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Case Report

Kidney Transplantation in a Patient with Smoldering Multiple Myeloma: A Case Report and Narrative Literature Review

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ABSTRACT

Chronic kidney disease and end-stage kidney disease are frequently observed in patients with plasma cell dyscrasias, including monoclonal gammopathy of undetermined significance, smoldering multiple myeloma, and multiple myeloma, although kidney failure is not always directly attributable to the hematologic disorder. Kidney transplantation represents the treatment of choice for end-stage kidney disease; however, the presence of an underlying plasma cell disorder poses significant clinical challenges and may limit access to transplantation.

We report the case of a 73-year-old woman with end stage kidney disease and low-risk smoldering multiple myeloma who underwent a comprehensive pre-transplant evaluation, including a kidney biopsy that excluded myeloma-related nephropathy and supported a non–plasma cell–related etiology of kidney failure.

The patient subsequently underwent deceased-donor dual kidney transplantation. Seventeen months after transplantation, she progressed from smoldering multiple myeloma to symptomatic multiple myeloma, requiring chemotherapy with a bortezomib-, thalidomide-, and dexamethasone-based regimen. Treatment resulted in a very good partial hematologic response according to International Myeloma Working Group criteria, accompanied by stable kidney graft function.

This case suggests that kidney transplantation may be feasible in carefully selected patients with SMM following thorough pre-transplant evaluation. However, it also highlights substantial risks of post-transplant disease progression and malignancy, underscoring the need for rigorous risk stratification, multidisciplinary decision-making, and close post-transplant surveillance.

1. Introduction

Smoldering multiple myeloma (SMM) is an asymptomatic plasma cell disorder associated with a variable risk of progression to symptomatic multiple myeloma (MM). It represents an intermediate clinical entity between monoclonal gammopathy of undetermined significance (MGUS) and MM [1].

According to the International Myeloma Working Group (IMWG) criteria, SMM is defined by the presence of a serum monoclonal (M) protein ≥3 g/dL and/or 10–59% clonal bone marrow plasma cells (BMPCs), in the absence of myeloma-defining events or end-organ damage or amyloidosis [2].

The risk of progression from SMM to MM is heterogeneous and influenced by several factors, including M-protein concentration and type, degree of immunoparesis, serum free light-chain ratio, extent of bone marrow involvement, immunophenotypic and cytogenetic abnormalities, plasma cell proliferation rate, and early organ involvement. Progression to MM is associated with increased morbidity and mortality [3].

The prevalence of chronic kidney disease (CKD) and MGUS increases with age. In the general population aged 50 years and older, MGUS has an estimated prevalence of approximately 3.2% [4]. This prevalence is significantly higher among patients with end-stage kidney disease (ESKD), in whom MGUS appears nearly three times more frequently than in the general population [5]. Kidney involvement occurs in approximately 20–30% of patients with MM at diagnosis and in up to 50% during the disease course [6].

Estimating the incidence and prevalence of SMM remains challenging due to evolving diagnostic criteria. In the general population, SMM prevalence is estimated at approximately 0.4–0.9 cases per 100,000 persons, while data in the ESKD population are scarce. Available literature suggests that among kidney transplant candidates with pre-transplant MGUS, approximately 15% progress to SMM and about 4% to symptomatic MM within five years after transplantation. In contrast, the reported cumulative probability of progression from SMM to MM of approximately 50% at five years derives from non-transplant cohorts, and transplant-specific progression risks remain poorly characterized due to limited and heterogeneous data [1, 7–10].

The identification of SMM in patients undergoing evaluation for kidney transplantation (KT) represents a significant clinical challenge.

