

Literature Review on Squamous Cell Carcinoma of the Kidney and Renal Pelvis

Anthony Kodzo-Grey Venyo

North Manchester General Hospital

Department of Urology

Manchester

United Kingdom

Correspondence to:

Mr Anthony Kodzo-Grey Venyo MB ChB FRCS(Ed) FRCSI FGCS Urol. LLM

North Manchester General Hospital Department of Urology Delaunay's Road Manchester

United Kingdom

Email: [akodzogrey@yahoo.co.uk](mailto:akodzogrey@yahoo.co.uk)

## **Abstract**

### **Background**

Primary squamous cell carcinoma of renal pelvis/kidney (PSCCRP/K) is rare with controversies regarding its histogenesis.

### **Aim**

To review the literature

### **Method**

Various internet data bases were searched.

### **Literature Review**

Few cases of primary squamous cell carcinoma of renal pelvis / kidney (PSCCRP/K) have been reported with only **three** cases of PSCC of the renal parenchyma without involvement of renal pelvis. Some PSCCRP/Ks have been associated with renal calculi, chronic infections, vesicoureteric reflux. Some cases had developed many years after successful percutaneous nephrolithotomy; a case was reported many years after curative radiotherapy for testicular tumour. The tumours tend to be initially diagnosed in advanced stages; generally the prognosis has been poor following nephrectomy/nephroureterectomy. Conventional radiological features of the disease are non-specific and cannot differentiate the lesion from other tumours or xanthogranulomatous pyelonephritis. Diagnosis is based upon the microscopic characteristics of the tumour. Primary tumour elsewhere should be excluded with radiological images. PSCCRP/K should be suspected when a renal/renal pelvis mass is found with a history chronic or past stone disease treatment. Perhaps if patients who have undergone treatment for kidney stones are carefully followed-up with radiological imaging using ultra-sound-scans especially, (avoiding CT scan which could possibly induce malignancy over many years and MRI scans which on the whole are expensive) for a long time PSCCR/Ks may be diagnosed at an early stage of the disease in order to provide early curative treatment.

### **Conclusions**

A multi-centre trial of long-term follow-up of patients who have undergone treatment for renal stone disease is required to see if interval follow-up ultrasound scans would help in diagnosing early cases of PSCCRP/K that would develop subsequently.

**Key Words:** Primary squamous cell carcinoma of renal pelvis; primary squamous cell carcinoma of kidney; calculi; Nephrectomy; metaplasia; chronic irritation; prognosis:

## **Introduction**

Primary squamous cell carcinoma of renal pelvis/kidney is a rare tumour that is reported sporadically. At the time of initial diagnosis the tumour tends to be in an advanced stage and hence the reported prognosis has so far on the whole been poor. Controversies exist regarding the histogenesis of the tumour. Because of rarity of the disease perhaps a number of clinicians would be unfamiliar with its biological behaviour. The ensuing literature review on primary squamous cell carcinoma of renal pelvis / kidney has been divided into two parts. (A) An Overview and (B) Miscellaneous narrations and discussions from some reported cases.

## **Aim**

To review the literature of primary squamous cell carcinoma of renal pelvis and kidney

## **Method**

Various internet data bases were searched including PUB Med, Google, Google Scholar and Educus. The key words which were used included Primary squamous carcinoma of kidney, primary squamous carcinoma of renal pelvis, squamous cell carcinoma of kidney and squamous cell carcinoma of renal pelvis. Twenty **nine** references were found suitable for the review article.

## **Literature Review**

### **(A) Overview**

#### **General Comments**

- It has been stated that Squamous Cell Carcinomas of the kidney tend to be associated with squamous metaplasia of renal pelvis, renal calculi or infection [1] [2]
- Cases of squamous cell carcinoma of kidney may be found associated with urothelial carcinoma or urothelial carcinoma in situ; however, it has been recommended such cases should be classified as urothelial carcinoma with squamous differentiation. [3] [3]
- Holmang et al. [2] stated that most often squamous cell carcinomas of the kidney are diagnosed in advanced stages of the disease and they tend to be associated with poor prognosis.
- With regard to the origin of the disease squamous cell carcinoma of the renal pelvis / kidney has been postulated to emanate from squamous metaplasia in response to chronic irritation. [3]

## Epidemiology

- It had been stated that SCCCK tends to present between 50 years and 70 years and about equally in men and women. [2]

## Presentation

- It had been stated that SCCCKs tend to present with haematuria, abdominal pain, and flank pain and that SCCCKs may produce para-neoplastic syndrome, similar to squamous cell carcinoma of lung. [3] It may also present with weight loss.

## Urine cytology

- Urine cytology may show evidence of abnormal cells which may be suggestive of squamous cell carcinoma,

## Radiological investigations

In squamous cell carcinoma of renal pelvis, radiological investigations may reveal a solid mass, with +/- hydronephrosis, calcifications, or a renal pelvis infiltrative lesion without any obvious distinct mass. The differential diagnosis of SCC of renal pelvis based upon radiological investigations include: primary and metastatic malignancies and Xanthogranulomatous pyelonephritis.

## Ultra-sound scan

- Ultrasound scan of abdomen and renal tract may be normal in some cases; it may show hydronephrosis plus or minus calculus in the renal pelvis; it may also show a lesion in the renal pelvis or kidney. Ultrasound scan of abdomen and pelvis can be done in the follow-up assessment of patients who had undergone nephrectomy/nephroureterectomy to exclude metastasis. If a patient needs fine needle aspiration biopsy of a subcutaneous lump or a lesion in the kidney the procedure can be done under ultrasound guidance.

## Computed tomography (CT) scan

- CT scan of abdomen and renal tract may be normal in some cases; it may show hydronephrosis plus or minus calculus in the renal pelvis; it may also show a lesion in the renal pelvis or kidney. CT scan can provide detailed assessment of the renal pelvis lesion and would show whether or not lymph nodes are enlarged in the abdomen and pelvis. The CT scan can also be used to confirm absence of a primary tumour lesion anywhere else in the abdomen. CT scan of abdomen and pelvis can be undertaken at follow-up of patients following nephrectomy or nephroureterectomy for squamous cell carcinoma of kidney/renal pelvis to exclude subsequent development of metastasis

## CT scan of thorax

- CT scan of thorax is undertaken to exclude a metastatic tumour lesion in the thorax and it would also exclude a primary tumour in the thorax. CT scan of thorax can be done in the follow-up of patients who had

undergone nephroureterectomy or nephrectomy for squamous cell carcinoma of kidney/renal pelvis to exclude subsequent development of metastasis in the thorax.

#### 18-Fludeoxyglucose Positron Emission Tomography (FDP- PET/CT)

- FDP- PET/CT scan can be used for metastatic tumour work-up assessment.

#### Magnetic Resonance Imaging (MRI)

- MRI scan of abdomen and renal tract may be normal; in some cases it may show hydronephrosis plus or minus calculus in the renal pelvis; it may also show a lesion in the renal pelvis or kidney. MRI scan can provide detailed assessment of the renal pelvis lesion and would show whether or not lymph nodes are enlarged in the abdomen and pelvis. The MRI scan can also be used to confirm absence of a primary tumour lesion anywhere else in the abdomen. MRI has an additional advantage in that it is not associated with radiation but it expensive to . MRI scan of abdomen and pelvis can also be undertaken in the follow-up of patients who had undergone treatment for squamous cell carcinoma of kidney/renal pelvis to exclude metastasis; however, perhaps the expensive cost of this radiological investigation would not make it possible for clinicians to undertake this investigation on regular follow-up situations.

#### MRI scan of thorax

- MRI scan of thorax is undertaken to exclude a metastatic tumour lesion in the thorax and it would also exclude a primary tumour in the thorax. MRI scan of thorax can be done in the follow-up of patients who had undergone nephroureterectomy or nephrectomy for squamous cell carcinoma of kidney/renal pelvis to exclude subsequent development of metastasis in the thorax. Because of the cost involved with regard to MRI scans globally, clinicians may request chest X-rays at follow-ups initially and if the x-ray shows any lesion in the lungs then either CT scan or MRI scan could then be requested.

#### Isotope bone scan

- Isotope bone scan can be used to exclude or confirm bone metastasis.

#### Radiological imaging guidance biopsy of lesions in kidney / renal pelvis

- Ultrasound-guided biopsy or CT-scan guided biopsy of renal masses can be undertaken to obtain specimens for histological examinations which could establish a diagnosis of squamous cell carcinoma of kidney/renal pelvis.

#### Fine needle aspiration for cytology

In the event of a lesion that is accessible for fine needle aspiration (for example a subcutaneous lesion), fine needle aspiration can be undertaken to obtain a specimen for cytological examination.

#### Cystoscopy and ureteric urine sample collection

- Cystoscopy and insertion of ureteric catheters by the retrograde approach can be undertaken to obtain urine for cytological examination which could show malignant cells

#### Ureteroscopy / Ureterorenoscopy and collection of urine as well as biopsy of lesion(s) in renal pelvis / calyx

- Ureteroscopy / Ureterorenoscopy and collection of urine as well as biopsy of lesion in the renal pelvis / calyx can be undertaken to obtain specimens of urine for cytology as well as biopsy specimens for histological examination which could be used to establish a diagnosis of squamous cell carcinoma. Ureterorenoscopy can also be used to treat associated renal pelvis stones by means of basket extraction or lithotripsy.

