Clinical Vignettes

Hypertension and Hydronephrosis: Rapid Resolution of High Blood Pressure Following Relief of Bilateral Ureteric Obstruction

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Hypertension secondary to hydronephrosis is not commonly reported in the medical literature. Tubuloglomerular feedback and the renin-angiotensin-aldosterone axis are thought to mediate this process. We describe a patient presenting with acute kidney injury and bilateral hydronephrosis secondary to pelvic malignancy in which peripheral venous renin and aldosterone were elevated. Her blood pressure improved rapidly following insertion of bilateral nephrostomies. The speed of resolution of hypertension following relief of obstruction suggests that humorally mediated vasoconstriction can play an important role in the mechanism by which hydronephrosis causes hypertension. We also discuss other causes of renal parenchymal compression that may lead to the development of hypertension.

KEY WORDS: hydronephrosis; hypertension; renin-angiotensin-aldosterone; tubuloglomerular feedback.
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INTRODUCTION

Hydronephrosis is a common cause of acute kidney injury. Less frequently, it may lead to hypertension. Proposed factors include vasoconstriction and salt and water overload, mediated by processes including tubuloglomerular feedback (TGF) and the renin-angiotensin-aldosterone (RAA) axis. We describe a patient in whom rapid improvement in hypertension following relief of hydronephrosis strongly suggests a vital role for vasoconstriction in the genesis of high blood pressure in this situation. We also discuss other conditions in which renal parenchymal compression may lead to the development of hypertension through similar mechanisms.

CASE HISTORY

A 32-year-old woman was admitted with lower abdominal and back pain in association with nausea, vomiting and headache. Her past medical history was notable for stage 2B squamous carcinoma of the cervix diagnosed 10 months before. She had been treated with chemotherapy, including carboplatin, and radiotherapy. Six months later magnetic resonance imaging (MRI) and a positron emission computed tomography scan demonstrated local tumor recurrence.

Her medications consisted of venlafaxine, cetirizine, lansoprazole, zopiclone (a cyclopyrrolone non-benzodiazepine hypnotic), acetaminophen, fentanyl, oral morphine and trimethoprim, but no anti-hypertensive therapy. On examination, she had a blood pressure of 220/148 mmHg, with a normal jugulovenous pressure and no peripheral edema. Fundoscopy showed no evidence of hypertensive retinopathy. Urine dipstick testing was remarkable for 3+ blood, 3+ leukocytes and 2+ ketones. Urine culture was negative. Laboratory data revealed an acute kidney injury with a sodium of 139 mmol/l, potassium 4.8 mmol/l, venous bicarbonate 24 mmol/l, urea 14.5 mmol/l (40.6 mg/dl) and creatinine of 254 μmol/l (2.87 mg/dl). Her creatinine had been 107 μmol/l (1.21 mg/dl) 9 days earlier and 66 μmol/l (0.75 mg/dL) 2 months before. Complete blood count and coagulation screen were normal. Recumbent peripheral blood renin and aldosterone were elevated at 64 mU/l (reference range 5.4 to 30) and 734 pmol/l (reference range 100 to 450), respectively. Amlodipine 10 mg daily and atenolol 50 mg daily were commenced, resulting in a slight improvement in her blood pressure to 180/120 mmHg. Her pain was controlled with analgesia but with little further improvement in blood pressure. Compared to 2 months earlier, MRI showed an increase in tumor bulk with invasion into the sigmoid colon and rectum. There was also new bilateral hydronephrosis with dilatation of both ureters extending into the pelvis (Fig. 1).

The acute kidney injury and bilateral hydronephrosis prompted insertion of bilateral nephrostomies under local anesthesia. Her blood pressure fell rapidly within a few hours (Fig. 2). Urine output during the 24 h following the procedure was 4 l. Blood pressure the following day improved to 130/80 mmHg with a serum creatinine of 229 μmol/l (2.59 mg/dL), which fell to 112 μmol/l (1.27 mg/dl) after 2 days. Her atenolol was stopped at this time. She underwent pelvic exenteration, which included hysterectomy, bilateral salpingo-oophorectomy, cystectomy, resection of the rectum and sigmoid colon,

