Resolution of proteinuria after transarterial embolization of aberrant renal artery in a patient with focal segmental glomerulosclerosis

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Abstract A 24-year-old man was admitted to our hospital for persistent proteinuria. He was born with a low birth weight but had grown up uneventful until the age of 20 when he was found to have proteinuria. Because his body mass index was 30.9 kg/m² at that time, he was diagnosed as obesity-related nephropathy. However, weight reduction and administration of ACE inhibitor were minimally effective for the amelioration of proteinuria. Ultrasound-guided percutaneous renal biopsy at the lower pole of right kidney was performed. As serious bleeding occurred from the right aberrant renal artery soon after biopsy, he was treated with transarterial embolization (TAE). The day after TAE, proteinuria completely disappeared. Renal biopsy showed benign nephrosclerosis with secondary focal segmental glomerulosclerosis (FSGS). Proteinuria could be induced by increased blood flow and pressure due to abnormal blood supply from aberrant renal artery. This is the first report of resolution of proteinuria after TAE of aberrant renal artery in a patient with FSGS.

Keywords Aberrant renal artery · Proteinuria · Focal segmental glomerulosclerosis · Transarterial embolization

Introduction

Focal segmental glomerulosclerosis (FSGS) is caused by various clinical conditions and it is therefore classified as either primary or secondary FSGS. Particularly secondary FSGS is linked to a variety of conditions that include kidney diseases, drug abuse, viral infections, cancers, hypertension, obesity, genetic mutations and others. Renal biopsy is usually necessary for definite diagnosis and proper management for the patients with FSGS. Ultrasound-guided percutaneous renal biopsy (PRB) is an important technique for making diagnosis and obtaining prognostic information for the treatment of glomerular diseases [1, 2]. Although PRB has some complications mainly related to bleeding [2, 3], life-threatening complications of PRB occur in only <0.1 % of cases [4–6].

The extra renal artery is a kind of renal vascular variation, which has been seen about 30 % in the anatomic and cadaver studies [7–9]. The aberrant renal artery is one of the extra renal arteries, which arises from aorta and directly enters the kidney [9].

In the present report, we describe a rare case of PRB-induced aberrant renal artery bleeding in the patient with secondary FSGS which showed resolution of proteinuria after transarterial embolization (TAE).

Case report

A 24-year-old man was admitted to our hospital for persistent proteinuria. He weighed 1,000 gram at birth but had grown up uneventful until the age of 20 when he was found to have proteinuria. Because his body mass index was 30.9 kg/m² at that time, he was diagnosed as obesity-related nephropathy and directed to lose weight. Although

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Table 1 Laboratory data on admission

Urinalysis		Transferrin saturation	38.2 %
Protein	0.5 g/day	Ferritin	132 ng/mL
Occult blood	(–)	Sodium	141 mEq/L
Red blood cells	1–4/HPF	Potassium	4.0 mEq/L
White blood cells	1–4/HPF	Chloride	103 mEq/L
Hematology		Calcium	8.4 mg/dL
Red blood cells	$592 \times 10^4/\mu\text{L}$	Phosphate	2.8 mg/dL
Hemoglobin	18.3 g/dL	Serology	
Hematocrit	53.5 %	CRP	<0.24 mg/dL
White blood cells	5,600/ μL	Antinuclear antibodies	(–)
Platelet	$22.1 \times 10^4/\mu\text{L}$	IgG	1,217 mg/dL
Erythrocyte sedimentation rate	1 mm/1 h	IgA	207 mg/dL
Chemistry		IgM	124 mg/dL
Total protein	7.2 g/dL	CH50	44.4 U/mL
Albumin	4.6 g/dL	C3	113 mg/dL
Creatinine	0.90 mg/dL	C4	25 mg/dL
Estimated GFR	87.4 ml/min/ 1.73 m^2	Hemostasis	
Blood urea nitrogen	12.1 mg/dL	Bleeding time	1.3 min
Uric acid	7.3 mg/dL	Prothrombin time	11.6 s
Fasting plasma glucose	102 mg/dL	Partial thromboplastin time	30.5 s
Glycated hemoglobin	5.2 %	Endocrinology	
Total bilirubin	0.9 mg/dL	Plasma renin activity	15 ng/mL/h
AST	19 IU/L	Plasma aldosterone concentration	120 pg/mL
ALT	36 IU/L		
γ -GTP	22 IU/L		
LDH	140 IU/L		

he lost 14 kg in 24 months, he had persistent proteinuria (0.5–1.5 g/day). Imidapril hydrochloride 10 mg/day was administered without apparent reduction of proteinuria.

