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Case Report

Multiple Hemodialysis Access Failures Due to Recurrent Thrombosis in a Patient with Antiphospholipid Antibody Syndrome

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Abstract

Introduction: The most common complication of permanent hemodialysis (HD) vascular access is thrombosis, with some cases being related to a hypercoagulable state. Antiphospholipid antibody syndrome (APAS) is a cause of increased thrombotic tendency, and this may complicate the management of such patients on HD.

Case report: We describe a 48-year-old man with end stage renal disease (ESRD) of undetermined cause who was referred to our tertiary care center for urgent renal transplantation. He was maintained on regular HD, but his dialysis care was complicated by recurrent vascular access thrombosis to the extent that no further access site was available for his routine renal replacement treatment. A thorough thrombophilia screen confirmed the presence of antiphospholipid antibodies. A diagnosis of APAS was made and he was anticoagulated with warfarin. A transhepatic dialysis catheter was inserted and HD was resumed, but this was complicated by a large intra-abdominal hematoma. His anticoagulation was reversed and he improved, but his transhepatic catheter got clotted. This catheter was removed and a translumbar dialysis catheter was inserted as a last resort. Within a week of his arrival to our hospital, he recieved a kidney transplant. Graft function was delayed, but eventually improved, though he has never regained normal renal function.

Conclusion: The presence of APAS can complicate HD management by causing recurrent vascular access thrombosis and failure, and nephrologists must remain alert to this possibility. Anticoagulation management of these patients must be handled with extra care to avoid bleeding complications.

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Introduction

The most common complication of permanent hemodialysis (HD) vascular access is thrombosis, accounting for 80 to 85 percent of arteriovenous (AV) access loss. Anatomic problems, mainly venous stenosis, are by far the major predisposing factors for thrombosis, being responsible for 80 to 85 percent of all cases [1-2]. Arterial stenoses and non-anatomic problems such as excessive post-dialysis fistula compression, hypotension and hypovolemia account for the remaining cases, with some cases being related to a hypercoagulable state [3-6].

In this case report, we describe a patient with the primary antiphospholipid antibody syndrome (APAS) complicated by recurrent AV fistulae and vascular access thromboses. We outline his management and conclude by summarising a guideline-based approach to the care of such problematic cases.

Case report

A 48-year-old man with end stage renal disease (ESRD) of undetermined cause was referred to our tertiary care center for urgent renal transplantation. He had a long history of hypertension but had no history of diabetes mellitus. He was maintained on regular HD, but his dialysis care was complicated by recurrent vascular access thrombosis to the extent that no further access site was available for his routine renal replacement treatment.

A thorough thrombophilia screen confirmed the presence of antiphospholipid antibodies, while antinuclear antibody and anti ds-DNA antibodies were negative. A diagnosis of APAS was made and he was anticoagulated with warfarin. On the day of arrival to our hospital, a transhepatic dialysis catheter was inserted and HD was resumed. During the ensuing days, the patient became

hypotensive and his hemoglobin dropped markedly. Investigations revealed the presence of a large intra-abdominal hematoma that was related to his transhepatic dialysis catheter. He was resuscitated, his anticoagulation was reversed and he improved. Unfortunately, his transhepatic catheter got clotted. This was removed and a translumbar dialysis catheter was inserted as a last resort.

Renal transplant workup was completed within a week of his arrival to our hospital. Soon afterwards, he received a cadaveric renal transplant. Graft function was delayed, but eventually improved, though he has never regained normal renal function.

Discussion

APAS is a disorder characterized by arterial and venous thrombotic events associated with the presence of the so called antiphospholipid antibodies, which are auto-antibodies directed against phospholipids or phospholipids binding proteins. APAS can either be primary or secondary; in the latter case it is associated with other autoimmune diseases, particularly systemic lupus erythematosus (SLE), or related to acute infections or certain drug exposures. Four types of antiphospholipid antibodies have been characterized: anticardiolipin antibodies, antiprothrombin antibodies, anti-ethanolamine antibodies and anti-beta2-glycoprotein I antibodies. It is not clear whether the presence of antiphospholipid antibodies is involved in the pathogenesis of APAS or is an epiphenomenon. However, the presence of these antibodies is strongly associated with lupus anti-coagulant activity of serum and to the risk of arterial and venous thrombosis, spontaneous abortion and thrombocytopenia [7].

