Systemic Lupus Erythematosus (SLE) is an autoimmune collagen vascular disease, which produces widespread damage to multiple organs. The spectrum of cardiac vascular involvement in young SLE is not elucidated completely. This report mainly describes a 27 year old girl with 20 year history of SLE presenting with both AMI (acute myocardial infarction) and PAH. Coronary angiography shows stenosis in LAD (left anterior descending artery), and occlusion in LCX (left circumflex artery). The right heart catheterization showed elevated pulmonary artery pressure (93/32/57 mmHg); acute vasoreactivity testing was negative to adenosine. Prothrombotic conditions such as homocysteine, anti-cardiolipin antibody, lupus anticoagulant levels were all normal. This is the first case that CAD and PAH happened together in one lupus patient in literature reported.

Keywords: Systemic lupus erythematosus; Myocardial infarction; Coronary artery disease; Pulmonary arterial hypertension

Introduction

Systemic Lupus Erythematosus (SLE) is a chronic inflammatory autoimmune disease that predominantly affects young women. It involves multiple organ systems, such as kidney, skin, and central nervous system. Coronary Artery Disease (CAD) is a potentially fatal complication of SLE [1]. Despite the published data, there remains limited awareness of this increased cardiovascular risk in SLE patients. Moreover, there are some reports that mentioned Pulmonary Arterial Hypertension (PAH) is the most ominous complication of collagen vascular diseases and its diagnosis and treatment has been a big challenge to clinicians. This report mainly describes a 27 year old girl with 20 year history of SLE presenting with both AMI (acute myocardial infarction) and PAH. After the prednisone and immunosuppressive drug treatment, combined with anticoagulation, antiplatelet, and vasodilator therapy the patient gained dramatic clinical improvement.

Presentation of Case

A 27-year-old girl with a 20 year history of SLE was admitted with acute chest pain for 34 hours. She had malar erythema, ulcer and alopecia 20 years ago. Her laboratory test showed thrombocytopenia, ANA (antinuclear antibody) positive (speckle 1:160), elevated anti double stranded DNA levels, then she was diagnosed as SLE based on the American College of Rheumatology’s criteria, and prescribed prednisone. Her symptom relieved and the treatment stopped. 13 years ago, she had cough and chest pain, X-ray showed lung infection and pleural effusion, after antibiotic therapy, her chest pain improved. However she began to have acuteness of vision, headache, restlessness, lumbar puncture showed elevated pressure (230 mm H2O), there were no evidence of central nervous system infection after the analysis of CSF (cerebrospinal fluid), so she was diagnosed NPSLE (Neuropsychiatric Systemic Lupus Erythematosus). Dosage of the glucocorticoid increased to 1 mg/kg again, cyclophosphamide and azathioprine were used, symptom of nervous system gradually relieved. 8 years ago, because of severe edema, large amount of protein in urine (10.95 g/d), hypoprotenemia (17.8 g/L), she had renal biopsy. The pathology was V type lupus nephritis. She used Mycophenolate Mofetil (MMF) 2 g/day, prednisolone 1 mg/kg, and decreased to 10 mg/day gradually within six months. She was a cigarette smoker and had the history of hyperlipidemia. There was no history of angina, hypertension and diabetes mellitus.

In May, 2009, the girl felt acute sustaining chest pain of 34 hours duration and she was admitted to the emergency department. Her chest radiography was no effusion and infarction. We attributed her chest pain to pleuritis according to her history, but after usage of antibiotics, her chest pain did not relieve. Her electrocardiogram showed 1mm ST segment depression in leads II, III, avF, T wave inversion in lead V1-V4, and there are small Q wave in lead V7, V8, V9. There were also increased levels of creatine kinase isoenzyme MB 170 ng/ml (N<5), cardiac-specific troponin I 11.76 ng/ml (N=0-0.5). Ultrasonogram detected hypokinesia in posterior segments of the left heart. At that time, the echocardiography showed right atrium and right ventricular enlargement, pulmonary hypertension and mild atrial septum defect. Then she was transferred to ward with the diagnosis of acute myocardial infarction.

