Insertion of Inferior Vena Cava Filters in Patients with the Antiphospholipid Syndrome

Eyal Zifman, MD, Pnina Rotman-Pikielny, MD, Tatiana Berlin, MD, and Yair Levy, MD

Background: The antiphospholipid syndrome (APS) is a disease with a high prevalence of thromboembolic events, especially pulmonary emboli (PE). These events may recur despite anticoagulation therapy. In such cases, placement of an inferior vena cava (IVC) filter may be considered to prevent propagation of a distal thrombus toward the pulmonary vessels. It is unclear whether the placement of such a filter is beneficial in patients with APS.

Objective: Retrospective evaluation of the value of IVC filter placement as prophylaxis against recurrent pulmonary emboli in patients with medically treated APS.

Methods: We identified 10 patients suffering from APS who, despite anticoagulation treatment, had recurrent thromboembolic events. All of them underwent placement of an IVC filter. We examined their medical files for further recurrences.

Results: Of the 10 patients in our study, only 1 had a documented PE following the intervention. The remaining patients had no evidence of PE after the filter insertion. Five of the 10 patients died, 2 of them suddenly. In those 2 patients, the cause of death is unknown, but PE cannot be excluded.

Conclusion: IVC filters seem to be protective against recurrent PE in APS patients but the true extent of their efficacy requires further study.

 Semin Arthritis Rheum 38:472-477

Keywords: *anti-phospholipid syndrome, inferior vena cava filter, pulmonary emboli, deep vein thrombosis, lupus anticoagulant, antiphospholipid antibodies*

Antiphospholipid antibodies (aPL) are a heterogeneous group of autoantibodies directed against phospholipid-binding proteins. These antibodies can be broadly categorized into those that prolong phospholipid-dependent coagulation assays, known as lupus anticoagulants (LAC), and anticardiolipin antibodies (aCL) or anti-β2-glycoprotein-I (anti-β_2GPI), which target a molecular congener of cardiolipin. The presence of these antibodies in patients with arterial or venous thrombosis or pregnancy morbidity comprises the APS. This syndrome is referred to as primary antiphospholipid syndrome (APS) when it occurs alone, and secondary APS when it occurs in association with other autoimmune conditions, such as systemic lupus erythematosus (SLE) (1,2).

The most common pulmonary manifestation of APS is pulmonary thromboembolic disease (3). Recurrent pulmonary embolism (PE) may give rise to pulmonary hypertension (PHT) (4) carrying with it significant morbidity and mortality. There have been several reports describing the occurrence of PHT in patients with primary and secondary APS (5).

The prevalence of PHT in patients with primary and secondary APS is estimated to be 3.5 and 1.8%, respectively (6). The prevalence of aPL in patients with chronic thromboembolic PHT varies between 10 and 20% (4,7). After the first episode of thrombosis, APS patients have a higher risk of recurrent thrombosis than do patients without aPL (8).

The standard approach to the management of this condition is the use of oral anticoagulants with or without low-dose aspirin to prevent thrombi formation (9). As opposed to the customary levels of anticoagulation used in other conditions such as atrial fibrillation, maintaining a target International Normalized Ratio (INR) of 2.0 to 3.0 is not enough to prevent these events in all cases. Indeed, even higher levels of INR (3.0-4.0) may not suffice, as there are some patients who experience thrombo-

Department of Medicine E, Meir Medical Center, Kfar-Saba, affiliated to the Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel.

Address reprint requests to: Levy Yair, MD, Department of Medicine 'E', Meir Medical Center, Kfar-Saba, 44261, Israel. E-mail: levy.yair@clalit.org.il.

 0049-0172/09/$-see front matter
doi:10.1016/j.semarthrit.2008.01.016

ses and its complications even at these levels of anticoagulation (10). Because of the high risk of recurrent thrombosis in APS patients, effective anticoagulation is of the utmost importance. However, the regimen of pharmacological therapy for each individual patient remains uncertain.

Inferior vena cava (IVC) filters are commonly used to prevent PE. The indications for their use are as follows: failure of anticoagulant therapy and/or a strict contraindication to anticoagulant therapy, such as active bleeding. Despite the common use of these filters (mainly the Greenfield stainless steel device), there is debate as to their effectiveness.

