Clinical Case Report

Nephrotic syndrome and recurrent pulmonary oedema in bilateral atherosclerotic renal artery stenosis: Resolution following renal angioplasty and stenting

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ABSTRACT

Hypertension and episodic pulmonary oedema are known complications of bilateral renovascular disease. However, significant proteinuria has not been reported in this setting. We describe a patient who presented with recurrent pulmonary oedema and nephrotic syndrome, and was found to have bilateral renal artery stenosis. Percutaneous angioplasty and stenting led to a complete resolution of both, confirming a causal relationship. This is perhaps the first report documenting the rare combination of nephrotic syndrome and flash pulmonary oedema due to bilateral renal artery stenosis.

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INTRODUCTION

Renal artery stenosis (RAS) is a well recognized cause of secondary hypertension. Its role in the genesis of other manifestations such as recurrent flash pulmonary oedema and, less frequently, nephrotic syndrome has been recognized recently. The former is encountered in patients with bilateral RAS whereas the latter occurs in unilateral disease. We describe a patient with recurrent pulmonary oedema and nephrotic syndrome who was found to have bilateral RAS. Correction of stenoses with percutaneous transluminal renal angioplasty (PTRA) and stenting resulted in complete resolution of both.

THE CASE

A 61-year-old woman was admitted in November 2001 to our hospital for the management of recurrent episodes of shortness of breath and generalized swelling over the body. She had been detected to be a hypertensive 15 years ago and was managed with calcium-channel blockers. She was well 6 months ago when she started having episodes of sudden shortness of breath that would increase on lying down. She was admitted to a local health facility for the management of recurrent episodes of shortness of breath and was subsequently admitted to our hospital. Initially the pedal oedema responded to diuretics, but later increased to involve the entire body and the patient became bed-bound. This was associated with progressively increasing weakness, anorexia and decreased urine volume. At this stage she was referred to our hospital. There was no history of haematuria or constitutional symptoms. She had also been diagnosed to have hypothyroidism 5 years ago, and was on regular thyroxine supplementation.

Physical examination revealed a pulse rate of 96 per minute, blood pressure 146/98 mmHg, respiratory rate 24/minute along with generalized oedema, pallor and distended jugular veins. Examination of the heart and central nervous system were unremarkable. Respiratory examination revealed right-sided pleural effusion. The liver edge was felt 4 cm below the right costal margin and she had ascites. Investigations revealed haemoglobin of 8.9 g/dl, total leucocyte count of 9400/cm² and a normal differential count. Blood urea was 102 mg/dl, serum creatinine 2.1 mg/dl, total proteins 5.4 g/dl, albumin 2.2 g/dl, calcium 8.7 mg/dl, phosphates 4.2 mg/dl, alkaline phosphatase 135 U/L, and fasting blood sugar 97 mg/dl. Urinalysis revealed ++ proteins, 6–8 pus cells and 1–2 red blood cells/high power field. The 24-hour urine protein excretion was 10.4 g. Chest X-ray confirmed the right-sided pleural effusion. Tests for hepatitis B surface antigen, antibody to hepatitis C virus, antinuclear antibodies and antineutrophilic cytoplasmic antibodies were negative. Abdominal fat pad aspiration did not show amyloid. Serum and urine electrophoresis showed no M spike. Echocardiography revealed a normal left ventricular systolic function and an ejection fraction of 65%. The left and right kidneys were 9.2 cm and 9.4 cm, respectively on ultrasound examination. Doppler examination revealed mean peak systolic velocities of 162 and 156 cm/second on the two sides and renal-to-aortic ratio of >2, suggestive of bilateral RAS. She was initially managed with oxygen inhalation, intravenous nitroglycerin, oral amiodipine and parenteral diuretics. However, she continued to have recurrent episodes of pulmonary oedema and there was little regression of anasarca. Initiation of ramipril at a dose of 2.5 mg twice a day was followed by a sharp increase in the level of serum creatinine to 4.2 mg/dl that returned to 1.7 mg/dl upon withdrawal. Coronary and renal angiographies were done. The coronary arteries were normal but both renal arteries showed >90% narrowing at the ostia (Fig. 1). Bilateral PTRA and stenting were done, and the respiratory distress improved within 48 hours. Over the next 7 days, the urine output improved, anasarca gradually regressed and proteinuria declined to 2.3 g/day. The blood pressure was controlled with amiodipine 7.5 mg/day. The proteinuria came down to 0.4 g/day at the end of 1 month and was undetectable at 3 months. As the nephrotic syndrome had completely resolved, kidney biopsy was deferred. She has now been followed up for over 4 years, with no recurrence of symptoms. The level of serum creatinine remains at 0.8 mg/dl and urinalysis reveals no abnormality.

