Segmental renal infarction in a stone former: possible relationship with NSAID administration

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Introduction

Renal infarction is a rare clinical problem, especially in young adult people. It is frequently misdiagnosed because of the unspecificity of its symptoms. One of the most frequent misdiagnoses is renal colic. We describe the case of a renal stone former in which a renal colic was complicated by a segmental renal infarction. We speculate that it was precipitated by NSAID administration.

Case report

A 40-year-old man was hospitalized for right flank pain of growing intensity, radiating to the lower abdomen and the groin, nausea, sweating, and low-grade fever. One year before he had a transient episode of dysuria and macrohaematuria. No personal or family history of diabetes, blood dyscrasia, cardiac disease, or renal disorder (including nephrolithiasis) was elicited. The father was hypertensive. The patient denied trauma or previous injury, and drug abuse.

The pain began at 5 p.m. increasing gradually, and at 11 p.m. the patient was evaluated at the emergency department of the University Hospital of Padua. He was considered to suffer from a renal colic, probably due to a stone, and received diclofenac 75 mg i.v. with almost complete resolution of pain; an extemporary urinary dipstick disclosed only haemoglobin, 2++. Four hours later the patient returned to the emergency department suffering from severe pain, received again diclofenac 75 mg i.v., and was admitted to a medical ward. Physical examination disclosed only tenderness at the right flank without rigidity. The temperature was 37.2°C. Blood pressure was normal and the pulse rate was regular, 70 beats per minute. No carotid or para-aortic bruit or heart murmur was ausculted. There was no peripheral oedema.

Urinalysis showed proteins (300 mg/l), glucose (8.3 mmol/l), and 10–20 red blood cells per high-power field (hpf). White blood cell count was 16 600 with 84% neutrophils, haematocrit 44%, platelet count 251 000; PT, PTT, fibrinogen, and plasma fibrin degradation products/D-dimer were within the normal ranges. Blood urea nitrogen (BUN) was 6.51 mmol/l and serum creatinine 112 μmol/l. Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were slightly increased (64 and 66 U/l respectively) and lactate dehydrogenase (LDH) was 579 U/l. Serum bilirubin, amylase, and creatinine phosphokinase were normal. Chest and the ECG were inconclusive. Direct abdomen X-ray showed a slender calcareous image in the left kidney region.

The patient was treated i.v. with butylscopolamine 40 mg, and amidopyrine 1 g, and hydrated with saline in the next 8 h, during which the pain was only partially relieved. Then, quickly, it almost completely disappeared, substituted by a modest flank discomfort which lasted for some days. Kidney, liver, and gall-bladder ultrasonography appeared normal. Fever, up to 38°C on day 4, lasted for 6 days, then completely disappeared. The patient received orally also trimethoprim/sulphamethoxazole 160/800 mg b.i.d. (for 10 days).

In the following days the patient’s physical conditions were unremarkable and blood pressure had normal or borderline values; however, laboratory examinations confirmed microhaematuria, glycosuria (which disappeared on the 10th day), and increased serum ALT, AST, and LDH with a zenith at the 5th day (1900 U/l) and gradual reduction in the following days (Figure 1). Analysis of serum LDH isoenzymes showed a marked increase of the LDH-1 (37%; NV 15–25%), marginally high LDH-2 (36%, NV 32–41%), and decreased or marginally decreased LDH-3 (14%, NV 18–26), LDH-4 (7%, NV 7–14%), and LDH-5 (6, NV 5–16). Hepatitis virus serology was normal and leukocytosis subsided. The intravenous urogram showed that the left calcareous image was located in middle calyces, and also showed a markedly hypertonic right kidney pelvis. The patient returned home at the 13th day.

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Three weeks later he passed a small calcium-oxalate stone. In the following week he started to complain of headache, and blood pressure was found to be 220/140 mmHg. Thus he came to our observation. Blood pressure was controlled with nifedipine.

BUN, serum creatinine, serum electrolytes, blood cell count, serum ALT, AST and LDH were all in the normal ranges. ECG disclosed only non-specific alterations. Ophthalmoscopy showed small flame haemorrhages, exudates, and narrowed arterioles. At urine examination more than 50 erythrocytes per hpf were present. Glycosuria was absent. Both plasma renin activity (12.90 μg/l/h in recumbency and >20 in standing position, NV 1.30–5.20 and 0.20–3.30 respectively) and serum aldosterone concentration (0.80 nmol/l and 1.60, NV 0.14–0.80 and 0.08–0.28 respectively) were high with abnormal response to upright posture. Urinary adrenaline and noradrenaline were both normal. A renal scintigram (RS) (Figure 2) revealed a right kidney with reduced perfusion and dimensions, and a perfusion defect in the mid-external part.

A computed tomography (CT) of the abdomen showed a right kidney of regular dimensions with reduction of the anterior part of the cortex. As segmental renal infarction was suspected, an arteriogram was performed. Selective right renal arteriography demonstrated that the anterior branch of the artery was almost completely occluded at its first bifurcation (Figure 3a); this branch further divided, showing occlusion of its cranial arm and partial obliteration of the caudal one with small thrombi in the lumen (Figure 3b). As a consequence, a wide ischaemic area in the anterior part of the upper and median portions of the right kidney was present. Only a narrow lumen of the caudal branch of the second bifurcation was still patent, which perfused the upper polar infarcted area, as demonstrated by the parenchymographic effect in the late images (Figure 3b).

