Case Report

Idiopathic acute granulomatous interstitial nephritis leading to renal papillary necrosis

P. Fong, F. Sepandj and A. Trillo

Division of Nephrology and Department of Pathology, Dalhousie University, Halifax, Nova Scotia, Canada

Introduction

Renal papillary necrosis (RPN) is a clinicopathological entity characterized by necrotic lesions of the kidney confined to the distal parts of the pyramids. The first description dates back to 1877 by Friedreich [1]. This condition has also been referred to as ‘renal medullary necrosis’, ‘suppurative necrotizing pyelonephritis’, and ‘renal necrotizing papillitis’ [2].

The fundamental mechanism in the pathogenesis of RPN is ischaemia of the inner medulla and papillae of the kidney, areas which have ordinarily low oxygen content and pH. The clinical course is variable. The subacute form of RPN (most common) usually presents insidiously over months to years with symptoms such as lumbar pain, haematuria, fever, and chills. There is also a rare acute fulminating type with acute onset of renal failure and sepsis and a latent form manifesting as asymptomatic passage of blood and papillary material.

RPN develops in a variety of diseases including diabetes mellitus, pyelonephritis, obstructive uropathy, analgesic abuse, sickle cell haemoglobinopathy, renal transplant rejection, cirrhosis of the liver, and dehydration [3]. We report development of an acute exsanguinating form of RPN in an otherwise healthy patient in association with histologic changes suggestive of granulomatous interstitial nephritis. Our literature review over the previous 30 years failed to identify idiopathic RPN specifically in conjunction with the above pathological changes. Earlier reports of idiopathic RPN were before discovery of association of RPN with analgesic abuse.

Case report

A previously healthy 30-year-old white male was admitted to a peripheral hospital on August 21, 1994 for an episode of gross haematuria followed by severe colicky right lumbar pain. There were no other associated symptoms including fever, chills, dysuria, frequency, or urgency.

There was no history of diabetes, sickle cell anaemia, nephrolithiasis, sarcoidosis, or exposure to tuberculosis. He had no unusual environmental or occupational chemical exposures and there had been no significant exposure to acetaminophen, non-steroidal anti-inflammatory drugs or any recreational drugs.

Physical examination was unremarkable except for some right-sided costovertebral angle tenderness. He was afebrile (temperature 36.8°C) and haemodynamically stable (blood pressure 155/85, no postural drop; pulse rate 80/min). Admission laboratory data were as follows: CBC revealed haemoglobin, 133 g/l (130–180 g/l) with normal white blood cell and platelet count; prothrombin time and partial-thromboplastin time were normal; serum electrolytes were normal as were blood urea nitrogen, 5.1 mmol/l (2.8–7.0 mmol/l) and creatinine 106 µmol/l (60–110 µmol/l); glucose and calcium were also normal; and the rest of the biochemical screen was unremarkable. His urine cultures were negative on two separate occasions. Abdominal X-rays were within normal limits. Intravenous pyelogram revealed only filling defects in the bladder and renal pelvis with no classical finding of RPN.

Serum immunopathology investigations were performed. Anti-nuclear antibody (ANA) and antideoxyribonucleic acid (anti-DNA) were negative. Anti-extractable nuclear antigens (anti-ENA) SM, RNP, and LA were negative but anti-Ro was marginally positive at 29 EU/ml (<25 EU/ml). Anticardiolipin antibody was negative. Complements C3 and C4 were normal. Quantitative immunoglobulins IgA and IgM were normal; IgG was slightly elevated at 13.10 g/l (6.60–13.00 g/l). Anti-neutrophilic cytoplasmic antibody (ANCA) was negative.

Cystoscopic examination revealed normal bladder, however, gross haematuria was noted to originate from the right ureteric orifice. Ten days after admission, he underwent right nephrectomy for exsanguinating hemorrhage (haemoglobin dropped from 133 to 79 g/l). He was subsequently transferred to our hospital for nephrologic assessment after demonstration of renal papillary necrosis on pathology.
Three weeks following surgery, the patient experienced another episode of hematuria with left lumbar pain. Hematuria spontaneously resolved over the next 10 days with no further recurrences. Mild intermittent left lumbar pain persisted for a number of months. He has since been followed up for 18 months and remains well and asymptomatic. Serum creatinine is slightly elevated at 114 µmol/l and urea is normal. Urinalysis is now entirely normal.