DISCUSSION

Major advances have been made in the past decade in understanding the renal and extra-renal manifestations of atherosclerotic renovascular disease. Recently recognized associations of bilateral
RAS include recurrent potentially life-threatening pulmonary oedema, chronic heart failure or crescendo angina. Pulmonary oedema is consequent to salt and fluid retention by the ischaemic kidneys leading to intravascular volume expansion. Hypertension is also sustained by the same mechanism. These patients have normal systolic cardiac function and normal coronaries on angiography. It has been suggested that the increased afterload leads to ventricular dilatation and reduced myocardial compliance, which adversely affect diastolic function. Several reports have documented disappearance of pulmonary oedema following percutaneous or surgical revascularization of narrowed renal arteries. In contrast to bilateral disease, unilateral RAS leads to stimulation of the renin–angiotensin system, vasoconstriction and compensatory natriuresis by the normal contralateral kidney and hence protects against pulmonary oedema.

The other presenting feature in this patient, i.e. nephrotic syndrome, is not common in RAS. In the cooperative study of renovascular hypertension, the average daily protein excretion was 500 mg. This degree of proteinuria can be due to renal parenchymal injury secondary to hypertension. Those with the worst renal function tend to have the greatest degree of proteinuria. The common secondary causes of nephrotic syndrome were ruled out in our patient. Although kidney biopsy was not done, the complete and sustained disappearance of proteinuria following revascularization strongly supports a causal relationship between the renovascular disease and nephrotic syndrome. To the best of our knowledge, this is the first report to document nephrotic syndrome in association with bilateral RAS and flash pulmonary oedema that was successfully treated by percutaneous revascularization.

The mechanism of proteinuria in this case was not clear. It has been postulated that high circulating angiotensin in patients with unilateral RAS causes proteinuria through its haemodynamic effect on the non-ischaemic kidney. Experimental studies have documented reversible nephrotic-range proteinuria following infusion of renin or angiotensin II in rats. By selectively catheterizing both ureters in patients with unilateral RAS and proteinuria, Kumar and Shapiro showed the urine from the ischaemic kidney to be free of protein, while the contralateral ureter showed proteinuria. Treatment with ACE-inhibitors or angiotensin receptor blockers is effective in amelioration of proteinuria, whereas removal of the ischaemic kidney leads to both normalization of proteinuria and elevated PRA levels. PTRA and stenting has been shown to reverse nephrotic syndrome in patients with unilateral RAS. We did not measure circulating renin or angiotensin levels. The circulating renin levels are high in unilateral RAS whereas bilateral high grade RAS (akin to Goldblatt one-kidney one-clip model) is usually associated with a low renin state. Therefore, it is difficult to provide an explanation for the nephrotic state, but prompt resolution following revascularization indirectly suggests that the renin levels might have been elevated in this patient despite the presence of bilateral disease. It can be speculated that because of differences in the degree of stenosis, one of the kidneys continued to overproduce renin. This issue could have been resolved only by selective renal vein renin measurements.

In conclusion, renovascular disease should be considered in the differential diagnosis of nephrotic syndrome, especially when the patient has other features that point to involvement of the renal arteries. Revascularization can lead to complete disappearance of proteinuria even in a patient with bilateral RAS.

REFERENCES