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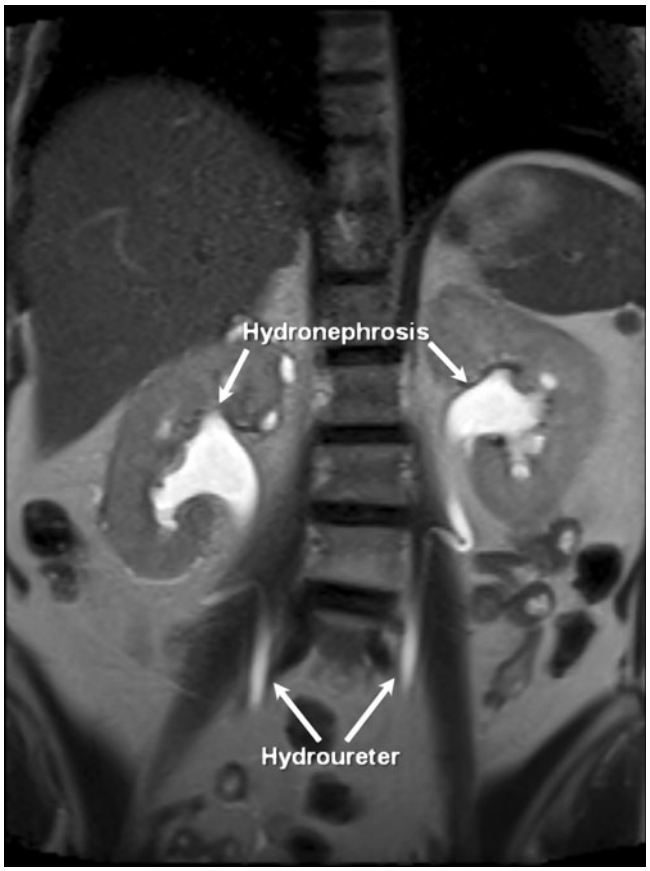

Figure 1. Contrast-enhanced magnetic resonance scan demonstrating bilateral hydronephrosis and hydroureter.

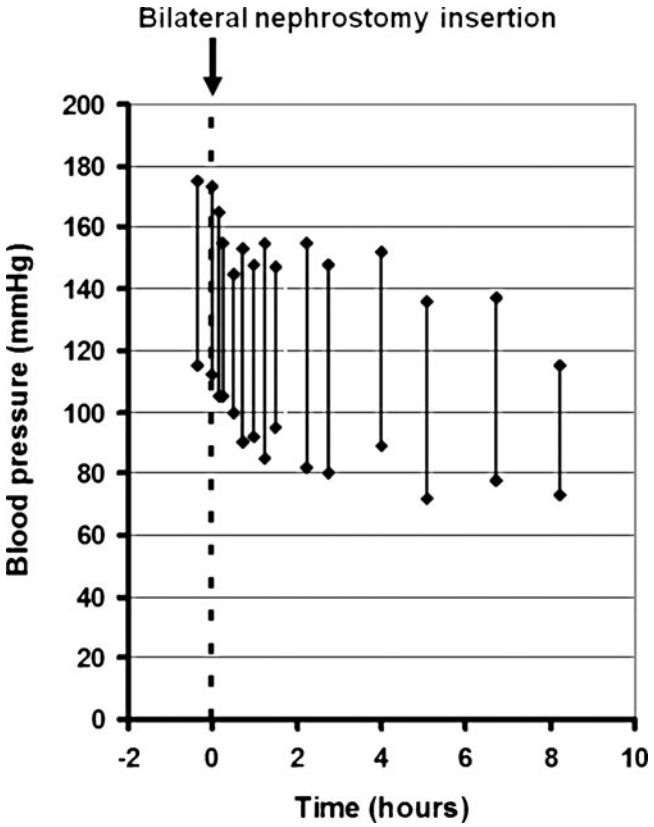

Figure 2. Blood pressure following insertion of bilateral nephrostomies.

and formation of a colostomy and urinary ileal conduit. Her recovery was otherwise unremarkable. She was discharged on postoperative day 10 with a serum creatinine of 61 μmol/l (0.69 mg/dl) and a blood pressure of 123/78 mmHg. She was still taking amlodipine 10 mg daily on discharge, but this was subsequently stopped.

