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Living-donor Kidney Transplantation After Resection of Mixed Epithelial and Stromal Tumor: A Positive Outcome Despite Not Observing the Recommended Waiting Period

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Abstract

Background/Aim: Mixed epithelial and stromal tumor (MEST) is a benign renal neoplasm. For MEST cases requiring kidney transplantation, a waiting period is essential. However, reports on the management of MEST cases awaiting kidney transplantation are limited. We report the case of a patient with end-stage renal disease and bilateral renal pelvic tumors who was pathologically diagnosed with MEST and successfully underwent living-donor kidney transplantation without the recommended waiting period.

Case Report: A 52-year-old woman had been diagnosed with mesangial proliferative glomerulonephritis 10 years earlier. Her renal function had gradually declined, and maintenance hemodialysis had been initiated 1 year before referral to us. She preferred living-donor kidney transplantation and was referred to our hospital after computed tomography at a previous institution revealed bilateral renal pelvic masses with well-defined margins and contrast enhancement. Voided urine cytology was classified as atypical urothelial cells. At the patient's request, ureteroscopic examination was not performed. For diagnostic and therapeutic purposes, robot-assisted left nephroureterectomy was performed. Histopathological examination revealed MEST, and this was confirmed *via* the histopathological examination of the right-sided lesion. Based on this diagnosis, right nephroureterectomy, followed by living-donor kidney transplantation up to the right iliac fossa, was performed 6 months after the left nephroureterectomy. The postoperative course was uneventful, and the patient was discharged on postoperative day 9. No evidence of recurrence or metastasis has been observed during 1 year of follow-up.

Conclusion: This case demonstrates that living-donor kidney transplantation without a mandatory waiting period may benefit patients with end-stage renal disease when a definitive diagnosis of MEST is established before transplantation.

Keywords: End-stage renal disease, kidney transplantation, mixed epithelial and stromal tumor.

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Introduction

Mixed epithelial and stromal tumor (MEST) is a rare renal neoplasm first reported by Pawade *et al.* in 1993 and is estimated to constitute approximately 0.2% of all renal tumors (1). From a histological perspective, MEST is composed of solid and cystic components and predominantly affects perimenopausal women (2), although cases in children and male patients have also been reported (3). MEST may be difficult to distinguish radiologically from cystic renal cell carcinoma or urothelial carcinoma of the renal pelvis (2), and understanding its diverse imaging features is important for appropriate clinical management and treatment decision-making (4). Although malignant variants of MEST have been reported (5), the tumor is regarded as a benign entity.

Regarding living-donor kidney transplantation, recipients with a history of malignant tumors are considered to be at increased risk of recurrence owing to postoperative immunosuppression (6). Therefore, a tumor-specific waiting period after curative treatment is recommended before transplantation (7). To our knowledge, reports on the management of MEST in candidates awaiting kidney transplantation are limited.

Here, we aimed to report a case of a patient with end-stage renal disease and bilateral renal pelvic masses who underwent left nephroureterectomy, was pathologically diagnosed with MEST, and subsequently had living-donor kidney transplantation without a waiting period, yet with a favorable clinical outcome.

Case Report

A 52-year-old Japanese woman had been undergoing maintenance hemodialysis for end-stage renal disease secondary to mesangial proliferative glomerulonephritis for 1 year before her initial presentation to our hospital. She desired kidney transplantation, and computed tomography performed as part of the pre-transplant work-up revealed bilateral renal pelvic masses. She was referred to our Institution for further evaluation.

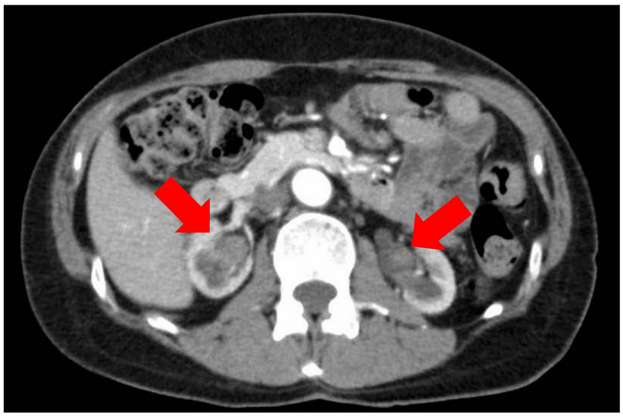

Figure 1. *Contrast-enhanced computed tomography at presentation revealed contrast-enhancing tumors in the bilateral renal pelvises (arrows).*

Voided urine cytology was classified as atypical urothelial cells. After referral, retrograde pyelography was performed, and bilateral selective urine cytology ranged from negative to suspicious for high-grade urothelial carcinoma. Contrast-enhanced computed tomography demonstrated enhancing solid lesions in the bilateral renal pelvises (Figure 1).