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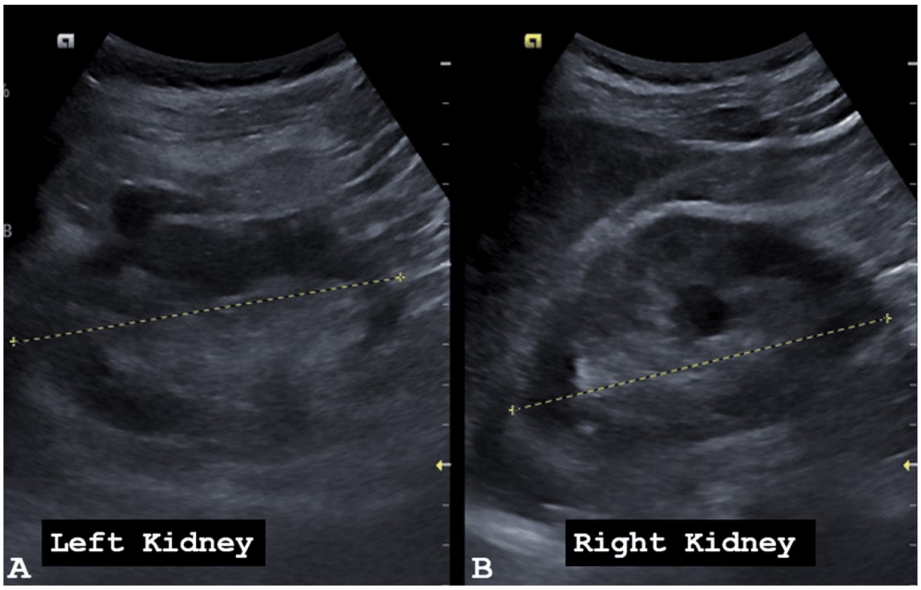

Figure 1: Bilateral Kidney Ultrasound. Bipolar kidney diameter (left kidney 10.66 cm, right kidney 10.68 cm).

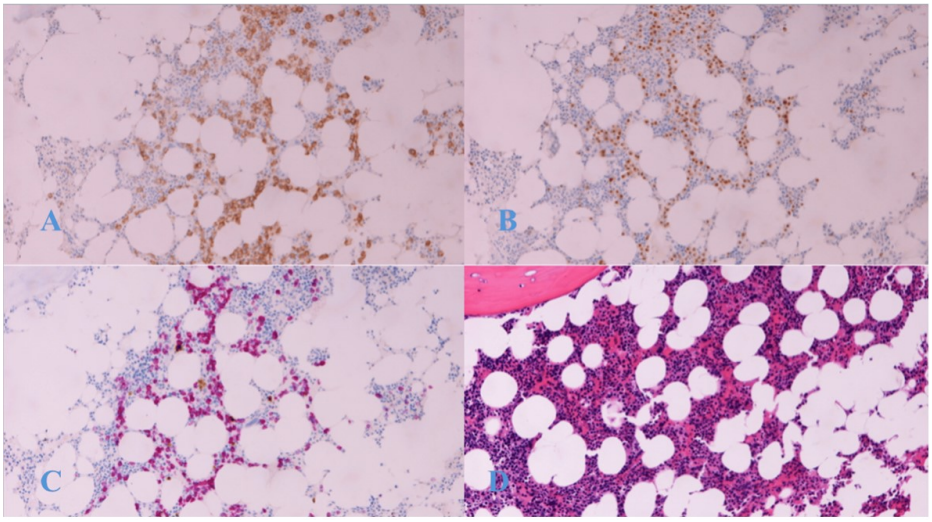

Figure 2: Bone marrow biopsy: **A.** Immunohistochemical staining for CD138 (Syndecan 1). **B.** Immunohistochemical staining for MUM1/IRF4 (Multiple myeloma oncogen-1/Interferon Regulatory Factor 4). **C.** Dual Immunohistochemical staining for kappa and lambda. Positive Immunohistochemical staining for Kappa light chain (magenta color). **D.** Haematoxylin and Eosin stain. Slight hypercellularity (10–20%) on bone marrow biopsy. Bone marrow biopsy demonstrated slightly increased cellularity (10–20%) on Hematoxylin and Eosin staining. Immunohistochemical staining revealed CD138 (Syndecan-1) positive plasma cells and MUM1/IRF4 positivity, consistent with plasma cell lineage. Dual immunohistochemical staining for kappa and lambda light chains demonstrated kappa-restricted staining (magenta), confirming monoclonality.