DISCUSSION

Hydronephrosis is a common condition. This may be unilateral (e.g., ureteric calculi or urothelial tumors) or bilateral (e.g., bladder outflow obstruction, most commonly as a result of benign or malignant prostatic enlargement). Secondary hypertension occurring as a consequence of hydronephrosis has been described in a small number of animal models[1] and clinical reports.[2–5] Interestingly, based upon the limited number of cases, unilateral hydronephrosis appears to be sufficient to cause hypertension.[2,4,5] The presence of a normal contralateral kidney may not be adequate to mitigate the effect of the hydronephrosis. Some authors describe resolution of hypertension following removal of the affected kidney,[5] while others show that relief of obstruction may also lead to normalisation of blood pressure.[2,3] It therefore appears that the intra-renal mechanism leading to the pressor effect is reversible. Increased activity of both the TGF system and RAA axis are thought to play an important role in this process.[6]

TGF is a physiological process involved in autoregulation of glomerular blood flow (Fig. 3). Increased sodium chloride delivery to the macula densa cells of the juxtaglomerular apparatus, such as when glomerular filtration rate (GFR) is high or in states of volume overload, leads to increased uptake via luminal Na-2Cl-K co-transporters in the loop of Henle. This results in release of adenosine, which acts on A_1 receptors on extraglomerular mesangial cells to trigger an increase in cytosolic calcium.[7] This signal is propagated to smooth muscle cells of the afferent arteriole, likely via gap junctions, where it results in afferent arteriolar vasoconstriction and a reduction in GFR.[8] TGF responsiveness and vasoconstriction are determined by several vasoactive compounds, including angiotensin II, thromboxane[9] and bradykinin.[10] It is important to note that the vasoconstrictor effect of these compounds is attenuated by locally produced nitric oxide.[11] In the hydronephrotic state, there is increased activity of the TGF system,[1] which appears to be due to reduced nitric oxide availability.[6] This pathologically increased activity of TGF reduces urine volume and thus may ameliorate the deleterious effect of high pressure within the renal pelvis that occurs in hydro-

