

## Nephrolithiasis Associated Rare Renal Tumors Masquerading Non-Functional Kidney

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### Abstract

Two cases - primary squamous cell carcinoma of renal parenchyma and adenocarcinoma of renal pelvis are added to those so far reported. There is very scant literature on primary squamous cell carcinoma of renal parenchyma making it a very rare tumor. Association with long standing chronic infection and nephrolithiasis is emphasized. Presence of a renal stone and occult gross appearance of most of these tumors and may lead the pathologist to overlook their presence and be overwhelmed with nephrolithiasis only. Hence, any kidney with nephrolithiasis should be examined carefully to look for the presence of any tumorous growth.

**Keywords:** Nephrolithiasis; Squamous cell carcinoma; Adenocarcinoma; Renal pelvis

### Introduction

Nephrolithiasis is a common entity encountered in general population. Nephrolithiasis refers to formation and impaction of stones in renal pelvis and calyces. Long standing stones cause irritation, chronic inflammation and may cause 'metaplasia' of lining epithelium. The metaplasia is commonly of squamous and glandular epithelium. Metaplastic epithelium may further undergo dysplasia and result in squamous cell carcinoma and adenocarcinoma respectively, both of which are very rare tumors of kidney. Tumors of the renal pelvis are uncommon, with relative frequency of transitional cell carcinoma (90%), squamous cell carcinoma (10%) and adenocarcinoma (1%) [1]. Hereby, we report two cases of primary squamous cell carcinoma of renal parenchyma and adenocarcinoma of renal pelvis. Both the cases are associated with nephrolithiasis, making chronic irritation the most probable cause of metaplasia and malignant transformation. The emphasis in this case report is careful examination of all cases of nephrolithiasis clinically, radiologically and histopathologically to look for any foci of malignancy because majority of them may be occult.

### Case History

#### Case 1

A 56-year-old male presented with right lumbar pain for 6 months with history of weight loss. Ultrasonography (USG) revealed right renal mass measuring 4 cm x 3.5 cm x 3.5 cm in middle and lower pole with multiple calculi. Computed tomography (CT) revealed a right distended kidney with solid-cystic mass in lower pole with multiple renal calculi with hyper-attenuated lesion in liver and right renal vein filling defect (Figure 1a). DTPA scan showed a non-functioning right kidney and left kidney with good cortical function. Right nephrectomy was performed. Right nephrectomy specimen measured 9 cm x 6 cm x 5 cm. Outer surface was irregular and ulcerated. Cut surface showed pale, solid areas of cystic degeneration with multiple impacted stones in dilated pelvi-calyceal system with a rim of yellow colored renal parenchyma (Figure 1b). Histopathological examination showed renal parenchyma infiltrated by malignant cells arranged in nests, islands and pseudoglandular pattern (Figure 1c). Individual cells showed moderate pleomorphism, hyperchromatic to vesicular nuclei, conspicuous to inconspicuous nucleoli and moderately abundant eosinophilic cytoplasm (Figure 1d). Atypical mitotic figures, areas of necrosis, inflammatory cell infiltrate and lymphoid follicles were also seen. Peripheral areas showed chronic pyelonephritis, lympho-vascular

invasion and perinephric fat involvement by tumor cells. The renal pelvis and ureter were lined by urothelium and showed no tumor invasion. A diagnosis of primary squamous cell carcinoma (moderately differentiate) – right kidney was given.

