Hypertension Due to Renal Artery Occlusion in a Patient With Antiphospholipid Syndrome

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We report an unusual case of renovascular hypertension in a 16-year-old boy with primary antiphospholipid syndrome (PAPS), admitted to our clinic for severe drug-resistant hypertension and hypokalemia. Hormonal investigation revealed secondary aldosteronism and positive captopril test for renovascular disease. Aortography confirmed the occlusion of the left renal artery. After nephrectomy, normalization of blood pressure and secondary aldosteronism occurred. Presently the patient remains in good health, receiving warfarin anticoagulant therapy.

PAPS is defined by the presence of antiphospholipid antibodies and recurrent thrombosis. Arterial thrombosis (29%) appears to be less prevalent than venous thrombosis. Thrombotic microangiopathy of the kidney is frequently observed but renal artery occlusion, as seen in our patient, is unusual. Am J Hypertens 2001;14:62–65 © 2001 American Journal of Hypertension, Ltd.

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Renovascular hypertension is believed to occur in a subset (1% to 4%) of the hypertensive population and is the result of a severe decrease (> 70%) in renal blood flow secondary to unilateral or bilateral branch or main renal artery stenosis with renal ischemia. In the young adult (age < 40 years), fibromuscular dysplasia of the renal arteries is the most common cause; this occurs predominantly in female patients. With aging, atherosclerosis becomes the most common underlying process, which can be identified in as many as 10% of hypertensive patients older than 60 years.

Renal artery thrombosis, arteritis (eg, Takayashu's arteritis), systemic vasculitis, and retroperitoneal fibrosis are less common causes of renovascular hypertension.[1] We report an unusual case of renovascular hypertension and renal artery occlusion in a 16-year-old boy with antiphospholipid antibody syndrome (APS).

Case Report

A previously healthy 16-year-old boy was admitted to our clinic for severe drug-resistant hypertension, hypokalemia, and suspected hyperaldosteronism with a periemphalic murmur at the physical examination.

Three months before admission he had tonicclonic and hypertensive crises (mean blood pressure [BP]: 140/100 mm Hg; highest BP: 200/120 mm Hg). A magnetic resonance imaging (MRI) scan showed multiple cerebral ab-

normal signals suggestive of flogosis or vasculitis. The search for neurotropic virus antibodies in serum and cerebrospinal fluid (CSF), as well as for *rickettsia* antibodies in the CSF, was negative.

Left renal biopsy showed no vasculitis but it caused a wide renal hematoma. Laboratory investigations revealed slight hypokalemia (3.3 mmol/L [3.3 mEq/L]), whereas prothrombin time (PT), partial thromboplastin time (PTT), platelet count, serum creatinine, and creatinine clearance were normal.

The hormonal investigation revealed secondary hyperaldosteronism with increased levels of plasma renin activity (PRA) and aldosterone, both in the supine and upright positions. The captopril test was positive for renovascular disease (aldosterone: from 832.2 to 3495.2 pmol/L [from 30 to 126 ng/dL], PRA: from 1.3 to 6.7 to 18.3 ng/mL/h [from 4.8 to 24 to 66 ng/mL/h]) (Table 1). The ACTH stimulation test showed normal plasma cortisol levels (270.4 to 772.5 mmol/L [9.8 to 28 mcg/mL]).

Renal Doppler sonography and scintigraphy (99-Tc-DTPA) showed a small-sized left kidney with hypoperfusion (Figure 1). Aortography showed occlusion of the left renal artery, close to its origin, and stenosis of the superior mesenteric artery with collateral revascularization (Figure 2). Pulmonary scintigraphy, fluoroangiography, and angio-MRI of the cerebral vessels excluded further vascular involvement.

We also found increased PTT, positive lupus anticoag-

Table 1. Laboratory investigations before and after left nephrectomy in paps patient

	Before Left Nephrectomy	After Left Nephrectomy	Normal Range
Creatinine (S)	85.7	89.3	53–123.7 μmol/L
Sodium ion (S)	141	143	136–145 mmol/L
Potassium ion (S)	3.4	4.5	3.5–5 mmol/L
Supine renin activity	1.3	0.08	0.05–0.7 ng/(Ls)
Upright renin activity	6.6	0.1	0.4–1.6 ng/(Ls)
Renin activity after captopril test	9.7	1.9	
Supine aldosterone	832.2	83.2	27.7–443.8 pmol/L
Upright aldosterone	3495.2	582.5	110.9–859.9 pmol/L
Aldosterone after captopril	970.9	194.2	
Urinary aldosterone	127		8.3–41.6 nmol/day
Platelet count	213	233	150–400 $\times$ 10^3/L
PT	96%	22%*	80–143
PTT	49 s	44 s*	< 36 s
LAC	Positive		Negative
aCL	IgG: 36		IgG < 10 GPL/mL
	IgM: 15		IgM < 7 MPL/mL
VDRL	Negative		Negative
Antinuclear antibodies	Absent		Absent
Anti-DNA antibodies	2 U/L		< 2 μ/L
Anti-ENA antibodies	Absent		Absent
Antiimmunoglobulin antibodies	Absent		Absent
Complement analysis	Normal		
Antithyroglobulin antibodies	17		< 100 UI/mL
Anti-TPO antibodies	5		< 70 UA/mL
TSH receptor antibodies	4		< 9 U/L

