



Bilateral Renal Papillary Necrosis: An Autopsy Study of 4 cases

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Abstract:

Renal papillary necrosis (RPN) is the coagulative necrosis of the renal medullary pyramids and papillae brought on by a host of associated conditions and toxins that exhibit synergism towards the development of severe pyelonephritis that is more devastating than usual because of associated disease states particularly diabetes and urinary tract obstructions. Infection is a frequent and important finding in the most of the cases, contributing significantly to the clinical presentation of RPN. We report 4 cases of bilateral renal papillary necrosis detected at autopsy which had associated conditions like diabetes mellitus, sepsis, analgesic abuse and sickle cell anemia respectively.

Key words: Analgesics, Anemia, Autopsy, Kidney, Kidney Papillary Necrosis, Pyelonephritis.

Introduction

Renal papillary necrosis (RPN) is the coagulative necrosis of the renal medullary pyramids and papillae brought on by a host of associated conditions and toxins that exhibit synergism towards the development of ischemia. The clinical course of RPN varies depending on the degree of vascular impairment, associated casual factors, health of the patient, unilateral or bilateral involvement and specifically the number of affected papillae. RPN is potentially disastrous and in the presence of bilateral involvement or an obstructed solitary kidney, may lead to renal failure. The infectious sequel of RPN is more serious if the patient has multiple medical problems, particularly diabetes mellitus.

Materials & Methods

A retrospective study of autopsy cases of adults was done over a period of 3 years and we archived 4 cases from the total of 650 autopsies which showed bilateral renal papillary necrosis at autopsy.

Results

Table 1 gives brief history of these 4 cases with clinical presentation, cause of death, gross and microscopic features of kidneys. There were 3 males and 1 female, age ranging between 40 to 55 years and in one case, the patient was a 15 year old boy.

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Table 1: Profile of patients with pathological findings.

	Age/Sex	Cause of Death & Associated Disease	Gross Kidney Examination	Microscopic features
1	40 / Male	Perforative peritonitis and septicaemia.	Kidney showing a bilateral diffuse grey-white soft papillary necrosis and small cortical abscess formation.	Section from the soft whitish areas shows coagulative necrosis with preserved tubule outline and moderate mixed inflammatory infiltrate.
2	55 / Male	Ischemic heart disease and diabetes mellitus and hypertension.	Kidney showed bilateral small granular kidneys. Cut section showed whitish soft papillae and few papillae showed fibrosed firm areas with focal calcification with hydroureter and dilated pelvis.	Section from the papillae showed evidence of acute renal papillary necrosis and areas of calcification suggestive of old healed papillary necrosis on the background of chronic pyelonephritis.
3	45 / Female	Acute renal failure and acute pyelonephritis with septicaemia. History of analgesic abuse for arthritis.	Normal sized kidneys with cortical abscess formation and papillae showed whitish grey areas and sloughing of papillae.	Section showed features of acute pyelonephritis and papillary necrosis.
4	15 / Male	Acute renal failure and sickle cell crisis in case of sickle cell anaemia.	Bilateral kidneys enlarged and white, cut section showed marked necrosis of all papillae.	The histomorphology was compatible with papillary necrosis with no evidence of inflammation.

Discussion

In 1877, Friedrich [1] first described renal papillary necrosis in a patient with urinary obstruction resulting from hypertrophy of the prostate, since then, researchers have reported the patients with renal papillary necrosis have diabetes, severe urinary tract obstruction as well as with analgesics and drug abuse nephropathy. Researchers report that 17%-90% of all patients with renal papillary necrosis have diabetes and 25%-73% of patients have severe urinary tract obstruction [2].

RPN is classified as one end of a spectrum of changes associated with pyelonephritis and tubulointerstitial nephritis. RPN is often considered as a complication or extension of severe pyelonephritis that is more devastating than usual because of associated disease states particularly diabetes and urinary tract obstructions. Infection is a frequent and important finding in the most of the cases, contributing significantly to the clinical presentation of RPN. (i.e fever and chills in approximately two

third of patients). However, RPN can occur in the absence of infection which indicates that infection may not be the primary process in the pathogenesis. Conversely, infection likely is a complication of RPN, the necrotic papillae acts as nidus for infection and lithogenesis [3]. Infection within necrotic material and calculi is often definitively treated with antibiotics alone, and infection often recurs as RPN progresses to chronic pyelonephritis.

In our four cases, the pathologic findings on a cut section of kidney grossly showed white to yellow necrosis on the tips in the distal two third of the pyramids [Fig.1]. Microscopically, the kidneys showed features of acute pyelonephritis with cortical abscesses and the sections from the papillae, the tissue showed characteristic coagulative infarction and necrosis, with preserved tubule outline [Fig.2]. The leucocytic response is limited to the junction between preserved and destroyed tissue. In septicaemia cases, there could be bacterial colonies in the background of acute inflammatory exudates [Fig.3]. After the acute phase, scars

that can be observed on the cortical surface as a fibrous depression replace the inflammatory foci. This pyelonephritic scar is usually associated with inflammation, fibrosis and deformation of underlying calyces and pelvis which was seen in our case of 55 year old male who had underlying diabetes [Fig.1 a].

RPN is considered a sequel of ischemia occurring in renal papillae and in the medulla. A host of insults generates this ischemia, one of which may be infection. The boggy inflammatory interstitium of the pyelonephritic kidney compress the medullary vasculature and, thus predisposes the patient to ischemia and RPN. This vasculature can become compressed, attenuated or impaired from several other associated diseases, most notably diabetes mellitus, urinary obstruction and analgesic nephropathy [4]. Therefore RPN is a distinct clinical and pathophysiological entity primarily caused by ischemia that can develop without pyelonephritis

or urinary tract infection and is likely a focus of infectious complications. RPN primarily is a bilateral process, as is expected when considering the systemic nature of the associated disease and the ischemic pathophysiological mechanism of RPN.



