

CASE REPORT



Squamous cell carcinoma of the renal pelvis in a patient with long-term spinal cord injury—a case report

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INTRODUCTION: For individuals with spinal cord injury/disease (SCI/D) the risk of developing a stone in the upper urinary tract is up to six times higher than in the able-bodied population. Upper urinary tract carcinomas, in general, are rare and account for only 5–10% of all urinary tract carcinomas. It is believed that chronic upper urinary tract irritation caused by e.g., kidney stones or recurrent upper urinary tract infections may be associated with an increased risk of renal squamous cell carcinoma (RSCC).

CASE PRESENTATION: We report on a 64-year-old male who suffered a spinal cord injury in 1981 resulting in a complete sensory and motor impairment below T6, AIS A. Recurrent left-sided kidney stone disease had to be treated repeatedly from 1984 onwards. Despite repeated surgical attempts, it was ultimately not possible to achieve stone clearance in the long term. Within the concept of life-long surveillance of SCI/D, the patient was examined regularly, including ultrasound examinations of the kidneys. Six months after the last control examination, the patient was admitted to our hospital with a locally advanced tumor of the left kidney, so that only the option of palliative treatment remained. Histologically an RSCC was found.

DISCUSSION: As people with SCI/D have a higher risk of developing kidney stones, it is of utmost importance to check regularly for stone disease and, if necessary, treat with the aim of long-term stone clearance in order to protect renal function and to avert potentially malignant changes at an early stage.

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INTRODUCTION

Individuals with spinal cord injury/disease (SCI/D) are at higher risk of developing the renal stone disease than the able-bodied population. Age-standardized annual incidence rates in the general population vary from 0.36 to 1.22 per 1000 person-years, whereas the rate rises up to 8 or even 9 per 1000 person-years within 1 year after SCI/D. Thus, the likeliness of developing a calculus translates to being up to six times higher than in the general population [1, 2]. In contrast to bladder stones, the way of bladder management does not relate to renal stone formation regarding the mean number of renal calculi [3]. Also, age at SCI/D, level of injury, and AIS classification do not appear to have a significant impact on the total stone burden of the kidney [4].

Though upper urinary tract carcinomas, in general, are rare and account for ~5–10% of all urothelial carcinomas, a history of chronic irritation of the upper urinary tract such as renal calculi or upper urinary tract infections is linked to the development of renal squamous cell carcinoma (RSCC), which accounts for ~0.5% up to 15% of all upper urinary tract cancers [5, 6]. This type of histological finding is usually being associated with a more advanced stage at the time of diagnosis and hence with a worse prognosis [7]. As of today, to our knowledge, there is no reported case in the literature relating renal calculi in individuals with SCI/D to developing a tumor of the upper urinary tract with unfavorable

histology such as RSCC. Among others, this aspect might be considered a crucial question concerning regular urological monitoring of individuals with SCI/D.

CASE PRESENTATION

We report on a 64-year-old man who was admitted to the Centre for Spinal Cord Injuries, at BG Trauma Hospital Hamburg. He suffered from a spinal cord injury in September 1981 as a result of dislocated fractures of the 6th and 7th thoracic vertebrae leading to a complete sensory and motor impairment below T6 AIS A and had been integrated in the life-long surveillance program of people with SCI/D at our institution since. Video-urodynamically diagnosed neurogenic bladder dysfunction was treated by sphincterotomy, bladder neck incision, and resection of the prostate in 1986 aiming to decrease micturition pressure in the bladder which had risen to pathological levels leading to vesicoureterorenal reflux on the right side. In addition, a bilateral vasectomy was performed to prevent the development of epididymitis.

