The Valvular Involvement of Lupus: Congestive Heart Failure Can Be The Presenting Feature of Systemic Lupus Erythematosus

Leonard Wei-Ren Lan, Cheng-Ting Tsai and Charles Jia-Yin Hou

Valvular heart disease is the most important cardiac manifestation of systemic lupus erythematosus (SLE). However, severe mitral valve regurgitation necessitating valvular surgery due to SLE is rare. We report a 22-year-old male patient presenting with symptoms of congestive heart failure initially in whom lupus and severe mitral valve regurgitation were diagnosed. In our patient, four of the American College of Rheumatology diagnostic criteria for SLE were present, including serositis, hematological abnormalities, positive ANA (640X), and positive double-stranded DNA (640X). This patient eventually underwent mitral valve surgery with good clinical results. Pathological examination of the excised mitral valve leaflet showed degenerated valve with chronic inflammatory cell infiltration which was consistent with Libman-Sacks endocarditis. It serves as a reminder that SLE (even in a male patient) may be an underlying cause for the development of severe mitral valve regurgitation.

INTRODUCTION

Valvular involvement is the most frequent cardiac manifestation in systemic lupus erythematosus (SLE). It has been shown that the prevalence of valvular disease in SLE can be up to 60-74% by transesophageal echocardiography (TEE). We herein describe a patient whose initial presentation of SLE was signs of congestive heart failure such as dyspnea on exertion and orthopnea due to severe mitral regurgitation rather than musculoskeletal or mucocutaneous presentations.

CASE REPORT

A 22-year-old man of well-controlled bronchial asthma came to our outpatient clinic in HsinChu in January 2003 due to sudden onset of intermittent chest pain with subsequent dyspnea and orthopnea for 3 days. Systemic blood pressure was 120/70 mmHg, and body temperature was 36.7 °C. Physical examination revealed no facial malar rash or generalized discoid rashes. The breath sounds at the lower left lung were decreased. Cardiac auscultation showed regular heart beat with a heart rate of 92 beats/min, a grade III/VI systolic murmur at the left lower sternal border and the apex, and a pericardial friction rub. Palpation of the abdomen showed neither splenomegaly nor hepatomegaly. The extremities were notable for mild pitting edema. There was no clubbing, cyanosis or deformity of joints. Neurologic examinations were unremarkable.

Electrocardiogram showed sinus rhythm. The chest x-ray revealed flask-shaped cardiac shadow, left pleural effusion and pulmonary edema. The electrolyte panel was

within normal limits. The patient's albumin was 2.9 mg/dL. Liver function test and renal function were unremarkable. Urinalysis showed no proteinuria, and the 24-hour urine collected showed daily protein loss of 0.15 gm/day. The complete blood count revealed white blood count 5120/uL without any left shift, hemoglobin 9.6 gm/dL, hematocrit 30.0%, mean corpuscle volume (MCV) 84.8 fl and platelets 116,000/uL. The coagulation parameters were normal.

A transthoracic echocardiogram demonstrated large amount of pleural effusion and moderate amount of pericardial effusion, with some fibrin formation in the pericardial space. The posterior mitral leaflet bulged into the left atrium during the systolic phase (Figure 1a). Color Doppler showed a severe eccentric mitral regurgitation jet toward the left atrial posterior wall (Figure 1b). An ejection fraction of 71% with good left ventricular systolic performance was noted.

Diagnostic thoracentesis revealed exudative effusion with no evidence of tuberculosis from culture and polymerase chain reaction. In addition, no microorganism was isolated from the four consecutive sets of blood culture.

Lupus work-up showed that there was a positive antinuclear (640X) and anti-double-stranded DNA antibody (640X), and low C3 and C4 levels. Antiphospholipid syndrome testing (lupus anticoagulants and anticardiolipin antibodies) was negative.

The patient was initially treated with angiotensin-converting enzyme inhibitor (captopril 25 mg Tid) and diuretic until SLE was diagnosed, when high-dose oral prednisolone (60 mg daily) was added.

