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Subacute bacterial endocarditis with vasculitis-like presentation; report of a case and literature review

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ABSTRACT

Infective endocarditis is a diagnostic challenge since it could manifest as a systemic disease mimicking rheumatologic disorders by immunological mechanisms. We introduced a case of infective endocarditis which was a 62-year-old man who presented with weakness, weight loss, myalgia, arthritis, petechiae, hematuria and proteinuria and was admitted by a rheumatologist for evaluation of possible vasculitis.

Keywords: Infective endocarditis, Vasculitis, Post-infectious glomerulonephritis

Case Report

Implication for health policy/practice/research/medical education:
Infective endocarditis is sometimes a challenging and misleading diagnosis, so that we should be aware of uncommon presentations of this disease. Here, we described an unusual case of infective endocarditis with vasculitis like presentations since no fever or defined risk factors were existed. Therefore, infective endocarditis should be considered in differential diagnosis of vasculitis like syndromes.

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Introduction

Infective endocarditis is a life-threatening and serious infection which presents in acute and subacute forms since it has high morbidity and mortality despite major improvements in medical and surgical approaches (1-3). Native valve infective endocarditis remains a diagnostic challenge with nonspecific signs and symptoms owing to extensive use of antibiotics and underlying conditions particularly in old patients (4,5). The most common pathogens are *Staphylococcus aureus* which causes acute endocarditis, while *Streptococcus viridans* leads to subacute bacterial endocarditis (SBE) (6).

Here, we report a case of SBE who had nonspecific clinical presentations associated with rheumatologic and renal findings with a delay in diagnosis.

Case Report

A 62-year-old man presented to Shariati hospital with dyspnea, lower limb edema and skin lesions. The patient was healthy with an unremarkable medical history until six months earlier when he gradually began to feel unwell associated with weakness, loss of appetite and weight loss (10 kg weight loss in six months period). He was referred to a gastroenterologist because of anemia and weight loss (hemoglobin level was 11.3 g/dL with MCV of 84fl). Upper gastrointestinal endoscopy was undergone which showed severe erosive gastritis and positive for *H. pylori*. His colonoscopy was normal. He was treated by proton pump inhibitors and drugs for *H. pylori* eradication.

Despite that, his condition was going worse until he suddenly started having arthralgia and non-tender, non-palpable and without blanchable erythema erythematous lesions in both legs (Figure 1). Then the patient was admitted by a rheumatologist for further investigation. On admission, his main complaints were weakness, weight loss, arthralgia and skin rashes but no chills and fever. His physical examination had revealed almost normal vital signs, paleness, weak systolic murmur, palpable spleen, pedal edema and skin rashes on his legs. A whole laboratory investigations revealed severe normocytic anemia (hemoglobin level; 6.8 g/dL and reticulocytes; 0.9%), a normal leucocyte (9230/µL) and platelet (225 000/µL) counts with normal LDH level (437 IU/l), slight increase in serum creatinine (1.6 mg/dL), severely

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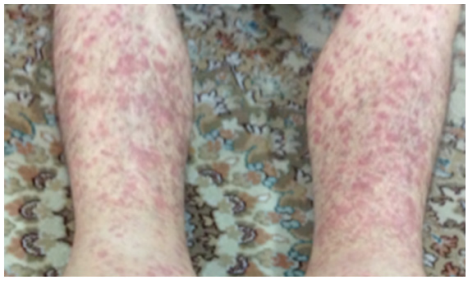

Figure 1. Petechial rashes of the patient diagnosed for subacute bacterial endocarditis.

increased erythrocyte sedimentation rate (138 mm/h) with mildly rise in C-reactive protein (17.5 mg/L). All serology of vasculitis and collagen vascular diseases were normal (FANA, anti-dsDNA, anti-myeloperoxidase and anti-proteinase 3) except for rheumatoid factor level (256 IU/mL) and slightly decreased complement level (C3; 72 mg/dL and C4; 10 mg/dL). Viral markers (hepatitis B and C and HIV) were negative. Serum iron level was low (25 mcg/dL) with normal level of transferrin (247 mg/dL) and high levels of ferritin (704 ng/mL). Report of urinalysis was as follows; specific gravity of 1005, protein; +1, blood; +4, RBC; many (30% dysmorphic), WBC; 5-8. Sub-nephrotic proteinuria was reported in 24-hour urine (protein; 2640 mg with creatinine of 1090 mg and volume of 2400 cc).