Fig.1: Gross of renal papillary necrosis. (a) External surface shows scar on the cortical surface, (b) Confluent areas of abscess seen with cavity formation (arrow), (c) Pale white necrosed area seen in the distal two third of the pyramids and papillae in fresh state and (d) shows the same in formalin fixed specimen.

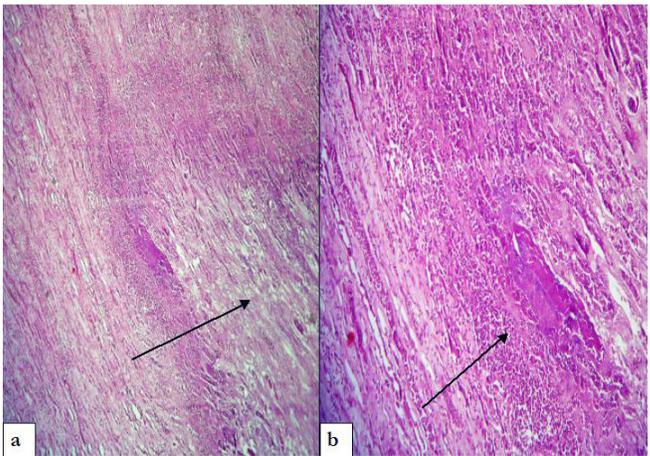


Fig.2: (a) Section of the kidney shows characteristic coagulative necrosis of papilla with preserved outline (arrow) and (b) Dense leucocytic response (arrow) at the junction between preserved and necrosed papilla [H & E stain x 100].

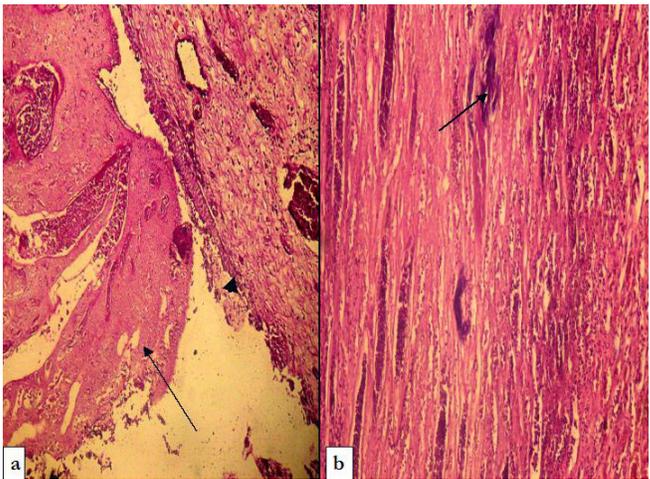


Fig.3: (a) Section of the kidney showing necrotic slough (arrow) lying in the calyces (a). (b) There is an acute inflammatory focus with bacterial colonies (arrow).

True unilateral RPN occurs when the predisposing factor is infection or obstruction that is limited to one kidney [4]. RPN generally affects elder patients with mean age of 53 years. Nearly 90% cases occur in the individuals older than 40 years [3]. RPN is uncommon in younger population and in paediatric group, except in patients with sickle cell hemoglobinopathy [5], hypoxia, dehydration and septicemia and substance abuse [6]. We have encountered renal papillary necrosis in a very young boy of 15 year old who had sickle cell anaemia and expired due to sickle cell crisis and acute renal failure.

Mandel [2] organised the first comprehensive review to focus attention on RPN. In his series, which examined 160 cases of RPN from the world wide literature, 96 (60%) patients had diabetes mellitus, 48 (30%) patients had urinary tract obstruction and 15 (9.4%) patients had both. In 1945, Spuhler and Zollinger [7] documented the first description of analgesic nephropathy. Since then, analgesic abuse has been increasingly significant in the development of papillary necrosis. In one of the four cases, there was a 45 year old female was on analgesics since last 15 years for rheumatoid arthritis in whom there was a bilateral papillary necrosis and presented as acute renal failure which was fatal.

Analgesic nephropathy is more common in females than in males. It is the one of the most common and preventable factor. A classic factor (drug) is phenacetin, with its highly toxic metabolite, P-Phenetidin [8]. Recently, however, the rising popularity of non-steroidal anti-inflammatory drugs (NSAIDs), particularly, those that inhibit cyclo-oxygenase (COX-1, COX-2) pathway, has led to a relatively high frequency of adverse events in patients at risk for RPN [8]. Thus most of the patients with RPN have a multifactorial origin and physician must consider the pathogenesis of RPN, a combination of detrimental factors that overlap and operate to cause RPN.

RPN has variable clinical course that ranges from a chronic, protracted and relapsing form to an acute, rapidly progressive form. The acute progressive is particularly rare, but the effects are devastating, resulting in death from septicaemia and renal failure. Patients with more common chronic form may remain asymptomatic until diagnosed incidentally through the appearance of ring shadow on a radiographic image [9], by the passage of sloughed papillae in the urine or during autopsy as noted in our cases.

The symptomatic form manifests as an episode of pyelonephritis and hydronephrosis and it mimics nephrolithiasis. The most common presenting symptoms of symptomatic patients are fever and chills, flank and/or abdominal pain and hematuria. Acute renal failure and oliguria or anuria occurs, but when it does, the disease may be fulminant, requiring dialysis and potentially resulting in death.

Conclusion

If the renal functions deteriorate suddenly in the patient with confirmed diabetes or a patient with a known history of chronic obstructive uropathy and/or pyelonephritis, consider the diagnosis of papillary necrosis.

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