

## Antiphospholipid antibody and anesthesia

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### INTRODUCTION

The presence of an anti-phospholipid antibody (also known as a lupus anticoagulant or anti-cardiolipin antibody) is uncommon in elective surgical patients. The literature to date mainly addresses the care of emergency or obstetric patients with an anti-phospholipid antibody (1, 2, 3). In this paper, a patient with a lupus anticoagulant undergoing major elective surgery is presented and relevant issues are discussed.

### CASE REPORT

A 49 year-old man presented for removal of a large tumor of his posterior thigh. He had a past history of end stage renal failure caused by IgA nephropathy and treated with hemodialysis until a renal transplant was performed in 1995. The transplant rapidly failed because of an ilio-femoral thrombosis with pulmonary embolism, and was removed. Since 1996, he was diagnosed with two deep venous thromboses. He had a second renal transplant at the end of 2001 and two new thromboses (of his arterio-venous fistula and internal jugular vein) in early 2002. At this point, an anti-phospholipid antibody was discovered. Long-term warfarin therapy was then commenced. The patient also has had hypertension since 1996, complicated by cardiomyopathy, but no documented ischemic heart disease.

At the preoperative visit, the patient was stable and the laboratory findings were as follows : hemoglobin 162 g/L, platelet count  $280 \times 10^9/L$ , activated partial thromboplastin time (APTT) 39 s, international normalised ratio (INR) 2.1, urea 4.7 mmol/L, creatinine 0.09 mmol/L.

Warfarin was ceased 5 days before surgery and the patient was administered low molecular weight heparin (LMWH) subcutaneously twice a day. On the day of surgery, no LMWH was given. The coagulation profile showed an APTT of 33 s, an INR of 1.1 and a thrombin clotting time (TCT) of 27 s.

The surgery was performed under general anesthesia. The patient was kept well hydrated and normothermic, and was not administered any medication increasing bleeding or thrombotic tendency. The procedure lasted one hour. Post-operative analgesia was achieved with patient-administered intravenous morphine. LMWH was continued postoperatively. Warfarin was commenced 3 days after surgery and the patient was discharged the fourth post-operative day. The histopathology of the tumor was a lipoma.

The patient was re-admitted the seventh post-operative day with a hematoma of the thigh wound. Warfarin was ceased ; 2 units of red blood cells were transfused and fresh frozen plasma was administered to antagonize the effects of warfarin. One litre of blood was surgically evacuated from the thigh wound. Warfarin was recommenced in a graded fashion on the first postoperative day and the patient was discharged 10 days after with a full oral anticoagulation.

### DISCUSSION

#### *What is Anti Phospholipid Antibody / Anti Phospholipid Syndrome ?*

Patients with an anti-phospholipid antibody (APA) and some clinical findings are often considered to have anti-phospholipid syndrome (APS). However, strictly speaking, an APA must be discovered at least twice, at least 6 weeks apart, for the diagnosis of APS to be made (4, 5). APS can occur primarily, or secondarily in patients with systemic lupus erythematosus (SLE) and many other disorders (6).

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Not all anti-phospholipid antibodies are the same. The first APA was discovered in a patient with syphilis (7). This APA bound to an antigen (a phospholipid) called cardiolipin. This first test was also positive in patients with SLE. Since the 1980s, with the development of a more sensitive test (8), many different antibodies have been discovered. These antibodies are mostly IgG, although IgM has been described, especially in SLE (9, 10), where they are termed lupus anticoagulants (11). In SLE, Lupus anticoagulant is strongly linked to thrombosis. This immune test is not positive for patients with syphilis. It can also identify another group of patients with an isolated thrombotic syndrome. So, patients with thrombosis can be divided in two groups: SLE with thrombosis (Secondary APS) and thrombosis only (Primary APS). For thrombosis to occur, it is necessary that:

- In the plasma of Secondary APS, the APA meets a Beta-2 glycoprotein-1 to bind its antigen (the cardiolipin).
- The same effect in Primary APS patients is achieved by a direct binding between APA and its antigen (10, 12), and the Major Histocompatibility Complex is involved in this immune reaction (10, 12, 13).

The paradox of APS is that coagulation tests indicate a bleeding tendency whereas clinically the patient is prone to thrombosis. However, occasionally a bleeding state can also occur (14), which results from immune thrombocytopenia. Cerebral hemorrhage, menorrhagia, macroscopic hematuria and gastrointestinal bleeding are recorded and are sometimes associated with anticoagulant treatment.

In some forms of APS, microvascular thrombosis is present in multiple organs such as brain, heart and lungs (15). This syndrome is named the catastrophic APS. APA has been involved in spontaneous abortion; women with a history of recurrent mid-trimester abortion associated with APS are usually treated with aspirin or/and heparin to reduce the risk of thrombosis (16, 17, 18).

APS also appears in young men. The prevalence is unknown but thrombosis is more frequent than bleeding in this group (9, 19).

Thrombosis may involve arteries and veins. Rare patients have Superior Vena Cava thrombosis (as did our patient) (14, 20).

The pathogenesis of thrombosis is not well described, although a few hypotheses are proposed (15). Furthermore a combination of hypotheses may be the best explanation (5).

#### PERI-OPERATIVE MANAGEMENT

In the final analysis, patients with anti-phospholipid antibodies should be considered at high risk of arterial and venous thromboembolism. Consequently, the preoperative assessment should concentrate on the prevention of that risk (21) taking the following measures: 1) avoid constrictive clothing; 2) stop smoking; 3) avoid oral contraceptive pill or oestrogen therapy; 4) facilitate venous drainage by careful positioning and 5) maintain adequate hydration.

For patients with APS, the major predictors of risk are: 1) previous thrombosis and 2) APA titers > 40 IU (10). The peri-operative risk of thromboembolism in a patient with an APA titer > 40 IU and previous thrombosis is up to 80% if no prophylaxis is given (14, 22). If the APA titer is > 40 IU, then it would be wise to defer elective surgery until the titer has fallen to < 40 IU (23).

During the preoperative assessment, the patient should be carefully questioned about bleeding, thrombosis and immune disorders. Hematological screening must include a complete coagulation profile and APA titers.

Patient with an APA and previous thrombosis usually are chronically anti-coagulated. (24, 25, 26). Oral treatment may be replaced with either unfractionated heparin or LMWH. (14). The advantages of LMWH include low cost, no need to stay in hospital preoperatively and fewer side effects (osteoporosis, allergy, thrombocytopenia). Treatment should be tailored so that on the day of surgery, the INR is normal. Venous compression stockings should be fitted to all patients preoperatively.

General anesthesia is usually preferred, although local anesthesia sometimes is employed. During surgery, patients must be kept warm and well hydrated. Medication increasing the risk of thromboembolism (e.g. hydralazine) should be avoided. Measures should be taken to avoid blood loss, as these patients may also be at risk of bleeding.

Patients with APA titers < 40 IU and with no past history of thrombosis also should receive LMWH in the peri operative period (19). The intra-operative management is the same for the two groups.

LMWH then oral anticoagulation should be re-instituted post-operatively. Optimal analgesia will help with early mobilisation to further reduce the risk of venous thromboembolism. If thrombosis is suspected then it should be aggressively diagnosed and managed in these patients.

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