The history of left-sided renal calculi began in 1984 and was initially treated by percutaneous nephrolithotomy. Regular neuro-urological assessments in 1–2-year intervals followed and revealed the recurrent stone disease of the left kidney with self-reported

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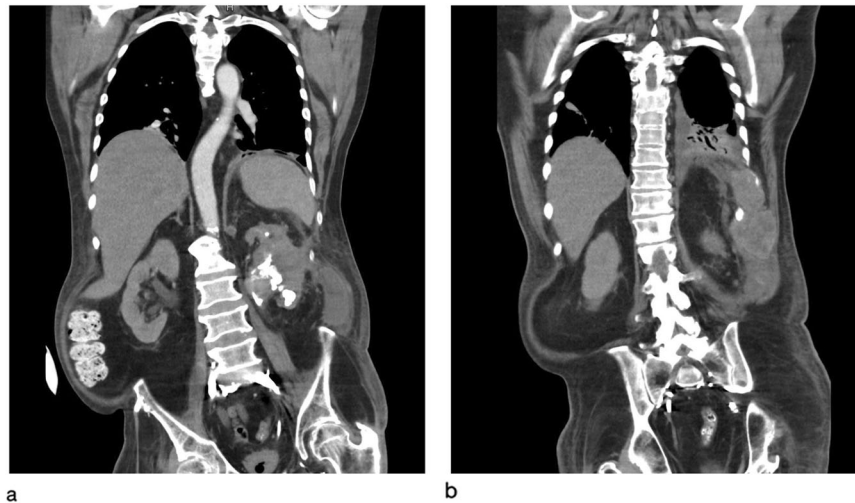


Fig. 1 Computed tomography images on admission of the patient. **a** Coronal section of abdominal and thoracic computed tomography showing the stone burden of the left kidney. **b** Coronal section of abdominal and thoracic computed tomography showing continuous inhomogeneous soft-tissue-like formation.

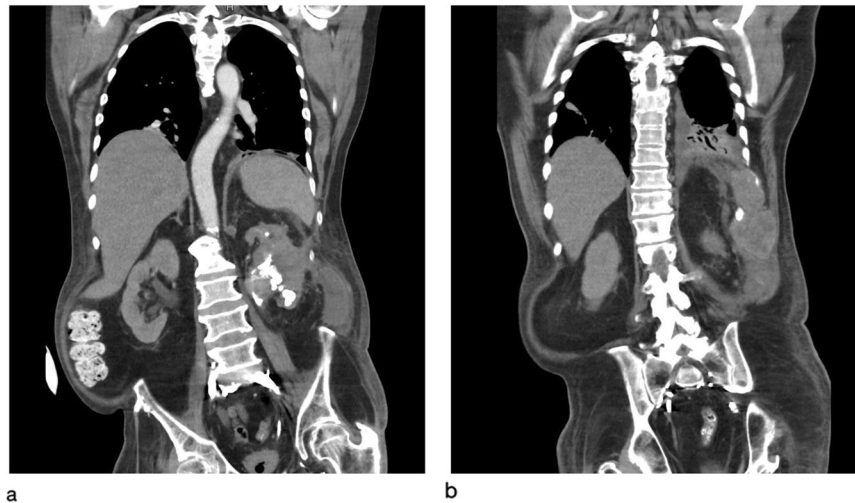


Fig. 2 Computed tomography images on admission of the patient. **a** Sagittal section of abdominal and thoracic computed tomography showing left-sided thoracic mass with partially hypodense, partially contrast agent accumulating structures. **b** Sagittal section of abdominal and thoracic computed tomography showing the stone burden of the left kidney and inhomogeneous, partially contrast agent accumulating structures at the upper pole of the left kidney.

recurrent urinary tract infections. Renal function determined by renal scintigraphy in 1993 showed a partial function of the left kidney of 36% (total clearance of 264 ml/min/1.73 m²). Owing to the significant gain of size in ultrasound imaging, recurrent stones were treated by extracorporeal shockwave lithotripsy and percutaneous nephrolitholapaxy in 1993 showing only minimal residual stones in the lower renal pelvis after therapy.

Neuro-urological checkups performed in 1996 revealed a gain of the size of the residual calculus of up to 1.5 × 2 cm. Treatment by extracorporeal shockwave lithotripsy and percutaneous nephrolitholapaxy followed later that year. Though ultrasound imaging showed a decrease of renal volume on the left side, renal function remained nearly stable as shown by another renal scintigraphy with a partial function of the left kidney of 31% (total clearance of 255 ml/min/1.73 m²) in 1998.