Her laboratory analysis was significant for hyperlipidemia, cholesterol 8.81 mmol/l (N=3.4-5.2), LDL cholesterol 5.51 mmol/l (N=2.1-3.1). Her serum albumin level was 24.3 g/l, level of protein in urine was 6 g/d. Serum urea and creatinine levels were normal. The other laboratory findings were as follows: erythrocyte sedimentation rate 58 mm/h, C-reactive protein 67.4 mg/l, antinuclear antibody positive, anti-double stranded DNA positive (IIF 1:10, ELISA 103 IU/ml), C3 0.74 g/L (N=0.6-1.5), C4 0.14 g/L (N=0.12-0.36). Other prothrombotic conditions such as homocysteine, anti cardiolipin antibody, lupus anticoagulant levels were all normal. Her chest radiography showed significant bulging in pulmonary artery segment (Figure 1). Computed Tomography (CT) scan of the chest showed a markedly enlarged main pulmonary artery with a diameter of 4.4 cm (Figure 2). No signs of pulmonary embolism detected in CT pulmonary angiogram and pulmonary ventilation perfusion scan.
She was diagnosed as having active SLE for SLEDAI (systemic lupus erythematosus disease activity index) was 27, and prescribed prednisolone 1 mg/kg after pulse methylprednisolone (three times), cyclophosphamide 1g per month, low molecular heparin, clopidogrel, pravastatin, and isosorbide dinitrate were used. After her chest pain was disappeared, she had coronary angiography and the right heart catheterization. There were 80% stenosis in LAD (Left Anterior Descending Artery), and occlusion in LCX (Left Circumflex Artery) (Figure 3). The right heart catheterization showed elevated pulmonary artery pressure (93/32/57 mmHg), pulmonary capillary wedge pressure was normal, and the pulmonary arteriolar resistance was 11 Wood units, acute vasoreactivity testing was negative to adenosine. There was no evidence of intra cardiac shunt by oximetry. We did not perform percutaneous coronary intervention for the active lupus. Warfarin were used as anticoagulants and bosentan (125 mg per day) to reduce the PA pressure.

Prednisolone decreased to 10 mg/day gradually within six months. In October 2009, the patient admitted to our hospital again for reevaluation the heart disease. Electrocardiogram and cardiac enzyme levels were normal. Coronary angiography showed recanalization in LCX, and still 80% stenosis in LAD (Figure 4), and the pulmonary artery pressure did not changed obviously (79/34/54 mmHg). Decision was made to proceed with PCI (Percutaneous Coronary Intervention), and 3 stents were placed in the coronary artery.

She has remained stable, asymptomatic without complications and normal renal function for the past follow-up year. She had quit smoking and gone back to work. The pulmonary pressure was 50 to 60 mmHg by echocardiography. Level of protein in urine decreased to 2 g/d, cholesterol and LDL cholesterol levels were in normal range (4.15 mmol/l, 1.9 mmol/l separately).

Discussion

This is the first case that CAD and PAH happened together in one lupus patient in literature reported. It is a rare phenomenon.

Due to the sex and young age of young patient, it may not be easy to consider AMI on her first visit. Then, diagnosis of AMI was confirmed until the elevation of myocardial enzymes, which could have resulted in an inappropriate treatment and undesirable results.

Although morbidity and mortality rates attributable to SLE itself have reduced with advances in the treatment of SLE, cardiovascular disease seems to be an important cause of increased mortality in SLE patients. Pathophysiology of AMI in the presence of normal coronary arteries remains unclear, but it can be explained on basis of coronary artery thrombosis with spontaneous thrombolysis, embolization with recanalization, coronary spasm, small-vessel vasculitis, or a combination of these processes [2]. Coronary thrombosis can be seen in hypercoagulable state, as in nephrotic syndrome [3], antiphospholipid syndrome [4], deficiencies of protein C, protein S and antithrombin III [5,6]. Renal involvement associated with nephritic syndrome may result in hypercoagulability, thus leading to AMI [3,7]. There are case reports and some small-sized series available that address development of AMI in young patients with SLE below 35 year [8]. Although clinically significant, CAD is prevalent among patients with SLE, it not often suspected even in the presence of clear anginal symptoms [1]. In our case, she had no other prothrombotic risk factors, apart from nephrotic syndrome and history of smoking. Angiography showed definitely stenosis in coronary. As well known, this patient has used long-term steroid, and steroid may accelerate atherosclerosis.