#### Macroscopic features

- Macroscopic examination of SCCPs, tend to show ulcerated tumours that are large and necrotic [3]

#### Microscopic features of SCCK

- On the whole microscopic examination of specimens of SCCPs, tend to reveal features that mimic squamous cell carcinoma of other organs. [3]
- Microscopic examinations of specimens of SCCPs tend to show infiltrating nests of atypical squamous epithelial cells which are associated with or not associated with keratinization and also there tends to be absence of a component of typical urothelial carcinoma. [3]

#### Differential diagnosis of SCCK

- It is important to differentiate SCCK from urothelial carcinoma with squamous differentiation and it should be appreciated that with regard to urothelial carcinoma with squamous differentiation a thorough examination of sections of the tumour would show areas of urothelial carcinoma but in SCCK there would not be any evidence of urothelial carcinoma anywhere in the tumour. [3]

#### Treatment

The surgical treatment options that had been used for squamous cell carcinoma of the renal pelvis / kidney include:

- Nephrectomy
- Radical Nephrectomy
- Nephroureterectomy

#### Chemotherapy and Radiotherapy

- Radiotherapy and chemotherapy or radiotherapy have also, been used in some cases in addition to surgery which has been used in most cases.

#### Outcome

- On the whole the outcome of SCCs or SCCRs have been poor due to the advanced stage of the disease at the time of initial diagnosis but in comparison with transitional cell carcinomas (urothelial carcinomas) of the renal pelvis / upper renal tract of the same stage there has not been any difference between the outcomes. It would therefore appear that if SCCs/SCCRs could be diagnosed earlier at less advanced stages, perhaps their prognosis would improve following treatment but this is conjectural and needs to be proven in due course.

(B) Miscellaneous narrations and discussions from some reported cases (see table 1 for a list of some of the reported cases and summary of various aspects of the cases and case series)

Vella et al. [4] reported a 73-year-old man, who had presented with visible haematuria. He had ultra-sound scan and CT scan which revealed a tumour mass in the right kidney associated with lymphadenopathy. He underwent nephrectomy and lymphadenectomy. Histological examination of the surgical specimen revealed squamous cell carcinoma of the renal pelvis which had involved the renal parenchyma and had extended into the peri-renal fat. The tumour had involved the regional lymph nodes and had also invaded the inferior vena cava. Histological examination had also shown squamous carcinoma in situ and squamous metaplasia in the urothelium adjacent to the tumour. He had another ultra-sound scan of abdomen and renal tract 3 months later which had revealed local recurrence of the tumour. He received adjuvant chemotherapy. Vella et al. [4] stated that the aggressive course of the disease is in concordance with the poor outcome of squamous cell carcinoma of the renal pelvis as was reported in the literature earlier.

Talwar et al. [5], reported a 69-year-old man who had presented with clinical features of pyonephrosis who had undergone nephrectomy. Histological examination of the nephrectomy specimen had shown an unsuspected squamous cell carcinoma of renal pelvis with concomitant pyonephrosis. Talwar et al. [5] stated the rarity of squamous cell carcinoma in the absence of renal calculi and highlighted its association with pyonephrosis.

Kayaselçuk et al. [6] reported two patients who had squamous cell carcinoma of the kidney. With regard to the first patient, Kayaselçuk et al. [6] reported that the patient was a 56-year-old man who manifested with haematuria, left lumbar pain fever and weight loss. He had a history of untreated

nephrolithiasis of his left kidney 20 years, earlier. His pre-operative radiological investigations as well as gross examination of the nephrectomy specimen did not reveal the tumour. The second patient was an 87-year-old woman who manifested with haematuria and left lumbar pain. She also had a long history of nephrolithiasis of her left kidney. Kayaselçuk et al. [6] stated that both patients had undergone left nephrectomy for non-functioning hydronephrotic kidney. In both cases microscopic examination of the nephrectomy specimens had revealed squamous metaplasia and dysplasia in the in the pelvi-calyceal mucosa, as well as islands of atypical squamous cells in the renal parenchyma. In the second case microscopic examination of the kidney additionally showed sarcomatous changes in the renal pelvis. [6]

Ito et al. [7] reported a 60-year-old man who had been admitted because of multiple bilateral renal calculi and visible haematuria. His radiological investigations had revealed non-functioning right kidney and marked left sided hydronephrosis. He underwent percutaneous nephrolithotomy for his left renal calculi. Squamous cell carcinoma involving the treated left kidney was several months subsequently diagnosed. He was treated by means of chemotherapy and radiotherapy but despite this treatment he died of renal failure.

Paonessa et al. [8] reported a 70-year-old woman who had had a long-history of renal calculi who had presented with vague abdominal pain. She had CT scan and MRI scan which had shown a mass in the upper pole of the left kidney. She had undergone percutaneous CT guided biopsy of the mass and histological examination of the specimen had revealed a poorly differentiated carcinoma but the features of the tumour were considered to be inconsistent with any definite cell type. She subsequently underwent left nephrectomy and histological examination of the specimen had revealed squamous cell carcinoma of the renal collecting system. Paonessa et al. [8] made the ensuing iterations:

- Chronic calculi of the kidney pose a risk for the development of squamous metaplasia which may emanate in squamous cell carcinoma.
- Despite the fact that squamous cell carcinoma of the upper urinary tract is rare, patients with long-standing nephrolithiasis should be monitored
- The diagnosis of SCCRP should be included in one's differential diagnoses in the evaluation of a renal mass that is associated with chronic inflammatory conditions.

Mikuriya et al. [9] reported a 49-year-old woman who had presented with left sided abdominal pain. She had various investigations which confirmed she had complete bilateral duplication of ureter and pelvis and vesico-ureteric reflux into the upper left part of the kidney. At operation, a tumour was found in the upper part of the left renal pelvis (upper moiety of the duplex system) and in the ureter belonging to the upper moiety of the left renal duplex pelvis. After a left nephro-ureterectomy, histological examination of the specimen had shown squamous cell carcinoma. She received 50 Gy of radiotherapy but despite this treatment, she died four months pursuant to her operation.

Sivaramakrishna et al. [10] reported a patient who had undergone successful percutaneous nephrolithotomy (PCNL) for a long-standing renal pelvis calculus and who eight months subsequently presented with a large squamous cell carcinoma in the same location in the renal pelvis.

Imbriaco et al. [11], reported a 69-year-old man with a past history of renal calculi who had presented with left flank abdominal pain and fever for several months. He had CT scan and MRI scan of abdomen which had revealed a large mass in the left side of his horseshoe kidney with associated large renal stones. He underwent partial nephrectomy with the removal of the left side of the horse shoe kidney. Pathological examination of the specimen showed squamous cell carcinoma arising in horse shoe kidney with associated renal stones.

Holmang et al. [2] reported a large series of patients with squamous cell carcinoma of renal pelvis/ ureter and compared them with patients who had had urothelial carcinoma. Holmang et al. [2] reviewed the histopathological records and the clinical records of an initial 808 patients who had renal pelvis and ureteral cancers. With regard to the results, Holmang et al. [2] reported that only 2 (4%) out of 65 patients with squamous cell carcinoma had had stage pTa/pT1/pT2 tumours and 96% of them had stages higher than T2 in comparison with 460 (62%) out of 743 patients with pTa/pT1/pT2 tumours who had urothelial carcinoma. Holmang et al. [2] also reported the following:

- The median survival was shorter for patients with squamous cell carcinoma who were treated surgically (7 months) in comparison with patients who had urothelial carcinoma (50 months).
- Nevertheless, there was no significant difference in the disease-specific 5-year survival rate between patients with squamous cell carcinoma and urothelial carcinomas in the same disease stage.
- Vascular invasion, microscopic solid tumour pattern, and large tumour size had negative prognostic significance in multi-variate analyses.
- The type of tumour based upon histopathology (squamous cell carcinoma or urothelial carcinoma) did not have any prognostic significance.

Holmang et al. [2] made the following conclusions:

- The prognosis for squamous cell carcinoma is poor; nevertheless, with regard to stage for stage comparison between squamous cell carcinoma and urothelial carcinoma, the prognosis is not different for tumours of the renal pelvis and ureter.
- It could be presumed that high stage squamous cell carcinoma and high stage urothelial carcinoma become symptomatic first at a time when the tumours are already large, deeply invasive, and most often incurable.
- New types of treatment are urgently required in order to improve upon the poor prognosis associated with patients who have advanced stage squamous cell carcinoma and urothelial carcinoma of the upper urinary tract.

O'Daly et al. [12] reported a 71-year-old man who was diagnosed with squamous cell carcinoma in the renal pelvis of a solitary functioning kidney. O'Daly et al. [12] stated that the patient had undergone radical orchidectomy and adjuvant radiotherapy for stage II seminoma 34 years preceding the diagnosis of the squamous cell carcinoma of the renal pelvis and that this rare second carcinoma had occurred within the radiotherapy treatment field.

O'Daly et al. [12] further stated the following:

- Second malignancies are uncommon but serious sequels of radiation treatment and they have a potential for the development of significant health problems in patients with complete remission of their primary disease.
- To their knowledge their case was the first reported case of squamous cell carcinoma of renal pelvis which had occurred after radiotherapy.

It would be argued that perhaps in this aforementioned case since there was no renal pelvis calculus and there was no history of chronic urinary tract infection or vesico-ureteric reflux, the radiotherapy might either have induced metaplasia within the cells lining the renal pelvis or induced de-differentiation of toti-potential cells within the lining of the renal pelvis and eventually resulted in squamous cell carcinoma.

