

# Successful Graft Recovery from Thrombotic Acute Kidney Injury in a Kidney Transplant Patient with Antiphospholipid Syndrome

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Antiphospholipid syndrome nephropathy (APSN) is well documented in the literature as the renal involvement of the antiphospholipid syndrome (APS). A review of literature also shows that among antiphospholipid antibodies, lupus anticoagulant (LA) positivity is recognized as the strongest risk factor for APSN. In addition, APSN is also known to be associated with a poor functional outcome in the first posttransplant year. Therefore, it is a general belief that renal transplantation may be life threatening in APS patients. Furthermore, the presence of LA at the time of transplantation is particularly associated with a high rate of allograft APSN and the consequent poor transplantation outcomes. Here, we report the case that thrombotic acute kidney injury due to APSN after kidney transplantation can be successfully treated if anticoagulation therapy is timely applied with a prompt diagnosis.

**Key Words:** Antiphospholipid syndrome nephropathy, Antiphospholipid syndrome, Antiphospholipid antibodies, Lupus coagulation inhibitor, Kidney transplantation

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## Introduction

The antiphospholipid syndrome (APS) describes a clinical entity with recurrent thrombosis, fetal loss and the presence of antiphospholipid antibodies (APAs)(1). Antiphospholipid syndrome nephropathy (APSN) is the renal involvement of the APS(2). The most frequently observed pathologic lesions are the thrombotic microangiopathy (TMA), characterized by the fibrin thrombi in glomeruli and/or arterioles in the absence of vascular immune deposits or inflammatory cells and more chronic vascular lesions such as fibrous intimal hyperplasia (FIH) of interlobular arteries, and focal cortical atrophy (FCA)(2,3). APSN is usually associated with grave functional outcome in the first posttransplant year(4). So renal transplantation may be life-threat-

ening in APS patients, and the presence of lupus anticoagulant (LA) at the time of transplantation is associated with a high rate of allograft APSN and poor transplantation outcome(3,4). Here we introduce the case that thrombotic acute kidney injury from APSN after kidney transplantation can be successfully treated if anticoagulation therapy is timely applied with prompt diagnosis.

## Case Report

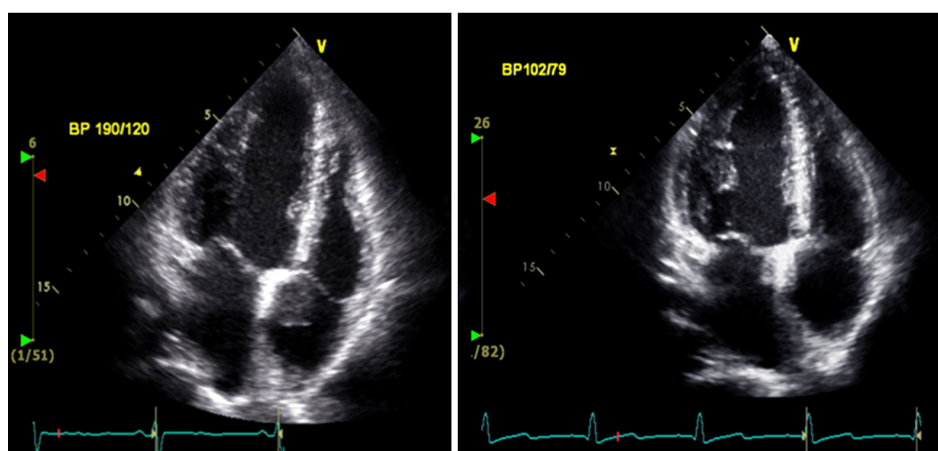
A 25-year-old woman was diagnosed lupus nephritis (class IV) in 2004. Despite of recurrent immunosuppressive treatment (steroid, cyclophosphamide, rituximab, and mycophenolate), her renal function had been decreased. Finally she was diagnosed end-stage renal disease and started hemodialysis from December 2010. Kidney transplantation was planned and while doing the preoperative evaluation right atrium myxoma was suspected in transesophageal echocardiography on May 16, 2011. Removal via submammary incision was conducted and organizing thrombus was found, thus coumadinization was started (Fig. 1). She