Treatment of recurrent calculi in the left kidney via shockwave lithotripsy followed in 2004 and 2007. For achievement of a complete stone, clearance was not possible in multiple attempts and the patient did not show any clinical symptoms, further invasive therapy was abandoned and switched to regular

surveillance of the upper urinary tract during neuro-urological checkups instead. As reported in May 2018, renal scintigraphy showed a deterioration of left-sided renal function to 26% (total clearance was not reported). The latest ultrasound performed in November 2019 showed a shrunken kidney on the left with the presence of a staghorn calculus without signs of dilatation of the upper urinary tract. The patient did not complain about any clinical symptoms at the time.

At the recent presentation in our institution after relocation from an external hospital, the patient showed a reduced general condition without fever. Except for fatigue and exhaustion, there were no constitutional symptoms like weight loss or night sweats. Clinical examination revealed multiple decubitus in the sciatic region on both sides, in the sacral and perianal region. Neurological assessment was carried out according to the International Standards for Neurological Classification of Spinal Cord Injury (ISNCSCI) and showed an unchanged status compared to the last consultation with a complete sensory and motor impairment below T6, AIS A [8]. Laboratory findings showed leukocytosis of 19.63 × 10⁹/l, a thrombocytosis of 497 × 10⁹/l, and

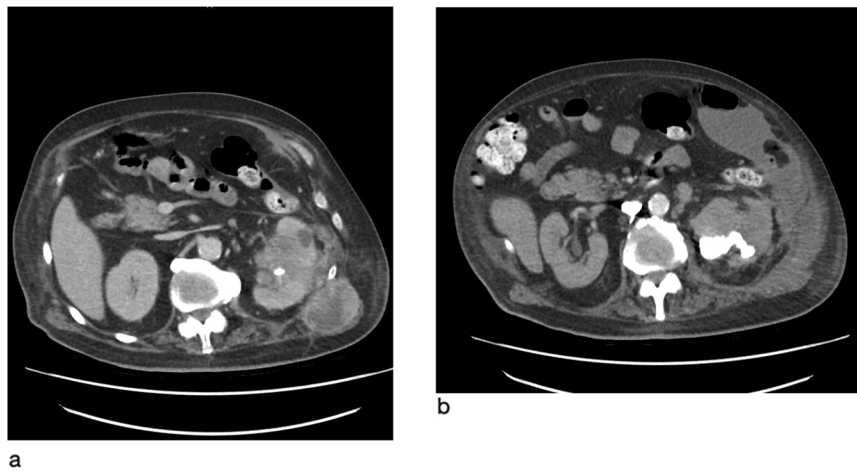


Fig. 3 Computed tomography images on admission of the patient. **a** Axial section of abdominal and thoracic computed tomography showing inhomogeneous soft-tissue-like formation reaching from the lateral middle pole of the left kidney into the retroperitoneum. **b** Axial section of abdominal and thoracic computed tomography showing the stone burden of the left kidney.

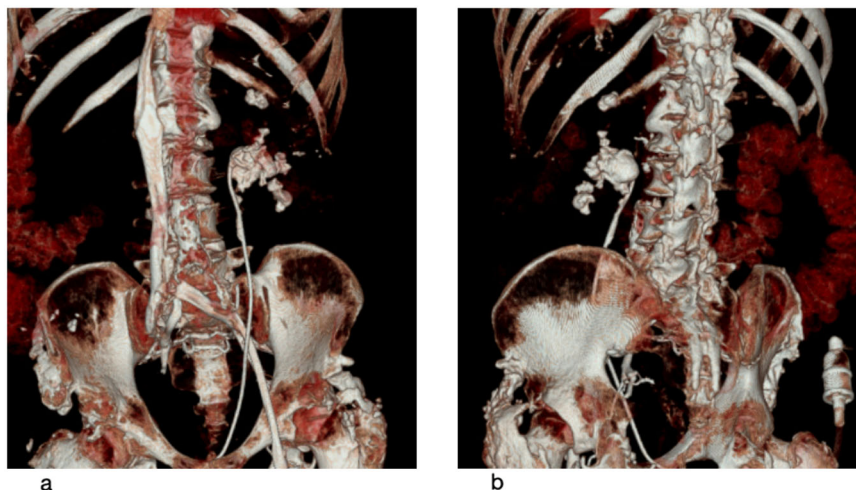


Fig. 4 Computed tomography images after insertion of a left-sided ureteral stent. **a** Computed tomography, 3D reconstruction, showing the stone burden of the left kidney, the position of the ureteral stent on the left side, and osteolytic destruction of costa X left, ventral view. **b** Computed tomography, 3D reconstruction, showing the stone burden of the left kidney, the position of the ureteral stent on the left side, and osteolytic destruction of costa X left, dorsal view.

an elevated CRP of 131.5 mg/l. In addition, anemia with hemoglobin of 8.8 g/dl and a deteriorated kidney function with a serum creatinine of 1.91 mg/dl and carbamide of 79 mg/dl were present.