Funez et al. [13] reported a 68-year-old woman who presented with visible haematuria and right flank pain. She had ultra-sound scan of abdomen and renal tract which showed a solid mass with probably calcified areas and cystic changes in the upper pole of the right kidney. She also had a CT scan which revealed a tumour in the upper pole of the right kidney with a heterogeneous contrast caption, calcification and no evidence of lymph adenopathy. She underwent right nephrectomy. Macroscopic examination of the kidney revealed a tumour in the upper pole which measured 4.6 cm in its maximum dimension, without involvement of the perinephric tissues or renal vein. Part of the tumour was brown and homogeneous and another part of the tumour was grey coloured with necrotic / haemorrhagic appearance as well as it had calcifications. There was no evidence of calculi in the renal pelvis. The tumour was related to the renal pelvis focally (see figure 1). Microscopic examination of revealed that the tumour consisted of a typical chromophobe renal cell carcinoma with positive Hale's colloidal iron stain and immunohistochemical staining of the tumour was negative for vimentin (Dakocytomation S. A.) in the areas that had brown, homogeneous appearance (see figure 2). There was another zone with necrosis, extensive calcification and solid epithelial nests with some keratin pearls and obvious squamous cell differentiation (see figures 3 and 4) close to these areas. These cells exhibited negative staining for Hale's colloidal iron stain and positive staining for cytokeratin 5/6(Dakocytomation S. A.). Sections which were taken from the area where both tumours were in contact did not show any evidence of collision effect (see figure 5). Focal relationship between both tumours and renal pelvis were observed. Extensive examination of the specimen did not reveal any urothelial malignancy or signs of chronic urinary tract infection or squamous metaplasia to suggest irritation of pelvic or calyceal epithelium. There was no evidence of invasion of the perinephric tissues, adrenal gland, or lymph nodes. The patient was alive after 32 months.

Bindra et al. [14] reported a 50-year-old woman who presented with a history of left flank lump, pain and fever. She had ultra-sound scan and intravenous pyelogram which revealed left sided hydronephrosis and multiple calculi in the lower calyx of the left kidney. On microscopic examination of her urine specimen, the urine cytology was positive for malignant cells and the cytomorphological characteristics of the cells were noted to be suggestive of squamous cell carcinoma (see figure 6). Fine needle aspiration cytology (FNAC) of the lump under ultra-sound guidance was undertaken and this was reported as follows:

- Fine needle aspiration cytology smears revealed acute inflammatory cells, a few a-nucleate squames, necrotic cellular material, and a few isolated and groups of occasional epithelial tumour cells.
- The cells exhibited pleomorphism, central hyperchromatic nucleus which had coarse irregular chromatin and nucleoli that were inconspicuous. It also showed irregular nuclear outlines and mild to moderate amount of ground glass-like basophilic cytoplasm. Rare tadpole cells were also found in a haemorrhagic background (see figure 7).

The aforementioned features were adjudged to be consistent with a diagnosis of squamous cell carcinoma.

Kalayci et al. [15] reported a 60-year-old man who had presented with weight loss. He had ultra-sound scan of abdomen and renal tract which revealed intra-parenchymal hypo-echoic solid mass which measured about 4.9 cm x 5.1 cm in size with lobulated contour and which had extended to the upper pole of the right kidney and absence of corticomedullary distinction (see figure 8a-8b). His Doppler ultra-sound scan did not show any significant vascularity in the mass. Staghorn calculi were also found in the right pelvi-calyceal system without any evidence of dilatation in the pelvi-calyceal system. He also had CT scan of abdomen which showed a large non-functioning right kidney with staghorn calculi and a hypo-dense mass in the renal parenchyma which had extended to the upper pole of the right kidney. He had radiological metastatic work up which showed absence of metastasis and the kidney tumour was staged stage III (pT3N0M0). T1-weighted imaging had shown a contoured homogeneous isointense mass within the upper pole of the right kidney which had invaded the renal sinus. On T-2 weighted imaging, a heterogeneous hyper-intense mass with some hypo-intense areas was seen with minimal enhancement on intravenous gadolinium contrast administration. Multiple millimeter hypo-intense foci in all sequences compatible with calculi or calcifications were seen (see figure 8c – 8e). He subsequently underwent right radical nephrectomy.

Macroscopic examination of the right radical nephrectomy specimen showed an enlarged kidney which on cut section was found to contain multiple yellow-brown colored staghorn calculi. An irregular gray-white solid tumor was seen which had replaced the renal pelvis and parenchyma. The surrounding renal parenchyma was not visible and the mass was found to have invaded the

perinephric and pelvic fat (see figures 9a and 9b). Serial sections of the tumour had revealed a haemorrhagic area in the superior pole.

Microscopic examination showed poorly differentiated squamous cell carcinoma (SCC) which had infiltrated the renal parenchyma and the perinephric-pelvic fat. The tumour had infiltrated the renal capsule, perinephric fat, and lymphovascular structures. A lot of necrosis was evident in the tumour mass (see figures 10a, 10b, and 10c). Kalayci et al. [15] stated the following:

- A pathological diagnosis of squamous cell carcinoma of renal pelvis which had extensively infiltrated the renal parenchyma and perinephric fat was made.
- Some authors [16] [17] had intimated that majority of squamous cell carcinomas of the renal pelvis tend to be moderately or poorly differentiated and thus the characteristics of squamous cell carcinomas including keratin pearls and intracellular bridges may not be readily apparent and that typically squamous cell carcinomas at the time of initial presentation and diagnosis on the whole tend to be more invasive in comparison with transitional cell carcinomas at diagnosis.
- Primary SCCRP is rare and accounts for 0.5% to 0.8% of malignant kidney tumours.
- On the whole these tumours are highly aggressive in nature and tend to manifest at an advanced stage at the time of initial diagnosis and tend to be associated with poor prognosis in comparison with other upper urinary tract malignancies. [18]
- Chronic irritation, inflammation, and infection induce squamous metaplasia of the collecting system of the kidney, which could develop into dysplasia and carcinoma in some patients. Whether the development of dysplasia is related to the presence of the calculus which finally emanates in carcinoma or the squamous cell carcinoma is responsible for the causation of calculus had not yet been clarified. [19]
- With regard to radiological characteristics of SCC of renal pelvis and kidney, the lesion may look like a solid mass, with evidence of hydronephrosis, calcifications, or it may look like an infiltrative lesion in the renal pelvis without any evidence of a distinct mass.
- The differential diagnoses of SCC of renal pelvis and kidney based upon the radiological features include primary and metastatic neoplasms of the kidney and xanthogranulomatous pyelonephritis associated with renal stones.
- Mardi et al. [16] had stated that xanthogranulomatous pyelonephritis tends to be frequently associated with lithiasis; nevertheless, it rarely causes keratinizing squamous metaplasia and because its

manifestations simulate neoplasm, it had tended to be misdiagnosed as malignancy.

- The radiological imaging features of squamous cell carcinoma of renal pelvis tend to be variable and some of the radiological findings include diffuse enlarged non-functioning kidney associated with renal calculi, radiological evidence of peri-renal infiltration, as well as, low-density or echogenicity in the renal parenchyma. Primary squamous cell carcinoma of the kidney cannot be differentiated from xanthogranulomatous pyelonephritis or other types of malignancies of the kidney based upon radiological features. The CT scan and MRI scan findings of a large urothelial carcinoma of the renal pelvis invading the renal parenchyma would tend to mimic that of xanthogranulomatous pyelonephritis.
- A number of authors [16] [17] [20] [21] had stated that in view of the non-specific clinical manifestations and non-specific radiological features of squamous cell carcinoma of the kidney, difficulties in the establishment of diagnosis would necessitate reliance on histopathological examination to confirm the diagnosis.

Raghavendran et al. [22] retrospectively reviewed 18 cases of malignancies associated with stone disease in the renal pelvis. They had noted 15 cases of squamous cell carcinomas associated with stone disease (high incidence) out of the 18 cases. They recommended that a patient with long standing stone and associated poorly functioning kidney or haematuria should have a screening CT scan. Considering the fact that squamous cell carcinoma of renal pelvis/kidney has been reported a long time after successful percutaneous nephrolithotomy even in the absence of a recurrent stone it would be argued that there is the need for patients who have undergone percutaneous nephrolithotomy for a long time with regular periodic / yearly imaging by means of ultra-sound scans of renal tract or at times other appropriate radiological imaging in order to detect early a possible SCC of renal pelvis/kidney.

Considering the fact that squamous cell carcinoma of the renal pelvis/kidney has been diagnosed many years after a patient had undergone radiotherapy for a testicular cancer and the involved kidney was in the radiation field of the radiotherapy, it is the view of the author that regular appropriate radiological imaging (for example ultrasound scans) should be done as surveillance. Perhaps long-term regular CT scans should be avoided in the long-term follow-up of such patients because of the potential possible risk of inducing another malignancy from repeated cumulative radiation effect (even though CT would be good for detecting any new malignancy).

Lee et al. [17] reported that the following CT features are helpful for the diagnosis of squamous cell carcinoma the kidney: presence of enhancing extra-luminal, and exophytic mass in some of the cases associated with intraluminal component. Lee et al. [17] recommended that considering the fact that it was not practical for every patient with renal stone to have a CT scan, intravenous urography (IVU) should be undertaken periodically, particularly,

in patients who have long-standing stones, and they should be assessed for split function for all areas of the renal parenchyma. It had been stated by some authors [17] [18] that the filling defect, the delay in appearance of pyelogram, renal parenchymal thickening in IVU may be suggestive of a renal tumour, despite preservation of renal contour and absence of mass effect.

