

Lupus Anticoagulant as a Risk Factor for Cerebral Infarction and Habitual Abortions

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Summary: A case involving a 34-year-old female with a progressive hemiparesis is described. She had a history of repeated spontaneous abortions. The CT and magnetic resonance imaging (MRI) showed a multiple cerebral infarction. A ^{99m}Tc perfusion lung scintigram demonstrated diffuse bilateral perfusion defects in the lungs. The presence of lupus anticoagulant (LA) was detected from the laboratory data and the thrombosis in the genital organ. The repeated abortions were probably due to thrombosis in the placental vessels caused by LA. High dose steroid therapy was effective in suppressing the LA activity and in preventing progression of the clinical symptoms.

Key words: lupus anticoagulant — thrombosis — cerebral infarction — habitual abortions — pulmonary infarction

Introduction

LA is an acquired IgG or IgM immunoglobulin which inhibits coagulation by interfering with the phospholipid portion of prothrombin activator complex. It is often associated with thrombosis in LA positive patients. The importance of LA as a risk factor for cerebral infarction and habitual abortions due to thrombosis in the placental vessels is described.

Case Report

A 34-year-old female was admitted to the hospital with weakness in all four limbs on April 11, 1988. She had noticed a left hemiparesis in 1981 and was diagnosed as having had a cerebral infarction.

Also, a right hemiparesis appeared in 1983. She was admitted to the hospital for further investigation because her symptoms progressed. She had a history of four spontaneous abortions from 1976 to 1979. She had no history of oral contraceptive use, hypertension, diabetes mellitus or heart disease.

On admission, the blood pressure was 140/96 mmHg, and the pulse was 92. The chest and abdomen were normal. There was no lesion in the genital organ. Neurological examination revealed that she had a slight reduction of mental state, bleeding in the corpus vitreum, a slight pseudobulbar palsy and a slightly spastic tetraparesis. Her deep tendon reflexes were increased with pathological reflexes. The urine was normal. The hematocrit was 35.0 percent; the white-cell count was

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Fig. 1 Technetium-99m (^{99m}Tc) perfusion lung scintigrams, showing diffuse bilateral perfusion defects in the lungs.



Fig. 2 Magnetic resonance imaging (MRI), showing a multiple cerebral infarction and bleeding in the corpus vitreum.

8000. The platelet count was 430,000, and the erythrocyte sedimentation rate was 36mm per hour. Liver and renal functions were normal. Serological tests for syphilis, anti-nuclear antibodies, anti-DNA antibodies, LE preparation and rheumatoid factor were negative. The cerebrospinal fluid (CSF) was watery clear with a pressure of 80mmH₂O. The CSF contained 3 cells per mm³. The sugar content was 55 mg/dl and the protein content was 86mg/dl. The EKG and echocardiography disclosed no abnormalities. A technetium-99m (^{99m}Tc) perfusion lung scintigram showed diffuse bilateral perfusion defects in the lungs, although chest X-rays disclosed no abnormalities (Fig. 1). The CT scan and MRI showed multiple cerebral infarctions and bleeding in the corpus vitreum, probably due to a left retinal central vein thrombosis (Fig. 2).

Coagulation study:

The bleeding and coagulation times, fibrin degradation product (FDP) and anti-thrombin III were within the normal limits. The prothrombin time (PT) was 13.1 seconds (normal <15 seconds). The activated partial thromboplastin time (APTT) was 57.9 seconds (normal <43 seconds) and when incompletely corrected (51.2 seconds) with a 1:1 dilution with normal plasma, it was at least 5 seconds longer than normal plasma. The presence of LA was recognized because the coagulation factors (II, V, VIII, IX, X, XI, XII) were within the normal limits.

Clinical course:

This case was diagnosed as a juvenile cerebral infarction due to LA. Pulse therapy (methylprednisolone, 1000mg/day) was performed for three days because the symptoms progressed. The APTT returned to the normal range (41 seconds) after three days. There has been no recurrence, and the patient has been maintained on prednisolone, 20mg/day.

Discussion

This was considered an idiopathic positive case of LA from the laboratory data, which was not associated with collagen disease. LA is an acquired IgG or IgM immunoglobulin which inhibits coagulation by interfering with the phospholipid portion of the prothrombin activator complex. Despite an in vitro anticoagulant activity, LA is most often paradoxically associated with thrombosis and not abnormal bleeding (Lechner and Pabinger-Fasching, 1985). Elias and Eldor (1984) reported that bleeding occurred in only five of forty patients, four of whom had severe thrombocytopenia; while excessive bleeding did not occur in thirty-five LA positive patients. Thrombosis was observed in both the arterial and venous systems, with deep venous thrombosis in the venous system and pulmonary infarction and cerebral infarction in the arterial system. In a case with a complicated pulmonary infarction (Anderson and Ali, 1984), a technetium-99m (^{99m}Tc) perfusion lung scintigram demonstrated perfusion defects, as in the present case. With pulmonary arteriography, most of the pulmonary arterial branches were either occluded or stenosed which was consistent with multiple pulmonary thromboemboli. That patient also had pulmonary hypertension and died of heart failure. At necropsy there were widespread organizing thrombi with focal intimal proliferation and medial hypertrophy within the pulmonary vasculature. The cerebral infarction indicated that the main cerebral arteries tended to be occluded (Hamada et al. 1987).

Thrombosis also tends to occur in the placental vessels and may cause an abortion due to infarction and necrosis (Firkin et al. 1980; DeWolf et al. 1982). Since the present patient had frequent abortions, it is possible that thrombosis was occurring in the placental and decidual vessels resulting in the abortions; because there

was no lesion in the genital organ that could induce an abortion and thrombosis had also occurred in other organs (brain, lung, eye). There was also no underlying disease that could cause only frequent abortions (Firkin et al. 1980). Accordingly, Lubbe et al. (1985) emphasized that the demonstration of LA in the plasma of a pregnant woman, even in the absence of other clinical or serologic evidence of connective tissue disease, should be regarded as a marker not only for potential intrauterine death but also for a high risk of maternal thrombotic complications.

Regarding therapy, anticoagulants may be needed (Elias and Eldor, 1984), and a successful pregnancy can be obtained on combination therapy with prednisolone and aspirin (Lubbe et al. 1983). Although combination therapy with prednisolone and aspirin is effective, it takes 4-8 weeks to develop a normal APTT, even with 40-60mg of prednisolone, daily. Therefore pulse therapy (methylprednisolone, 1000 mg/day) was performed, because the symptoms were progressing. The APTT returned to the normal range after three days of pulse therapy. There has been no change of APTT, since the patient has been maintained on prednisolone, 20mg /day daily.

There is no agreement on therapy for LA, as mentioned above. High dose steroid therapy at an early time in this patient did reduce LA activity and normalize APTT, and recurrences were prevented by maintenance doses of prednisolone.

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