The patient had been initially hospitalized during a vacation trip and was being treated for a complicated urinary tract infection with ciprofloxacin and amoxicillin/clavulanic acid intravenously. In the course of treatment (in addition to the known staghorn calculus of the left kidney) he received the presumptive diagnosis of a locally advanced renal cell carcinoma of the left kidney detected via computed tomography. He, therefore, was transferred to our institution for further diagnostics and treatment. Ultrasound imaging at admission revealed left-sided hydronephrosis with an unclear perirenal mass in addition to the previously known staghorn calculus. Abdominal and thoracic computed tomography without and (after having placed an indwelling ureteral stent (double-J stent) in the left ureter in local anesthesia the same day) with contrast agent showed an inhomogeneous distribution in the renal parenchyma as well as in the perirenal fatty tissue. In addition, a continuous inhomogeneous soft-tissue-like formation

reached from the lateral middle pole of the left kidney into the retroperitoneum over a distance of up to 20 cm. Furthermore, the scan revealed the presence of a left-sided thoracic mass (8 × 5 × 5 cm) with partially hypodense, partially contrast agent accumulating structures and also osteolytic destruction of costa X on the left side, highly suspicious of a malignant process originating from the left kidney (Figs. 1–4). Owing to rising systemic infectious parameters, the antibiotic therapy was escalated to meropenem intravenously.

For surgical treatment, the patient was admitted to the Department of Urology in University Clinic Hamburg Eppendorf. Owing to hypokalemia of 3.0 mmol/l and hypercalcemia of 2.25 mmol/l surgical treatment was delayed as surveillance in the intensive care unit and later in the department of nephrology became necessary. Having planned an open radical nephrectomy, the intraoperative situs showed a vast abscess with partially necrotic detritus infiltrating the perirenal fat and reaching into the thoracic cavity. Owing to the inoperable and locally advanced disease, open drainage of the abscess with the placement of two antibiotic sponges (gentamicin), of two drains in the retroperitoneal and one in

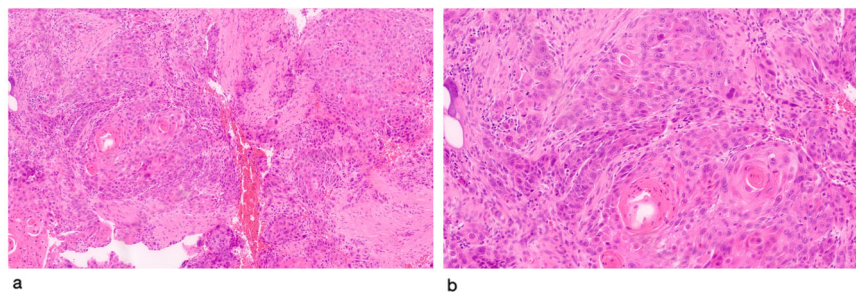


Fig. 5 Histopathologic findings. **a** Microscopic finding of the resected specimen of the retroperitoneal region of the left kidney with infiltrating, squamous cell-like differentiation and partial cornification (hematoxylin–eosin stain, 80-fold magnification). **b** Microscopic finding of the resected specimen of the retroperitoneal region of the left kidney with infiltrating, squamous cell-like differentiation and partial cornification (hematoxylin–eosin stain, 200-fold magnification).

the thoracic cavity followed after the assertion of specimens for histopathological work-up.

The histological finding (Fig. 5) showed a squamous cell carcinoma, described as transitional cell carcinoma of the renal pelvis with squamous cell-like differentiation and partial cornification. PD-L1-status showed a positivity of 10% for tumor cells and 20% for tumor-associated histiocytes. Because of the locally advanced disease, the recommendation of palliative check-point inhibitor systemic therapy with pembrolizumab was given in an interdisciplinary tumor conference. The dosage of 200 mg every 3 weeks intravenously was recommended.

