



## Case Report

# Management of Squamous Bladder Cancer post Bladder-drained Kidney-Pancreas Transplantation

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### Abstract

A 53-year-old female patient with a previous kidney-pancreatic transplant connected to the bladder, developed muscle-invasive bladder cancer with direct invasion of the duodenal wall of the transplant. A curative approach was undertaken, with radical cystectomy with ileal conduit diversion and pancreatic-duodenal graft explant, with excellent oncological and clinical outcomes. Bladder cancer following kidney-pancreas transplant with bladder drainage is rare with only a few cases reported in the literature. However, it is crucial in these cases not to underestimate symptoms such as hematuria or dysuria, in order to avoid a diagnostic delay. The rare case we report highlights the importance of fast management of this challenging clinical condition, without delay and with radical intent.

### Introduction

Kidney-Pancreas Transplantation (KPT) is a procedure performed in patients with type 1 diabetes mellitus complicated by End-Stage Renal Disease (ESRD). This procedure improves the quality of life of the patients and decreases the mortality rate. After transplantation, exocrine pancreatic secretion can be drained to the bowel or via the bladder. The latter implies the implantation of a whole pancreas graft, with a duodenal segment forming a side-to-side anastomosis to the bladder. In this paper we report about a case of muscle-invasive urothelial cancer involving the bladder and the transplanted duodenum in a patient who had previously undergone KPT with bladder drainage.

**Keywords:** Bladder cancer; Cystectomy; Kidney-pancreas transplant; Squamous cancer

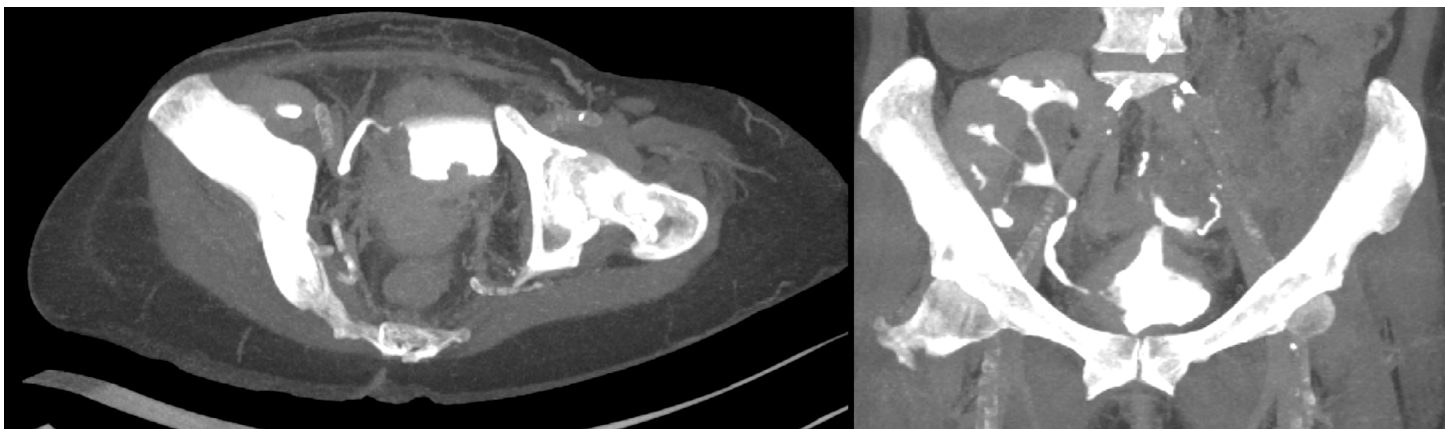
### Case Report

C.R., a 53 year-old woman suffering from type 1 diabetes mellitus, underwent kidney transplantation in 1996 for ESRD, after dialytic treatment. In 2002 she received a pancreatic transplantation; the pancreaticoduodenal graft was anastomosed to the bladder for the exocrine drainage (pancreas-duodeno-cystostomy). In 2000 she underwent VLS surgical removal of an ovarian cyst, in 2002 she had two transitory ischemic episodes treated with aspirin; two laser treatments for diabetic retinopathy; hypothyroidism in replacement therapy and, in 2018, surgical correction of an incisional hernia. The immunosuppressive therapy included 2 mg/day of tacrolimus, 720 mg/day of mycophenolic acid and 5mg of prednisone every other day. In June 2019, the patient went to the Emergency Room with hematuria and dysuria. Abdomen US showed parietal thickening on the right posterolateral side of the

