are a few cases in the literature reporting an infective endocarditis presenting with renal failure. Lopez Garcia et al.<sup>5</sup> reported a case of infective endocarditis presenting with acute renal failure and leukocytoclastic vasculitis. Masuda et al.<sup>6</sup> reported an infective endocarditis case presenting with macroscopic hematuria, marked anemia, leukocytosis and azotemia. After the antimicrobial treatment, renal failure gradually disappeared. They considered the cause of renal manifestations to be an immune complex glomerulonephritis. Martinez-Costa et al.<sup>7</sup> described a 27-year-old intravenous drug addict (IVDA) patient with tricuspid endocarditis caused by *S. aureus* whose first manifestation was an acute

renal failure. It was treated with antibiotics and hemodialysis, obtaining normal levels of plasma creatinine. However, the presented patient was not an IVDA and the antibiotic treatment combined with surgery did not lead to an abstinence from hemodialysis by progressing to chronic renal failure.

Conlon et al.<sup>8</sup> reported that one-third of the patients developed acute renal failure in a retrospective chart review of 204 consecutive episodes of definite bacterial endocarditis and the presence of acute renal failure increased the odds (OR) of dying by 5 ( $p=0.0001$ ). Age and thrombocytopenia were independent risk factors for developing acute renal failure. They also concluded that patients who developed acute renal failure as a result of septic syndrome or following cardiac surgery had a higher mortality when compared to other causes of acute renal failure. In another study, multivariate analysis showed that presence of acute renal failure on admission was the single independent greatest risk factor for a fatal outcome. Thirteen (39%) patients out of 33 patients with infective endocarditis admitted to the intensive care unit were found to have acute renal failure.<sup>9</sup> Miyake et al.<sup>10</sup> also reported a recent case of renal failure that developed as an initial manifestation of infective endocarditis. The authors emphasize that renal failure necessitating hemodialysis is not generally recognized as a complication of infective endocarditis. They suggest that uremia can develop as an initial manifestation of infective endocarditis, and removal of an infected heart valve can improve renal function despite persistent renal failure.

The presented case is interesting in various parts: a) infective endocarditis is still surprising and needs high suspicion, b) it should be considered early in every patient with fever or septicemia and cardiac murmurs, c) early diagnosis of infective endocarditis may prevent complications and may be life-saving, d) renal impairment may be the sole manifestation of infective endocarditis, e) the acute impairment of renal functions will end up with a diagnosis of chronic renal failure and hemodialysis may be the final outcome.

In summary, acute admission with impairment of renal function should raise a suspicion of infective endocarditis since it might be the first manifestation of the disease. If the diagnosis is delayed or appropriate therapeutic measures postponed, morbidity and mortality are still high.

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