Ureteroscopic evaluation was proposed to obtain a definitive diagnosis; however, given the patient's firm preference for early kidney transplantation, she opted for surgical treatment. In addition, 3 months after her initial visit, robot-assisted left nephroureterectomy was performed. The operative time was 146 min, and the estimated blood loss was 5 ml.

Postoperatively, she developed *Clostridioides difficile* colitis, which was successfully treated with antibiotics; nevertheless, this prolonged her hospital stay. She was discharged on postoperative day 22.

Histopathological examination revealed proliferation of various-sized tubular structures and stromal components, without evidence of malignancy (Figure 2). Immunohistochemistry indicated that the stromal cells were positive for estrogen receptor (ER) and progesterone receptor (PgR) (Figure 3), focally positive for CD10, but negative for melanosome-associated antigen (detected by HMB45 antibody). The epithelial cells were positive for GATA

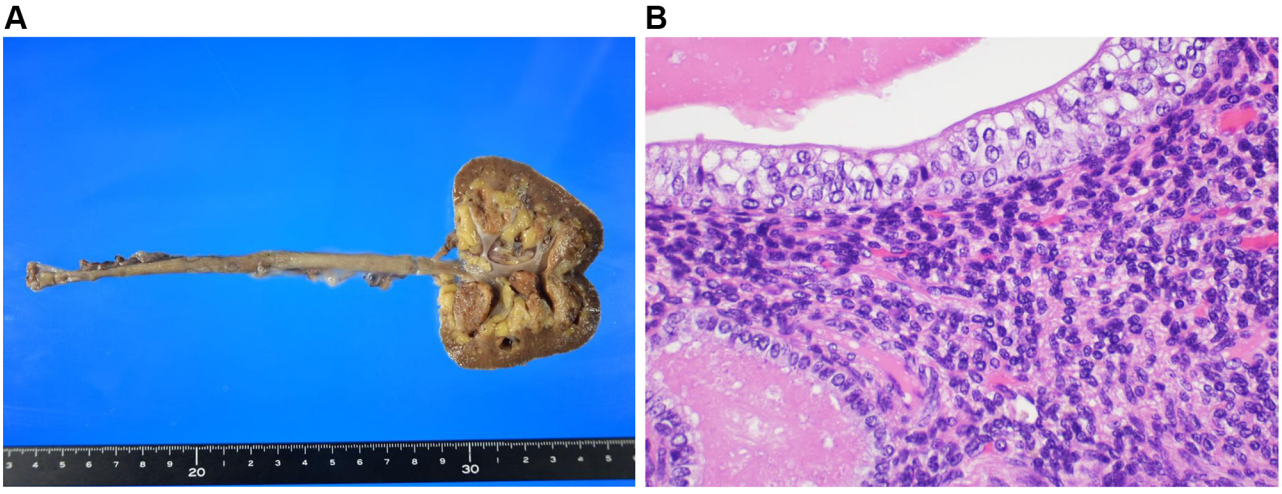

Figure 2. *Resected specimen of the left kidney and ureter (A) and the corresponding hematoxylin and eosin-stained histological findings (B). Original magnification, ×400. Proliferation of variably sized glandular/tubular structures and stromal components was observed, both demonstrating minimal cytological atypia, prompting the diagnosis of renal mixed epithelial and stromal tumor.*