Ghosh and Saha, [23] reported a 51-year-old man who presented with a history of his right upper abdomen and intermittent right loin pain. He had a contrast-enhanced computed tomography scan (CECT) of abdomen which revealed a solitary heterogeneously enhancing relatively well-delineated mass in the lower pole of the right kidney. There was no evidence of infiltration of the adjacent organs (see figure 11a), and there was no evidence of lymph node involvement. There was no evidence of hydronephrosis or calculi in the renal tract. He also had contrast-enhanced CT scan of thorax and isotope bone scans which excluded metastasis. He underwent right radical nephrectomy.

Macroscopic examination of the specimen revealed a variegated, light tan to yellow friable mass (see figure 11b), which measured 5.8 cm x 5.5 cm x 4.5 cm confined to the lower pole of the kidney with haemorrhagic and necrotic areas seen on sectioning. The pelvicalyceal system was not involved. There was no calculus in the kidney and the pelvi-calyceal system was not dilated. The histopathological examination findings of the specimen was reported as consistent with well-differentiated squamous cell carcinoma with nests of atypical squamous epithelial cells, keratin pearl formation, and focal areas of necrosis in the parenchyma of the kidney with entrapped glomeruli and tubules (see figures 12a, 12b, and 12c). There was evidence of chronic inflammatory reaction in the surrounding areas. The tumour was staged T1bN0M0. Microscopic examination of the pelvicalyceal system revealed that there was no tumour in the nearest urothelium, there was no evidence of squamous metaplasia or carcinoma in situ (see figure 12d). He had an 18-Fludeoxyglucose positron emission tomography / computed tomography (FDG – PET/CT) which excluded any other unknown primary malignancy. He did not receive any adjuvant therapy and he remained well without any evidence of local recurrence or distant metastasis at his 12 months follow-up. Ghosh and Saha [23] stated that their reported case in 2014 was the second case of primary squamous cell carcinoma of the parenchyma of the kidney to be reported without involvement of the urothelium. Ghosh and Saha [23] stated the following:

- Primary squamous cell carcinoma of the renal pelvis would present at an advanced stage with infiltration of adjacent tissue although both squamous cell carcinoma and transitional cell carcinoma in advanced stages have similar poor prognosis. [24]
- Their case presented at an earlier stage and was associated with excellent-outcome following treatment.
- Squamous cell carcinoma of the urothelial tract is believed to arise through a process of metaplasia usually keratinizing squamous metaplasia of the urothelium which leads to an increase in the chance for the development of squamous cell carcinoma in the future.

- The concept of squamous metaplasia preceding squamous cell carcinoma of the urothelial tract had been associated with controversies with different results in previous studies. The disagreement may partly be because of the relative rarity of the upper urinary tract. [25]
- If an identifiable urothelial dysplastic element is found including urothelial carcinoma in situ (cis) then the tumour should be classified as primary urothelial carcinoma with squamous differentiation. Nevertheless, the conspicuous presence of keratinizing squamous metaplasia of the adjacent flattened urothelium, particularly if associated with dysplasia would be in support of primary squamous cell carcinoma of the renal pelvis which is rare. [26] [27]
- In their case there was no evidence of dysplastic urothelial component or metaplastic and/or dysplastic squamous lining of urothelium.
- The leading aetiological factors for the development of squamous cell carcinoma of the renal pelvis include recurrent urinary tract infections without or with vesicoureteric reflux, long-standing staghorn calculi, smoking, schistosomiasis, endogenous and exogenous chemicals, vitamin A deficiency, hormonal imbalance and others. Only anecdotal cases of squamous cell carcinoma of renal pelvis had been reported where no apparent aetiological factors had been identified. [5] [25]
- Their case lacked the association of the carcinoma with any predisposing factors.
- Primary squamous carcinoma of the kidney should be differentiated from metastatic squamous cell carcinoma with the primary tumour elsewhere by means of a combination of clinical history, imaging studies, and histopathology. [21] [25]

The first case of primary squamous cell carcinoma that involved the renal parenchyma without the involvement of the renal pelvis urothelium was reported in 2012 by Kulshreshtha et al. [28] in a 60-year-old woman who presented with a history of weight loss.

Sahoo et al. [29] reported a 50-year-old woman who presented with pain in the right side of her abdomen of 6 months duration. She did not have any history of kidney stones, urinary tract infection or pyelonephritis. She had ultrasound scan of the renal tract which revealed mild right hydroureteronephrosis and a hypo-echoic lesion in the upper pole of her right kidney. She had a contrast enhanced CT-scan of abdomen and pelvis and thorax which did show a mild to moderate enhancing mass of about 6 cm x 8 cm in the upper pole of the right kidney (see figure 13 a) and right sided dilated ureter (see figure 13 b) and the CT scan did not show any lesion anywhere else. She underwent right radical nephrectomy and histological examination of the specimen showed normal looking glomeruli and renal tubules (see figure 13 c) together with squamous carcinoma component with keratin pearls (see figure 13 d) which established the diagnosis of squamous carcinoma of kidney. The histological

examination also showed that the renal capsule was involved but the perirenal fat and hilar lymph nodes were not involved and the renal pelvis was normal. The patient was well without any evidence of recurrence at her 6-month follow-up.

## **Summary**

Primary squamous cell carcinomas of the kidney / renal pelvis are rare tumours that are reported sporadically. Majority of reported cases of these carcinomas involve the renal pelvis and invade the kidney. Only **three** cases of primary squamous cell carcinoma involving the renal parenchyma but not involving the renal pelvis have been reported. Primary renal cell carcinomas of renal pelvis / kidney tend to be diagnosed in advanced stages of the disease and on the whole associated with a poorer prognosis in comparison transitional cell carcinomas of the renal pelvis with a 5-year-survival of less than 10% [16] [21] and a mean survival of 7 months. Nevertheless, the mean survival of patients with squamous cell carcinoma of the kidney/renal pelvis when compared with transitional cell carcinomas of the renal pelvis of the same stage would appear to be similar. A number of cases of primary squamous cell carcinomas of the renal pelvis / kidney have been associated with calculi and some have had a past history of successful treatment for stones (Percutaneous nephrolithomy). Radiological imaging characteristics in conventional studies are non-specific. Squamous cell carcinoma of the renal pelvis/kidney should be suspected when a patient is found to have a renal / renal pelvis mass and when the patient has a history of treatment for renal calculi or chronic long-term renal pelvis calculi. Considering the fact that squamous cell carcinomas of the renal pelvis/kidney tend to be associated with previous treatment for stones, perhaps if patients who have undergone treatment for renal stones are followed up for a long time with appropriate radiological imaging (for example ultrasound scans at yearly intervals) may be diagnosis of squamous cell carcinoma would be made when the tumour is less advanced which would enable early curative surgical treatment as an attempt to improve the prognosis

## **Conclusions**

Primary squamous cell carcinomas of the renal pelvis / kidney have been reported sporadically and a number of them have been associated with renal calculi and chronic infections of the urinary tract. These malignancies on the whole are initially diagnosed in advanced stages of the disease and hence associated with poor prognosis. Conventional radiological investigations are non-specific with regard to the diagnosis of squamous cell carcinoma of renal pelvis / kidney. CT and MRI scans cannot fully differentiate between xanthogranulomatous pyelonephritis, squamous cell carcinomas and other tumours of the kidney and renal pelvis. Histopathological examination of the lesion so far is the definite way to confirm the diagnosis. Clinicians should have a high index of suspicion for the possibility of squamous cell carcinoma of renal pelvis / kidney when they encounter patients with a history of chronic renal calculi or previous treatment for renal calculi.

Ethical Approval

Not required for literature review

Consent

Not applicable in cases of literature review

Conflict of interest

None

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Figure 1: Macroscopical aspect of the neoplasm. Squamous cell carcinoma (sq) and Chromophobe renal cell carcinoma (chr). Reproduced from: [13] Fúnez R, Pereda T, Rodrigo I, Robles L, Gonzalez C. Simultaneous Chromophobe renal cell carcinoma and squamous renal cell carcinoma.