He had no family history of collagen vascular disease or kidney disease. He was a college student and non-smoker and had no history of illicit/recreational drug use.

On admission he was afebrile, normotensive (114/68 mmHg) with a pulse of 60/min. He was 164.5 cm tall and weighed 63.2 kg. Physical examination was unremarkable. Laboratory examination revealed that 24-h urinary excretion of protein was 0.5 g, serum creatinine concentration and estimated glomerular filtration rate were 0.90 mg/dl and 87.4 ml/min/ 1.73 m^2 , respectively (Table 1). Since the effects of weight reduction and administration of ACE

inhibitor were insufficient for the amelioration of proteinuria, it was considered to be appropriate to investigate renal histology. After we explained to the patient and his family the risk and benefit of renal biopsy, ultrasound-guided PRB was performed at the lower pole of right kidney using the 16-gauge needle. Two hours after biopsy, he had nausea, abdominal pain, sweating, and discomfort on the right side of the waist. Abdominal computed tomography (CT) showed hematoma in perinehritic and retroperitoneal space, and the aberrant renal artery at the lower pole of the right kidney was found (Fig. 1). Renal artery angiography demonstrated severe bleeding from the aberrant renal artery (Fig. 2b). TAE was performed and aberrant renal artery bleeding was satisfactorily controlled (Fig. 2c). During the bleeding episode, he was hemodynamically stable and did not need a transfusion. One day after TAE, he was found to have dramatically reduced proteinuria to 0.06 g/day. He had maintained complete remission of proteinuria since then (Fig. 3).

Renal biopsy samples were examined. Light microscopy showed that sampling tissues consisted of renal cortex. There were 34 glomeruli, 11 of which were globally sclerotic, one showed segmental sclerosis resembling the

Fig. 1 Abdominal computed tomography (CT). Abdominal CT showed hematoma in perinehritic and retroperitoneal space, and the aberrant renal artery at the lower pole of the right kidney was found, which arised from aorta and directly entered the kidney (white arrow)

Fig. 2 Images of the renal angiography. **a** Right renal angiography revealed a defect of the blood flow in the lower segment of right kidney despite a presence of the upper and middle segmental blood flow. **b** The angiography of the right aberrant renal artery demonstrated the blood flow of lower segment of right kidney and severe bleeding of lower pole of right kidney (*black arrow*). **c** The right aberrant renal artery bleeding was satisfactorily controlled after transarterial embolization

perihilar variant of FSGS, and remaining ones exhibited glomerulomegaly without any glomerular injury (Fig. 4b, c). There was mild tubular atrophy and interstitial fibrosis involving approximately 40 % of the cortex (Fig. 4a). Moderate intimal thickening and moderate hyalinosis were noted in the small arteries (Fig. 4c). Immunofluorescence was negative for IgG, IgA, IgM, and C3. Electron microscopic examination showed mild focal foot process effacement (Fig. 4e). According to these findings, he was diagnosed as benign nephrosclerosis with secondary FSGS.

Discussion

Renal artery variations are common [9] and it is reported that the incidence of extra renal artery is approximately 30 % in the general population [7–9]. Recently, renal artery variations are becoming more important, because interventional radiological procedures, urological and vascular operations, and renal transplantation have been widely available [8, 9]. As computed tomographic angiography and renal angiography are not routinely performed in the patients with glomerular disease, it is difficult to evaluate the extra renal artery before renal biopsy. The extra renal arteries are divided into 2 groups: accessory (hilar) and aberrant (polar). The accessory arteries enter kidneys from the hilus with main renal artery, whereas aberrant arteries enter kidneys directly from capsule outside the hilus [9]. In the present case, the angiographic findings were compatible with aberrant renal artery and renal biopsy injured the artery when the biopsy was performed from the lower pole of the right kidney. It was reported that significant biopsy-induced renal artery bleeding rarely occurred because renal artery was contracted when the kidney was punctured [2]. However, because of higher perfusion pressure of aberrant renal artery, vascular constriction induced by tissue biopsy could not prevent from clinically significant bleeding from the artery. Conservative bleeding control was considered to be difficult and TAE was performed.

