

## CASE REPORT

# Donor-derived duodenal adenocarcinoma of a bladder-drained pancreas allograft

Dylan Isaacson<sup>1,2</sup>  | Justin Steggerda<sup>1</sup>  | Yue Xue<sup>3</sup> | James Wren<sup>2</sup> | Mohammed Javed Ansari<sup>1,4</sup> | Gregory B. Auffenberg<sup>5</sup> | Nitin Katariya<sup>6</sup> 

<sup>1</sup>Department of Surgery, Comprehensive Transplant Center, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

<sup>2</sup>Department of Urology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

<sup>3</sup>Department of Pathology, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

<sup>4</sup>Division of Nephrology and Hypertension, Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois, USA

<sup>5</sup>Urology of St. Louis, St. Louis, Missouri, USA

<sup>6</sup>Department of Surgery, Division of Transplant and Hepatobiliary Surgery, Mayo Clinic, Alix School of Medicine, Phoenix, Arizona, USA

## Correspondence

Nitin Katariya, Department of Surgery, Division of Transplant and Hepatobiliary Surgery, Mayo Clinic, Alix School of Medicine, Phoenix, Arizona, USA.  
Email: katariya.nitin@mayo.edu

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The subset of the population that received bladder-drained allograft pancreata during peak utilization of the technique in the 1990s is approaching 20–30 postoperative years. This time frame is salient, as it parallels the time in which patients in the urologic literature develop adenocarcinomas after bladder reconstruction using gastrointestinal segments. We present the case of a 57-year-old simultaneous pancreas/kidney recipient who presented with microhematuria twenty-four years after transplantation and was found to have an adenocarcinoma of the duodenum of his failed, bladder-drained pancreas. After allograft pancreatectomy/duodenectomy, he remains disease-free eleven months postoperatively. As this patient population ages, practitioners should consider pathology of the donor duodenum and pancreas in recipients who present with gross or microscopic hematuria.

## KEYWORDS

cancer/malignancy/neoplasia, cancer/malignancy/neoplasia: risk factors, clinical research/practice, pancreas/simultaneous pancreas-kidney transplantation, pathology/histopathology, urinalysis, urology

## 1 | INTRODUCTION

In solid organ transplantation, donor-derived malignancies refer to those originating from donor cells, but not present prior to the transplant event.<sup>1</sup> Relative to cancers in transplant recipients overall,

donor-derived malignancies are rare.<sup>1,2</sup> However, outcomes in the literature are poor, with a recent Organ Procurement and Transplantation Network (OPTN) Disease Transmission Advisory Committee (DTAC) report describing a 38% mortality rate for donor-derived cancers and 70% for donor-derived adenocarcinomas over ten years of observation.<sup>2</sup>

**Abbreviations:** DTAC, disease transmission advisory committee; ESRD, end stage renal disease; H&E, hematoxylin and eosin; OPTN, organ procurement and transplantation network; SPK, simultaneous pancreas/kidney [transplant].

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For much of the history of pancreas transplantation, exocrine drainage was accomplished via anastomosis of allograft duodenum to recipient bladder as opposed to gastrointestinal tract.<sup>3</sup> Bladder drainage allowed for graft monitoring via urinary lipase and amylase and enabled cystoscopic biopsies. However, by the late 1990s, high rates of urologic and metabolic complications in bladder-drained pancreata along with improvements in surgical technique and immunosuppression precipitated a drastic change. In 1995, 85% of pancreas transplants in the United States utilized bladder drainage as compared to 15% with enteric drainage. By 2000, the proportion had shifted to 35% bladder-drained vs. 65% enteric-drained,<sup>4</sup> progressing to less than 10% bladder-drained over the decade prior to this publication.<sup>3</sup>

Most reports of donor-derived malignancies after pancreas transplantation have been pancreatic adenocarcinomas,<sup>5,6</sup> although sarcomas<sup>7</sup> have also been described. These have been managed with cessation of immunosuppression, allograft resection and systemic antineoplastic therapy.<sup>5,6</sup> In bladder-drained pancreata, urothelial carcinomas have been noted at the junction of the duodenal mucosa and bladder urothelium.<sup>8</sup> Consistent with OPTN/DTAC events reporting data,<sup>2</sup> these donor-derived cancers have frequently been aggressive with unfavorable outcomes.