Limited evidence and the absence of standardized guidelines necessitate individualized decision-making based on multidisciplinary assessment and careful risk–benefit evaluation.

Here, we report the case of a patient with ESKD unrelated to SMM who underwent KT, highlighting the clinical challenges associated with transplant candidacy and post-transplant disease evolution in the setting of SMM.

2. Case Presentation

Our patient is a 73-year-old woman admitted in May 2015 for advanced kidney insufficiency (creatinine 4.19 mg/dL) and hyperproteinemia (8.9 g/dL) detected on outpatient testing due to asthenia. No prior medical records were available. At presentation, she had hypertension, but no diabetes or other systemic diseases, and no exposure to nephrotoxic medications was reported.

Kidney ultrasound showed slightly reduced renal size and cortical thickness, without hydronephrosis or calculi (**Figure 1**). Laboratory evaluation confirmed impaired kidney function (creatinine 5.2 mg/dL), anemia (Hb 8.6 g/dL), and proteinuria (1130 mg/24h), with negative Bence Jones proteinuria. Secondary hyperparathyroidism was present (PTH 157 pg/mL) with normal serum calcium (9 mg/dL). Autoimmune screening was negative.

Serum protein electrophoresis revealed an IgG-kappa monoclonal band, confirmed by immunofixation. The serum free light chain (FLC) kappa/lambda ratio was 1.73 (kappa 580 mg/L, lambda

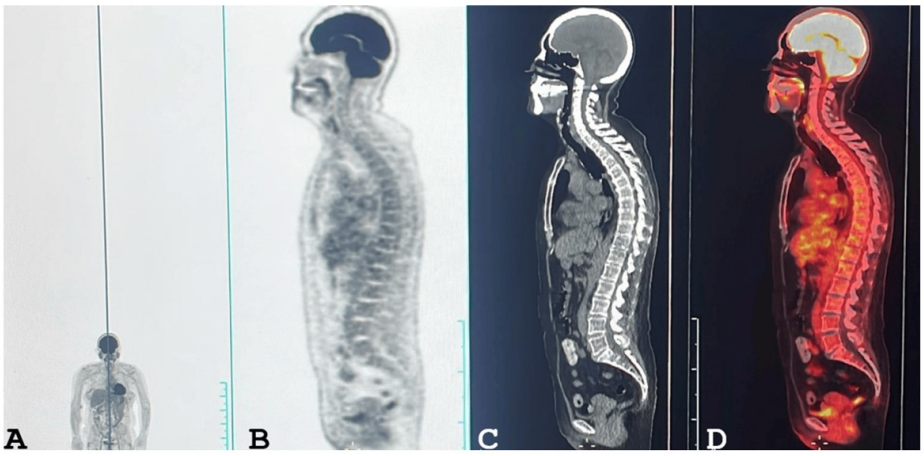

Figure 3: Positron Emission Tomography (PET). Negative for Multiple Myeloma bone disease and extra-medullary sites of metabolically active myeloma foci.