#### Case 2

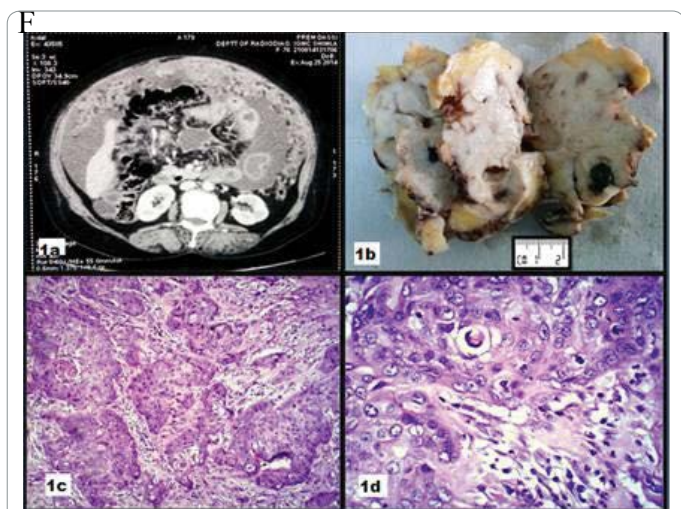
A 50-year-old male presented with history of pain in right flank and intermittent fever for two years. USG abdomen revealed single calculi in the lower pole of right kidney. On renal scan, posterior images of abdomen were acquired immediately after intravenous injection of 99m TcEC. The scan revealed normal appearing left kidney, normal perfusion and cortical tracer uptake. The right kidney showed no tracer uptake at the end of 3 hour study (Figure 2a). A right nephrectomy was performed for non-functioning kidney. Right nephrectomy specimen measured 6x5 x 4 cm with attached 6 cm ureter. Outer surface was unremarkable. Cut surface revealed tan-brown calculi impacted in the collecting system near the lower pole. The pelvis and collecting system were dilated by grey-white papillary growth and the growth was infiltrating the renal parenchyma. (Figure 2b) A thin rim of cortex was identified at the periphery. HPE of growth showed an epithelial tumor comprising of irregular glands and papillae lined by tall columnar epithelial tumor cells showing high nucleo-cytoplasmic ratio, round to ovoid moderately pleomorphic hyperchromatic nuclei, conspicuous nucleoli and eosinophilic cytoplasm. Prominent mucus vacuoles (goblet cells) were seen in some tumor cells. (Figure 2c,2d) mitotic figures were also seen. The renal parenchyma was infiltrated by tumor cells, showed extensive fibrosis, atrophic tubules and dilated tubules containing inspissated secretions (thyroidization). Few glomeruli showed peri-glomerular fibrosis, marked chronic inflammatory cell infiltrate in stroma comprising of lymphocytes, plasma cells, histiocytes, and lymphoid follicles with germinal centers. Arterioles showed hyaline arteriosclerosis and medium sized arteries show duplication of internal elastic lamina. Tumor cells involved the

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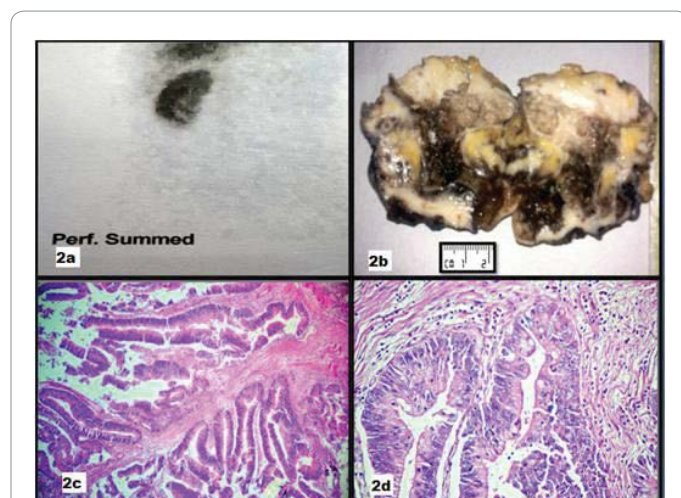
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**Figure 1:** (a) CT revealing a right distended kidney with solid-cystic mass in lower pole with multiple renal calculi; (b) Cut surface of right kidney showed pale, solid areas of cystic degeneration with multiple impacted stones in dilated pelvi-calyceal system with a rim of renal parenchyma; (c) HPE showing renal parenchyma infiltrated by malignant cells arranged in nests, islands and pseudoglandular pattern (H&E  $\times 10$ ); (d) The tumor cells showed moderate pleomorphism, hyperchromatic to vesicular nuclei, conspicuous to inconspicuous nucleoli and moderately abundant eosinophilic cytoplasm (H&E  $\times 40$ ).



**Figure 2:** (a) The renal scan revealing normal perfusion and cortical tracer uptake in left kidney and no tracer uptake in right kidney at the end of 3 hour study; (b) Cut surface of kidney revealing pelvis and collecting system dilated by grey-white papillary growth and a tan-brown calculi impacted in the collecting system near the lower pole; (c) & (d) HPE showing an epithelial tumor comprising of irregular glands and papillae lined by malignant tall columnar epithelial tumor cells (H&E  $\times 10$ ). Some cells are showing mucus vacuoles / goblet cells (H&E  $\times 40$ )

peri-renal fat and lymphatics showed tumor emboli formation. Segment of ureter showed epithelial metaplastic change to columnar intestinal type of epithelium with presence of goblet cells and severe dysplasia (ureteritis glandularis with dysplasia). Pelvic mucosa adjacent to tumor shows features of intestinal metaplasia (pyelitis glandularis). Special stains with PAS and Alcian blue showed positive results. A diagnosis of primary adenocarcinoma of the renal pelvis with infiltration into the renal parenchyma and peri-renal tissue with chronic pyelonephritis, benign nephrosclerosis, pyelitis glandularis and ureteritis glandularis was signed out.