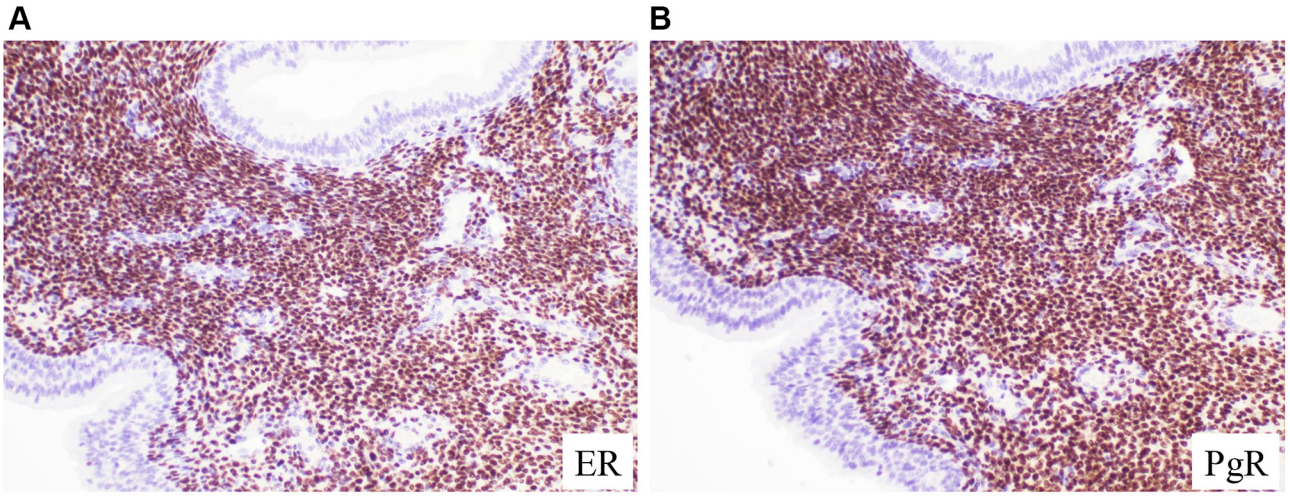

Figure 3. *Immunohistochemical staining of the resected left kidney specimen. The specimen demonstrated positivity for estrogen receptor (ER) (A) and progesterone receptor (PgR) (B). Original magnification, ×100.*

binding protein 3 (GATA3) and paired box 8 (PAX8) (Figure 4). Based on these findings, the tumor was diagnosed as MEST.

Although malignancy of the contralateral renal pelvic lesion could not be completely ruled out, it was considered highly likely to be MEST. Given the patient's firm desire for prompt transplantation, open right nephrectomy, followed by living-donor kidney transplantation to the right iliac fossa, was performed 6 months after the left nephroureterectomy. The donor was her husband, whose blood type was O, and the recipient's blood type was A. Donor-specific antibodies were not detected preoperatively. Standard immunosuppressive therapy consisting of tacrolimus, mycophenolate mofetil, methylprednisolone, basiliximab, and rituximab was administered according to our institutional protocol.

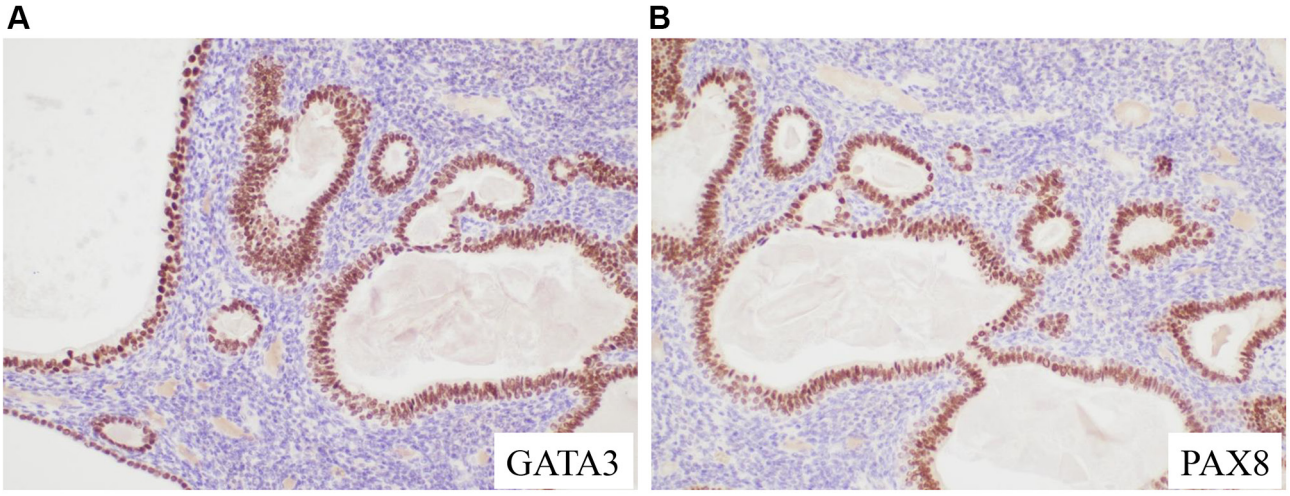

Figure 4. *Immunohistochemical staining of the resected left kidney specimen. The specimen demonstrated positivity for GATA binding protein 3 (GATA3) ×100 (A) and paired box 8 (PAX8) (B). Original magnification, ×100.*