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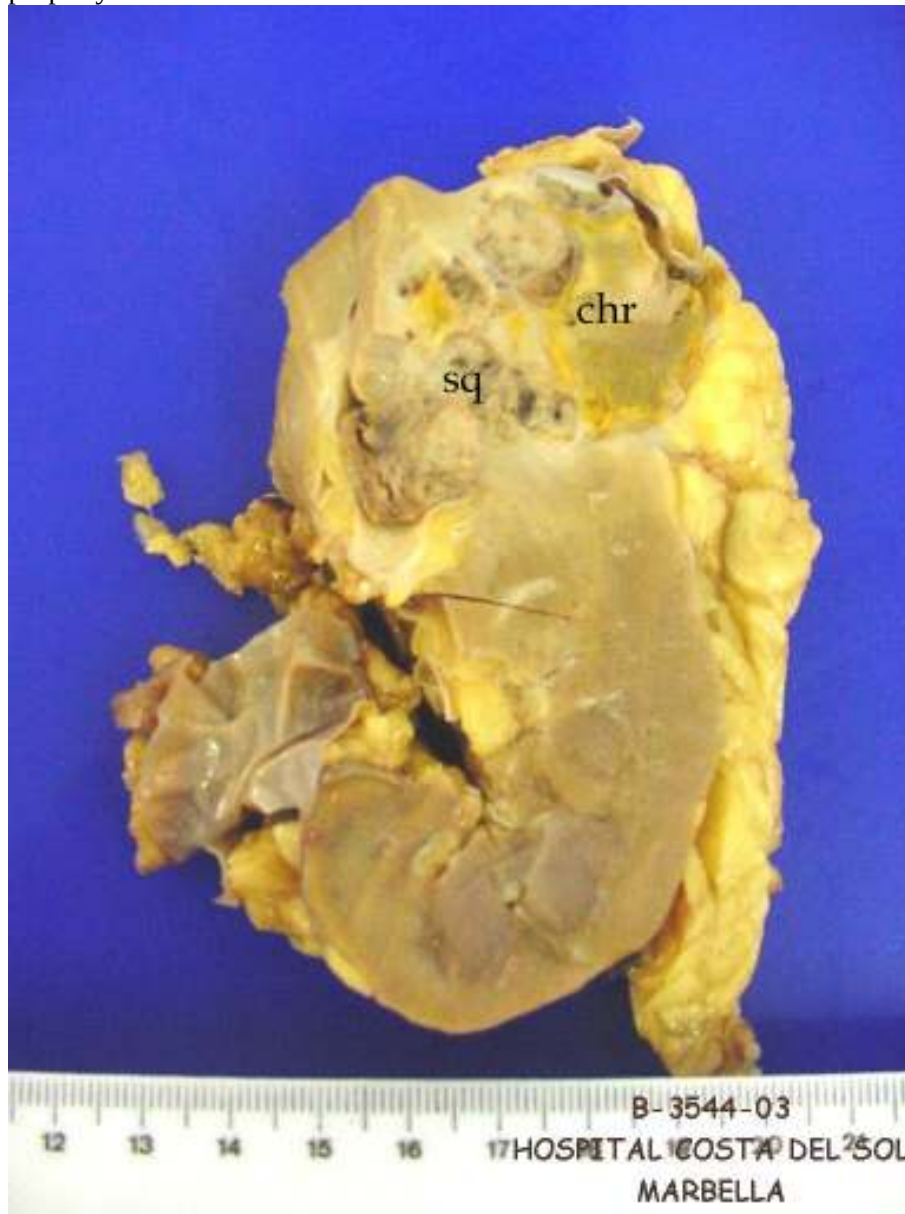


**Figure 2**

**Areas with typical chromophobe renal cell carcinoma HE x 200.**

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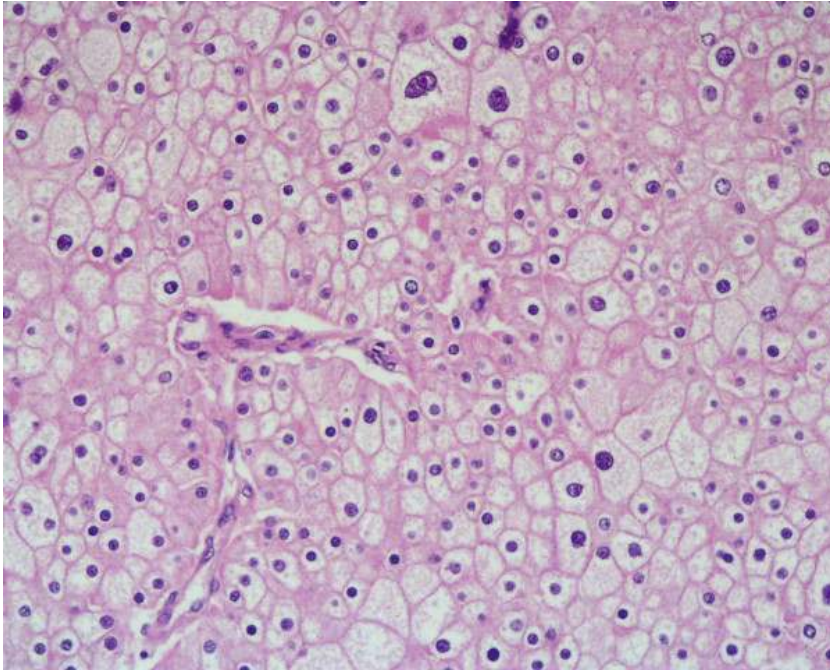


**Figure 3: Zone with squamous cell carcinoma HE x 200.** Reproduced from: [13] Fúnez R, Pereda T, Rodrigo I, Robles L, Gonzalez C. Simultaneous

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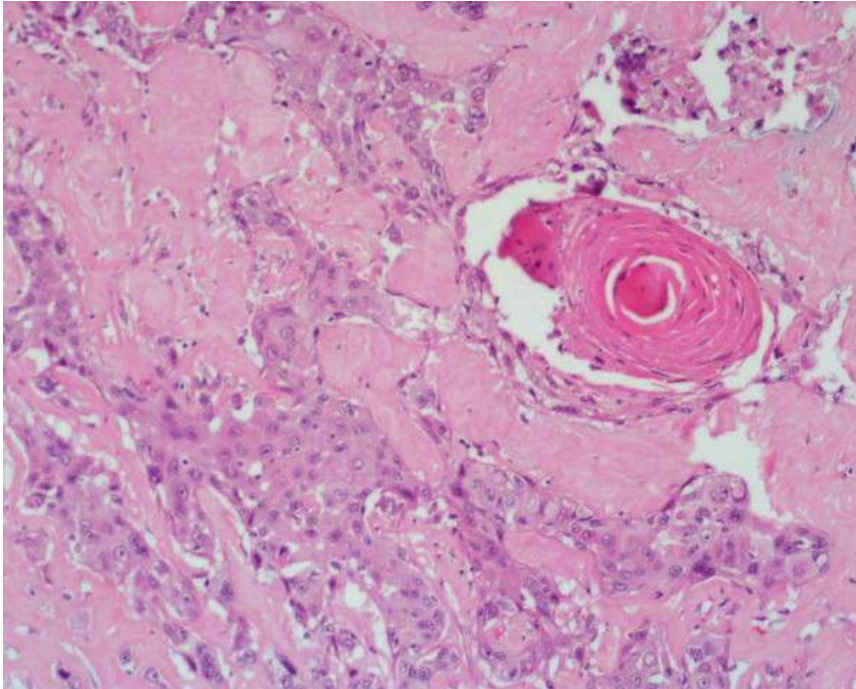


Figure 4: Zone with squamous cell carcinoma HE x 400. Reproduced from: [13] Fúnez R, Pereda T, Rodrigo I, Robles L, Gonzalez C. Simultaneous

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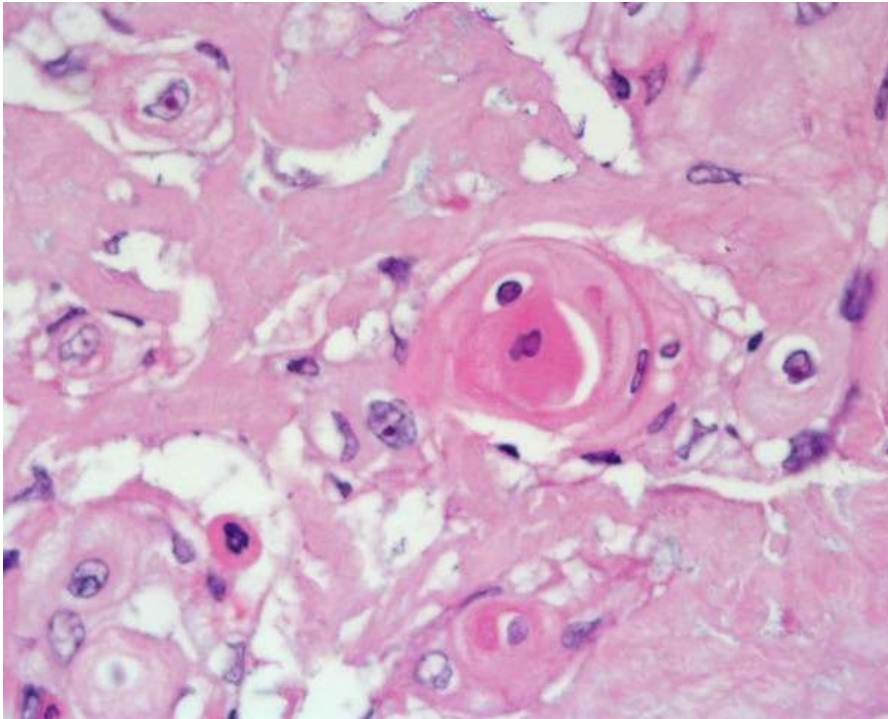


Figure 5: Border region of the two tumors .There was no collision effect. HE x 100 Reproduced from: [13] Fúnez R, Pereda T, Rodrigo I, Robles L, Gonzalez C. Simultaneous Chromophobe renal cell carcinoma and squamous renal cell carcinoma Diagnostic Pathology 2007; 2:30 doi: 10.1186/1746-1596-2-30. URL: <http://www.diagnosticpathology.org/content/2/1/30> © Fúnez et al; licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/2.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

