Medical Journal of the
Islamic Republic of Iran

Volume 10
Number 1
Spring 1375
May 1996

ANTIPHOSPHOLIPID ANTIBODY SYNDROME–A CASE OF AORTIC VALVE INSUFFICIENCY

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ABSTRACT

A 31 year old woman was hospitalized for evaluation of aortic valve insufficiency and her present cardiac status. Clinical and paraclinical findings strongly suggested the presence of a collagen vascular inflammatory process–precisely, the antiphospholipid antibody syndrome (APS), with systemic lupus erythematosus as the underlying disease.

MJIRI, Vol. 10, No. 1, 85-88, 1996.

CASE REPORT

A 31 year old woman was admitted to Shahid Rajai Cardiovascular Center because of palpitation and dyspnea on exertion of 5 years' duration. She was in New York Heart Association (NYHA) functional class III.

The past medical history revealed that she had had ten pregnancies leading to two healthy living children, five stillbirths, and three abortions. There was no history of acute rheumatic fever. She had experienced a transient paresis of both lower extremities, and frequent episodes of transient scotoma, diplopia, and sudden reduction of visual acuity. She suffered from migraine-like headaches and infrequent episodes of transient severe arthralgia.

On physical examination she did not look very ill, was oriented, and had a depressed mood. She was pale. JVP was normal, BP: 140/80mmHg, HR: 100/ min, her carotid pulse was hyperactive and the apical impulse was wide and laterally displaced. S_1 was normal and S_2 (A_2) reduced in intensity. There was a loud and moderately long diastolic blowing murmur, best heard in the mid LSB with radiation to the apex. There was no lymphadenopathy. The liver and spleen were not palpable, although the spleen was found to be significantly enlarged sonographically. The skin showed livedo reticularis on the hands, forearms, trunk, knees and feet (Figs. 1, 2, 3). There was also periungual hyperemia, telangiectases and peripheral cyanosis. Ophthalmologic examination revealed the presence of retinal vascular sheeting and a few cotton wool spots.

The chest roentgenogram revealed a moderately increased cardiothoracic ratio in the long axis. The ECG showed a normal sinus rhythm and some evidence of LVH. Echocardiography showed a moderate degree of aortic valve insufficiency (Fig. 4), and the three cusps of the aortic valve were thickened, and showed incomplete coaptation in diastole (Fig. 5). The mitral valve leaflets showed diastolic fluttering and were mildly thickened, with no restriction of motion or

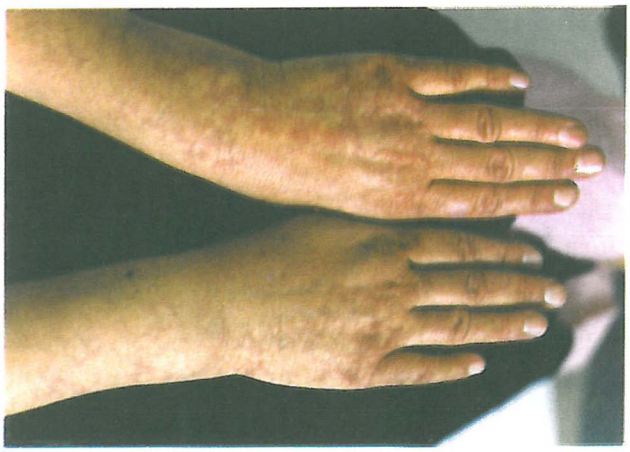

Fig. 1. Livedo reticularis on the hands and forearms.

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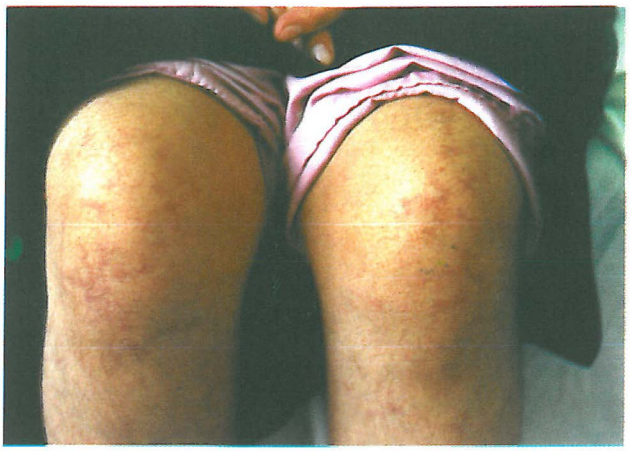

Fig. 2. Livedo reticularis on the knees.