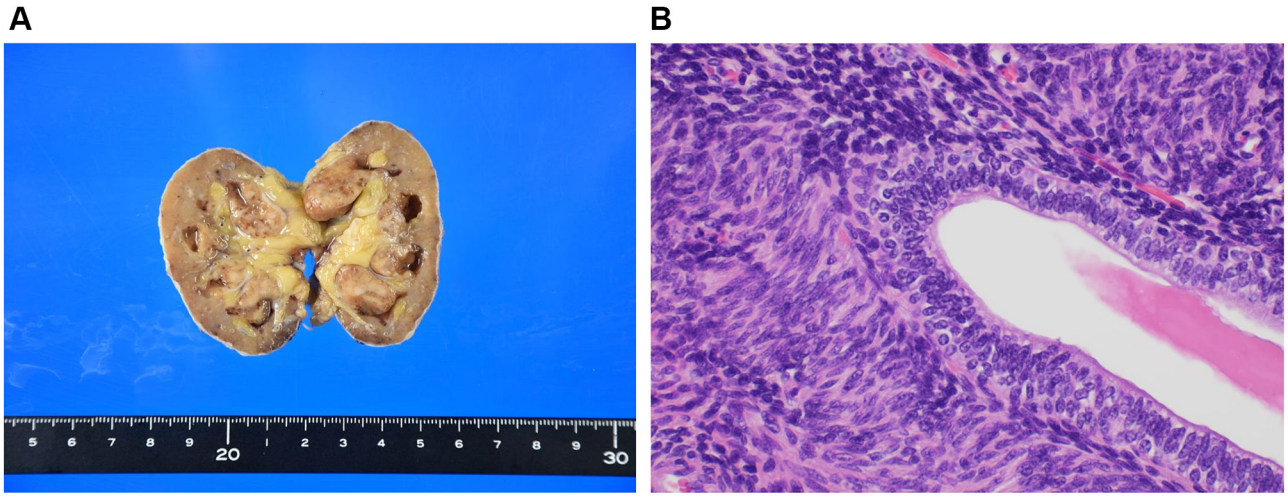

Figure 5. *Resected right kidney specimen (A) and its hematoxylin and eosin-staining findings (B). Original magnification, ×400. The tumor in the right kidney demonstrated features closely resembling those of the left renal tumor, prompting its diagnosis as renal mixed epithelial and stromal tumor.*

The operative time was 229 min, and the estimated blood loss was 69 ml. The total ischemic time was 53 min, and the warm ischemic time lasted 4 min. The graft had a single renal artery and vein. The renal artery was anastomosed end-to-side to the external iliac artery, and the renal vein was connected end-to-side to the external iliac vein.

The postoperative course was uneventful, and the patient was discharged on postoperative day 9. Histopathological examination of the right kidney confirmed MEST, similar to the left renal tumor, with no evidence of malignancy (Figure 5).

Renal graft function improved promptly after transplantation. A protocol graft biopsy performed 3 months postoperatively showed no evidence of rejection. At 1-year follow-up, the patient maintained stable graft function with no evidence of tumor recurrence or metastasis.

Discussion

In the present case, bilateral renal pelvic tumors were identified, the patient underwent robot-assisted nephroureterectomy and the tumors were pathologically diagnosed as MEST. Based on this diagnosis, living-donor kidney transplantation was performed without a waiting period, and the procedure was successful. The postoperative course has been uneventful, with no deterioration of graft function or evidence of rejection up to 1 year after transplantation. To our knowledge, this is the first report of living-donor kidney transplantation in a patient bearing MEST.