DISCUSSION

Recent studies have shown an association between traumatic SCI [9] or congenital SCI/D [10] and developing malignancy of the lower urinary tract with unfavorable histology and advanced disease at the time of diagnosis. Interestingly, a recent study also showed an increased incidence and mortality of bladder cancer in patients with multiple sclerosis, who also frequently suffer from neurogenic dysfunction of the bladder [11]. Recurrent urinary tract infections and urolithiasis, which both increase the risk of bladder and renal pelvic carcinoma in non-paralyzed patients, are frequently seen in patients with SCI-associated neurogenic bladder dysfunction. Long-term spinal cord injury affects the development of bladder cancer, thereof about one-third are squamous cell carcinomas as two comprehensive reviews recently revealed [12, 13] (normal population: ~5%). However, there are only a few data on the association of SCI with renal pelvic carcinoma, and none for the rare squamous cell carcinoma. In analogy to the data on bladder carcinomas, it can be assumed that the squamous cell carcinoma of the renal pelvis reported here in a long-term SCI patient with neurogenic bladder dysfunction is a consequence of recurrent urinary tract infections and renal stone formation. The association of these squamous cell carcinomas with recurrent urinary tract infections is impressively backed by a recently published, country-wide Danish study on 333 squamous cell carcinomas of the urinary bladder [14], which reported a 15-fold risk of squamous cell carcinoma for the patients who received 20 or more prescriptions of antibiotics for urinary tract infections.

For upper urinary tract tumors an even more aggressive behavior in comparison to the counterpart in the urinary bladder is known, usually showing a higher histological grade and presenting at a more advanced stage of disease [15]. Individuals with SCI/D and neurogenic bladder are at significantly higher risk of developing renal stones and urinary tract infections than in the able-bodied population due to additional risk factors such as immobility, bacteriuria, hydronephrosis, renal scarring, reflux, and metabolic changes [1, 2, 16].

In case of incidental and small non-obstructing renal stones, regular upper urinary tract monitoring may be a viable option providing a

careful selection of patients [4]. For a connection between upper urinary tract infections, renal calculi, and developing RSCC is known, persons suffering from spinal cord injury may be at a higher risk for upper urinary tract tumors. Since RSCC is a very rare tumor and lacks specific symptoms which may be identical to those caused by renal stones, definitive diagnosis is difficult and thus delayed. Hematuria, flank pain, and abdominal mass may be present, yet these are non-specific. Also, paraneoplastic symptoms such as hypercalcemia, thrombocytosis, and leukocytosis have been described [17]. Even though RSCC shows an association with a renal stone disease which may result in repeated radiological imaging, it lacks specific radiological features making it hard to identify the disease at an early stage [6, 7, 17]. Also, sensory impairment, which is very often associated with SCI/D, can also mask the aforementioned symptoms and thus add to the risk of a delayed diagnosis.

Our patient had a long history of renal calculi with multiple attempts including surgery to accomplish a stone-free condition, in vain. Renal function was monitored regularly and showed only minor deterioration over the years. Even though repeated ultrasound examination owing to SCI/D and accompanying stone disease was performed continuously over the years, a definitive diagnosis of RSCC could only be given by surgical assessment and histopathological work-up after computed tomography had shown a locally advanced disease—leaving palliative treatment as the only option in our patient. Due to the listed conditions and difficulties in identifying the tumor at an early stage, the prognosis of RSCC is poor and even worse compared to other malignancies of the upper urinary tract [18, 19].

In summary, RSCC is a very rare tumor that may originate from a preexisting condition such as the presence of renal calculi or chronic or recurrent inflammation. Commonly, it presents with a higher histopathological grade and locally advanced status. Thus, with respect to treatment under a curative intent, an early diagnosis is crucial. Since individuals with SCI/D are at higher risk of developing renal stones and urinary tract infections, it is of high interest to regularly screen for and if necessary to manage stone disease in order to protect the kidney function and to avert potentially malignant changes to the urothelium due to chronic irritation at an early stage.

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COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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