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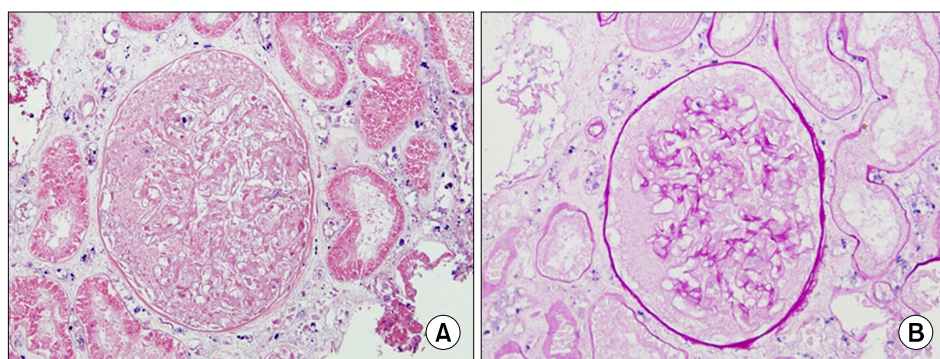
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was hospitalized on September 3, 2011, had heparin 5,000 unit subcutaneous injection daily for 3 days and stopped the day before the operation. On September 7, 2011 (day 0) she had living-related kidney transplantation from her cousin. Immunosuppressive therapy consisted of prednisolone, mycophenolate, and tacrolimus. Heparin 5,000 unit subcutaneous injection daily was started again on day 2. Doppler Ultrasonography on the graft proceeded on day 3, and cortical echogenicity was in normal range. But serum crea-

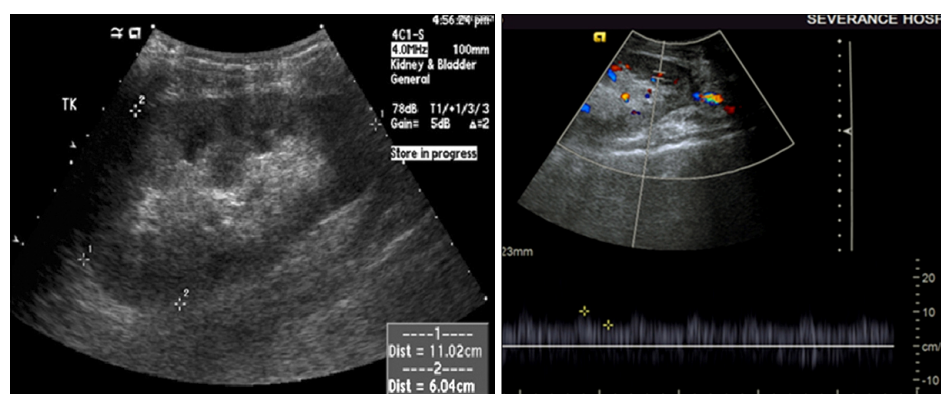
tinine (sCr) level was elevated continuously (5.16 mg/dL). Empirical steroid pulse therapy for acute rejection was done on day 3. In the Doppler ultrasonography on day 7, echogenicity of cortex slightly increased as well as the blood flow to the graft decreased. So graft biopsy was performed on day 8. Two-third of renal cortex showed ischemic necrosis and the remaining parenchyma showed tubular necrosis and interstitial edema (Fig. 2). APA was analyzed: LA (+), anticardiolipin antibody (aCL) immunog-



**Fig. 1.** Echocardiogram showing right atrium thrombus. After removal via submammary incision, thrombus was disappeared.

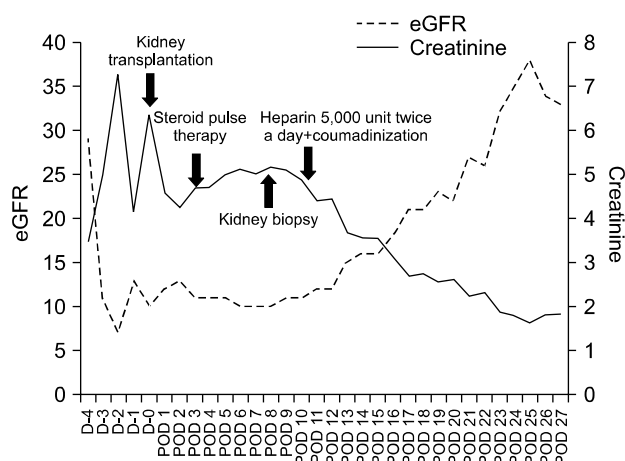


**Fig. 2.** The biopsy slide of transplanted kidney showing cortical necrosis, focal (postoperative day 8) (A, HE stain,  $\times 120$ ; B, PAS stain,  $\times 120$ ).



**Fig. 3.** Sonography of transplanted kidney (postoperative day 15). The transplanted kidney size was 11.4 cm. The echogenicity of the cortex was increased and blood flow was decreased. The resistive index of upper, mid, and lower pole was 0.56.

lobulin M (IgM) (-), aCL IgG (-), anti- $\beta$ 2GPI(a $\beta$ 2GPI) IgG (-), and a $\beta$ 2GPI IgM (-). With the diagnosis of APSN, anticoagulation therapy was continued. From day 10, 5,000 unit of heparin was subcutaneously injected twice a day. Since then, sCr decreased continuously. In the Doppler ultrasonography on day 15, echogenicity of allograft cortex still increased, however the blood flow to the graft was improved (Fig. 3). Heparin was changed to coumadin with target prothrombin time international normalized ratio 2~3. Finally on day 25 sCr was decreased to 1.64 mg/dL (Fig. 4). After 12 weeks, LA was weak positive and