For patients with a history of malignancy, Kidney Disease Improving Global Outcomes recommends a waiting period before kidney transplantation, depending on the cancer type (7). For upper tract urothelial carcinoma, a waiting period of 2 years after nephroureterectomy is recommended for patients with localized tumors and 5 years for cases with invasive tumors. For renal cell carcinoma, a waiting period is not necessarily required in the case of incidentaloma cancer (<3 cm) that have been completely excised with negative margins. In contrast, a waiting period of approximately 2 years is generally recommended for patients with localized tumors and 5 years for those with invasive tumors (7). In the present case, as the diagnosis was MEST (a benign tumor) and no specific Kidney Disease Improving Global Outcomes guidance exists, transplantation without a waiting period was performed after a careful discussion with the patient.

Although MEST is regarded as benign, a few cases with malignant transformation have been reported. To our knowledge, 28 cases with malignant features have been reported (5, 8-28). The median age was 55.5 (range=42.5-67) years, and 75% of the patients were female. Some cases demonstrated extension into the renal vein or inferior vena cava, and others developed distant metastases. In cases with recurrence or metastasis, chemotherapy or radiotherapy has been administered, and tumor shrinkage has been reported for treatment with doxorubicin plus ifosfamide (22). From a pathological perspective, sarcomatous transformation of the stromal component was observed in 79% (22 cases); nevertheless, malignant changes in the epithelial component have also been described. In our case, the epithelial and stromal components showed no malignant features. Moreover, no reports have described cases initially diagnosed as benign MEST to subsequently demonstrate malignant transformation upon recurrence. MEST is usually unilateral; only three bilateral cases have been reported, and none showed malignant features (29-31). Although MEST is a rare entity and may not always be managed in the same manner as other benign tumors, based on these findings, living-donor kidney transplantation without a waiting period was considered feasible in the present case. However there have been seven reported cases of MEST with malignant features that developed recurrence after surgery, with a median time to recurrence of 4 months (range=2-12 months) and a maximum of 24 months (8, 10, 11, 17, 22, 28). In the present case, the follow-up period was limited to 1 year; therefore, careful long-term surveillance is warranted. Furthermore, follow-up adherence among living kidney donors has been reported to be potentially associated with graft survival and recipient survival (32), suggesting that long-term follow-up of donors may be necessary.

The precise pathogenesis of MEST remains unclear. However, it predominantly occurs in perimenopausal women (2), frequently shows positivity for ER and PgR in the stromal component (ER positive in 62% and PgR positive in 85%) (33), and has been reported in men receiving estrogen therapy for prostate cancer (16). These observations suggest that hormonal stimulation promotes the proliferation of hormone-sensitive stromal cells, leading to the formation of a biphasic tumor incorporating epithelial elements (34). Malignant transformation may occur through additional genetic alterations or aging-related factors during this process. Although immunosuppressive agents are associated with an increased risk of malignancy (6), MEST emerges primarily through hormonal mechanisms. Therefore, whether immunosuppression contributes to the

malignant transformation of MEST remains unclear. While immunosuppressive therapy is associated with increased malignancy risk, no evidence suggests that benign MEST undergoes malignant transformation under immunosuppression. To our knowledge, this is the first reported case of immunosuppressive therapy in a patient with bilateral MEST.

Conclusion

We reported a case of successful living-donor kidney transplantation without the recommended waiting period in a patient with renal pelvic tumors pathologically diagnosed as MEST. In carefully selected patients with confirmed MEST without malignant features, kidney transplantation without a waiting period may be considered. Nevertheless, careful long-term follow-up remains essential.

Conflicts of Interest

The Authors declare no conflicts of interest.

Authors' Contributions

Keisuke Nakai was involved in patient care, reviewed the literature, collected the patient data, and prepared the manuscript. Yuki Kobari prepared and revised the manuscript. Toshio Takagi revised the manuscript. Mayu Hakozaki and Yoji Nagashima performed the pathological evaluation and interpretation. Takashi Ikeda, Saito Ayaka, Daigo Okada, Arisa Wada, Hironori Fukuda, Takayuki Nakayama, Kohei Unagami, Kazuhiko Yoshida, Toshihito Hirai, Tomokazu Shimizu, Junpei Iizuka, and Hideki Ishida were involved in the clinical management of the patient. All Authors have read and approved the final version of the manuscript.

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Artificial Intelligence (AI) Disclosure

During the preparation of this manuscript, a large language model (ChatGPT, OpenAI) was used solely for language editing and stylistic improvements in select paragraphs. No sections involving the generation, analysis, or interpretation of research data were produced by generative AI. All scientific content was created and verified by the authors. Furthermore, no figures or visual data were generated or modified using generative AI or machine learning–based image enhancement tools.

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