Renal biopsy

The main lesions in this nephrectomy specimen consisted of necrosis of the tips of many of the papillae. In some of the intact papillae, there was superficial ulceration of the papillary epithelium. In both necrotic and non-necrotic papillae there was calcification of the basement membranes of the limb of Henle’s loops. There was no relation between inflammatory infiltrates and calcification (Figure 1). The blood vessels, particularly the vasa recta, were patent and appeared relatively unremarkable. In areas showing papillary necrosis at the viable portion, there were scattered granulomata. No inclusions were observed in the reactive multinucleated cells (Figure 2). Stains for acid fast bacilli and fungal organisms were negative. The interstitium in both necrotic and non-necrotic papillae showed varying degrees of inflammatory infiltrate. The inflammatory infiltrate was mostly lymphoplasmacytic with presence in some areas of numerous eosinophils (Figure 3). In some of the partly dilated limbs of Henle’s there were luminal accumulations of polymorphonuclear cells. Microscopic examination of the cortical portion was relatively unremarkable with no glomerular abnormalities and only isolated foci of interstitial mononuclear inflammatory infiltrates.

Discussion

RPN has been reported in association with various conditions [3]. In a review of the literature over a thirty year period (1966–1996) using the software program Medline for previous documentation of idiopathic RPN, we could only identify one study from Kuwait [4]. In this study, the authors believed the
cause in their large group of patients with unexplained RPN to be either analgesic abuse or subclinical dehydration. Analgesic intake is high in Kuwait and it is also one of the hottest countries in the world, hence dehydration is not uncommon.

We report a patient who developed unrelenting hematuria complicating RPN who required nephrectomy for control. The etiology of this patient’s RPN is unclear as he had no clinical or pathological evidence of any of the recognized predisposing conditions. The most common condition associated with RPN is diabetes mellitus, accounting for approximately 60% of all cases of RPN in the United States [3,5,6]. We excluded diabetes in our patient by history, documentation of normal blood sugars, and lack of histological evidence of diabetic nephropathy. It is unlikely that pyelonephritis can explain our patient’s RPN since urine cultures throughout hospitalization remained sterile including those obtained during cystoscopie exam from right ureter. Analgesic abuse is commonly associated with RPN especially in Australia and parts of Europe [3]. We could not get a history of analgesic abuse in our patient who was interviewed by several physicians. We excluded sickle cell haemoglobinopathy on the basis of absence of ethnic background for sickle cell disease, lack of anaemia, and a normal blood smear. The immunopathological work-up was, for the most part, negative except for a minimally positive anti-Ro autoantibody which could suggest presence of Sjogren’s syndrome but our patient did not have any of the clinical manifestations of this syndrome. He denied any history of alcohol intake or use of recreational drugs. He had no risk factors for dehydration and there was no clinical evidence for dehydration on admission.

We are quite uncertain as to the pathogenesis of RPN in our patient, however, possibility of acute drug/chemical allergic interstitial nephritis with eosinophilic infiltrate or acute granulomatous interstitial nephritis with scattered granulomatosis was raised by the pathologist. As mentioned previously patient denied any unusual drug, food item, or chemical exposure and to this date he has no clinical or laboratory evidence of sarcoidosis or other systemic granulomatous condition. The patient was not hypercalcaemic and did not have any condition associated with high bone turnover; therefore, the calcification in the tubular basement membranes was likely the result of dystrophic calcification secondary to toxic renal injury resulting in papillary necrosis. No clear etiological evidence was however ascertained as mentioned above.

RPN may develop in the absence of any underlying risk factors. It should be included in the differential diagnosis of patients presenting with gross haematuria even in the absence of classical disease associations.

References


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