To our surprise, we detect the patient not only had CAD, but also had pulmonary artery hypertension when we looked at her chest X ray and CT, right heart catheter confirmed sever PAH and negative acute
vasoreactivity test in this patient. Pulmonary hypertension is another major cardiac vascular complication of SLE. Calcium channel blockers and prostaglandins showed effectiveness to some extent. Although sildenafil and bosentan were added recently to the treatment with great expectations, effectiveness for the acute exacerbation of PAH is not fully examined [9]. Based on recommendations for efficacy of specific drug therapy for pulmonary arterial hypertension according to WHO-FC (World Health Organization Functional Class), non-responder to acute vasoreactivity test who are in WHO-FC II should be treated with endothelin receptor antagonists or phosphodiesterase type-5 inhibitor. However, our patient did not prescribed sildenafil because of acute myocardial infarction.

Immunosuppressive treatment, cyclophosphamide infusions once a month for 6 months in combination with steroid treatment resulted in recanalization of coronary artery together with dramatic clinical improvement, but no decrease of pulmonary pressure. Improvement might have resulted from treatment with high dose steroids or cyclophosphamide, or both, and could not be attributable to cyclophosphamide only. The association of vasodilator and anticoagulant with immunosuppressive drug treatment might have been helpful, even though the initial treatment with vasodilator alone was ineffective. None of improvement with immunosuppressive drug treatment had reported about CAD in SLE patient. This is the first time that we found steroids and cyclophosphamide can partly improve the CAD. Although neither angiographic features suggestive of arteritis include isolated segments with tapered narrowing, nor coronary ectasia or aneurysm existed, sequential angiographic studies showed a rapid change in coronary luminal diameter, which would be an unusual manifestation of atherosclerotic CAD [10]. We presumed coronary vasculitis in our patient.

There are some cases of improvement with immunosuppressive drug treatment have been reported about PAH in lupus. Corticosteroids alone are rarely efficient. In 1996, Karmochkine et al. first reported a severe PAH SLE patient successfully treated with corticosteroid and cyclophosphamide [11]. Goupille et al. reported the case of a lupus patient with precapillary pulmonary hypertension who was successfully treated with high doses of corticosteroids, with an appreciable follow up of 18 months [12]. Groen et al. described a prolonged-but only partial improvement with low dose prednisone and quarterly cyclophosphamide infusions in a woman with SLE and pulmonary hypertension [13]. Sanchez et al. mentioned 18% PAH associated with SLE might respond to a treatment combining glucocorticoid and cyclophosphamide, and responders had a better survival than non-responders [14]. Jais et al. found that 50% SLE or mixed connective tissue disease associated PAH were responders to immunosuppressive therapy alone. These patients had a significantly improved NYHA functional class, 6 minute walking distance, and mean pulmonary artery pressure. Patients in NYHA functional class I or II and/or a cardiac index>3.1 liters/minute/m2 at baseline were more likely to benefit from immunosuppressive therapy [15]. Our patient had none of the variables associated with poor survival rates in patients with pulmonary hypertension, such as New York Heart Association functional class IV, presence of Raynaud’s phenomenon, or decreased cardiac index. She had a better life during the following year.

In conclusion, the prolonged and excellent outcome seen in our patient supports treatment with immunosuppressive drugs associated with vasodilator agent in cardiac vascular disease arising in SLE. Controlled trials of immunosuppressive drug treatment in patients with SLE and cardiac vascular disease are needed.

**Conclusion**

This is a rare case that a young lupus patient had cardiac involvement not only myocardial infarction but also pulmonary hypertension. After the prednisone and immunosuppressive drug treatment, combined with anticoagulation, antiplatelet, and vasodilator therapy the patient gained dramatic clinical improvement. Further clinical study may help us to know the pathology mechanism and efficiency of treatment.

**References**