

Case Report

Antiphospholipids (Hughes) Syndrome in Pregnancy: A Report of Three Cases and Review of the Literature

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ABSTRACT

Since the discovery of the antiphospholipids syndrome in the early eighties, many clinical conditions have been described in patients with antiphospholipid antibodies. Complications include infertility, recurrent miscarriage and increased perinatal mortality. A more serious complication, however, are episodes of arterial thrombosis during pregnancy and puerperium. We have had six such cases in the last three years, of which, the three with major complications are reported here.

The first patient had a combination of sickle cell disease, β -thalassaemia and antiphospholipid antibodies during pregnancy. Put on heparin prophylaxis, she was delivered at 38 weeks by Caesarean section, but died postnatally of a massive pulmonary embolism. The

second patient reported at eight weeks of gestation with evidence of a cerebro-vascular accident. Her condition improved and her pregnancy was terminated. The third, a young woman with a history of infertility, was treated with assisted reproductive technology and became pregnant but had a mid-trimester abortion. Eventually she had a normal gestation with heparin prophylaxis and delivered a live baby.

Antiphospholipids syndrome is not uncommon in Bahraini pregnancies. Considering the impact of this disease on reproduction and the range of complications involved, screening of pregnant women with a bad obstetric history or recurrent miscarriage is essential.

KEY WORDS: Antiphospholipids syndrome; complications; pregnancy.

INTRODUCTION

Antiphospholipids syndrome (APS) is an autoimmune and thrombophilic disorder^[1] characterized by a high level of anticardiolipin (aCL) and/or lupus anticoagulant antibodies (LA)^[2]. The condition is associated with the tendency for arterial and venous thrombosis^[3], strokes and neurological features^[4] and has a strong association with recurrent fetal loss, and a tendency for thrombocytopenia^[5]. Hughes and co-workers first described the condition in the early eighties^[6].

While the earlier reports concentrated on systemic lupus, it immediately became clear that the syndrome was also found in mild lupus, or in discoid lupus. It was soon found that the aCL was raised in patients with no lupus, giving rise to the beginning of the antiphospholipid syndrome^[7]. Several issues regarding this condition such as the precise nature of the clotting mechanism and the level of antibodies, which does not always correlate with the clinical intensity of APS, remain unsettled. Phospholipid antibodies may also be

high in cases of systemic lupus and APS where they are seen equally in 10%-20% of cases. Some patients may become negative for antibodies at a later date. Screening for APS^[8,9] is simple and usually carried out using two tests:

- Measuring the titre of cardiolipin antibody
- The lupus anticoagulant is more complicated and less reliable

The incidence of APS is found in approximately 1% of all women. Women of childbearing age with a history of recurrent fetal loss represent the majority of cases. The condition nevertheless is found in all age groups including children. In 1990, it was reported that there are 100,000 patients with APS in the United States of America alone. In Bahrain no data is available on the incidence, but an ongoing screening survey is being conducted in our laboratory. It is interesting that most of the international surveys emphasize the effect of confounding factors such as smoking, thrombophilia and the oral contraceptive pill. Here we report another factor - sickle cell disease, which is common in Bahrain.

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Screening for APS is done in women with a history of recurrent pregnancy losses in addition to other routine tests. A history of unexplained poor fetal growth and/or the early onset of severe pre-eclampsia or unexplained placental abruption are all indications for testing. Any history of thrombosis, cerebro-vascular accidents, myocardial infarction, thrombocytopenia, presence of other autoimmune disorders such as lupus, an abnormal venereal disease, research laboratory finding or prothrombin time blood test is an indication for testing^[10,11].

Steroids, such as prednisone, have been used in this case, but prednisone has been associated with side effects such as prematurity. The optional therapies today are heparin prophylaxis throughout pregnancy, either alone, or in combination with a small 75 mg dose of aspirin daily. Recent reports have shown that there is no difference in the results between the two regimens. The pregnancies should be monitored closely by ultrasound every month to check fetal growth and well-being. Non-stress testing and biophysical profile should be performed weekly in the last six weeks. The reported success of this form of management is 50-75%^[12,13].

With regards to labor, patients should be encouraged to have a normal spontaneous vaginal delivery. Caesarean section should be avoided except when there are strong surgical indications. Expert anesthesia is required and conduction anesthesia (epidural or spinal) is superior to general anesthesia. Anticoagulants should be resumed as soon as possible after the delivery^[14].

Three cases will be described here, which have been encountered in our practice. We believe that these cases present a considerable range of problems that may be encountered among pregnant patients with APS.