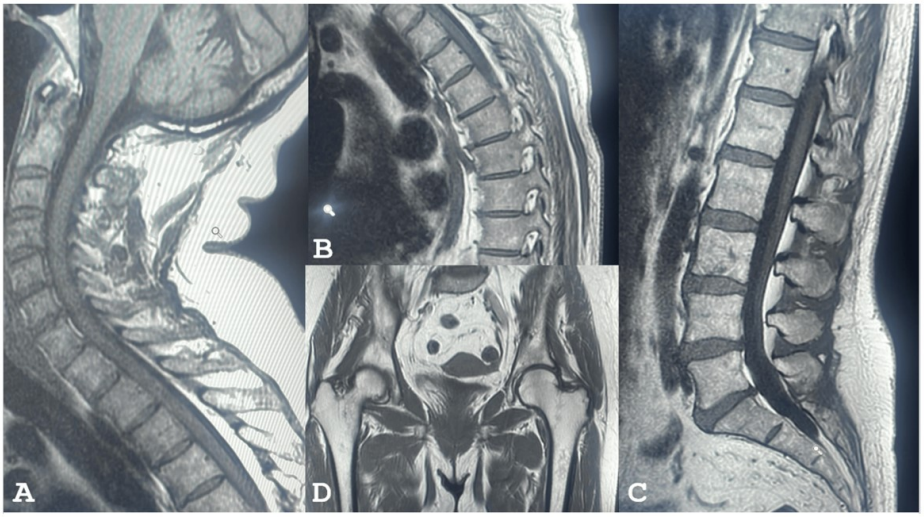

Figure 4: Magnetic Resonance Imaging. Spinal column and pelvis magnetic resonance imaging was negative: **A.** cervical segment, **B.** thoracic segment, **C.** lumbar and sacral segment, **D.** pelvis.

377 mg/L), measured using the Freelite® assay (The Binding Site, Birmingham, UK). Reference ranges were kappa: 3.3–19.4 mg/L; lambda: 5.7–26.3 mg/L; and ratio: 0.26–1.65. Given the patient's ESKD, absolute FLC levels were elevated; renal-adjusted interpretation was applied using the ratio 0.3–3.1 as described by Hutchison CA et al. [11]. Although the renal-adjusted FLC ratio was within the expected range, the presence of a monoclonal IgG kappa band on immunofixation warranted further hematologic evaluation, including a bone marrow biopsy, to accurately assess the patient's plasma cell disorder.

This approach allowed hematologic risk stratification in SMM by integrating FLC levels, bone marrow plasma cell infiltration, imaging, and clinical context.

Based on the above findings, a kidney biopsy (KB) and bone marrow biopsy (BMB) were performed.

The kidney tissue biopsy sample contained 10 glomeruli; 2 (20%) were globally sclerotic, and the remaining glomeruli showed no significant changes. Severe tubular atrophy and interstitial fibrosis were present (IF/TA grade III), accompanied by a diffuse moderate lymphocytic-plasmacytic infiltrate. Numerous tubules contained intraluminal and intracytoplasmic calcium oxalate crystals that were diffusely birefringent under polarized light. Immunofluorescence was negative for monoclonal deposits (IgG, IgA, IgM ±; kappa ++ along capillary walls; lambda +), and electron microscopy did not reveal lesions suggestive of myeloma-related kidney injury. These findings supported a non–plasma cell–related etiology of CKD, ultimately attributed to adenine phosphoribosyltransferase (APRT) deficiency. Following the biopsy, the patient started xanthine oxidase inhibitor therapy and a vegetarian diet.

The BMB demonstrated interstitial plasma cell aggregates comprising 10–20% of cellularity, CD138-positive, with kappa light chain restriction, confirming monoclonality **(Figure 2)**. Fluorescence in situ hybridization (FISH) analysis was negative for all cytogenetic abnormalities tested. These findings were integrated with serum FLC and immunofixation results to assess hematologic risk and guide further monitoring for smoldering multiple myeloma progression.

Radiologic evaluation, including positron emission tomography (PET) and spinal and pelvic magnetic resonance imaging (MRI), showed no evidence of active disease **(Figs. 3 and 4)**.

