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Neoplastic Sequelae of a Retained Ureteric Stent? The First Case of a Retained Stent Subsequently Presenting with Upper Tract Urothelial Carcinoma

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ABSTRACT

We present the first case of a patient with a retained ureteric stent subsequently presenting with upper tract urothelial carcinoma (UTUC). A 43-year-old male, who was lost to follow-up after stent insertion for ureteric stones in 2016, presented with haematuria and weight loss. Imaging revealed a renal mass, retroperitoneal lymphadenopathy and a retained ureteric stent. Radical nephroureterectomy and retroperitoneal lymph node dissection confirmed UTUC with squamous differentiation. This case demonstrates a potential relationship between long-term mechanical irritation in the upper urinary tract and UTUC, but given the absence of prior reports, highlights the need for further investigation into chronic irritation as a risk factor for UTUC.

Keywords

Upper tract urothelial carcinoma, UTUC, Retained ureteric stent, Forgotten ureteral stent, Chronic ureteric irritation.

Body

Upper and lower tract urothelium are embryonically distinct [1] and upper UTUC and bladder urothelial carcinoma (BUC) have clinical, pathological and epidemiological differences [2]. UTUC is far less common and accounts for only 5-10% of all urothelial carcinomas [3], and our understanding of its risk factors is less established.

It is well described that tobacco smoking and aromatic amine exposure are risk factors in the development of both BUC and UTUC [4]. Chronic inflammation secondary to recurrent urinary tract infection, *Schistosoma haematobium* infection or mechanical irritation has strongly associated with BUC and bladder squamous cell carcinoma [1,5]. In the upper tract population chronic irritation is commonly referred to as a risk factor [6], however the evidence is contradictory. For example, UTUC and stone disease are associated in large population studies [7], but the causal mechanism is debated given shared risk factors between both conditions [8]. Conversely, large retrospective reviews of cohorts of patients who are lost to follow up with retained ureteric stents have not previously described urothelial malignant transformation, and reviews of over 50,000 ureteric stents (15,000 of which were long term) have never observed malignancy as a potential risk [9,10].

A 43-year-old man presented with weight loss, night sweats and haematuria. He was a non-smoker without significant past medical history or history of familial cancers. Nine years prior, he had a left ureteric stent inserted for the management of acute renal colic, after which he was lost to follow-up. Computed tomography (CT) imaging revealed a left lower pole exophytic mass in the renal parenchyma, a large left retroperitoneal mass abutting the aorta and invading psoas, and a retained left ureteric stent with heavy proximal and distal encrustation. A biopsy of the retroperitoneal mass showed likely squamous cell carcinoma and FDG-PET demonstrated intense avidity in both the renal and retroperitoneal

mass suggesting a primary renal squamous cell carcinoma with malignant lymphadenopathy. Following a multidisciplinary review, it was decided to proceed with radical surgery.

Via a midline laparotomy, the left renal unit was exposed and a radical left nephroureterectomy was performed. A limited left retroperitoneal node dissection was then performed to remove the retroperitoneal mass. The patient was admitted to ICU for routine monitoring; he had an uncomplicated post-operative stay and discharged home day seven post operatively. Post-operative histopathology revealed focal mucous secretion and strong staining for CK7, and favoured high grade urothelial carcinoma with extensive squamous differentiation in both the renal and retroperitoneal specimen.

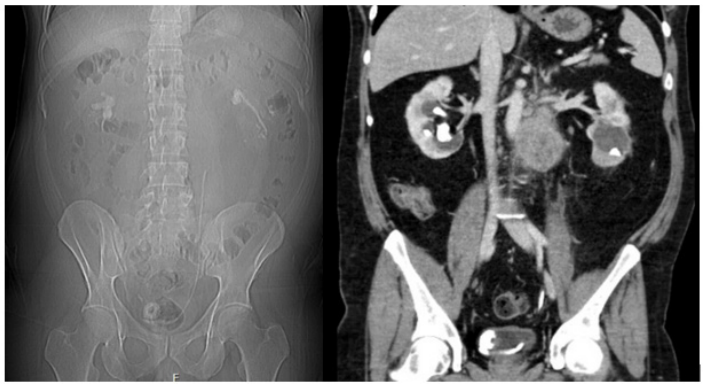

Figure 1: Computed tomography imaging of a retained stent.

The link between chronic mechanical irritation and development of UTUC has been debated in the literature, with conflicting factors on both sides. Large population data out of the Netherlands examining over 120, 000 people demonstrates an increased risk of UTUC in people with kidney stones with a hazard ratio of 1.66, (95% CI 1.03-2.68). It is debated whether the stone itself versus the greater biological environment that predispose an individual to forming stones are key in malignant transformation [8]. Risk factors such as smoking, alcohol, diet, and gender are shared between both pathologies. Chronic kidney disease has also been strongly associated with both stones and UTUC formation [11,12].

Large retrospective reviews of up to 50,000 patients with ureteric stents, including subgroups of patients with long term stents (n= >15,000) have never observed malignant transformation as a risk [9,10]. A meta-analysis of over 1200 patients specifically with non-intentionally retained ureteric stents did not demonstrate a single case of malignant transformation, and over 250 patients in this meta-analysis had stents left in situ for greater than 10 years [13-15]. Reviews of simple nephrectomy specimens for management of stone disease or xanthogranulomatous pyelonephritis rarely describe incidental UTUC [16,17], although this is occasionally reported in international data [18,19] and may be of a higher incidence in countries with less timely access to stone management [20].

Squamous differentiation is the most common histological variant in UTUC, quoted at about 15% and considered as an adverse prognostic factor [21]. It is thought to be related to advanced tumour stage and a high rate of lymphovascular invasion [22]. The relationship between upper tract pure SCC and UTUC with squamous differentiation is poorly understood given the rarity of the disease. In bladder cancer, pure squamous cell carcinoma compared to urothelial carcinoma with squamous differentiation is differentiated with careful immunohistochemistry [23]. Interestingly in our case, non-keratinizing squamous metaplasia was noted in the renal pelvis and ureter, and squamous metaplasia has long been interlinked in the carcinogenesis in the bladder urothelial carcinoma population [24].

We describe a case in which long term mechanical irritation of the upper collecting system precedes the development of UTUC with extensive squamous differentiation. This is the first documented case of malignancy following a retained ureteric stent and asks the question of a potential relationship or just a rare entity. There is a paucity of data and research into the mechanism and relationship between long term inflammation of the upper tract urothelium and development of UTUC.

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