A transthoracic echocardiogram was repeated 1 month later showing moderate pulmonary hypertension with estimated systolic pulmonary artery pressure of 48 mmHg. In addition, a transesophageal echocardiogram was performed at the same time, where heterogenous echogenic vegetations of variable size without independent movements were seen on the mitral and tricuspid valves (Figure 2). The posterior mitral leaflet was thickened, immobile and destroyed.

The patient was then treated with oral prednisolone (30 mg daily) for the vegetations, which were suspected caused by Libman-Sacks endocarditis, and ACE inhibitor and diuretic for symptoms of acute heart failure. No antibiotics were prescribed, since there was no toxic sign or evidence of infection clinically. Cardiac catherization on 17th February 2004 revealed normal coronary angiogram, elevated pulmonary capillary wedge pressure (28 mmHg) and left ventricular end-diastolic pressures (mean 30 mmHg). There was no pressure gradient across the aortic valve. Left ventriculography demonstrated normal left ventricular systolic function with severe mitral regurgitation. Consequently, operative replacement of the mitral valve was initiated. During the surgery, the anterior and posterior mitral leaflets were observed to be totally destructed (Figure 3). The subvalvular apparatus was thickened, but the annulus was intact and normal. There was dense pericardial and pleural adhesion.

Pathological examination of the excised mitral valve leaflet showed degenerated valve with chronic inflammatory cell infiltration, which was consistent with
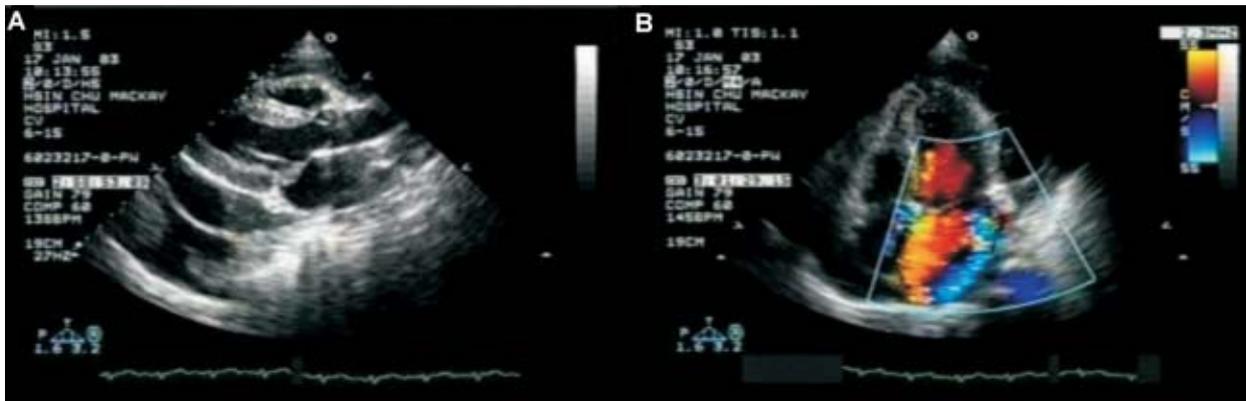

Figure 1. *Transthoracic echocardiography obtained on admission. In a parasternal long-axis view (A), an echolucent space posterior to the LV posterior wall and pericardium, fibrinous stranding within the echo-free space and late systolic displacement (bowing) of mitral leaflets toward the left atrial side are shown. An apical four-chamber view (B) showed eccentric mitral regurgitation jet toward the left atrial posterior wall.*

Libman-Sacks endocarditis (Figures 4A and 4B)

The postoperative course was uncomplicated, and the patient remained free from symptoms of heart failure
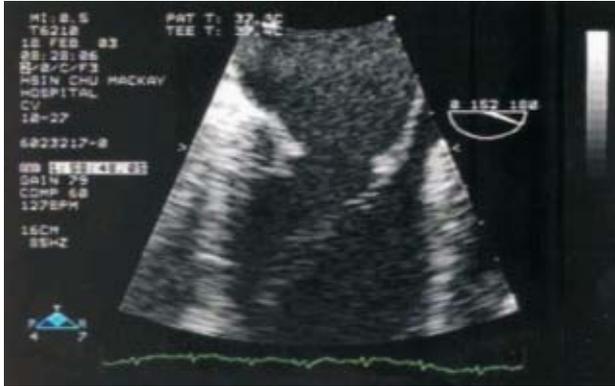