The insertion of an IVC filter carries with it the risk of complications. The risk of death during the procedure is very low, amounting to less than 0.5% of patients (11). Several serious complications may occur during or shortly after the procedure, including IVC perforation, hemothorax, and IVC occlusion. These too are quite rare (12). Later, IVC obstruction is more frequent and is reported to occur in 5 to 18% of patients (11). Another important complication is venous thrombosis, especially at the insertion site, which has been reported to take place in up to 40% of cases (13). The risk of additional events of deep vein thrombosis (DVT) in patients with IVC filters for has been found to be higher, nearly 2.5 times that of patients receiving standard anticoagulation (14). We could not find significant data indicating how long these filters may be effective. However, estimations are in decades.

APS remains a relatively uncommon disease with varying modes of presentation. As a result, there are few studies in the current medical literature about the role of IVC filters in this setting (15,16). In this article we present and discuss 10 patients with the APS who underwent placement of an IVC filter for the prevention of recurrent PE.

METHODS

We retrospectively reviewed the charts of 110 patients with APS from the Meir Medical Center and the Sheba Medical Center (Israel). To be included in the study, patients had to fulfill all of the following criteria:

1. Definite APS according to the Sapporo criteria (2). Thus, only patients who tested positive for aCL antibodies at medium or high titers and/or LAC antibodies twice (at least 12 weeks apart) were enrolled in the study.
2. A history of thrombosis: PE was diagnosed by a high-probability lung scan, spiral computed tomography, or pulmonary arteriography. DVT was documented by appropriate imaging studies (ultrasonography and/or venography).
3. Treatment with oral anticoagulants to a target INR range of 2.0 to 4.0 during the previous 12 months.
4. Insertion of a filter in the IVC due to thromboembolic events, despite compliance with oral anticoagulant therapy. The decision to place each filter was made on an individual basis, based on the clinical circumstances at the time.

The aCL testing was performed by enzyme-linked immunosorbent assay (ELISA) (R&D, Minneapolis, MN). A positive aCL result was an immunoglobulin G (IgG) titer >10 GPL units and immunogloblin M >7 MPL units.

All patients had normal levels of protein S, protein C, and Antithrombin 3 levels.

In patients number 3 and 6 the homocysteine level was 18 and 23 μM/L, respectively (abnormal cutoff <15 μM/L) and their methylenetetrahydrofolate reductase (MTHFR) was homozygous. In all other patients it was negative.

The test for Factor V was performed in 6 patients of 10 (patients number 1, 2, 3, 6, 8, and 9). It was normal in patients 1, 3, 8, 9 and heterozygous in patients 2 and 6.

A test for a mutation in Factor II was not performed.

Overall 10 patients fulfilled the above criteria and were included in our study. We reviewed the data in their medical files from October 2004 to May 2007, noting all the events mandating hospitalization in the time period of March 1998 through May 2007. The extracted data were abbreviated to include only those details relevant to our current study.

CASE REPORTS

Case 1

A 70-year-old woman with a history of paroxysmal atrial fibrillation chronically treated with warfarin was hospitalized after being diagnosed with both a DVT and PE. On admission, her INR value was 2.5. Previous blood tests revealed moderate levels of aCL IgG antibodies (48 IU/mL) without the presence of LAC antibodies. Echocardiography performed during the workup showed an increased pulmonary blood pressure of 50 mmHg, moderate tricuspid insufficiency, and mild right ventricle dysfunction. Following evaluation, the team decided to insert an IVC filter. One year after these procedures, the patient died suddenly at home; cause of death was not established.

Case 2

A 52-year-old woman had Coombs-positive hemolytic anemia, SLE, and extremely elevated levels of aCL and LAC antibodies. While being chronically treated with anticoagulants, she had recurrent PE. Over the years, serial INR tests indicated a range of 2.5 to 3.5, which was her target level. The pressure in her pulmonary vessels reached values of 80 mmHg. Reevaluation of her status prompted the insertion of an IVC filter. No clinical evidence of recurrent PE was documented after the insertion of the IVC filter.

She died a year after the placement of the filter from sepsis caused by *Staphylococcus aureus* bacteremia.