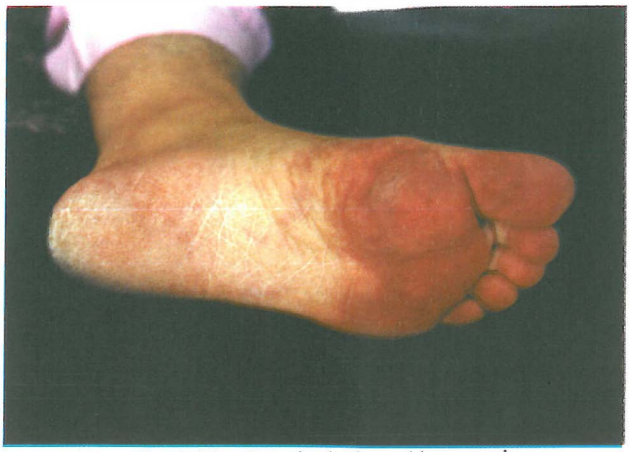

Fig. 3. Livedo reticularis and hyperemia.

insufficiency. There were not any visible vegetative lesions, and the LV was mildly dilated with symmetrically increased wall thickness and an EF of about 50-55 percent.

Significant laboratory findings at the time of admission are presented in Table I.

The clinical and paraclinical findings including recurrent pregnancy loss, livedo reticularis, aortic insufficiency, neurological complaints, Coombs' positive immunohemolytic anemia, a markedly elevated ESR, false-positive VDRL and weakly positive ANA were all highly suggestive for the presence of the antiphospholipid antibody syndrome and systemic lupus erythematosus. The response to treatment with prednisolone (60 mg per day) was favorable. The patient's appetite improved remarkably, the Hb increased from 5.5 g/dl to 10.6 g/dl and the ESR decreased from 160mm/h to 70 mm/h after about 20 days. The false-positive VDRL and CRP became negative. Then, cardiac catheterization and selective coronary angiography were performed, revealing a slightly enlarged LV with slightly decreased contractility. LVEF was about 50%. The mitral valve was normal with no MR. Aortic root injection showed a dilated ascending aorta and 3 to 4+ AI. Coronary arteries

Table I. Significant laboratory findings at the time of admission.

Hb	5.5 gr/dl
Hct	17.2%
MCV, MCH, MCHC	WNL
Retic. count	7%
Platelet count	170.000/mm^3
WBC count	WNL
Peripheral blood smear	Infrequent basophilic stippling, rouleaux formation and a few microspherocytes
Serum iron	70 µg/dl (40-145)
TIBC	324 µg/dl (250-400)
Serum ferritin	320 mg/dl (2.5-212)
Direct Coombs'	Positive
Indirect Coombs'	Positive
Cold agglutinin titer	Negative
ESR	160 mm/h
CRP	3+
VDRL	4+
FTA-ABS	Negative
ANA	Weakly Positive
LE cell	Negative
RF	Negative
CIC	Weakly Positive
C_3	85 IU/ml (67-154)
C_4	50 IU/ml (65-157)
CH_{50}	120 IU/ml (70-150)
Serum IgG, IgM, IgA	High
Uric acid	10 mg/dl
Serum creatinine	1.8 mg/dl
BUN	33 mg/dl
24-hour urinary protein	100mg
Estimated GFR	50 ml/min
Urinalysis	Unremarkable
Hemosiderinuria	Negative
Bence-Jones Protein	Negative
PT, PTT	WNL
Anti HIV	False Positive (by ELISA)

and pulmonary arterial pressure were normal. After about 2 months, as the dosage of prednisolone had been tapered to 30 mg/day, Hb was 13 gr/dl, the ESR 15 mm/hr, and the patient Cushingoid. We planned to continue medical treatment and to follow up and re-evaluate the patient periodically.

DISCUSSION

A novel type of autoimmune cardiovascular damage has been characterized during the past few years associated with the presence of antiphospholipid antibodies.[1] This family of autoantibodies includes the biologic false-positive tests for syphilis, anticardiolipin and the lupus anticoagulant.[2] In this patient, the test for lupus anticoagulant was not available and the test for anticardiolipin, although reported to be

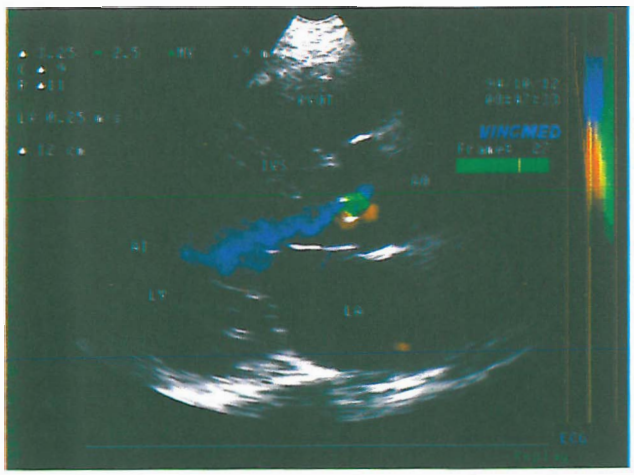

Fig. 4. Parasternal long-axis view; arrow denotes AI.