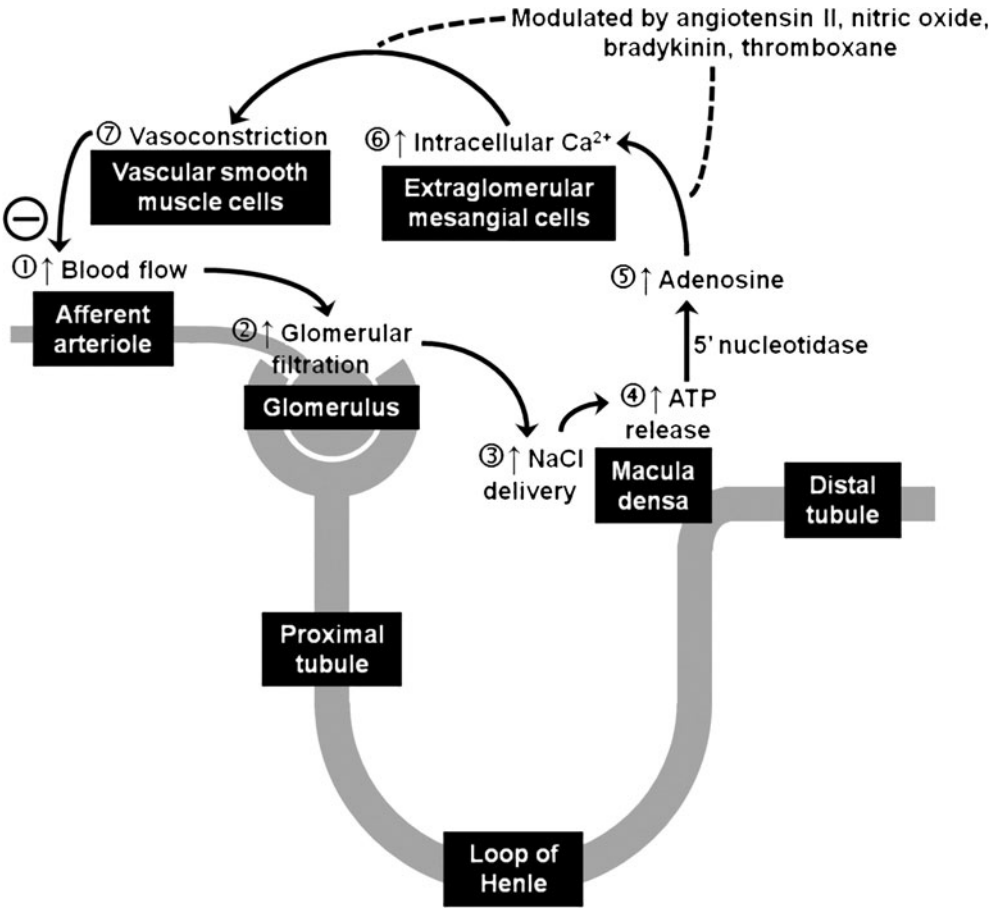

Figure 3. The role of tubuloglomerular feedback in regulation of the glomerular filtration rate.

nephrosis,[12] but also results in salt and water retention and development of salt-sensitive hypertension.[6]

Increased activity of the RAA axis in hydronephrotic states also contributes to the development of hypertension. In animal studies and clinical reports on hydronephrosis, peripheral plasma renin activity has been shown to be elevated.[1,2,5] In cases of hypertension and unilateral hydronephrosis, selective renal vein sampling generally shows elevated renin secretion from the affected kidney and suppressed levels from the contralateral side.[5] High preoperative plasma renin levels are predictive of improvement in blood pressure following surgery in hypertensive hydronephrotic patients.[4] The cause for the increased activity of the RAA axis that occurs in hydronephrotic kidneys is unclear, but may, in part, be a consequence of the reduced renal blood flow that occurs as a result of the heightened TGF.

There are two key mechanisms by which over-activity of the RAA axis may lead to hypertension. The first is through the systemic vasoconstrictor effect of angiotensin II. The second, as with increased TGF sensitivity, is a result of aldosterone-mediated intra-renal salt and water retention. The observation that unilateral hydronephrosis can be sufficient to cause hyper-reninemic hypertension suggests that, at least in some cases, the former mechanism predominates since the pressure natriuresis occurring in the normal contra-lateral kidney is unable to compensate completely. In our patient, the rapid improvement in blood pressure following nephrostomy tube insertion and before significant diuresis is more consistent with a humorally mediated vasconstrictive cause of hypertension than simply salt and water overload.

Other forms of renal parenchymal compression can result in hypertension. Irwin Page first described an experimental canine model in 1939 in which hypertension was induced by extrinsic compression of one kidney by wrapping it in cellophane.[13] The first clinical report of a so-called "Page kidney" was by Engel in 1954 in a patient who developed hypertension as a result of a renal sub-capsular hematoma.[14] There have since been multiple descriptions of this phenomenon, for example following trauma or renal biopsy with increased renin secretion from the affected kidney and normalisation of blood pressure following surgical intervention.[15–18] There have similarly been clinical case reports of hypertension due to extrinsic renal compression from other causes such as paragangliomas[19] or splenic cysts.[20]

Parenchymal compression by renal cysts may also lead to hypertension. There have been several descriptions of

simple cysts resulting in hypertension with elevated renin from the affected kidney, which resolves following cyst decompression.[21–23] Interestingly, a longitudinal study has demonstrated an increased risk of developing hypertension in middle-aged men with renal cysts,[24] and a case series of patients undergoing aspiration of simple cysts has shown that hypertension is more common among those with larger cysts.[25]

Adult polycystic kidney disease (APKD) frequently leads to the development of hypertension, which can occur before there is a significant decline in renal function.[26] Hypertensive APKD patients have a greater total renal volume, due to expansion of cysts, than their normotensive counterparts,[27] and cyst decompression can result in improvement in blood pressure.[28] Activity of the RAA axis is increased in hypertensive APKD patients compared to those with essential hypertension.[29] Taken together, these observations suggest that parenchymal compression by cysts, with consequent intra-renal ischemia, plays a role in the genesis of hypertension in APKD.

In summary, this case demonstrates that hydronephrosis can lead to the development of reversible hyper-reninemic hypertension. While salt and water retention may contribute partly through increased TGF activity, the rapid normalisation of blood pressure following relief of obstruction strongly suggests that systemic vasoconstriction plays an important role in this process. Renal parenchymal compression (which may also be due to cysts or sub-capsular or extrinsic lesions) should be considered as a cause in the assessment of patients presenting with hypertension, and renal imaging may therefore play a valuable role in their evaluation.

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