Figure 2. *A transesophageal echocardiography before valve replacement: Echogenic masses of variable size on the mitral valve.*
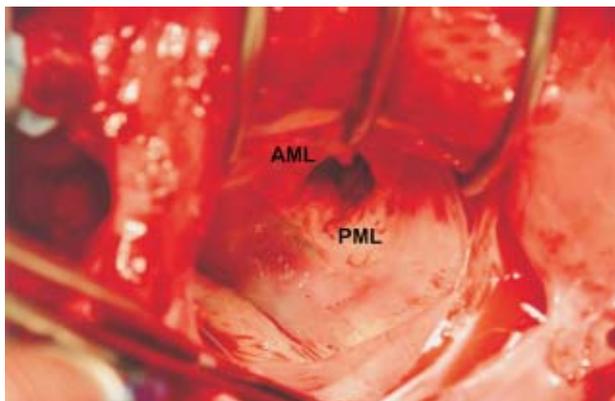

Figure 3. *Gross morphology of the excised mitral valve. Totally destroyed mitral valve including anterior mitral leaflets (AML) and posterior mitral leaflets (PML).*

2 months later. Oral steroids had been tapered to 10 mg daily. The follow-up echocardiograms showed preservation of left ventricular function with only trivial mitral regurgitation.

DISCUSSION

Systemic lupus erythematosus (SLE) is an autoimmune disease that primarily affects young women. The diagnosis of SLE requires four or more of the American College of Rheumatology criteria. In our patient, the diagnosis of SLE was based on the following criteria: serositis, haematological abnormalities, positive ANA, and positive double-stranded DNA.

In patients with SLE, the clinical expression of the musculoskeletal and mucocutaneous disease predominates, even in patients with cardiovascular disease.[1] However, in our case, there were no musculoskeletal and mucocutaneous presentations clinically. He had in fact presented with symptoms of congestive heart failure, which was the sequela of severe mitral regurgitation. According to the literature, the prevalence of cardiovascular involvement in patients with SLE has been estimated to be more than 50%. Valvular involvement is the most commonly encountered form of heart disease in SLE. Thickening of the valves is encountered more frequently (51~52%) than valve masses/vegetations (34~43%).[2] Functionally, valvular regurgitation has been reported to occur in up to 74% of patients, 7~41% of cases having moderate or severe regurgitation, while
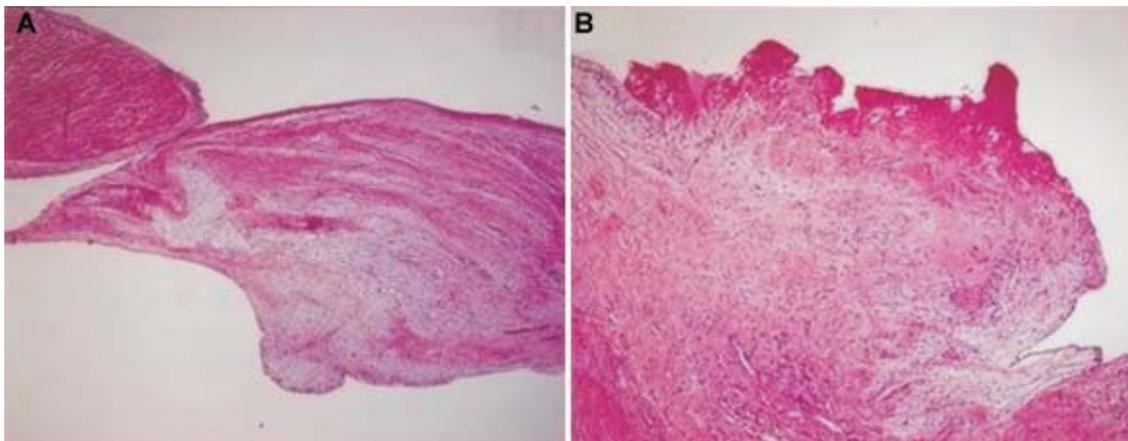