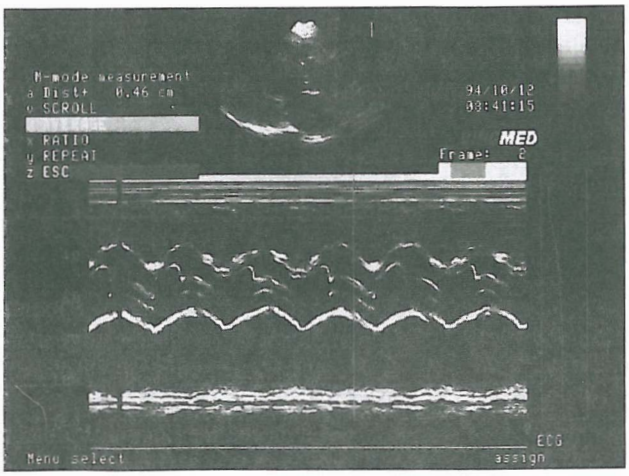

Fig. 5. M-mode echocardiogram shows thickened aortic valve cusps with incomplete diastolic coaptation.

negative, was unreliable. APS is now recognized as a distinct clinical entity; prominent clinical features include arterial and venous thromboses, fetal loss, livedo reticularis, thrombocytopenia, and cardiac and neurologic manifestations.[3] It is common in patients with SLE but may occur as primary APS without other evidence of systemic collagen vascular disease.[3] The prevalence of valvular disease in patients with APS appears to be higher (36%) than in patients with SLE (18%).[5] Patients with cardiac valvular lesions are typically young women and the lesions are left-sided, causing regurgitation that may be clinically relevant.[4] Although the most common manifestations of APS are deep vein thrombosis (DVT), pulmonary embolus and stroke,[2] in the presented case there was no apparent clinical evidence of these problems except for very transient neurological and ocular manifestations.

Other possible cardiac manifestations and vascular associations of APS are summarized in Tables II and III.[1,2] Livedo reticularis, a lattice-like pattern of superficial dilated

Table II. Cardiac manifestations of the antiphospholipid syndrome.

Valvular Disease
Nonbacterial vegetations
Valvular thickening
Aortic and mitral insufficiency
Fibrocalcific changes
Myocardial Dysfunction Including Dilated Cardiomyopathy
Coronary Artery Disease
MI in young patients
Restenosis after CABG
Intracardiac Thrombosis
Pericardial Effusion

Table III. Vascular associations of antiphospholipid antibodies.

Arterial Disease
- Thrombosis of large arteries leading to stroke, splenic infarction, mesenteric infarction, etc.
- Coronary thrombosis
- Pulmonary hypertension
- Retinal artery disease, deafness and vestibular failure
- Multi-infarct dementia
- Adrenal infarction
- Marrow necrosis
- Skin necrosis
Venous Disease
- Recurrent DVT with or without emboli
- Budd-Chiari syndrome
- Superior vena cava syndrome
Placenta
- Thrombosis of placental vessels

veins, is considered a feature of APS. The relative odds of a lupus patient having livedo reticularis are 23 times greater in those with elevated anticardiolipin antibodies.[3]

The estimated risk for deep vein thrombosis or pulmonary embolus in persons with a high anticardiolipin antibody level is similar to that of other well-established risk factors for venous thrombosis, such as intermediate-dose estrogen oral contraceptive use, smoking, hypertension and obesity.[7]

Recurrent pregnancy loss occurs in 0.5 to 1 percent of women with this disorder. In one study, APS appeared to be the cause of recurrent pregnancy loss in 5% of cases.[8] Patients with SLE have a higher incidence of pregnancy loss (30%). Women with antiphospholipid antibodies have rates of fetal loss estimated to be as high as 96%.[3] In the presented

case the rate of fetal loss was 80%. The incidence of cerebrovascular disease in patients with APS appears to be 25%. It is suggested that antiphospholipid antibody screening be included in the investigation of all young patients (less than 45 years of age) with idiopathic or unexplained cerebrovascular thrombotic episodes, even in the presence of other risk factors such as hypertension. Echocardiographic evaluation of these patients, even in the absence of clinical evidence of valvular involvement, is also advised.[6] Treatment of antiphospholipid associated complications usually involves anticoagulation, although in severe cases immunosuppressive therapy may be initiated as well.[3] Increased recognition of this syndrome and early anticoagulant therapy in high-risk patients may help reduce the mortality and morbidity of this disorder.[2]

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