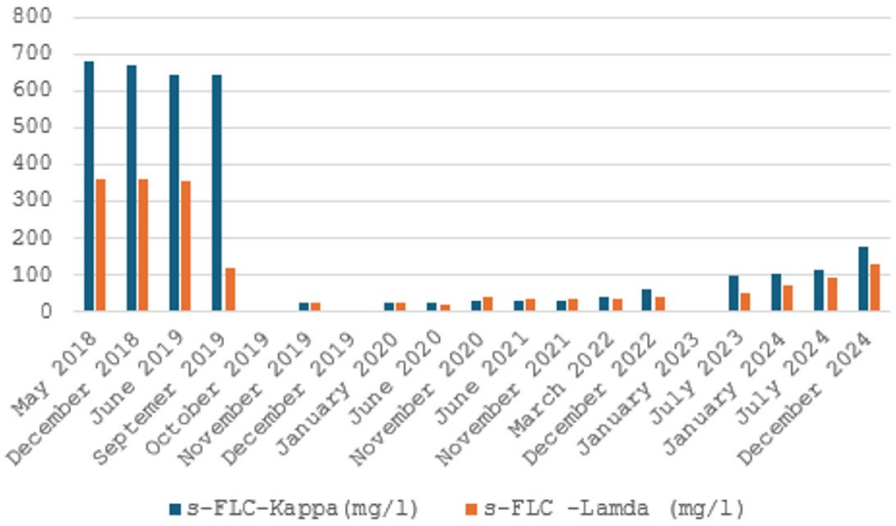

Figure 5: FLC trend.

Hematologic assessment classified the patient as having low-risk SMM according to the IMWG [2]. risk model, which considers serum M-protein, bone marrow plasma cell percentage, and immunoparesis. At baseline, the patient had a serum M-protein of 2.1 g/dL, bone marrow plasma cells of 10–20%, and normal immunoglobulins, consistent with low-risk SMM. This classification informed the decision to proceed with active hematologic surveillance without pre-transplant therapy.

In the context of ESKD, maintenance hemodialysis was initiated three times per week, and the patient was subsequently placed on the KT waiting list.

The patient was placed under close hematologic surveillance, with regular laboratory testing and imaging follow-up.

In 2016, one year after the SMM diagnosis, a skeletal survey revealed no evidence of disease progression. Laboratory parameters remained stable, consistent with the indolent nature of the underlying plasma cell disorder. During follow-up, serum-free FLC levels and ratios were monitored longitudinally using renal-adjusted reference ranges to ensure accurate interpretation in the context of ESKD.

In 2017, during routine hematologic surveillance, a second monoclonal component, typed as IgA-lambda, was detected on serum and urine protein electrophoresis and confirmed by immunofixation, in addition to the previously known IgG-kappa component, resulting in a biclonal gammopathy. This finding was associated with increased serum FLC levels and an abnormal kappa/lambda ratio, prompting a repeat BMB.

BMB evaluation showed findings comparable to those of the previous 2015 biopsy, with plasma cell infiltration of approximately 20%, predominantly small CD138-positive aggregates. Repeat FISH analysis did not identify high-risk cytogenetic abnormalities, and skeletal magnetic resonance imaging showed no evidence of focal lesions or active disease.

During subsequent follow-up, serum FLC levels remained stable between 2017 and early 2018, with stabilization of the kappa/lambda ratio. Given the absence of myeloma-defining events, stable bone marrow involvement, negative imaging findings, and preserved clinical status, the emergence of biclonality was interpreted as a marker of clonal heterogeneity rather than overt disease progression. After multidisciplinary discussion, a strategy of close hematologic surveillance was adopted, and the patient remained active on the KT waiting list.

In April 2018, the patient underwent dual KT from a 78-year-old male deceased donor (cause of death was cerebral hemorrhage). The Kidney Donor Profile Index (KDPI) was 85%. Pre-implantation biopsy demonstrated a Karpinski score of 4, considered acceptable for dual kidney transplantation. Cold ischemia time was 10 hours. There were four HLA mismatches (two at HLA-A, one at HLA-B, and one at HLA-DR). At the time of transplantation, the recipient's panel-reactive antibody (PRA) score was 10%. These donor and transplant parameters were incorporated into baseline graft risk assessment and post-transplant management.

Induction immunosuppressive therapy consisted of anti-thymocyte globulin (ATG) and high-dose intravenous methylprednisolone, followed by a tapering regimen. Maintenance immunosuppression included tacrolimus (a calcineurin inhibitor), low-dose corticosteroids, and mycophenolate mofetil.