Figure 4. *Photomicrography of the excised mitral valve: (A) Degeneration with an increase of myxoid connective tissue. (Hematoxylin-eosin stain, 20X). (B) Fibrin deposition on the surface of the valve which may be consistent with disrupted vegetation.*

valvular stenosis is seen in only 3~4% of patients and usually accompanies regurgitations. Involvement of the mitral valve is most frequently encountered. However, any valve or multivalvular affection may occur.[3]

The most classic cardiac valvular abnormality in patients with SLE is known as Libman-Sacks endocarditis, which consists of noninfective, verrucous vegetations (marantic endocarditis). They occur most frequently on the mitral valve. The verrucae are generally small (1~4 mm in diameter), cauliflower-like or flat, red-colored and can be multiple.[1-3] Most of the valves that have vegetations are usually associated with diffuse thickening or regurgitation.

The mechanism for the development of valvular damage in SLE is not completely understood. It is thought that immune complex deposition and complement activation cause acute, chronic or reccurent inflammation of the valve leaflets.[4,5] These processes can lead to valvular regurgitation, stenosis or both. Such hypothesis is in fact proven in our patient, where severe destruction of the mitral valve was seen during surgery. The microscopic examination of the excised mitral valve showed degenerated mitral valve with chronic inflammatory cell infiltration and fibrin deposition on the surface of the valve which was consistent with disrupted vegetation. However, several studies have suggested that antiphospholipid antibodies can also contribute to the pathogenesis of the valvular disease.[6]

Transesophageal echocardiography is the modality of choice for detecting valvular involvement in SLE, but a definitve diagnosis can be made only on pathologic examination of affected tissue.[1] Libman-Sacks vegetations are described on TEE as being usually smaller than 1 cm^2, with irregular borders, heterogenous echogenecity and no independent movement. In contrast, infective vegetations have a homogenous echogenecity, and present with vibratory or rotary motion independent of leaflet motions.

Treatment of valvular manifestations of SLE depends on the type and severity of involvement. Some investigators have suggested that the introduction of corticosteroids as treatment of SLE may have decreased the frequency.[7] However, Bulkley and Roberts stated that corticosteroid therapy may lead to healing of the verrucous lesions, with subsequent scarring and shortening of the posterior mitral valve leaflet and chordae tendinae, increased adherence to the endocardium, and valvular insufficiency.[3,8]

Our patient had undergone valve replacement due to hemodynamically significant valvular dysfunctions. Review of the literature has shown that mitral valve replacement is superior to valve repair in patients who have SLE.[9] Outcome is good in most patients who have undergone successful valvular surgery, but it should be noted that an increased perioperative mortality (up to 25%) and recurrent valvulitis on bioprosthetic valves have also been reported.

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全身性紅斑性狼瘡可以以鬱血性心臟衰竭來表現

藍偉仁　蔡政廷　侯嘉殷

台北市　馬偕紀念醫院　心臟內科

辦膜性心臟病是紅斑性狼瘡最重要的心臟表現，然而因為紅斑性狼瘡造成需要開刀的嚴重二尖辦閉鎖不全很少見。我們報告一個 22 歲的男性病患一開始是以鬱血性心衰竭的症狀表現，而最終是診斷為紅斑性狼瘡併二尖辦閉鎖不全。這個病人符合四個 American College of Rheumatoloy 的診斷準則包括漿膜炎，血液學異常，陽性抗核抗體 (ANA:640X)，陽性雙螺旋脫氧核糖核酸 (anti-dsDNA:640X)。這病人後來接受了二尖辦手術且結果不錯。切除的二尖辦病理學上的檢驗呈現退化性且發炎細胞浸潤的辦膜，符合 Libman-Sacks 心內膜炎的診斷。這個病例提醒我們，紅斑性狼瘡 (即使對男性病患) 也是造成嚴重二尖辦閉鎖不全的其中一個可能原因。

關鍵詞：全身性紅斑性狼瘡、辦膜性心臟疾病、辦膜置換術。