Chest X-ray and abdominopelvic ultrasound were reported normal (except for mild cardiomegaly). CT scanning was positive for mild bilateral pleural effusion, cardiomegaly with mild pericardial effusion, and mild hepatosplenomegaly with hypodense lesions in spleen compatible with old infarcts. Transthoracic echocardiography, which has been conducted by on-call cardiology resident, was reported about normal.

Serum protein electrophoresis, which had been done because of high ESR and anemia, had revealed hypoalbuminemia (2.6 g/dL) and hypergammaglobulinemia (1.5 g/dL) with no spike. Because of clinical features of peripheral neuropathy, electromyography with nerve conduction velocity (EMG-NCV) and sural nerve biopsy had been performed with evidence of subacute axonal sensorimotor polyneuropathy and bilateral ulnar neuropathy, however sural nerve biopsy was reported about normal.

Diagnosis had been still in doubt despite these extensive works-up, so that on consultation with a nephrologist, kidney biopsy was performed. Finally, he was discharged on tapering prednisolone with possible diagnosis of vasculitis, while waiting for result of kidney pathology.

One week after discharge, he came to nephrology clinic because of progressing dyspnea without any cough or hemoptysis and worsening lower limb edema. On

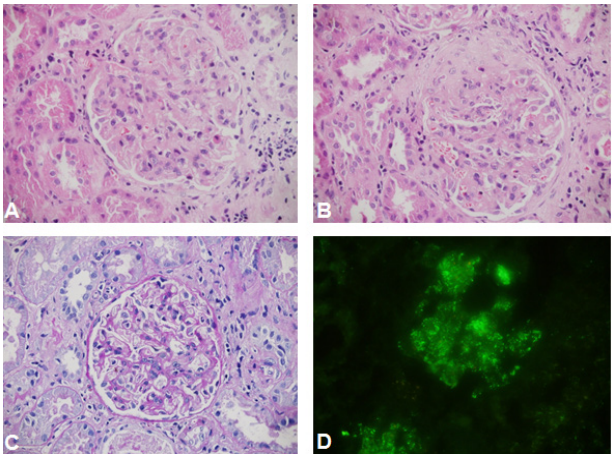

Figure 2. Kidney pathology of the patient diagnosed for subacute bacterial endocarditis, presenting focal proliferative and sclerosing glomerulonephritis on light microscopy (A, B, and C); and starry sky pattern with granular deposition of IgG and C3 in mesangial and capillary wall on immunofluorescence microscopy (D) compatible with post-infectious glomerulonephritis.

examination he was oriented, ill and afebrile. His vital signs were as followings; temperature of 37°C, blood pressure of 140/70 mm Hg, PR: 100 beats/min, and RR of 32/min. He had orthopnea and elevated jugular venous pressure with fine crackles in both lungs and a 3/6 systolic murmur at apex and also generalized edema. His skin rashes were disappeared. Other examinations were unremarkable except for mild splenomegaly and clubbing. Kidney pathology was described as a focal proliferative and sclerosing glomerulonephritis on light microscopy, and starry sky pattern with granular deposition of IgG and C3 in mesangial and capillary wall on immunofluorescence microscopy compatible with post-infectious glomerulonephritis (Figure 2). Electron microscopy revealed minimal effacement of the foot processes, subendothelial and mesangial electron dense deposits, segmental endocapillary proliferation, and segmental duplication of the GBM.

After admission, blood was taken for routine laboratory works and cultures. Because of serum creatinine of 5.2 mg/dL and volume overload hemodialysis was commenced. Empirical antibiotics were instituted and prednisolone was tapered off to 15 mg/d. Transthoracic echocardiogram and transesophageal echocardiography revealed severe mitral regurgitation with multiple highly mobile masses attached to mitral valve compatible with endocarditis, since one of three blood cultures was positive for *S. viridans*. The complete description of echocardiography was as follows; mitral valve is myxomatous and prolaptic with flail P2 scallop and severe anterior directed mitral regurgitation. There are multiple highly mobile masses attached on atrial surface of anterior mitral leaflet and

posterior mitral leaflet which the largest one was 2×0.9 cm consistent with vegetation based on clinical history. There was also moderate left ventricular enlargement, moderate to severe pulmonary artery hypertension (PAP; 63 mm Hg) and mild pericardial effusion.

In 3 weeks the patient serum creatinine declined to 1.4 mg/dL and surgical replacement of the mitral valve was successfully performed. After 5 weeks, he was discharged in a fairly good condition. In the last follow-up visit (three years later), he still was healthy and on warfarin therapy.