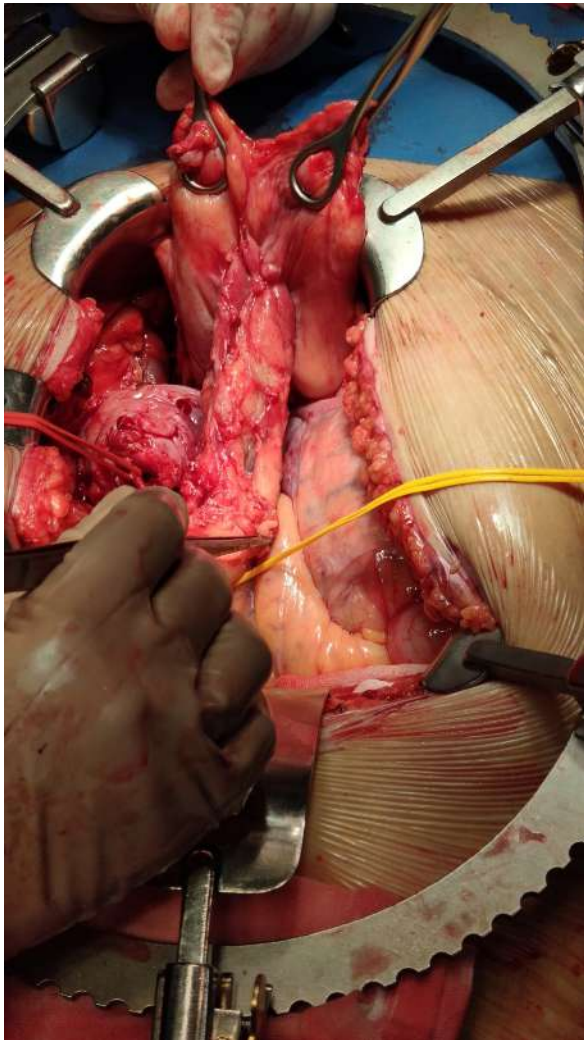
bladder, with evidence of clots. A cystoscopy was performed and showed the presence of a bladder tumor. Trans-urethral resection of the bladder tumor (TURBT), performed elsewhere, documented a high-grade muscle-invasive transitional cell carcinoma (TCC), with squamous aspects and Carcinoma in Situ (CIS). The patient came at this point to our attention and was admitted to the Urology, part of the ERN eUROGEN, a European network for treatment of rare and complex urological conditions [1]. A rigid cystoscopy under anaesthesia showed the presence of neoplasia in the bladder lumen, reaching the anastomosis of the pancreaticoduodenal graft. A contrast-enhanced CT-scan (Figure 1) showed the bladder with neoplastic wall, atrophic native kidneys and no hydronephrosis in the renal graft. Complete angiographic rendering was obtained in order to have clear information on the vascular anatomy of the grafts. A radical cystectomy with ileal conduit diversion and pancreatic-duodenal graft explant was performed (Figure 2: intraoperative view). The bladder with the pancreas-duodenum graft was isolated and the bladder-duodenum anastomosis was resected. The sample was sent for frozen section, showing a squamocellular infiltration. This, due to oncological reasons, requested the explant of the whole graft (Figure 3). The

ureter of the kidney graft and the native ureters were isolated and accurately dissected from the bladder. The ureteral sections, sent for extemporaneous histological exams, were negative for neoplastic infiltration. Radical cystectomy and ileal conduit according to Wallace technique was performed. Pelvic lymph node dissection was carried out with the limitations of the presence of the kidney graft. Only the ureter of the transplanted kidney was anastomosed, while the two native ureters were ligated due to absence of residual diuresis from the native atrophic kidneys.

