Learning from errors

Sarcomatoid carcinoma of the bladder after simultaneous kidney-pancreas transplant: a case report and review of the literature

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Summary

Carcinosarcoma and sarcomatoid carcinoma of the bladder after organ transplantation is higher in comparison to the general population but overall occurrence is still very uncommon. Due to the decreased immunitary response effects of antirejection drugs, these cancers have aggressive course and respond poorly to treatment. Bladder drained pancreatic transplants are associated with a number of urologic challenges that can delay the diagnosis and the treatment of malignancies of the genito-urinary system. The authors present a case of a rare sarcomatoid carcinoma of the bladder following bladder drained simultaneous kidney and pancreas transplant and discuss its pathogenesis and clinical management.

BACKGROUND

Bladder malignancies following solid organ transplantation are rare, with a demonstrated rate of 0.1–0.3% across multicentre reviews in kidney transplant recipients.^{1 2} These tumours demonstrate aggressive behavior with rapid invasion of surrounding organs and poor response to treatments.³ We present a case of sarcomatoid carcinoma of the bladder diagnosed after 12 years following simultaneous kidney-pancreas (SPK) transplant with bladder drainage of the exocrine pancreatic secretions (figure 1). To our knowledge, this is the only report of a sarcomatoid carcinoma of

the bladder after simultaneous kidney and pancreas transplantation and there has been only one previous reported case of adeno-squamous-transitional carcinoma of the bladder following cystic drainage of SPK.⁴

CASE PRESENTATION

A 45-year-old man with type diabetes for 35 years underwent a SPK with bladder drainage of the exocrine pancreatic secretions 12 years before being assessed at our transplant centre for chronic allograft nephropathy and recurrent renal failure.

Figure 1 Anatomy of bladder drained simultaneous pancreas-kidney transplant.

Figure 2 Cystoscopic appearance of the tumour that appeared like a sessile papillary polypoid mass.

At the time of his presentation, his pancreatic endocrine function was preserved with hemoglobin A1C (HbA1C) level of 6.1% (normal range 3.5–5.5%). He was anuric and required renal replacement therapy by haemodialysis every other day. After completing a series of investigations, he was listed for second cadaveric kidney transplantation. Three months before being identified as the recipient of his second renal transplant, he had experienced one episode of haematuria associated with increasing burning pain in his pelvis, urgency and frequency. His symptoms progressed to the point that required the use of narcotics. Further history revealed a self-limited gross haematuria 2 years earlier that was not investigated by his primary physician as he lived in a very remote rural area with suboptimal access to specialised medical services. At his home hospital, it was suspected that the bladder-drained pancreas graft caused chemical cystitis and prostatitis due to the lack of urinary output that initially diluted the pancreatic enzymes. A non-contrast CT showed thickening of the bladder wall interpreted as postinflammatory changes. No other abnormalities were detected by cross sectional imaging modalities.

His medical history was significant for retinopathy and hypertension and he denied any smoking history or any other substance abuse. Family history was non-contributory and his immunosuppressive regimen at the time of admission to our transplant centre was: sirolimus (2 mg/day), tacrolimus (4 mg/day) and prednisone (5 mg/day) with drug levels within the normal limits.

In March 2010, he underwent a second cadaveric kidney transplant with insertion of a ureteral stent; during the formation of the uretero-cystic anastomosis no abnormalities were noted at the level of the dissection of the

bladder wall. Postoperatively, the patient had persistent low abdominal and pelvic pain with irradiation to his perineum. A renal scintigraphy detected a contained urinary leak that was managed by the reinsertion of the Foley catheter in the lumen of his bladder. During the 2 weeks after his surgery, the patient continued to experience progressive pelvic pain despite the resolution of his urinoma with normalisation of serum creatinine levels.

A urologic consultation was obtained and it was recommended to perform an enteric drainage of his pancreatic graft to reverse the exposure of the exocrine secretions that may have caused his chronic cystitis.