PT = prothrombin time; PTT = partial thromboplastin time; LAC = lupus anticoagulant; aCL = anticardiolipin antibodies; VDRL = venereal disease research laboratory; TPO = thyroid peroxidase antibodies; TSH = thyrotropin.

* Receiving warfarin anticoagulant therapy.

ulant (LAC) and anticardiolipin antibodies (aCL), a normal complement analysis, and negative antinuclear antibodies. All these findings suggested the diagnosis of primary antiphospholipid syndrome (PAPS) (Table 1).

After left nephrectomy, normalization of the blood pressure and resolution of the secondary hyperaldosteronism occurred. Histologic examination of the removed kidney revealed interstitial nephritis with recanalized left renal arterial thrombosis.

Two years after the nephrectomy, the patient is still in good health, receiving warfarin anticoagulant therapy.

Discussion

The PAPS is characterized by the presence of both venous and arterial occlusive events associated with antiphospholipid antibodies (LAC and aCL) and, especially, high levels of IgG, often accompanied by thrombocytopenia and false-positive VDRL tests. This syndrome does not appear to have any of the clinical or serologic features of systemic lupus erythematosus (SLE) or of autoimmune disease, which characterizes secondary APS.[2–5]

Antiphospholipid antibodies are a heterogeneous group of antibodies that appear to react with negatively charged phospholipids. The antigen is now thought to be $\beta2$ glycoprotein 1, even if the exact nature of the epitope(s) remains uncertain.[6–8]

Antiphospholipid antibodies are found with frequencies of 1% to 2% in the normal population and in 25% to 50% of patients with SLE. In APS patients, the male-to-female ratio is 1:4 and patients with non-SLE disorders are older than those with SLE. The presence of antiphospholipid antibodies alone, without clinical manifestations, does not define APS. Antiphospholipid antibodies without associated APS symptoms are present in patients with infections, particularly viral ones, AIDS, and hematologic disorders such as idiopathic thrombocytopenic purpura. They may also be induced by certain drugs (procainamide and sulfonamides), as well as by oral contraceptives. In most of these conditions, the antibodies are at low levels and predominantly of the IgM istotype, and they are not associated with thrombotic events.[3,4]

Thrombosis is the most distinctive lesion of APS and may occur in any venous and arterial vessels. In a retrospective study of 70 patients with antiphospholipid antibodies, Rosove and colleagues found that the site of a first event (arterial or venous) could be predictive of future locations in 91% of cases.[4]

Venous thrombosis is more common than arterial thrombosis and it involves particularly the deep veins of the lower extremities, less commonly the retinal, renal, and hepatic veins. The clinical presentation is variable, from a superficial or deep thrombophlebitis to severe mul-
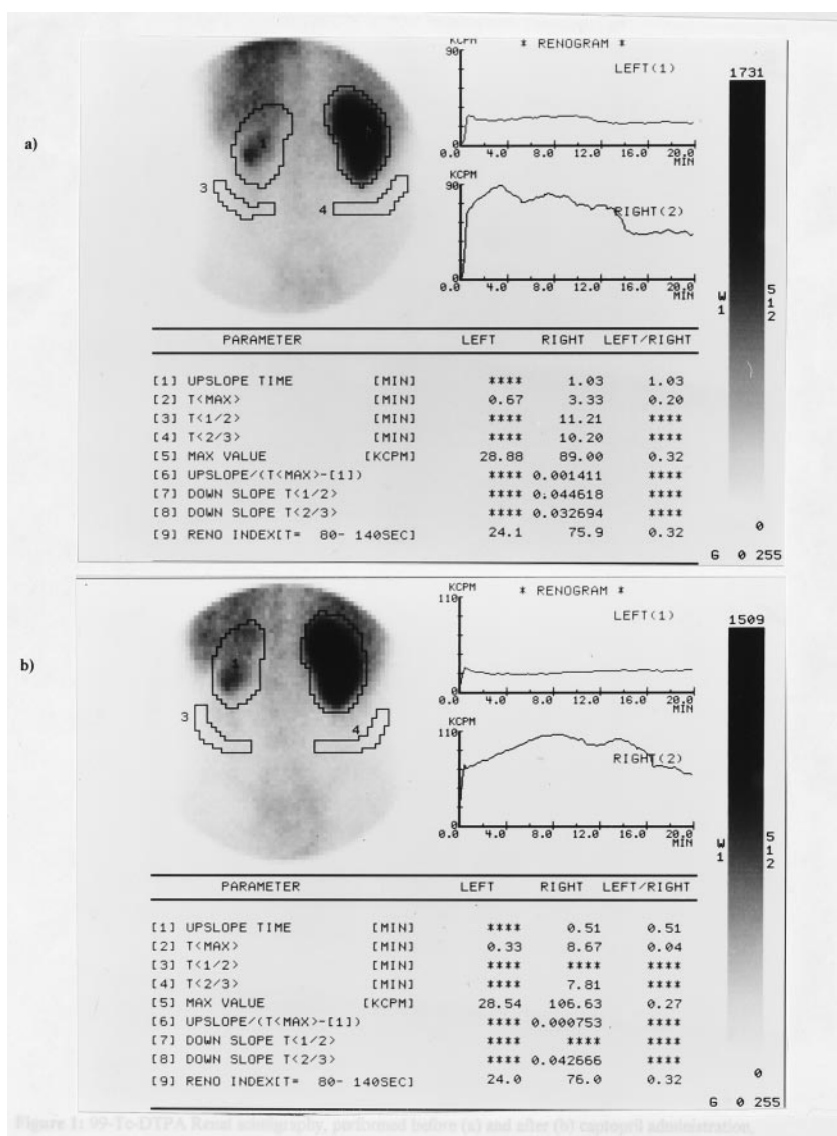
FIG. 1. 99-Tc-DTPA renal scintigraphy, performed before **(a)** and after **(b)** captopril administration, showed a small-sized left kidney with hypoperfusion.