An echocardiogram and a biplanar abdominal aortogram showed no source of embolic disease (Figure 4). Serum anti-HIV, antinuclear, ANCA, lupus anticoagulant, and anticardiolipin antibodies, and neoplastic markers were all negative. A further workup for hypercoagulopathy, including antithrombin III, protein S, protein C, activated protein C resistance, plasminogen, and plasminogen activator inhibitor, was in the normal range. Finally, homocysteine in serum and in 24-h urine was normal.

Blood pressure was controlled to normal values with a calcium blocker and an ACE inhibitor at full ordinary dosages.

Five months later the patient had a typical left renal colic, with microhaematuria and no glycosuria. The
Fig. 3. Wide ischaemic area in the anterior part of the upper and median portions of the right kidney can be seen.
(a) The right renal arteriography shows that the anterior branch of the artery is almost completely occluded at its first bifurcation.
(b) The anterior branch further divided, showing occlusion of its cranial arm and partial obliteration of the caudal one with small thrombi in the lumen. The latter or the small apical arterial branches maintain the perfusion of the upper polar ischaemic area as demonstrated by the parenchymographic effect in this late image.

patient was treated only with i.v. spasmolytic drugs and passed the small stone previously observed at the intravenous urogram. In fact, a direct abdomen roentgenogram failed to show the calcareous image previously reported. The stone chemical nature was calcium oxalate. Microhaematuria rapidly disappeared. An attempt to reduce the antihypertensive dosage was unsuccessful.

Fig. 4. The biplanar abdominal aortogram appears normal.

Discussion

The patient here described had a pain syndrome which was considered, at the beginning, to be of renoureteral origin, and to have been caused by a stone, but that was unexpectedly complicated by a renal infarct.

No known risk condition for renal infarct was found. There was no embolic cardiac or arterial disease, no renal artery dysplasia with intimal dissection, and no vasculitis [1]. Immunological diseases and hypercoagulable [2] states were ruled out. An extrarenal mass invading the renal artery [3], or a phaeochromocytoma determining renal artery stenosis and occlusion or severe renal arterial spasms [4] were also excluded. The patient denied recent trauma, and use of cocaine [5]. The only alternative to ‘idiopathic renal infarct’, a rare condition [6], is the assumption that a relationship exists between the renal stone colic and its pharmacological treatment on the one hand and segmental renal infarction on the other.

Renal infarction should be included in the differential diagnosis for any pain possibly related to the kidney. It is not a common disease. Furthermore symptoms are variable and non-specific so that its diagnosis is difficult. Based solely on clinical findings the correct diagnosis was made only in two of 205 cases of renal infarction who had come to postmortem [7]. It is likely that many cases are erroneously diagnosed as renal colic and urolithiasis. We do not think that this patient had a pure renal infarction which was misdiagnosed as a simple colic, but rather assume that he had a stone-related renal colic which was complicated by a renal infarct.

There are two reasons favouring this idea. First, this patient is certainly a renal stone former since he passed two small calcium-oxalate stones, the first one few days after the episode of renal infarct. Generally the pain due to a renal infarct is a flank pain and the
radiation to the groin is unusual; when this happens, it might be due to the ureteral passage of a blood clot (but this possibility seems unlikely since the patient had only microhaematuria), or of a sloughed papilla (but no papilla was passed in the urine, nor were typical changes present at urography). Second, microhaematuria was present in the first urinalysis (at 11 p.m.) (this is compatible with a moving stone), and glycosuria was shown only in the subsequent urinary examination (5 h later). Concerning the cause of such an abnormality, a toxic effect of diclofenac (the only drug that the patient received before the onset of glycosuria), i.e. selective inhibition of proximal tubular reabsorption of glucose, or interference of NSAIDs with the chemical assay for glucose, have never been reported. An acquired proximal tubular lesion seems to be the most logical cause of this urinary abnormality because of its disappearance in the following days. In our opinion, this tubular lesion was the earliest marker of the underlying renal infarct that was complicating a trivial renal–ureteric colic.

To the best of our knowledge this is the first case in which a stone colic was complicated by a renal infarct; however, even the most extreme speculation that we are able to propose does not offer any chance to link pathogenetically the two conditions. What we indeed suspect is that diclofenac played a role. Although a number of adverse renal effects have been reported for NSAIDs, renal infarct has never been reported.

Renal prostaglandins play an important part in the maintenance of renal blood flow, that consequently, in risky patients, may be deranged by NSAIDs because of the interruption of the balance between hormonally mediated pressor mechanisms and prostaglandin-related vasodilatory effects. When this happens, an acute renal deterioration leading to renal failure might ensue. At-risk conditions for NSAID-induced acute renal failure are all those settings in which volume contraction activates pressor systems (congestive heart failure, cirrhosis, chronic renal disease, advanced age, dehydration). We propose that in our patient the acute obstruction of the urinary tract by a stone provoked acute renal vasoconstriction. In the dog, experimental ureteric occlusion, causes transient vasodilatation for 2 h followed by renal vasoconstriction with marked reduction of renal blood flow [8]. Possibly vasoconstriction is not homogeneously distributed in the kidney, but rather has a segmental distribution as in reflux nephropathy [9,10].

Thus we suggest that in this patient the ureteric obstruction by a stone led to renal segmental vasoconstriction that, not being counterbalanced by prostaglandins because of diclofenac administration, caused renal infarction. Perfusion of the upper pole of the right kidney through the partially patent caudal branch of the second bifurcation of the renal artery may have caused ischaemia of the upper pole, renin release, and hypertension [11].

References


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