CASE REPORT

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C4 deficiency state in antiphospholipid antibody-related recurrent preeclampsia evolving into systemic lupus erythematosus

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Abstract The case of an apparent healthy woman who developed recurrent preeclampsia with antiphospholipid antibodies and evolved towards systemic lupus erythematosus during her last pregnancy is presented. The diagnostic dilemma between lupus renal flare and toxemia is discussed. The potential role of immunological alterations, such as complement genetic deficiencies, in women with primary antiphospholipid syndrome who develop systemic lupus erythematosus is also discussed.

Keywords Preeclampsia · Antiphospholipid syndrome · C4 null alleles · Lupus

Introduction

In normal healthy women, the recurrence rate of preeclampsia is generally low (<10%). However, some experiences suggest that aPL are found in a substantial proportion of recurrent cases of early-onset severe preeclampsia. In addition, women with preeclampsia and aPL may be at significant risk for serious peripartum morbidity (i.e., thromboembolic events), and some authors argue that women with primary antiphospholipid syndrome (APS) who develop amaurosis fugax and transient ischemic attacks (TIA) may be prone to systemic lupus erythematosus (SLE) development [1, 2].

Antiphospholipid syndrome was first recognized in association with SLE, in which the frequency of aPL is about 10–30%. However, the notion of a primary APS has led to the relation between the two conditions being questioned [3]. Some works have suggested that there is a different genetic background for the two groups of patients with APS, and this has led to renewed interest in the concept that the primary APS could switch to full-blown SLE [4].

We present the case of a young healthy woman who developed recurrent preeclampsia followed by a full-blown SLE during her fourth pregnancy. This is an unusual event that poses some diagnostic and therapeutic challenges, and therefore it is important to be cautious about this possibility.

Case report

A 27-year-old Caucasian woman was transferred to our rheumatology clinic on the 10th week of her last gestation with acute arthritis, malar rash, and malaise. Her obstetric history included preeclampsia with intrauterine growth retardation (IGR) and fetal intrauterine deaths at 28, 30, and 27 weeks' gestation over a 3-year period. Intergestational periods had been remarkably normal from the serological and clinical perspectives, and the patient denied a history of hypertension, thromboembolic events, or data suggesting active lupus. Necropsy of her third gestation showed a placenta with multiple infarcted areas. Prior investigations of the last two gestations – including cariotype, antinuclear antibodies (ANA), anti-DNA antibodies, anti-Ro, anti-La, rheumatoid factor, full blood count, and complement – revealed positive tests on only two occasions for anticardiolipin antibodies (aCL) and low C4 levels, and therefore a diagnosis of primary APS was made.

At age 27, she became pregnant again and was prescribed aspirin 125 mg daily with subcutaneous heparin (15,000 IU daily). In the 10th week, she developed a butterfly rash, Raynaud's syndrome, vasculitic digital lesions, metacarpophalangeal joint arthritis, and severe malaise and was referred to a rheumatology clinic. Complementary data showed hemoglobin 11.5 g/dl, normal white cell count, platelet count 100,000 per μl, erythrocyte sedimentation rate (ESR) 45 mm/h, ANA 1/2560 (indirect immunofluorescence with homogeneous pattern), positive anti-DNA antibodies (C.rithidia), positive anti-Ro (CIE), C3 68 mg/dl (normal 100–185 mg/dl), C4 8 mg/dl (normal 20–47 mg/dl), negative lupus anticoagulant (Russell vipes venom test), aCL (enzyme-linked immunosorbent assay, or ELISA) IgG 80 GPL/ml (normal 0–13 GPL/ml), and IgM 120 MPL/ml (normal 0–11 MPL/ml). Tissue typing by serological testing showed HLA A1, A3, B7, B8, Cw5, Cw7, DR3, DR7, and DQ2. Her total hemolytic complement

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and marked proteinuria. Laboratory showed hemoglobin 10.5 g/dl, cause of hypertension (170/100 mmHg), rapid weight gain, edema, and proteinuria. She remained well until 28 weeks’ gestation, when she was admitted because of hypertension (170/100 mmHg), rapid weight gain, edema, and marked proteinuria. Laboratory showed hemoglobin 10.5 g/dl, 10,200 WBC per µl, 980 lymphocytes per µl, ESR 50 mm/h, normal renal function (creatinine clearance), 5.6 g per day proteinuria with positive casts and cells in urinalysis, low serum albumin, high serum cholesterol, ANA 1:320, anti-DNA +, anti-Ro +, C3 59 mg/dl, C4 <8 mg/dl, negative lupus anticoagulant, IgG aCL 50 GPL/ml, and IgM aCL 67 MPL/ml; other results were not remarkable. Serial ultrasound scans had shown oligohydramnios and intrauterine growth retardation with Doppler flow studies revealing poor placental blood flow, so a cesarean section was performed for fetal distress and a live, 1,200-g female infant was delivered.

The patient was diagnosed as having nephritic lupus flare with preeclampsia and started on metyldopa and 1 mg/kg per day prednisone in divided doses. After delivery, she normalized her tension values, and the proteinuria disappeared in few weeks. During a 4-year follow-up period, the patient and her child have remained symptom-free. The mother is being controlled with 7.5 mg deflazacort on an alternative dose scheme and the child has remained well, without any neonatal lupus stigmata.