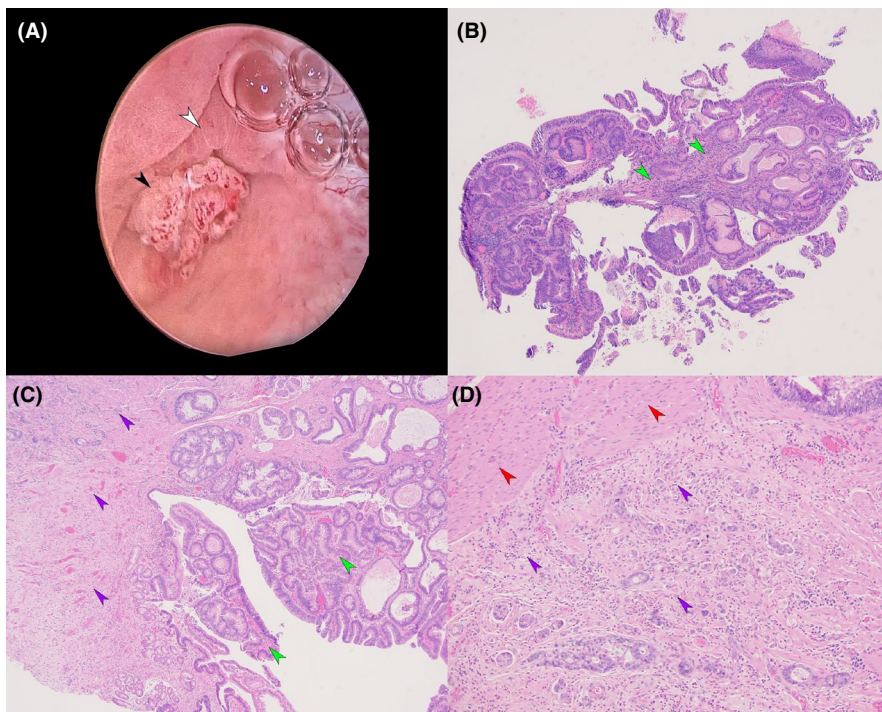
## 2 | CASE DESCRIPTION

A 57-year-old man with type 1 diabetes mellitus and prior bladder-drained simultaneous pancreas/kidney transplant (SPK) in 1996, 24 years prior to presentation, was referred to urology for asymptomatic microhematuria. His pancreas and kidney were previously donated after brain death by a 39-year-old woman who died from

a cerebrovascular accident. Induction immunosuppression was antithymocyte globulin and steroids, followed by maintenance with tacrolimus, mycophenolate and prednisone. He restarted insulin two years after his SPK but retained partial pancreas function and therefore continued maintenance immunosuppression through the time of presentation. He returned to dialysis 21 years after his SPK and subsequently received a second deceased donor kidney one year prior to presentation (see Table S1 for detailed donor/recipient clinical data). After his second kidney transplant, multiple urinalyses demonstrated microhematuria with up to 51-100 red blood cells/high-powered field. He was referred to urology, where cystoscopy revealed what was initially thought to be a 5mm papillary bladder tumor at the duodenocystostomy.

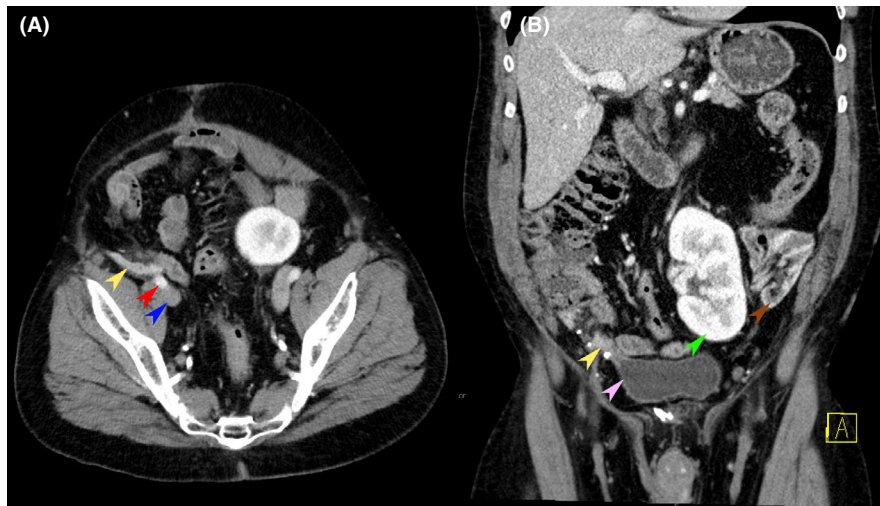
Biopsies of the lesion revealed a tubular adenoma with focal high-grade dysplasia (Figure 1A,B). CT urography revealed no additional concerning findings (Figure 2). The patient was counseled that transplant pancreatectomy would be the most definitive treatment if the high-grade dysplasia was associated with an occult malignancy in the donor duodenum. He therefore elected to proceed with transplant pancreatectomy/duodenectomy. His abdomen was entered via a midline incision. The tail of the allograft pancreas was identified, and the pancreas mobilized towards its head. The donor superior mesenteric artery/splenic artery Y-graft was located and the arteries sequentially stapled, followed by the donor portal vein. The bladder was mobilized away from the abdominal wall to circumferentially visualize the duodenal anastomosis. The donor duodenum was then excised with a 5mm margin and sent for frozen pathologic analysis, which was negative. The bladder was closed with a two-layer cystorrhaphy.