CASE REPORTS

Case 1: A 35-year-old G5, P0, Ab1 Bahraini patient who was known to have recurrent abortions, sickle cell disease and antiphospholipids syndrome. In early pregnancy, she was referred from the Medical Department with the above history. Her antenatal care was conducted jointly with both a hematologist and a rheumatologist. She was started on heparin and aspirin prophylaxis right from the beginning of her pregnancy. Two years earlier, she had been admitted to hospital with a cerebral infarction and right-sided hemiparesis. The patient had a circlage inserted at 13 weeks of gestation. The remaining part of her antenatal care was uneventful, until she was admitted as an emergency at 33 weeks of

gestation with a history of bilateral shoulder-joint pains and backache. The condition was diagnosed as vasoocclusive sickle cell crisis and treated with hydration, oxygenation and analgesics. Pregnancy ultrasound, arterial blood gases, chest radiographs, cardiac enzymes and CBCs were all normal. On the fourth day of admission, the circlage was removed. That same day she developed pain in the right side of the abdomen, and the non-stress test showed a lack of fetal heart variability. The heparin and aspirin were discontinued and two units of packed cells were transfused prior to surgery. An elective Caesarean section was performed and a live and healthy 3070 gram baby was born. The Apgar scores were normal.

Heparin was resumed six hours later. One day after the operation, she had a sudden onset of severe chest pain. The CPR (Resuscitation) team carried out resuscitation, but she expired despite all efforts of the team. Cause of death was determined to be pulmonary embolism.

Case 2: A 28-year-old G5, P0, Ab4 patient was admitted through Accident and Emergency at the eighth week of gestation with a history of severe headaches, blurring of vision in both eyes and vomiting for two days. She was a known case of APS and a carrier of the sickle cell trait. In the previous four years, she had had three early miscarriages and a premature labor at 24 weeks of a macerated stillbirth weighing 250 grams. She had been fully investigated one year earlier for habitual abortion, and all results were normal with the exception of raised anticardiolipin antibodies. An MRI (magnetic resonance imaging) was advised immediately and this revealed an early thrombosis of the right lateral cerebral sigmoid sinus. She also had bilateral papilloedema, but no focal deficits. Thrombophilia screening was negative. Gradually, the patient lost her vision and was found to have ophthalmoplegia involving the abducens muscles, the left rectal muscle and the oculomotor nerve as well as the trochlear. In view of this situation, termination of pregnancy was recommended. This was performed and the postoperative period was normal. A lumbar puncture was done with no untoward results and patient was placed on dimox 250 mg bid. Her vision gradually returned and patient was discharged home on the seventh day.

Case 3: A 41-year-old Bahraini female originally presented with history of primary infertility. Initial investigations of the patient and her husband were all normal. She went to London for further investigations, and the conclusion was that her human leukocyte antigen (HLA) compatibility was too close and that she may need immunological

treatment. The husband was also found to have antisperm antibodies. She eventually resorted to *in vitro* fertilization (IVF), but was unsuccessful despite seven attempts. On the eighth attempt, she was treated with intra-cytoplasmic sperm injection (ICSI) resulting in a pregnancy.

Unfortunately, she had a mid-trimester abortion at 24 weeks. Postnatally she was further investigated and found this time to have a low titre of anticardiolipin antibodies. Six months later, following another ICSI procedure she again became pregnant. She was put on prophylactic aspirin 75 mg daily, along with persantin and artralous throughout her pregnancy. At 38 weeks of pregnancy, the non-stress test (NST) showed evidence of fetal distress. So an elective Caesarean section was performed and a live, healthy male baby weighing 2500 grams was born.

She was heparinized after delivery for ten days. Mother and child remained healthy and both were discharged home six days later.

DISCUSSION

One of the most common and distressing problems associated with APS is recurrent miscarriage and episodes of thrombosis during pregnancy. The condition is, however, amenable to treatment. It has also been found that the chances of untreated pregnancy in a patient with APS resulting in a normal delivery are 10%, while treatment can improve the outcome by between 50% and 70%. In Bahrain, cases are either diagnosed in the Rheumatology Clinic or by sending blood samples overseas for screening, and in some cases these were diagnosed overseas. The incidence of APS, as quoted in the West is approximately 1% of all women, although in pregnancy it is much less. The incidence in Bahrain is approximately 0.01% of all pregnant women, determined by a review of all cases admitted to Salmaniya Medical Complex between 1991 and 2001. A current survey of the prevalence of APS is in progress. Two patients of the ten seen in the last three years in the maternity suite provided a very strong family history.

In Bahrain, there are several confounding factors added such as hemoglobinopathies, diabetes and hypertension. These conditions make the management of APS more complicated. We report these three cases to illustrate the range of problems encountered, the importance of screening and early management of such cases. Not only is the screening not always accessible, but patients' compliance to prophylactic treatment with heparin is also poor. The situation has recently been ameliorated by the availability of low-molecular weight heparin, which can be given once daily and

does not need frequent monitoring of the clotting profile.

There is now a need for development of selective screening for pregnant women at risk for antiphospholipid antibodies and to develop specialized anticoagulation clinic for multidisciplinary treatment of cases of APS complicated by sickle cell disease or other hemoglobinopathies.

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