According to the Sapporo criteria for the diagnosis of the APAS, which are adopted by the American College of Rheumatology, the isolated detection of antiphospholipid antibodies in a patient's serum is not enough to make the diagnosis of APAS [8]. For a diagnosis of APAS to be made, the patient must have at least one clinical criterion and one laboratory criterion for APAS. Clinical criteria include one or more confirmed episodes of vascular thrombosis, or three un-explained consecutive abortions, or an un-explained late pregnancy loss, or a premature birth due to pre-eclampsia or placental insufficiency. Laboratory criteria include the detection of anicardiolipin antibodies in high titer or lupus anticoagulant activity in the patient's serum on at least two occasions, six weeks apart [8].

Renal complications occur in as many as 25% of patients with the APAS [9]. For the most part, these complications are directly related to thrombotic occlusions of glomerular capillaries; however, they occasionally involve the renal veins and renal arteries. Clinical manifestations include acute and subacute renal failure, active urinary sediment, the nephrotic syndrome and hypertension [9, 10]. Pathological entities include thrombotic microangiopathy, focal segmental glomerulosclerosis, ischemic interstitial nephritis with fibrosis and renal infarction [9, 10]. In addition, the presence of antiphospholipid antibodies in patients with ESRD often complicates their management. The presence of the antiphospholipid antibodies doubles the frequency of thrombotic occlusion of vascular access sites in HD patients [4].

The development of these antibodies may be related to the type of HD access used, since they are more frequent in patients with AV grafts compared to patients with AV fistulae. In a cross-sectional study that evaluated HD patients at a single dialysis facility, 22% of patients with AV grafts had a raised titer of anticardiolipin antibodies, while only 6% of patients with AV fistulae had similarly raised titers [5]. However, another likely explanation for the higher incidence of antiphospholipid antibodies in patients with AV grafts is that patients who already have the antiphospholipid antibodies are more likely to suffer from repeated vascular access failure and are more likely to require the placement of a synthetic AV graft. The development of antiphospholipid antibodies may also be related to the type of dialysis membrane used, with a greater incidence being associated with frequent use of cuprophane membranes (68% versus 34%, $P<0.05$) [6].

Vascular thrombosis is usually recurrent in APAS and all patients who have major or recurrent thrombotic event should receive life-long warfarin therapy with a target INR of 3.0 or higher [11, 12]. In a retrospective study of 147 patients with the APAS, recurrent thrombosis affected 30% of patients per year in those who did not receive long-term anticoagulation therapy. Aspirin alone was of no benefit, while low intensity warfarin (INR<3) with or without low dose aspirin offered only modest protection against recurrent thrombosis (23% of patients per year). High intensity dose warfarin (INR>3) with or without low dose aspirin markedly reduced the incidence of recurrent thrombosis (1.3% of patients per year) [11]. Treatment with warfarin may also be successful in increasing AV graft survival in HD patients with elevated anticardiolipin levels and a history of vascular access failure [11, 12].

The thrombophilic potential of these antibodies extends to the post-renal transplant stage as well, leading to a much higher early as well as late renal allograft loss in those who are not properly anticoagulated [13, 14]. In a study of 11 renal transplant recipients with APAS, all seven patients who did not receive anticoagulants lost

their allografts due to renal thrombosis within one week of surgery, while three of the four patients who received anticoagulation had functioning grafts for over two years post transplantation. However, among another group of 37 patients who had high titers of anticardiolipin antibodies without previous history of thrombosis, no allograft was lost to renal thrombosis [13].

In another study, nine patients with APAS received cadaveric kidney transplants, seven of whom were treated with warfarin and the remaining two were treated with heparin. Of the seven patients treated with warfarin, five did not have thrombotic complications post-transplant. However, three of these patients were taken off warfarin due to bleeding complications 6-12 months post-transplant; they all returned to dialysis shortly thereafter. The remaining two patients have maintained their allograft on warfarin therapy for three and five years post-transplant. The other two patients had post-transplant renal thrombosis within 24 hours of their transplantation despite warfarin therapy. Of the two patients treated with heparin, one was doing well at 6 years post-transplant while the other had early allograft loss due to thrombosis [14].

Recommendations for managing antiphospholipid antibody-positive patients on HD, peri-operatively and post-transplantation are [15]:

• If warfarin is used preoperatively, it must be stopped a few days prior to surgery.

• For general surgery prophylaxis, 5000 units of unfractionated heparin or 30 mg of enoxaparin is given subcutaneously one or two hours preoperatively.

• If there are no immediate postoperative bleeding complications, warfarin can be resumed the evening after surgery. Prophylactic heparin is continued until the INR is in therapeutic range.

A possible future role for the use of hydroxychloroquine in the management of APAS in renal patients is suggested by its efficacy in reducing thrombotic tendency in experimental animal studies [16].

Conclusion

Nephrologists must remain alert to the possibility of APAS being the cause of repeated vascular access thrombosis and failure in HD patients. Anticoagulation management of these patients must be handled with extra care to avoid bleeding complications.

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