INVESTIGATIONS

Preoperatively, a cystoscopy performed to confirm the diagnosis of chronic cystitis revealed a flat mass measuring 6 centimetres in maximum diameter involving the dome, posterior wall of the bladder and surrounding the duodenal-cystic anastomosis of the pancreatic graft (figure 2). An incomplete transurethral resection of the lesion was performed. The new kidney transplant uretero-vesical anastomosis with the double J stent were visualised in proximity but not infiltrated by the tumour. Towards the right edge of the mass there appeared to be papillary growth, suggestive of urothelial cell carcinoma. Intraoperative frozen section biopsies showed poorly differentiated carcinoma.

Final pathology revealed a high-grade urothelial cell carcinoma with sarcomatoid differentiation. Axial imaging with MRI of the abdomen and pelvis showed tumour extension into perivesical fat, cystoduodenostomy stoma and duodenum without involvement of the donor pancreas or the presence of lymphadenopathy (figure 3).

Figure 3 Sagittal (A) and coronal (B) views of the MRI of the abdomen and pelvis: the tumour is infiltrating the cranial and left lateral aspect of the wall of the bladder (white arrows).

DIFFERENTIAL DIAGNOSIS

- ▶ Tuberculosis
- ▶ Lymphoma
- ▶ Chronic haemorrhagic cystitis
- ▶ Granulomatous cystitis
- ▶ Periarthritis nodosa of the bladder
- ▶ Malignancies from rectus, prostate, or other metastases invading the wall of the bladder

TREATMENT

Treatment options were discussed at a multi-disciplinary oncology conference: surgical resection with total cystectomy, prostatectomy and resection of the kidney and pancreas transplants was recommended.

OUTCOME AND FOLLOW-UP

The patient declined the treatment and he expired 7 months after his diagnosis with a still functioning kidney transplant.

DISCUSSION

Pancreatic bladder drainage and management of urologic complications

SPK can be drained either enterically or via the bladder. Bladder drained SPKs usually do not cause mucosal changes to the bladder⁵ and this technique is advantageous because pancreatic graft rejection can be monitored by urine concentration of amylase and lipase.⁵ The transplantation includes a whole pancreas graft with a duodenal segment which forms a side-to-side anastomosis to the bladder (figure 1).

Well-described urologic complications of bladder drainage include haematuria, bladder/duodenal segment leak, reflux pancreatitis, recurrent urinary tract infections (UTI), urethritis that can result in urethral strictures, metabolic acidosis and dehydration secondary to bicarbonate and fluid losses, and the formation of urinary calculi.^{6 7}

Reflux pancreatitis may present with pelvic pain and elevated pancreatic enzymes and is usually relieved by placement of a Foley catheter, and can be differentiated by imaging studies. Failure of conservative therapy requires

conversion to enteric drainage. Conversion is also indicated for acidosis/dehydration and recurrent UTI. The overall conversion rate from bladder drainage to enteric drainage is in the range of 10–35%.⁸

Malignancy and immunosuppressive therapy

The incidence of malignancy in SPK is not well described. For kidney transplants, the incidence of cancer (not including non-melanotic skin cancers) is three to five times more frequent than the general population and about half of recipients experience some sort of malignancy after 25 years of immunosuppression regimen.⁹ The incidence of bladder cancer is approximately five times baseline but still a rare event.^{10 11} Overall, immunosuppressant exposure is thought to correlate with malignancy risk due to impaired immune surveillance and antiviral activity that can promote tumour formation. The oncogenicity of agents used for induction and maintenance immunosuppressive therapy is variable. The specific effect of antirejection therapy on bladder cancer has not been a topic of many investigations.

Despite a greater amount of physician contact, bladder and most other cancers are diagnosed at a more advanced stage as the tumours behave more aggressively than in the general population.¹² Also, when stage stratified, transplant patients have worse outcomes.^{12 13}

Diagnosis, surveillance and treatment of bladder cancer

In the non-transplant population, cystoscopy and upper urinary tract imaging (ultrasound, CT, or retrograde pyelograms) are used to rule out genitourinary malignancy in the setting of haematuria or unexplained bladder irritability. Haematuria affects up to 80% of patients with bladder cancer, and it is the most common clinical presentation. Bladder irritability (frequency, urgency, dysuria) is the second most frequent symptom, and is usually associated with invasive carcinoma or diffuse carcinoma in situ.¹⁴