Final pathology revealed a 1.0 cm moderate-to-poorly-differentiated duodenal adenocarcinoma with micropapillary



**FIGURE 1** (A) Cystoscopic image of lesion (black arrow) adjacent to duodenal mucosa of duodenocystostomy (white arrow). (B) 40 × magnification hematoxylin and eosin (H&E) stain of the same lesion after biopsy, revealing tubular adenoma with areas of focal high-grade dysplasia (green arrows). (C) 40 × magnification H&E stain of resected allograft duodenum demonstrating tubular adenoma with high-grade dysplasia (green arrows) with invasive adenocarcinoma immediately adjacent (purple arrows). (D) 100 × magnification H&E stain of resected duodenum demonstrating duodenal adenocarcinoma with micropapillary features (purple arrows) invading muscularis propria of the duodenum (red arrows)

**FIGURE 2** Preoperative CT abdomen/pelvis with contrast. (A) Axial cut revealing body of extraperitoneal pancreas allograft (yellow arrow) located in the right lower quadrant adjacent to the external iliac artery (red arrow) and vein (blue arrow). (B) Coronal cut demonstrating the head of the allograft pancreas (yellow arrow) and duodenum anastomosed to the bladder (pink arrow). Also visible are the patient's initial failed extraperitoneal kidney allograft (brown arrow) and second intraperitoneal transplant kidney (green arrow)



features invading the muscularis propria of the duodenum, stage pT2 (Figure 1C,D). Adjacent to the adenocarcinoma were areas of duodenal adenoma with high-grade dysplasia as demonstrated on the initial biopsies. All surgical margins, the pancreas and the resected portion of bladder were negative. Given the patient's poorly-differentiated histology, he was treated with reduction in immunosuppression and adjuvant capecitabine/oxaliplatin with an intended three-month course. However, chemotherapy was discontinued after one cycle due to severe nausea/vomiting. He has been surveilled for the last eleven months with cystoscopy and cross-sectional imaging with no evidence of recurrent disease.

### 3 | DISCUSSION

We describe what we believe to be the first case of donor-derived adenocarcinoma of the duodenum of a bladder-drained pancreas allograft. Our patient was transplanted in 1996, when exocrine drainage trends were rapidly shifting in favor of enteric drainage.<sup>3,6</sup> Although estimates of graft failure have been limited by a lack of universal definitions, International Pancreas Transplant Registry data note that 50% of pancreata will fail between 6–12 years depending on whether they were transplanted as pancreas alone or as part of a SPK.<sup>3</sup> A corollary to these statistics is that the majority of bladder-drained pancreata are now likely nonfunctional. Many failed pancreas recipients may, however, still have a functioning first or second kidney allograft requiring immunosuppression—a well-established risk factor for malignancy.<sup>9</sup>

Studies in the urologic literature have assessed malignancy risk after urinary reconstruction with gastrointestinal segments.<sup>10,11</sup> In urology, gastrointestinal tract is used to replace or augment dysfunctional ureters and bladders or to create new urinary diversion after cystectomy. Ureterosigmoidostomy was once the most common form of urinary diversion, however it fell out of favor after it became apparent that 2%–15% of patients develop colonic adenocarcinomas at the ureterosigmoid junction 20–26 years later.<sup>11,12</sup> Augmentation cystoplasty, in which bladder volume and compliance

is increased through anastomosis of a detubularized gastrointestinal segment, has also been associated with tumor risk. A study of 17,758 patients with urinary diversions at 44 German centers revealed a 1.71% tumor incidence in patients with prior ileocystoplasties, all of which were adenomas or adenocarcinomas of the ileal segment or the ileovesical anastomotic junction.<sup>10</sup> Their observed mean latency period of 21.5 years is consistent with the broader literature.<sup>11</sup> These rates are contrasted with the lower lifetime incidence of small bowel adenocarcinoma which is estimated at 0.3%.<sup>13</sup> Other forms of urinary diversion using isolated bowel without native bladder such as ileal conduits, ileal neobladders and ileocecal pouches have not demonstrated the same risk of carcinogenesis.<sup>10,11</sup> A caveat is that these diversions are often performed after radical cystectomy for bladder cancer and this population may not routinely survive for the decades required to develop secondary malignancies.

Despite the elevated cancer risk for patients with these forms of urinary system reconstruction, surveillance protocols have not been demonstrated to be cost-effective<sup>14</sup> or fully consistent with principles of disease screening.<sup>15</sup> A prospective study of 92 consecutive enterocystoplasty patients surveilled with annual cystoscopy and random biopsies for fifteen years did not identify any cancers.<sup>16</sup> As such, despite multiple potential risk factors for malignancy, we cannot advocate for routine screening of bladder-drained pancreas recipients based on this initial case. However, as these recipients continue to age, it will be essential to maintain long-term follow-up, infrastructure for tracking donor-derived malignancies, and to suspect pathology of the donor duodenum and pancreas in any patients who present with gross or microscopic hematuria.

#### DISCLOSURE

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

#### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request

## ORCID

Dylan Isaacson  <https://orcid.org/0000-0003-1791-504X>

Justin Steggerda  <https://orcid.org/0000-0001-9320-9871>

Nitin Katariya  <https://orcid.org/0000-0001-6706-666X>

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## SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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