Acute Interstitial Nephritis in the Course of Primary Antiphospholipid Syndrome

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Abstract: Renal involvement in the course of primary antiphospholipid syndrome (APS) is exceptional and typically results in vascular nephropathy. Other nephropathies are rarer. We report an unusual case of acute interstitial nephritis associated with primary APS in a 38-year-old man with a history of recurrent venous thrombosis of the lower and upper limbs which was admitted for exploration of organic acute renal failure with creatinine level at 700µmol/l and both normal-sized kidneys. Biology showed a prolonged activated partial thromboplastin time; protein C, S, and anti-thrombin III were at normal levels; the antiphospholipid antibodies were positive at significant levels: Ig G at 38 GPL and IgM at 25 MPL. Nuclear antibodies were negative. Renal biopsy concluded to an isolated acute interstitial nephritis (AIN). There was no prior history of suspicious drug intake, nephrolithiasis, and neither old nor recent urinary tract infection. Under anticoagulants and corticosteroid therapy at full dose, the outcome was favorable with a check-up of creatinine level at 82µmol/l after 2 months.

To the best of our knowledge, the isolated AIN has not been described during the primary APS. This nephropathy could be a new event enriching the spectrum of renal complications during this syndrome.

Keywords: Acute interstitial nephritis; primary antiphospholipid syndrome; nephropathy.

INTRODUCTION

The primary antiphospholipid syndrome (APS) is a clinico-biological entity characterized by the recrudescence of arterial and/or venous thrombosis, the permanent presence of auto-antibodies directed against membrane phospholipids, and the exclusion of any other associated autoimmune diseases [1]. This definition distinguishes the primitive APS from the secondary APS that can be associated with multiple infectious, neoplastic or autoimmune diseases, particularly systemic lupus erythematosus [1,2].

The diagnosis of APS is based on specific clinico-biological criteria first developed in 1998 (Sapporo criteria) and then revised and validated in 2004 (Sydney criteria) [2].

To retain the diagnosis of an APS, we require the combination of a clinical criterion (arterial or venous thrombosis or recurrent miscarriages) and a biological criterion (lupus anticoagulant or anti-cardiolipin antibodies or anti-β2 glycoprotein 1 antibodies positive at least 12 weeks apart) [1,2].

In addition to the very specific vascular and obstetrical manifestations, several other visceral disorders can be seen during this syndrome (cardiac, pulmonary, neurological, renal, gastrointestinal, etc...). The most serious form of this syndrome with multi-visceral involvement defines the catastrophic syndrome of anti-phospholipids [3].

Apart from this serious form, renal involvement is exceptional and is classically characterized by vascular nephropathy: thromboses in major renal arteries or veins or thrombotic microangiopathy [4-6]. Other nephropathies (non-vascular) are very rarely reported during APS.

We report an exceptional and unusual case of isolated acute interstitial nephritis (AIN) associated with primary APS.

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CASE REPORT

A 38-year-old Tunisian patient, with a history of recurrent venous thrombosis of the limbs (right lower limb and left upper limb at an interval of one year) was admitted to our department (Department of Internal Medicine at Gabès Military Hospital, Tunisia) on September 2017 for exploration of organic acute renal failure with creatinine level at 700 μmol/l and two normal-sized kidneys on ultrasound. The diagnosis was made in the emergency room because of repetitive vomiting and asthenia. The patient was apyretic with stable hemodynamic status.

The basic biological tests (complete blood count, transaminases, blood electrolytes, calcium, phosphorus, muscle enzymes, C reactive protein, sedimentation rate, serum protein electrophoresis, and thyroid function) showed no abnormalities.

In front of the recurrent venous thrombosis, a screening of thrombophilia objectified a prolonged activated partial thromboplastin time (patient/control=2.5), protein C, S and antithrombin III at normal levels, positive antiphospholipid antibodies (anti-cardiolipin and Anti-β2GP1) at significant levels: IgG at 48 GPL and IgM at 35 MPL. The antinuclear, anti-native DNA, and anti-soluble antigens antibodies were negative.

Thus the diagnosis of primary APS was retained due to the association of recurrent venous thrombosis and the positivity of antiphospholipid antibodies. Systemic investigations (cardiac, pulmonary, neurological and digestive) were normal eliminating the catastrophic form of this syndrome.

Renal biopsy concluded to an isolated acute interstitial nephropathy with renal interstitial infiltration by polymorphic inflammatory cells without signs of vasculitis or micro thrombosis. There was no focal cortical atrophy or interstitial fibrosis.

The etiological research has not objectified suspicious drug intake, or nephrolithiasis (ultrasound and CT scan) and no recent or old urinary tract infection (urine culture, blood cultures and urinary tuberculosis tests). This nephropathy, in front of the negativity of the etiological investigations, was related to the primary APS.

The patient was treated with an effective curative anticoagulation (low molecular weight heparin relayed withacenocoumarol) and systemic corticosteroids at full dose (1mg/kg/day) for four weeks followed by a gradual decrease. The evolution was favorable with rapid disappearance of functional complaints and progressive normalization of creatinine level: 250 μmol/l at 2 weeks, 103 μmol/l at 1 month and 82 μmol/l at 2 month control.

The check-up of antiphospholipid antibodies after an interval of twelve weeks was always positive confirming the diagnosis of primary APS.

DISCUSSION

The exact prevalence of renal complications during the APS is not well known but they are recognized as uncommon [4]. Indeed, in the largest European series of Cervera R. et al., (Euro-Phospholipid Project Group) comprising 1,000 cases of APS, renal involvement was noted only in 2.7% of cases [7].

Clinically, the nephropathy secondary to APS includes hypertension, nephritic syndrome, nephrotic syndrome, acute renal failure, chronic vascular nephropathy and the reduction of renal graft’s survival [8,9]. This renal disease typically results from thrombosis and/or stenosis of the intra-renal arteries and/or arterioles, renal vein thrombosis or diffuse intra-renal micro-thrombosis [5,9,10].

The histological appearance of this antiphospholipid-related nephropathy associates, to varying degrees, typically diffuse thrombotic lesions and ischemic glomeruli with classically negative glomerular and arterial immunofluorescence [5]. Diffuse micro-thrombosis of the intraparenchymal renal arteries and glomerular capillaries is histologically manifested by thrombotic microangiopathy [5,6]. In late-diagnosed forms, histological features such as

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American Research Journal of Clinical Case Reports
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fibrous intimal hyperplasia, focal cortical atrophy fibrous occlusions of the arteries, indicative of chronic vaso-occlusive lesions, can be seen on renal biopsy specimens [6].

Exceptionally other types of kidney disease (non thrombotic), especially glomerular nephropathies, have been related to the primary APS as sporadic cases: focal segmental glomerulosclerosis [11], extra-membranous glomerulonephritis [10], membrano-proliferative glomerulonephritis [4], Pauci-immune glomerulonephritis [12] or diffuse renal vasculitis [4].

To the best of our knowledge, no other cases of isolated tubulo-interstitial nephritis have been previously reported as renal manifestation of primary APS. Even in the series of five cases of renal biopsy performed during the APS of Saracino A. et al., the tubulo-interstitial disease was attached to one or several other nephropathies: thrombotic microangiopathy (4 cases), focal segmental glomerulosclerosis (4 cases) and the double outline of the capillary walls (2 cases) [13].

**Conclusion**

Our observation is, to the best of our knowledge, the first reporting this association. The acute tubulo-interstitial nephritis could be a new event enriching the spectrum of renal complications during the primary APS.

**REFERENCES**