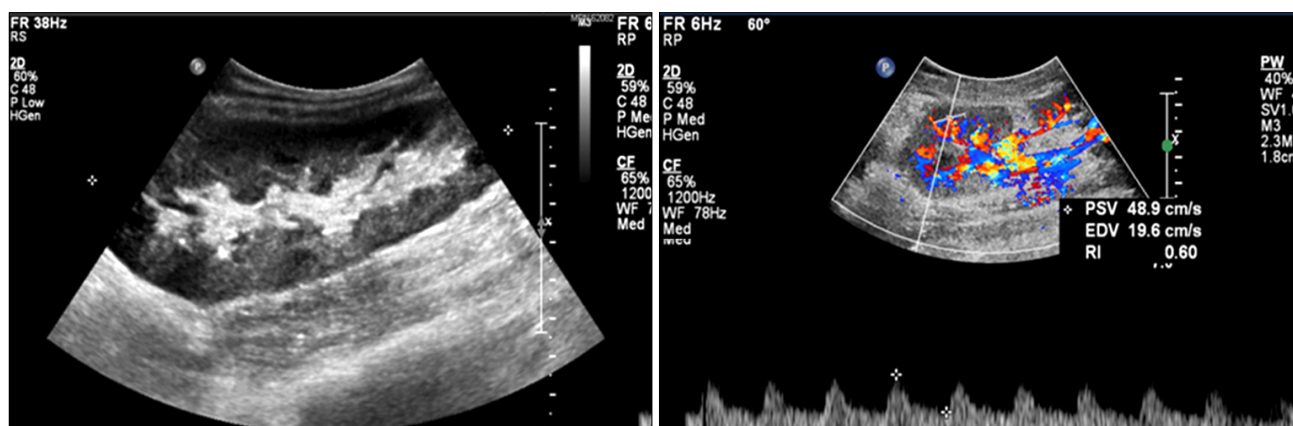
**Fig. 4.** Change of renal function. After anticoagulation therapy was started the transplanted kidney function was improved. Abbreviations: eGFR, epidermal growth factor receptor; POD, postoperative day.

sCr was 1.28 mg/dL. Doppler ultrasonography performed 3 months after transplantation showed the normal echogenicity of the cortex and improved blood flow (Fig. 5). She takes coumadin currently without additional complications.

## Discussion

The manifestations of APSN are the renal artery thrombosis/stenosis, renal infarction, hypertension, renal vein thrombosis, end-stage renal disease, increased allograft vascular thrombosis, some types of glomerular disease, and a small vessel vaso-occlusive nephropathy(2). The most frequently observed pathologic lesions are the TMA, characterized by the fibrin thrombi in glomeruli and/or arterioles in the absence of vascular immune deposits or inflammatory cells and more chronic vascular lesions such as FIH of interlobular arteries, and FCA(2,3).

In APSN, APAs are directed against phospholipid-protein complexes and include LA, IgG or IgM aCL, and IgG or IgM a $\beta$ 2GPI(1,2). Antibodies should be demonstrable on at least two occasions separated by 12 weeks(1). These antibodies may be associated with connective tissue diseases such as systemic lupus erythematosus (secondary APS) or be found in isolation (primary APS)(5). However, the most recent international consensus statement on classification criteria for APS advises against this terminology because the clin-



**Fig. 5.** Sonography of transplanted kidney (postoperative day 3 months). The transplanted kidney size was 11.8 cm. The echogenicity of the cortex was normal and there was no hydronephrosis or fluid collection. The resistive index of upper, mid, and lower pole was 0.60~0.64.

ical consequences in both groups appear to be the same(5).

Among APAs, LA positivity is recognized as the strongest risk factor for APSN(2). And APSN is associated with grave functional outcome in the first post-transplant year(4). So renal transplantation may be life-threatening in APS patients, and the presence of LA at the time of transplantation is associated with a high rate of allograft APSN and poor transplantation outcome(3,4).

In this case, the APA status had not been worked up before the kidney transplantation. Although thrombus was not found in the pathology, evidence of vascular obstruction and decreased blood flow from Doppler ultrasonography suggested the high probability of thrombotic lesion. Considering the previous history of atrial thrombus and the serologic evidence, we concluded that APS involved the grafted kidney in this case. The improved blood flow of the grafted kidney after 3 months with continuous anticoagulation therapy also suggested the APSN. APSN is usually associated with a catastrophic functional outcome in the first posttransplant year(5). However in our case, renal function was improved dramatically with the appropriate anticoagulation therapy after the early detection of allograft APSN. Our experience suggests that kidney transplantation can be performed successfully in APS patients if timely anticoagulation therapy is performed. However, there are no recommendations on immediate postoperative thromboprophylaxis after kidney tran-

splantation(6-8). Guideline recommendations and standardized protocols for the use of anticoagulation after kidney transplantation in APS patients should be developed.

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