FSGS is thought to be a group of clinical-pathologic syndromes sharing a common glomerular lesion and mediated by diverse insults directed to the podocyte [10]. It

Fig. 3 Clinical course. Despite weight reduction and administration of imidapril hydrochloride, proteinuria was not improved significantly. Ultrasound-guided percutaneous renal biopsy was performed and serious bleeding occurred from the right aberrant renal artery

soon after biopsy. He was treated with transarterial embolization (TAE). The day after TAE, proteinuria completely disappeared. Imidapril hydrochloride was discontinued 4 weeks after TAE, however, he had maintained complete remission of proteinuria

is well known that FSGS is the podocyte disease or podocytopathy [11, 12], and classified according to the cause of podocyte injury; primary and secondary form. Among the secondary FSGS, adaptive response has been reported to be associated with the development of secondary FSGS. Adaptive response include intrarenal vasodilatation, increased glomerular capillary pressure, and enhanced plasma flow rate [10, 13], which were induced by various structural and functional alterations, and all of which could lead to glomerular scarring and FSGS. The adaptive form of FSGS is often characterized by normal serum albumin levels despite nephrotic-range proteinuria, and pathological findings show the presence of glomerular hypertrophy, the relatively mild foot process effacement, and the perihilar distribution of segmental sclerosis [10, 11, 14]. The present case was considered to be the adaptive form of FSGS because of the presence of subnephrotic proteinuria without nephrotic syndrome, enlargement of glomeruli, perihilar sclerosis, and mild degree of foot process effacement. In this case we initially assumed that glomerular hypertension induced by the relative reduction of the number of

glomeruli due to low birth weight and the obesity-induced glomerulomegaly was associated with the development of FSGS, however, ACE inhibition and weight reduction were only minimally effective for the amelioration of proteinuria. Notably, proteinuria was completely resolved after the cessation of blood flow from the aberrant renal artery after TAE. This finding encouraged us to reevaluate the role of extra renal artery flow for the development of FSGS. Previous reports showed that extra renal artery was related to various renal diseases, such as renal artery stenosis, renovascular hypertension, renal bleeding, hydronephrosis and secondary FSGS [2]. We assume that higher blood flow, which was delivered by aberrant renal artery to the lower portion of the right kidney, could produce glomerular hypertension with resultant glomerular scarring and FSGS. This hypothesis would be supported by the complete improvement of proteinuria after normalizing the blood flow to the right kidney by shutting down the aberrant renal artery flow. However, the incidence of FSGS is disproportionately low compared to that of renal artery variations. We assume that not all renal artery variations affect

Fig. 4 Renal biopsy findings (**a** Masson trichrome stain, **b**, **c**, **d** periodic acid silver methenamine stain, **e** electron microscopy). In the renal biopsy specimens, 34 glomeruli were contained. Eleven of them were globally sclerotic, one showed segmental sclerosis (**d**), and remaining ones exhibited glomerulomegaly (**c**). There was mild

glomerular hemodynamics. Because of various protective mechanisms to maintain steady glomerular hemodynamics, only a small number of cases in renal artery variations

tubular atrophy and interstitial fibrosis involving approximately 40 % of the cortex (**a**). Small arteries showed multiple hyalinized glomeruli moderate intimal thickening and moderate hyalinosis (**c**). Electron microscopy showed mild focal foot process effacement (**e**)

could cause increased glomerular hypertension and glomerular scarring. In our case extra renal artery flow was significantly abundant enough to affect glomerular flow

and pressure, which resulted in glomerular scarring and FSGS.

This is the first report of resolution of proteinuria after TAE of aberrant renal artery in a patient with secondary FSGS. In conclusion, caution should be taken for possible association between the presence of extra renal artery and the development of secondary FSGS.

Conflict of interest There is no conflict of interest statement for all authors.

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