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“Tumorous nodules” in the native kidney in a woman transplanted 3 years earlier because of “chronic pyelonephritis”-induced renal failure

Case presentation
In May 2007, a 54-year-old woman with chronic renal failure due to “bilateral chronic pyelonephritis” received an allograft from a deceased donor. Between 2007 and 2010, we examined biopsy samples of the allograft on 3 occasions, with the following results: September 2007 (protocol biopsy): no alteration; May 2008 (protocol biopsy): coinciding tacrolimus toxicity and acute T-cell-mediated tubulointerstitial rejection; and July 2010 (biopsy for cause; serum creatinine 221 µmol/L): C4d-positive chronic antibody-mediated rejection.

In October 2010, with the clinical diagnosis of tumour at the pyeloureteral border, the right native kidney of the patient was removed and submitted to our department for evaluation. Grossly, the right kidney was markedly shrunken, and several tumorous nodules were observed in the pelvis, calyces and parenchyma. The largest nodule, measuring 70x70x30 mm and situated at the pyeloureteral border, bulged into the pelvis and infiltrated the renal sinus. The pelvis and calyces were dilated; the papillae, medulla and cortex were atrophied. The tips of the papillae were pale and displayed calcified foci. The changes indicated end-stage kidney, multifocal tumourous involvement of the pelvis and the right kidney, and tumour-induced pyelectasis.

A representative right kidney slide, stained with haematoxylin and eosin, is submitted for examination by the participants of the slide seminar. What is your diagnosis?

Description of the histological changes, histopathological diagnosis, and follow-up of the patient
The cortex and medulla were severely atrophied and thinned. The majority of the glomeruli were sclerotic, while the few glomeruli with patent capillaries appeared to be atubular. The majority of tubuli and the interstitium had extensively disappeared. Hyaline casts in the remaining atrophic tubules (thyroidization) and lymphocytic interstitial infiltrates were present focally. The arteries exhibited pronounced fibroelastosis. The papillae were hyalinized and calcified, and the outlines of the ducts were no longer visible. The calyces and the pelvis displayed dilation. The urothelium exhibited foci of high-grade dysplasia/in situ carcinoma. The tumorous nodules, observed grossly, proved focally high-grade invasive papillary urothelial carcinoma, infiltrating the papillae, the medulla and the renal sinus. The findings led to the histopathological diagnosis of phenacetin kidney-induced end-stage kidney and multifocal urothelial carcinoma of the pelvis and calyces.

Subsequently, the nephrology departments at the hospitals where the patient had been treated in the pretransplantation period were consulted for a review of the patient’s medical history. It emerged that the woman, who had a personality of depression, had consumed phenacetin-containing analgesic agents for at least 15 years because of headaches and pains due to osteroarthrosis in the vertebral joints due to osteoarthrosis since the age of 35. She had been operated on for a lumbar disc prolapse at the age of 47 years. Hypertension had been diagnosed at the age of 50 years. In 2006, a chronic renal insufficiency attributed to analgesic nephropathy had ensued and had been treated with chronic ambulatory peritoneal dialysis. For some reason that in retrospect is unclear, while she had been on the waiting list to receive a renal transplant, the diagnosis of interstitial nephritis induced by phenacetin containing analgesics had been amended to chronic pyelonephritis. The transplant surgeons who had led the posttransplantation management and regularly controlled the allograft function had not been aware that the woman’s native kidney disease was phenacetin kidney. The allograft had functioned well for 3 years, but laboratory signs of a chronic allograft dysfunction had then developed, and the evaluation of the renal biopsy specimen revealed chronic active antibody-mediated rejection. Prior to the biopsy, the radiologist had performed an ultrasonographic examination only of the transplanted kidney; the native kidneys had not been scanned. In September 2010, the patient was admitted to the county hospital with fever, vomiting, oliguria and a markedly elevated serum creatinine level. The abdominal ultrasonographic examination revealed a tumour in the shrunken right native kidney, which caused hydronephrosis. Microhaematuria was noted in the urinary sediment. Bolus steroid therapy, conservative anturiaemic treatment and broad-spectrum antibiotics were administered. 3 weeks later, the patient was transferred to the Department of Renal Transplantation for removal of the tumorous kidney. The nephrectomy did not prove curative, and she died of recurrence-induced intestinal bowel obstruction and disseminated haematogeneous metastases in April 2011.

Comment
The presented case is an example of how the pathologist can sometimes put things order. The characteristic alterations in the renal papillae led to the histopathological diagnosis of end-stage kidney due to phenacetin kidney, which was in accord with the patient’s medical history. The multifocal carcinoma of the pelvis and calyces was obviously induced by the analgesic abuse. The association between a severe abuse of phenacetin-containing analgesics and the development of urinary tract carcinoma was first reported from Sweden in 1965. Subsequent studies from other parts of the world revealed that patients with phenacetin kidney were at an
increased risk of the development of urothelial cell carcinoma of the urinary tract.²⁻⁸ The induction time was calculated between 20 and 25 years.⁴⁻⁹ Despite regular tumor screening via urine cytology and abdominal sonography in patients with phenacetin kidney after renal transplantation in a study from Germany, the diagnosis of urothelial carcinoma was still made late.⁵ The prohibition of phenacetin-containing analgetics in European countries including Hungary, led to a significant decrease in the incidence of phenacetin kidney, and a potential long-term consequence of analgesic consumption, the development of urothelial carcinoma of the urinary tract, has subsequently become exceptional. In contrast with the rarity of urothelial carcinomas in end-stage kidneys, renal cell carcinomas are relatively common. The most frequent subtype seems acquired cystic disease-associated renal cell carcinoma, which may be multifocal and bilateral. The tumorous nodules are usually well-circumscribed, and may arise within cysts. Histologically, the observation of multiple small lumina/sieve-like, cribriform architecture and the presence of intratumoural oxalate crystals are diagnostic. Other subtypes include clear cell papillary, papillary, clear cell, and chromophobe renal cell carcinoma.¹⁰

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References