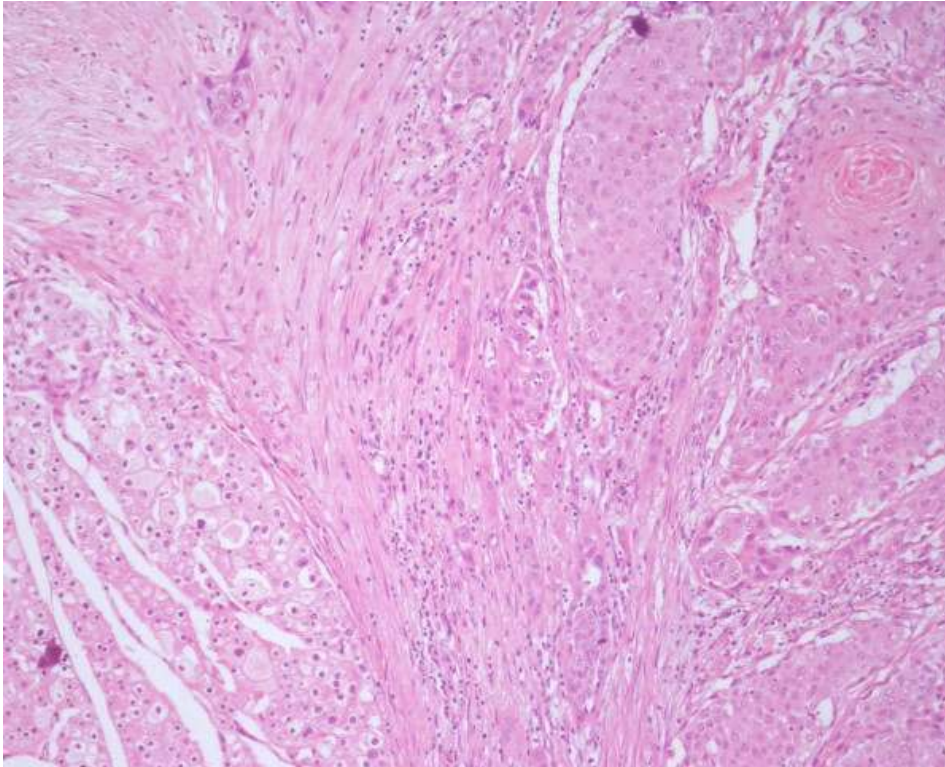


Figure 6: Fine needle aspiration cytology smear shows pleomorphic squamous cells in a hemorrhagic background. (Giemsa stain, x 400) Reproduced from: [14] Bindra R, Gupta S, Gupta N. Cytological diagnosis of squamous cell carcinoma of renal pelvis J. Cytol 2010 Apr; 27(2): 76 – 77. Doi: 10.4103/0970-9371.70756 Copyright © Journal of Cytology. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction, in any medium provided the original work is properly cited.

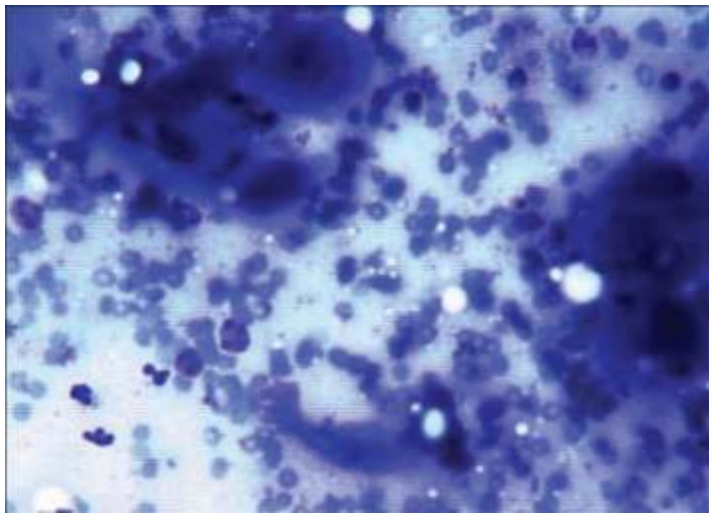
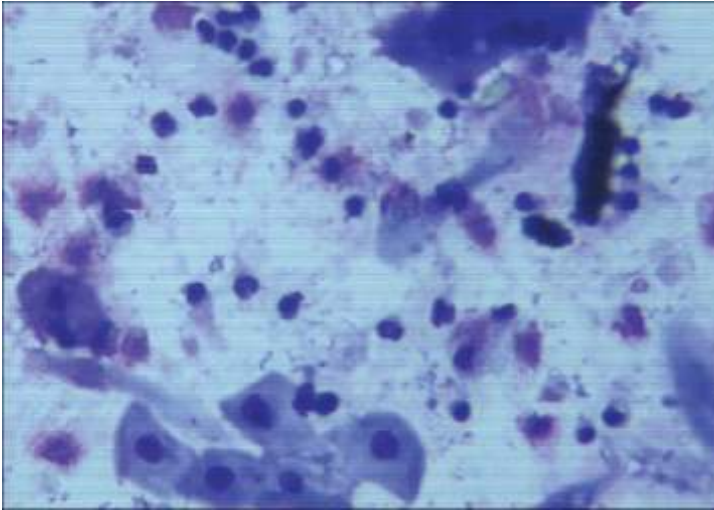


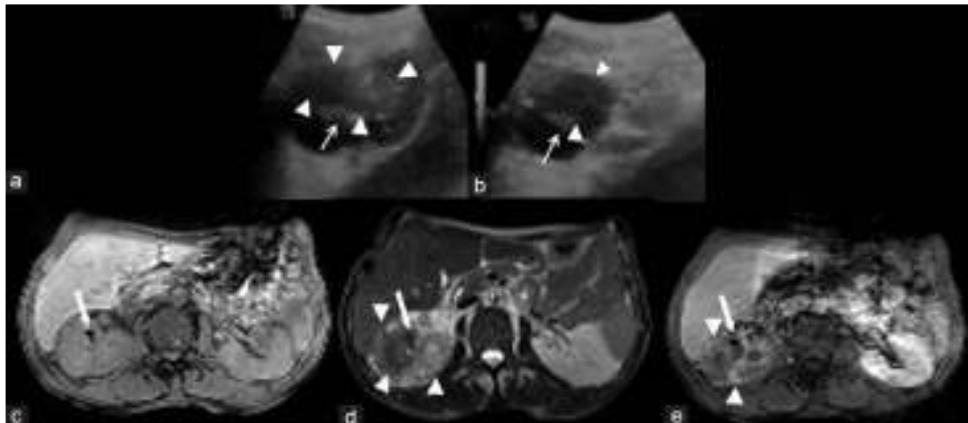
Figure 7

Urine smear shows benign urothelial cells and pleomorphic squamous cells (Giemsa stain, x 400). Fine needle aspiration cytology smear shows pleomorphic squamous cells in a hemorrhagic background. (Giemsa stain, x 400) Reproduced from: [14] Bindra R, Gupta S, Gupta N. Cytological diagnosis of squamous cell carcinoma of renal pelvis J. Cytol 2010 Apr; 27(2): 76 – 77. Squamous cell carcinoma of renal pelvis J. Cytol 2010 Apr; 27(2): 76 – 77. Doi: 10.4103/0970-9371.70756 Copyright © Journal of Cytology. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction, in any medium provided the original work is properly cited.



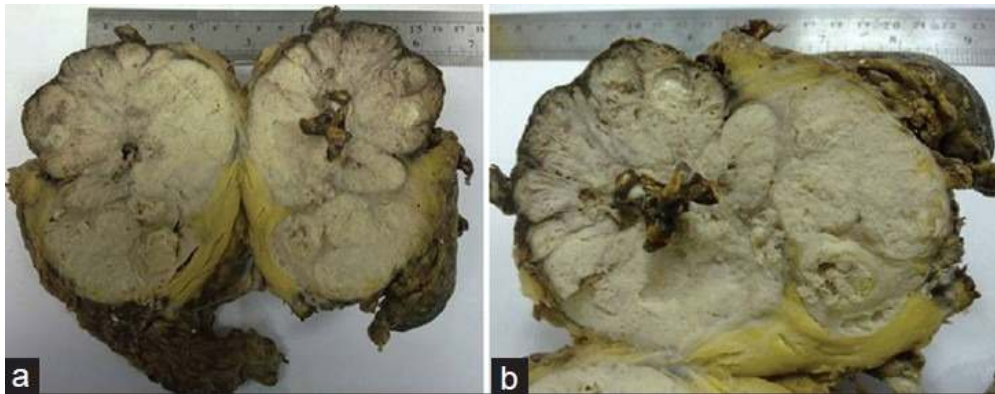
Figures 8a; 8b; 8c; 8d; 8e:

- (a) Coronal and (b) axial ultrasound (US) imaging show intra-parenchymal hypo-echoic heterogeneous solid mass with lobulated contour in the upper middle portion of right kidney (arrowhead). (c) Axial T-1 weighted magnetic resonance image (MRI), (d) T-2 weighted image (WI) show an increase in the size of the right kidney and reveal a heterogeneous hyper-intense mass (arrowheads) (e) Post-contrast T-1 WI reveals a heterogeneous isointense mass lesion invading renal sinus parenchyma, and the mass shows minimal enhancement after administration of intravenous contrast medium, and note hyper-echoic foci on US imaging and hypo-intense foci in all MRI sequences compatible with stones (white arrows). Reproduced from: [15] Kalayci O T, Bozdag Z, Sonmezgoz F, Sahin N. Squamous Cell Carcinoma of Renal Pelvis Associated with Kidney Stones: Radiologic Imaging Features with Gross and Histopathological Correlation. *J Clin Imaging Sci.* 2013; 3:14 doi: 10.4103/2156-7514.109741 Copyright © 2013 Kalayci O T; This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.