Discussion

Annual incidence of infective endocarditis is estimated to be 3 to 9 cases per 100 000 persons in developed countries (6,7). Infective endocarditis is nearly 2.5 times more common in males than females (8,9). Nowadays, because of a decrease in the incidence of rheumatic valvular disease and an increase in percentage of old patients with more degenerative valvular disease, more than half of infective endocarditis is happening in patients older than 50 years (9). In-patient mortality rate of infective endocarditis is 15-22% with a 5-year mortality of around 40% (4,8,11,12).

Infective endocarditis is usually diagnosed by 1) clinical manifestations such as heart failure and new or changing murmurs; presence of micro or macro-emboli like focal neurologic deficits and pulmonary, splenic, and renal infarcts; cutaneous or mucocutaneous lesions including petechiae, Janeway lesions, Osler's nodes, splinter hemorrhages, and Roth spots; systemic immune responses such as arthritis and glomerulonephritis, 2) microbiologic studies (particularly persistent bacteremia in 2-3 sets of blood cultures), and 3) echocardiographic findings (combined transthoracic and transesophageal echocardiography reveals vegetations in more than 90% of cases) (4, 13). High titer of rheumatoid factor (50% positive in SBE) and classic pathway hypocomplementemia (C3 and C4) associated with glomerulonephritis are part of minor Duke Criteria for infective endocarditis diagnosis.

Clinical course of SBE is frequently indolent. Alpha-hemolytic streptococci of viridans streptococci (50%-60% of cases), *Streptococcus bovis*, and enterococci are the prevailing involved microorganisms. The underlying predisposing condition is usually routine activities of brushing teeth and bowel movements which lead to bacteremia. The early clinical manifestations of SBE are mostly nonspecific including weakness, anorexia, weight loss, abdominal symptoms, flue-like syndromes, headache, and low-grade fever (which is absent in 3 to 15% of cases). Embolic or immunologic clinical manifestations are developed if the diagnosis and treatment of SBE is postponed. The risk of embolization is much more common when the mitral valve is involved. Arthritis is immunologically mediated synovitis which usually implicates 1 to 3 joints in an asymmetrical pattern. Splenomegaly and clubbing is another feature of long-established SBE (14-19).

Immune complex-mediated glomerulonephritis, antibiotic-induced acute interstitial nephritis, acute tubular necrosis, and renal infarction due to embolic diseases are the renal manifestations associated with infective endocarditis. Histologic findings of extensive subendothelial and subepithelial immune complex depositions associated with capillary wall thickening are appreciated because of the longer duration of antigenemia. Variable degrees of hematuria, RBC casts, proteinuria sometimes associated with nephrotic syndrome, hypertension, and renal failure are common clinical findings (15,20,21).

The most common indications for surgery are congestive heart failure (resistant to standard medical therapy), a second relapse during or after completion of treatment, and severe mitral or aortic regurgitation with evidence of abnormal hemodynamics (22,23).

In-hospital mortality is less than 10% among patients with streptococcal, left-sided, native-valve infective endocarditis. Outcomes of patients with timely surgery intervention are usually favorable. Moderate to severe heart failure, perivalvular abscess, cerebrovascular and embolic events, and *S. aureus* infection are predictors of short-term mortality. Recurrent infection and old age have adverse impacts on long-term outcomes (4,6,8).

Conclusion

Here, we sought to emphasize the diagnostic challenge of infective endocarditis, because it could present as a multisystem fashion and mimics other systemic diseases particularly vasculitis. Some interesting points in this patient are absence of fever, no known underlying heart disease, no previous intervention leading to bloodstream infection, multisystem manifestations, and immunological involvements of skin (petechiae), musculoskeletal (myalgia and arthritis) and kidney (glomerulonephritis). There was high titer of rheumatoid factor and typical renal pathology of post-infectious glomerulonephritis. The patient also had scanty old embolic infarct of spleen. As noted, these non-specific presentations led to the treatment of patient by different subspecialists while they had no definitive diagnosis. Therefore, we should consider SBE as an important differential diagnosis of patients who have multisystem manifestations.

Authors' contribution

HK as visiting rheumatologist collected some history of the patient and helped to prepare the primary draft. TS completed both history of the patient and draft. TS also edited the final draft.

Conflicts of interest

The authors declared no competing interests.

Ethical considerations

Ethical issues including plagiarism, double publication, and redundancy have been completely observed by the authors. The patient gave his consent to publish as a case report.

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