With pancreas grafts draining into the bladder, haematuria is observed in up to 28% of patients who are also prone to irritative voiding symptoms.¹⁵ Buzzee¹⁵ and Highshaw⁴ recommend a thorough urologic evaluation in renal and pancreas transplant patients presenting with haematuria

outside of the immediate postoperative period or in the absence of infections as neoplastic lesions can be easily missed. For this reason, regular cystoscopy for 5 years in all recipients of bladder-drained pancreatic transplants has been put forth by Hickey *et al.*¹⁶ Highshaw⁴ suggested extending the follow-up period even longer although there is no evidence that this strategy is cost-effective or that it would prevent tumour related deaths.

The standard surgical treatment for muscle-invasive bladder cancer in the absence of metastatic disease is radical cystoprostatectomy with en bloc pelvic lymphadenectomy and Master *et al.*¹⁷ described a survival rate of 60% at 48 months in five cases of early stage (pT2) invasive bladder cancer in renal transplant recipients quite comparable to non-transplant patients.

Multi-modal approach is the only chance for cure in locally advanced disease (tumours stage higher than T2); preoperative radiotherapy may improve control of loco-regional advanced disease (ie, T3) but a clear survival advantage has not been demonstrated.¹⁸ Adjuvant and neo-adjuvant chemotherapy have shown small but measurable survival benefit in meta-analyses of advanced bladder cancers.^{19–20} There is very limited experience with adjuvant cisplatin based chemotherapy in renal transplant recipients as indicated only in well functioning allografts.²¹ Chemotherapeutic cytotoxic agents are immunosuppressive and the risks and benefits of continued immunosuppression must be carefully weighed while facing an aggressive malignancy.

Bladder cancer following SPK transplant with bladder drainage is an extremely rare clinical presentation with only 13 cases reported in the literature before this one (transitional cell carcinoma: eight; squamous cell carcinoma: three; Kaposi's sarcoma: one).²³ The disease may be accelerated by the combination of chronic cystitis and immunosuppressant therapy although experience with this occurrence is very limited and rarely observed. Of course, pancreas bladder drainage might complicate the clinical presentation of bladder tumours and therefore it is important to keep in mind this possibility and exclude malignancy early as soon as symptoms present. Although the treatment of these patients is complicated by need for immunosuppressant regimens to be adjusted and reassessed often while on chemotherapy, it is worth considering as the prognosis is poor. In this case, the patient was offered aggressive surgical and adjuvant chemotherapy with the intent to radically excise his bladder, pancreatic and renal graft leaving him diabetic and in the need of renal replacement therapy. After a very careful assessment of the potential benefits and risks, he opted for the best supportive care and he spent the remaining part of his life back with his family and community in Newfoundland.

The review of this case has several teaching points. The most important is that for this patient appropriate investigation for haematuria was not completed before his second kidney transplant. One of the several reasons was that he did not have easy access to urologists and transplant specialists as he lived in a poorly served rural area.

Second educational point is that transplant physicians often are in the position to make decisions on patients' suitability for transplantation with limited information and in a very short time limit. Our patient was scheduled to undergo a cystoscopy but he was called in for his

transplant before he could complete the endoscopic assessment and our team was not fully aware of his previous pelvic symptoms, haematuria and the findings of the CT scan performed a few months before his transplant-related admission.

The third teaching point is that in circumstances where quality of life versus quantity is at stake, patients' preferences should be fully elicited by caregivers as we did for this unfortunate patient.

Learning points

- ▶ Sarcomatoid carcinomas of the bladder, although rare, can occur in recipients of solid organ transplants.
- ▶ Patients who are immunosuppressed have higher risk of developing cancer in comparison to the general population; lower thresholds to investigate signs and symptoms should be considered by primary physicians as well as by specialists involved in their care.
- ▶ Persistent haematuria in patients with bladder drained pancreatic transplant grafts should be aggressively investigated and malignancy should be ruled out.
- ▶ Immunosuppressed patients affected by malignancies have poorer outcomes in comparison to the general population when affected by the same tumour stage.

Competing interests None.

Patient consent Obtained.

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