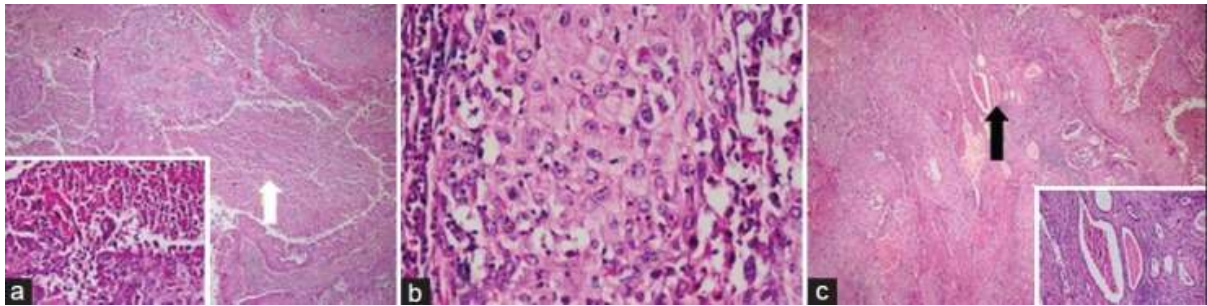
Figures 9a and 9b

Cut sections of the nephrectomy specimen (a, and b) after the right radical nephroureterectomy show an irregular gray-white solid tumor in total kidney and multiple yellow-brown colored staghorn stones. Surrounding renal parenchyma is not visible and the ... Reproduced from: [15] Kalayci O T, Bozdog Z, Sonmezgoz F, Sahin N. Squamous Cell Carcinoma of Renal Pelvis Associated with Kidney Stones: Radiologic Imaging Features with Gross and Histopathological Correlation. J Clin Imaging Sci. 2013; 3:14 doi: 10.4103/2156-7514.109741 Copyright © 2013 Kalayci O T; This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.



Figures 10a, 10b, and 10c:

Histopathology samples stained with H and E x 40 (a, b, c) show poorly differentiated squamous cell carcinoma of renal pelvis, extensively infiltrating the renal parenchyma and perinephric fat. Sample shows intensive necrotic areas within ... Reproduced from: [15] Kalayci O T, Bozdag Z, Sonmezgoz F, Sahin N. Squamous Cell Carcinoma of Renal Pelvis Associated with Kidney Stones: Radiologic Imaging Features with Gross and Histopathological Correlation. J Clin Imaging Sci. 2013; 3:14 doi: 10.4103/2156-7514.109741 Copyright © 2013 Kalayci O T; This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.



Figures 11a and 11b:

- (a) CECT of abdomen on coronal plane showing a solitary mass in the lower pole of the right kidney.
- (b) Photograph of bisected specimen of nephrectomy showing a well-delineated mass in the lower pole.

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[a]



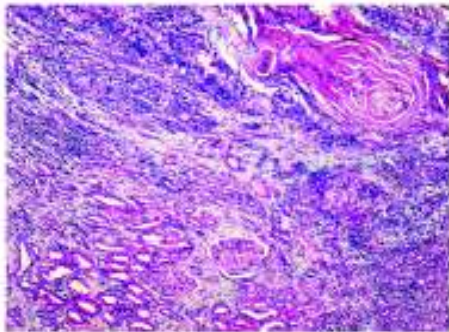
[b]



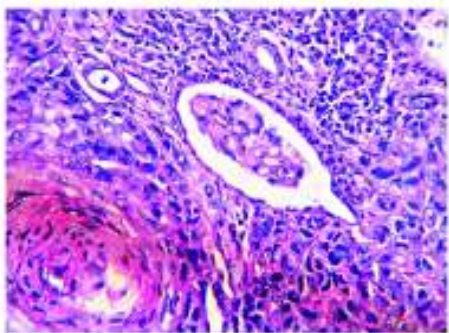
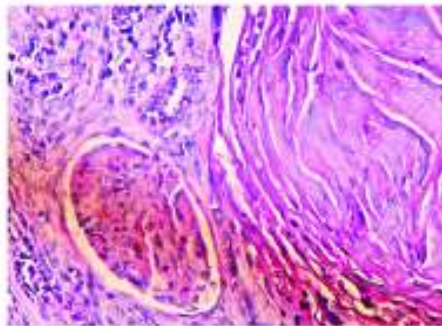
Figures 12a, 12b, and 12c:

- (a) Photomicrograph of well-differentiated squamous cell carcinoma with keratin pearl formation along with glomeruli and tubules (H and E, x 100). (b) Glomerulus and tubules in close relation to keratin pearl of squamous cell carcinoma (H and E, x 400). (c) Photomicrograph of entrapped glomerulus and renal tubules within squamous cell carcinoma (H and E, x 400). (d) Photomicrograph of uninvolved flattened urothelium of pelvicalyceal system (left) keeping a distance from sheets of malignant squamous cells (right) (H and E, x 100). Reproduced from: Ghosh P, Saha K. Primary Intraparenchymal Squamous Cell Carcinoma of the Kidney: A Rare and Unique Entity. Case Reports in Pathology Volume 2014 (2014), Article ID 256813, 3 pages <http://dx.doi.org/10.1155/2014/256813> with copyright permission: Copyright © 2014 Prithwijit Ghosh and Kaushit Saha; This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

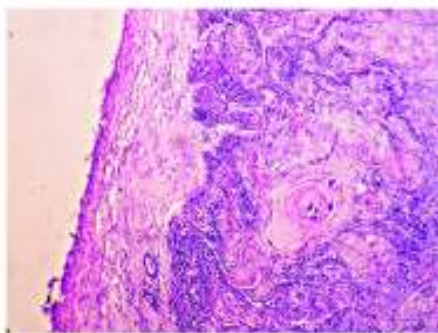
[a]



[b]



[c]

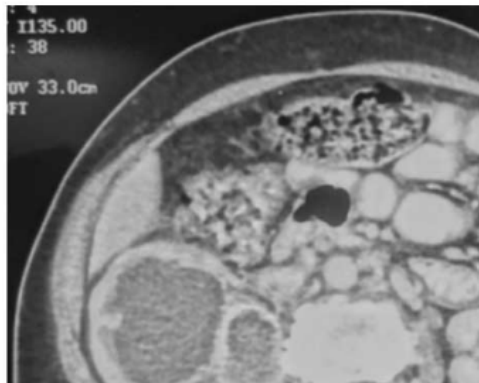


[d]

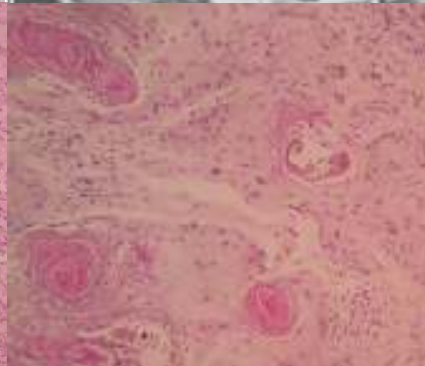
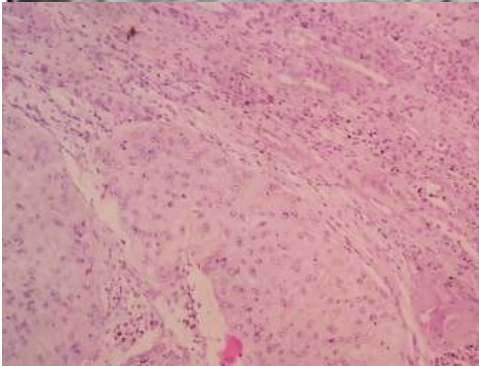
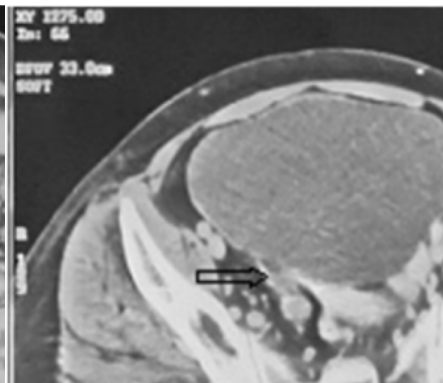
Figures 13 a; 13 b; 13 c; and 13 d:

- (a) Figure (13 a) Presence of a hypodense renal mass of size approximately 6 x 8 cms in upper pole of right kidney with mild to moderate enhancement in nephritic phase; Figure (13b) Presence of dilated ureter up to terminal part; Figure (13c) Normal glomeruli adjacent to focus of squamous epithelial carcinoma; Figure (13d) Normal tubular structures entrapped within the squamous cell carcinoma focus showing characteristics squamous pearls. Reproduced from: [29] Sahoo T K, Das S K, Mishra C, Dhal I, Nayak R, Ali I, Panda D, Majumdar S K D, Parida D K. Squamous Cell Carcinoma of Kidney and Its Prognosis: A Case Report and Review of the Literature. Case Reports in Urology Volume 2015 (2015), Article ID 469327, 3 pages <http://dx.doi.org/10.1155/2015/469327> Copyright © 2015 Tapan Kumar Sahoo et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

(13a)



(13b)



(13c)

(13d)

Table 1:

Table of some of the reported cases of squamous cell carcinoma of kidney and renal pelvis with summary of presentation, treatment and outcome

| Authors/reference/year | Age/sex/presentation/site                             | Radiological Investigation findings                    | Histological findings                                                                                                                                                                                                                                                                                                                  | Treatment                                                   | Outcome                         |
|------------------------|-------------------------------------------------------|--------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------|---------------------------------|
| Vella et al. [4] 1995  | 73; Male; haematuria; right kidney + lymph adenopathy | Ultrasound scan; CT scan – tumour mass in right kidney | Squamous cell carcinoma of the renal pelvis which had involved the renal parenchyma and had extended into the peri-renal fat. The tumour had involved the regional lymph nodes and had also invaded the inferior vena cava and also shown squamous carcinoma in situ and squamous metaplasia in the urothelium adjacent to the tumour. | Right nephrectomy + lymphadenectomy + adjuvant chemotherapy | He was alive at months          |
| Talwar et al. [5] 2006 | 69 years; male; features of pyonephrosis              |                                                        | An unsuspected squamous cell carcinoma of renal pelvis with                                                                                                                                                                                                                                                                            | Nephrectomy                                                 | Outcome not available to author |

|                       |                                                                                                                                        |                                                                                                 |                                                                                                                                                                                          |                                                                    |         |
|-----------------------|----------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------|---------|
|                       |                                                                                                                                        |                                                                                                 | concomitant pyonephrosis                                                                                                                                                                 |                                                                    |         |
| Kayaselçuk et al. [6] | [1] 56 years; male; haematuria; left lumbar pain; fever; weight loss, history of untreated nephrolithiasis of his left kidney 20 years | Radiological investigations did not detect a tumour, non-functioning hydronephrotic left kidney | squamous metaplasia and dysplasia in the in the pelvi-calyceal mucosa as well as islands of atypical squamous cells in the renal parenchyma.                                             | Eventual long-term outcome not Available to author                 |         |
|                       | [2] 87 years; female; haematuria, left lumbar pain, a long history of nephrolithiasis of her left kidney                               | non-functioning hydronephrotic left kidney                                                      | Squamous metaplasia and dysplasia in the in the pelvi-calyceal mucosa as well as islands of atypical squamous cells in the renal parenchyma and sarcomatous changes in the renal pelvis. | Eventual long-term outcome not Available to author                 |         |
| Ito et al. [7]; 1988  | 60-years; male; multiple bilateral renal calculi and visible haematuria Left                                                           | Non-functioning right kidney and marked left sided hydronephrosis. Squamous cell carcinoma      | Squamous                                                                                                                                                                                 | Percutaneous nephrolithotomy for his left renal calculi. Initially | he died |

|                                  |                                                                                                                                                                                                 |                                                                                                                       |                                                         |                                                                                                                                                                                                                                                                         |                                                 |
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|                                  |                                                                                                                                                                                                 | involving the treated left kidney was several months subsequently diagnosed.                                          | cell carcinoma involving the treated left kidney        | Chemotherapy and radiotherapy                                                                                                                                                                                                                                           | of renal failure                                |
| Paonessa et al. [8]; 2011        | 70-years; Female; a long-history of renal calculi who had presented with vague abdominal pain. Left                                                                                             | A mass in the upper pole of the left kidney.                                                                          | Squamous cell carcinoma of the renal collecting system. | Percutaneous CT guided biopsy of left renal mass<br><br>Left nephrectomy                                                                                                                                                                                                | Alive with short history post-operatively       |
| Mikuriya et al. [9]; 1989.       | 49 years; Female; left sided abdominal pain.                                                                                                                                                    | A complete bilateral duplication of uretero-pelvis and vesico-ureteric reflux into the upper left part of the kidney. | Squamous cell carcinoma.                                | Left nephroureterectomy. Plus She received 50 Gy of radiotherapy At operation, a tumour was found in the upper part of the left renal pelvis (upper moiety of the duplex system) and in the ureter belonging to the upper moiety of the left renal duplex renal pelvis. | She died four months pursuant to her operation. |
| Sivaramakrishna et al. [10] 2004 | Details not available. A patient, who had undergone successful percutaneous nephrolithotomy (PCNL) for a long-standing renal pelvis calculus and who eight months subsequently presented with a | -Previously had stone in renal pelvis but details of subsequent findings not available-                               | Squamous cell carcinoma in renal pelvis                 | Details of all the treatment is not available to author                                                                                                                                                                                                                 | Outcome details not available                   |

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|                             | large squamous cell carcinoma in the same location in the renal pelvis.                                                                                                                                                                                                                                 |                                                                                         |                                                                                                                                                                                                                                                                                                         |                                                                                 |                                  |
| Imbriaco et al. [11]; 2011. | 69 years; man; with a past history of renal calculi who had presented with left flank abdominal pain and fever for several months.                                                                                                                                                                      | Large mass in the left side of his horseshoe kidney with associated large renal stones. | Squamous cell carcinoma arising in horse shoe kidney with associated renal stones.                                                                                                                                                                                                                      | Partial nephrectomy with the removal of the left side of the horse shoe kidney. | Details of outcome not available |
| Holmang et al. [2]; 2007.   | Holmang et al. [2] reported that only 2 (4%) out of 65 patients with squamous cell carcinoma of renal pelvis/ureter had had stage pTa/pT1/pT2 tumours and 96% of them had stages higher than T2 in comparison with 460 (62%) out of 743 patients with pTa/pT1/pT2 tumours who had urothelial carcinoma. | Details not available                                                                   | Holmang et al. [2] reported that only 2 (4%) out of 65 patients with squamous cell carcinoma of renal pelvis/ureter had had stage pTa/pT1/pT2 tumours and 96% of them had stages higher than T2 in comparison with 460 (62%) out of 743 patients with pTa/pT1/pT2 tumours who had urothelial carcinoma. | Details not available                                                           | Details not available            |
| O'Daly et al. [12]; 2007.   | 71years; Male; man who was diagnosed with squamous cell carcinoma in the                                                                                                                                                                                                                                | Details not available                                                                   | Squamous cell carcinoma of renal pelvis                                                                                                                                                                                                                                                                 | Details not available                                                           | Long-term outcome details        |

|                          |                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                         |                                                                                                      |                                  |                       |
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|                          | renal pelvis of a solitary functioning kidney. The patient had undergone radical orchidectomy and adjuvant radiotherapy for stage II seminoma 34 years preceding the diagnosis of the squamous cell carcinoma of the renal pelvis and that this rare second carcinoma had occurred within the radiotherapy treatment field. |                                                                                                                                                         |                                                                                                      |                                  | not available         |
| Funez et al. [13]; 2007. | 68 years; Female; visible haematuria and right flank pain.                                                                                                                                                                                                                                                                  | A solid mass (a tumour) in the upper pole of the right kidney with a heterogeneous contrast caption, calcification and no evidence of lymph adenopathy. | Two tumours [1] Chromophobe renal cell carcinoma and squamous cell carcinoma with keratinization     | She underwent right nephrectomy. | Alive after 32 months |
| Bindra et al. [14]; 2010 | 50 years; Female; Left flank lump, pain and fever.                                                                                                                                                                                                                                                                          | Left sided hydronephrosis and multiple calculi in the lower calyx of the left kidney.                                                                   | Urine cytology On microscopic examination of her urine specimen, the urine cytology was positive for | Details not available            | Details not available |

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|                            |                                    |                                                                                                                                                                    | <p>malignant cells and the cytomorphological characteristics of the cells were noted to be suggestive of squamous cell carcinoma</p> <p>Pathological examination of the ultrasound-guided fine needle aspiration biopsy of the renal mass showed features consistent with squamous cell carcinoma.</p> |                           |                               |
| Kalayci et al. [15]; 2013. | 60 years; Male; Weight loss; Right | A large non-functioning right kidney with staghorn calculi and a hypo-dense mass in the renal parenchyma which had extended to the upper pole of the right kidney. | Poorly differentiated squamous cell carcinoma (SCC) which had infiltrated the renal parenchyma and the perinephric-pelvic fat. The tumour had infiltrated the renal capsule, perinephric fat, and lymphovasc                                                                                           | Right radical nephrectomy | Outcome details not available |

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|                                 |                                                                                                                                                                                      |                                                                                                             | ular structures.                                                                                                                                                                                                                  |                                  |                                                                                                   |
| Raghavendran et al. [22]; 2003. | 18 cases of patients of various ages with renal stone disease and presentations / sex groups not included in analysis of data; 15 had squamous cell carcinoma of renal pelvis/kidney | Various                                                                                                     | They retrospectively reviewed 18 cases of malignancies associated with stone disease in the renal pelvis. They had noted 15 cases of squamous cell carcinomas associated with stone disease (high incidence) out of the 18 cases. | Individual details not available | Details not available                                                                             |
| Ghosh and Saha [23]; 2014;      | 51 years; Male; - Pain in right upper abdomen and intermittent right loin pain; Right                                                                                                | A solitary heterogeneously enhancing relatively well-delineated mass in the lower pole of the right kidney. | Well-differentiated squamous cell carcinoma with nests of atypical squamous epithelial cells, keratin pearl formation, and focal areas of necrosis in the parenchyma of the kidney with entrapped glomeruli and tubules           | Right radical nephrectomy        | He was alive at his 12-month follow-up with no evidence of local recurrence or distant metastasis |
| Sahoo et al. [29]; 2015         | 50 years; Female; Right sided abdominal pain.                                                                                                                                        | Mild to moderately enhancing mass in upper                                                                  | Squamous cell carcinoma of kidney                                                                                                                                                                                                 | Right radical nephrectomy        | Alive at 6-month follow-                                                                          |

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|  |  | pole of right<br>kidney and<br>right<br>hydroureterone<br>phrosis | with keratin<br>pearls |  | up with<br>no<br>eviden<br>ce of<br>disease |
|--|--|-------------------------------------------------------------------|------------------------|--|---------------------------------------------|