tiple thrombotic events, as in catastrophic syndrome. In a recent literature review, including 50 patients with catastrophic APS, Asherson et al have found major venous occlusion in 36% of cases and major arterial occlusion in 24% of cases.[8,12]

Recurrent spontaneous abortions in the first trimester, caused by placental thrombosis, also can be associated with APS. Dermatologic manifestations (as in livedo reticularis) are probably the most common manifestations of APS. Early recognition of these signs is important because they can be harbingers of major later thrombotic events in many patients.

Twenty-five percent of thrombosis occurs in cerebral and 16% in peripheral arteries. Transient ischemic attacks, ischemic strokes, chorea, epilepsy, and cognitive function deficits are the most common neurologic manifestations. Strokes are often multiple and are followed by multiinfarct dementia. Sometimes these neurologic disorders follow embolic strokes secondary to valvular vegetations.[5,9]

Ischemic events can also involve the enterohepatic circulation, causing a Budd-Chiari Syndrome or angina abdominis. In our case, even if the aortography showed stenosis of the superior mesenteric artery, there were no symptoms or signs of ischemia because of the presence of collateral revascularization.

Both angina and myocardial infarction have been reported in patients with antiphospholipid antibodies and, at present, 30 cases of acute adrenocortical insufficiency due to adrenal artery thrombosis have been described. In our patient we have observed a normal adrenocortical function.

Although scant attention has been paid, at present, to the renal manifestations of the APS, the kidney is probably a major target organ. Thrombosis may develop at any location within renal vessels: renal artery trunk or branches, intrarenal arteries or arterioles, glomerular capillaries, and the renal vein. The clinical manifestations consist of highly variable degrees of renal failure and

FIG. 2. Aortography showed occlusion of the left renal artery, close to its origin, and stenosis of the superior mesenteric artery, with collateral revascularization.

systemic hypertension ranging from mild to malignant.[10,11] These events can occur both in primary and secondary APS and, most commonly, in the catastrophic form, which is caracterized by a rapid clinical course with involvement of at least three organs.[9] Biopsy findings are often consistent with a thrombotic microangiopathy involving glomerular capillaries.[13–15]

To our knowledge, this is an unusual case of primary APS, in which renal artery occlusion caused renal hypertension. Our patient also had diffuse thrombotic arterial damage affecting the superior mesenteric artery and the cerebral arterial circle. Only five other cases of PAPS have been reported in the literature with unilateral or bilateral renal artery occlusion. Although most major clots occur in persons with high levels of antibody, our patient had a moderately positive titer. We are not able to explain such a phenomenon. In any case, other reports of PAPS have showed lower levels of antibody with respect to the case we have described here.[16] A laboratory variability can be evoked as responsible for such differences as well as for the latency time between antibody titer determination and the acute events.

These patients are now in good health and normotensive after percutaneous transluminal balloon angioplasty and/or antihypertensive therapy. Prophylactic anticoagulant therapy with warfarin was always performed.[3,16–19] According to data in the literature, the best treatment to prevent secondary thromboses in the APS is warfarin anticoagulation.[5] In our case, nephrectomy had to be performed because the kidney was seriously and irreversibly damaged.

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