Case Report

Transient Low Levels of Antibodies at Initial Presentation of Primary Anti-Phospholipid Syndrome

S Divate, P Hardikar, LS Bichile*, A Rajadhyaksha*

Abstract

We present, herein, a case of venous thrombosis who was lupus anticoagulant negative and had low levels of anticardiolipin antibodies at the time of initial presentation. A definite diagnosis of antiphospholipid syndrome (APS) could be made only when repeat testing, six months later, revealed a dramatic rise of these antibodies.

INTRODUCTION

The anticardiolipin antibody (aCL) test is a critical factor in identifying patients with antiphospholipid syndrome (APS).1 At times, patients present with a clinical picture of this syndrome but without evidence of antiphospholipid antibodies in their sera and a definitive diagnosis of APS cannot be made in such cases. Two studies of patients with systemic lupus erythematous2,3 have been reported and aCL do appear in such patients in subsequent blood samples and the term “seronegative APS” has been proposed for this uncommon entity.3 Herein we present a case of primary APS who was negative for aCL and lupus anticoagulant (LAC) at the time of initial presentation with venous thrombosis. However, on follow-up, a marked rise in the concentrations of serum aCL was seen a few months later.

CASE REPORT

A 26 years old female presented with complaints of severe right temporal headache and weakness of her left upper and lower limbs since one day with one episode of vomiting two days earlier. There was no history of slurring of speech, facial deviation or convulsions. There was no history of a similar episode in the past. She also did not have hypertension, diabetes mellitus, ischemic heart disease or any major illness in the past. On clinical examination, she was afebrile, conscious, co-operative and well oriented with a pulse rate of 82 per minute, blood pressure of 130/86 mm of Hg and a normal jugular venous pressure. There was no pallor, icterus, lymphadenopathy, clubbing, cyanosis or oedema feet. The central nervous system examination revealed a mild decrease in power (4/5) accompanied by mild hyper-reflexia in the left upper and lower limbs with upwardly moving plantars and a left upper motor neuron (UMN) facial palsy while her other functions were normal. Examination of other systems revealed no abnormality. Blood investigations showed haemoglobin of 10.7 gms/dl, haematocrit 32%, total white cell count 11,700 per cu/mm. and a differential count : neutrophils 83%, lymphocytes 17%. The erythocyte sedimentation rate was 30 mm at the end of one hour and the peripheral smear showed adequate number of plateles and a mild hypochromic microcytic anaemia. Fasting and post-prandial blood sugar levels were 112.0 mg% and 126.0 mg%, respectively and the blood urea nitrogen was 11.0 mg%. Anti-nuclear antibodies, anti-double stranded deoxyribonucleic acid antibodies and tests for LAC were negative. The IgG and IgM isotypes of serum aCL were quantitated by enzyme linked immunosorobent assay (ELISA) against a beta2 glycoprotein I (β2-GP1) conjugated cardiolipin antigen, using commercial kits (Genesis Biotechnology, USA) calibrated with international standards. The test revealed aCL-IgG = 6.0 GPLU/ml and aCL-IgM = 11.0 MPLU/ml. As per the normal ranges for the kits used aCL-IgG was negative and aCL-IgM was only borderline positive. Protein C and protein S were within normal limits. Magnetic resonance imaging of the brain showed a superior sagittal sinus (SSS) thrombosis with ischemic changes in the posterior parafalcine regions bilaterally. The patient was immediately administered heparin 5000 units intravenously and subsequently 25,000 units of heparin in 5% dextrose was infused per day. Mannitol and dexamethasone injections were also administered. The heparin was later overlapped with warfarin 5 mg per day. The patient’s power improved and she was discharged in a stable condition eleven days after admission on a maintenance dose of warfarin 2.5 mg per day. She remained asymptomatic thereafter. The borderline elevation of aCL prompted a repeat aCL test which was done six months later. This revealed a dramatic rise of serum aCL-IgG to 107.0 GPLU/ml with a mild increase of serum aCL-IgM to 17.0 MPLU/ml. In a third test performed another
six months later, the aCL-IgG had decreased to 9.0 GPLU/ml and aCL-IgM to 8.0 MPLU/ml and she continued to remain asymptomatic.

**DISCUSSION**

The diagnostic serological hallmarks of APS are aCL and LAC. Two studies had reported a decrease of aCL at the time of the thrombotic episode in patients with systemic lupus erythematosus. A subsequent study by the Drenkard’s group described that both aCL as well as anti-β2-glycoprotein1 (β2GP1) levels decreased at the time of thrombosis and increased thereafter. The decrease in concentration of these antibodies has been attributed by Drenkard et al to their consumption in the course of the thrombo-embolic episode. It has been shown that aCL persist for several years with fluctuations in titres from time to time. The reasons for neither these fluctuations nor the triggers, which cause the sudden development of thrombosis in these patients, are yet identified.

In the index case, aCL was not significantly elevated nor were LAC detected at the time of occurrence of the SSS thrombosis. A definite diagnosis of APS could therefore be made only when follow-up testing, months later, provided evidence of high titres of aCL. To our knowledge, this is the first case of a decrease of aCL, at the time of thrombosis, in a patient with a primary APS. This case has been presented to highlight the need for repeated testing of aCL/LAC negative patients with thrombosis, in order to avoid missing a diagnosis of APS.

**REFERENCES**