Operative time was 360 minutes with a blood loss of 1000 mL, three blood units were transfused during the surgical time. The postoperative course was characterized by challenging glycemic peaks, which required multiple adjustments of insulin doses, and difficult pain management. 24 days after surgery the patient was discharged in good clinical conditions. Definitive histologic examination showed an invasive urothelial and squamous carcinoma of the bladder, with infiltration of the detrusor muscle, the peripheric fat tissue (pT3b pN0), and the duodenum of the pancreatic graft. No adjuvant chemotherapy treatment was advised due to the post-transplantation status and multiple comorbidities. The patient is alive and disease-free at follow-up after 36 months.



**Figure 1:** Contrast-enhanced CT scan.



**Figure 2:** Intraoperative view.



**Figure 3:** Resected pancreatic graft with duodenum.

## Discussion

Bladder cancer is not uncommon after a kidney transplant. A meta-analysis by Yan et al. in 2014 showed a 3.18-fold risk of developing bladder cancer in renal transplant populations [2]. A recent cohort study reported a standardized incidence ratio of 6.67 (95% CI 2.15–15.57) for bladder cancer after kidney transplant [3].

As a consequence, each kidney transplant patient with unexplained hematuria should undergo a careful urological examination, and a cystoscopy. This is especially true in female patients, like the one presented in our case, where diagnosis can be delayed due to gender-related issues: prolonged hematuria treatment with antibiotics in the assumption of a recurrent cystitis is a possible factor contributing to delayed bladder cancer diagnosis in women [4]. On the other hand, squamous bladder cancer after KPT with bladder drainage has been reported rarely, and literature is scarce on this topic. In the few published cases, the presentation is aggressive [5] and in an advanced stage [6]. Possible mechanisms explaining increased risk of bladder cancer in this setting are the cytotoxic effect of the immunosuppressive agents [7] and possibly viral infections, as HPV [8].

Bladder drainage after KPT is known to be prone to urologic complications such as hematuria, urinary stones, reflux pancreatitis, urinary tract infections and/or urethritis, bicarbonate and fluid loss with metabolic acidosis and dehydration. The risk of developing bladder cancer in transplant populations is increased, in particular in the renal transplant recipients. However, these tumors usually demonstrate local and distant aggressiveness and respond poorly to treatments. Bladder cancer following kidney-pancreas transplant with bladder drainage is exceedingly rare with only a few cases reported in the literature [6,7]. Chronic exposure to pancreatic secretion with possible chemical cystitis, together with immunosuppression, may play a role in the development and progression of bladder cancer in these patients, especially in cases with squamous histotypes. However, due to the rarity of the disease, it is not possible to draw definitive recommendations on treatment strategies. A multidisciplinary discussion between experts, like urologists, transplant surgeons and medical oncologists is strongly advisable [1]. Upfront radical surgery is a good option in most cN0 cM0 cases, due to the very aggressive behavior of the disease and the scarce response to oncological treatments. Usually, the squamocellular subtypes are associated with a worse prognosis [9].

The decision of removing the pancreatic graft (with the return of the patient to lifelong insulin therapy) is definitely a difficult one to make. In our case, the invasion of the bladder-duodenum anastomosis by the tumor shown by the intraoperative frozen sections, did not leave us many options. The definitive histopathology examination performed on the rest of the explanted pancreas did not show additional disease areas, thus confirming the oncological radicality of the surgical procedure.

## Conclusion

In KPT patients, it is important not to underestimate symptoms such as dysuria and/or hematuria, in order to avoid a diagnostic delay, especially in the case of bladder drainage of exocrine pancreas. Cystoscopy under anesthesia and TURBT should be performed without delay. In case of diagnosis of bladder cancer with invasive histology, prompt and upfront radical surgery appears to be the best therapeutic modality.

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