## Discussion

Primary renal SCC is a very entity and very few cases have been reported in literature till date [2]. SCC constitutes only 0.7-7% of all urothelial malignancies [3]. Of all renal SCC, majority are centered in renal pelvis [4]. Urothelium does not have squamous cells thus a 'metaplastic' process is assumed to initiate the development of SCC. Urothelial metaplasia results from reaction to chronic irritation, leading to dedifferentiation, dysplasia and finally to SCC [5]. Women are affected more commonly and the most common age group is 50-70 years [6]. Etiological factors which have implicated are long standing renal calculi especially stag horn calculi, infections, endogenous and exogenous chemicals, schistosomiasis, smoking, hormonal imbalance and vitamin A deficiency [6]. These etiological factors have been found to be associated with SCC of renal pelvis however, genesis of renal parenchymal SCC is unknown, although similar mechanism probably underlies. In our case, multiple calculi were present in the affected kidney, thus, renal calculi are the most probable etiological agent for causing renal SCC.

When SCC is found infiltrating renal parenchyma, three possibilities should be considered - metastasis from distant site, metaplastic change accompanying urothelial malignancy and primary renal SCC. Tumor with squamous cell morphology should be meticulously sampled to differentiate between primary SCC of renal pelvis, metastatic SCC to kidney and primary SCC of renal parenchyma. The pelvic urothelium is the key structure to reach at correct diagnosis. In the presence of urothelial dysplastic element in the form of urothelial carcinoma in situ or area of transition from urothelial carcinoma to squamous differentiation, the tumor should be classified as primary urothelial carcinoma with squamous differentiation which is common in high grade and sarcomatoid variants of urothelial carcinoma. However, conspicuous presence of keratinizing squamous metaplasia of the adjacent flattened urothelium, especially if associated with dysplasia supports a diagnosis of primary SCC of renal pelvis. Absence of all the above findings in the urothelium is seen in primary SCC of renal parenchyma. Further primary SCC of renal parenchyma should be distinguished from metastatic SCC. With the help of clinical history imaging studies and histopathology, most of the secondary SCC has been found from lung, few from esophagus, hypopharynx and adenosquamous cell carcinoma of intra-hepatic bile ducts [7]. The prognosis of renal SCC is poor and radical nephrectomy is the mainstay of treatment [8].

In this current case, no dysplastic/metaplastic changes were seen in urothelium and clinically there was no evidence of metastasis from any distant site. Thus, the case was labelled as primary SCC of renal parenchyma. The current data regarding incidence, pathogenesis, course and prognosis of renal parenchyma SCC is inadequate, thus, future evaluation is needed to give comprehensive data on the entity.

Primary adenocarcinoma of the renal pelvis and ureter is an extremely rare tumor, representing < 1% of all renal tumors [9]. Adenocarcinoma of the renal pelvis and ureteral system usually occurs following glandular metaplasia of the transitional epithelium (pyelitis or ureteritis glandularis and cystica) induced by long-standing chronic inflammation, sometimes secondary to renal stones [9]. Glandular metaplasia of the urothelium that develops as a response to injury may progress to dysplasia and adenocarcinoma [1]. Some authors have postulated that formation of the calculi might be the result of over secretion of glycoproteins by the tumor and binding of that with cations such as sodium, calcium, and magnesium, forming larger calculi. Thus, calculi may not be the cause of the neoplasm [10]. The term

adenocarcinoma is reserved for the rare tumors that form unequivocal glandular structures, and not applied to urothelial carcinomas that have small pools of mucin in between the tumor cells [11]. Adenocarcinomas at this site have been subdivided into tubulovillous, mucinous, papillary nonintestinal, and signet ring cell types [9]. A hepatoid variant secreting alpha fetoprotein has also been described [12]. Patients are often asymptomatic. Hematuria is the most common presenting sign and loin pain and palpable abdominal mass are the late presentation of this tumor [13]. The treatment of these tumors is radical nephrectomy and total ureterectomy, including the intravesical part [14].

## Conclusion

In conclusion, both primary squamous cell carcinoma and adenocarcinoma of renal pelvis are rare tumors. Exact pathogenesis of both tumors is not proven but chronic irritation and inflammation most commonly associated with nephrolithiasis are the most probable causes. Meticulous search for a malignancy should be made in all cases of nephrolithiasis since many associated tumors are occult. In both instances presentation was that of non-functional kidneys emphasizing the need for good pathological examination.

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