Early post-transplant, tacrolimus target trough levels were maintained between 5–8 ng/mL, lower than the standard regimen. This approach was adopted because the patient underwent ATG induction, which reduced tacrolimus exposure and minimized additional immunosuppression given her risk of hematologic malignancy.

The immediate post-transplant period was complicated by delayed graft function (DGF), requiring two sessions of hemodialysis. A graft biopsy was performed and revealed acute antibody-mediated rejection (AMR), C4d-negative, classified according to the Banff 2017 criteria [12]. Histologic findings included glomerulitis (g1) and peritubular capillaritis (ptc2). Immunofluorescence for kappa and lambda light chains showed no monoclonal deposits. Donor-specific antibodies (DSAs) were detected against HLA class II antigens: DRB3 (MFI 550) and DPB (MFI 6,970). Based on these findings, the patient underwent three sessions of plasmapheresis and received low-dose intravenous immunoglobulin (IVIG), resulting in a gradual improvement in graft function. During the immediate post-transplantation period, multiple blood transfusions were required because of persistent anemia, with a hemoglobin level < 8 g/dL. At discharge, serum creatinine was 1.17 mg/dL.

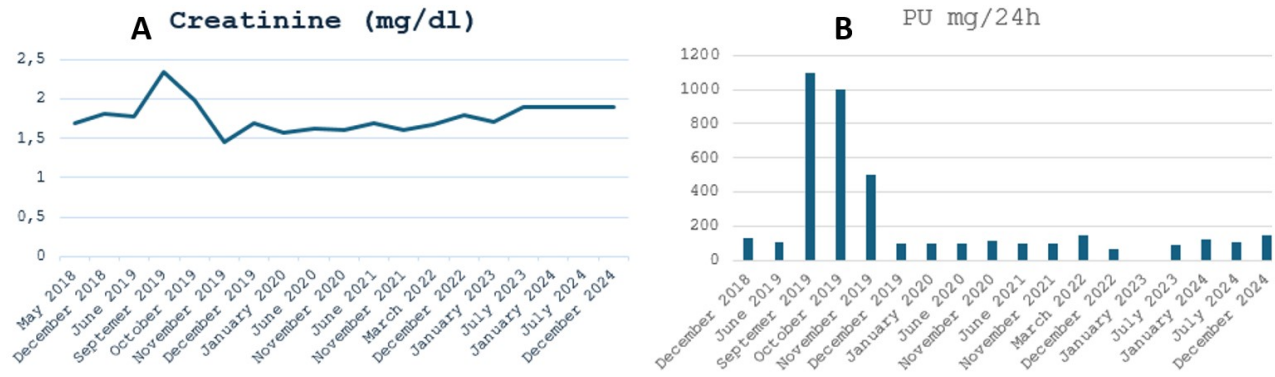

Figure 6: Kidney graft function (**A**) and 24h Proteinuria (**B**) trend.

The patient was closely monitored through coordinated hematological and nephrological follow-up in the early and long-term post-transplant period. In September 2019, a progressive increase in serum monoclonal (M) protein was observed, accompanied by a marked rise in serum FLC (kappa 642 mg/L; lambda 119 mg/L; kappa/lambda ratio 5.42), declining graft function (serum creatinine 2.35 mg/dL), and increased proteinuria (1100 mg/24 h). Bence Jones proteinuria was newly detected. Laboratory evaluation also revealed anemia (hemoglobin 10 g/dL) and a trend toward hypercalcemia (serum calcium 10.5 mg/dL).

In this clinical context, both a BMB and a kidney allograft biopsy were performed. The BMB demonstrated clonal plasma cell infiltration exceeding 30%. Progression to symptomatic MM was defined according to IMWG criteria, based on clonal bone marrow plasma cell infiltration > 30% associated with anemia, abnormal FLC ratio, hypercalcemia, and new Bence Jones proteinuria.

The KB excluded acute cellular and antibody-mediated rejection, calcineurin inhibitor toxicity, and intragraft infection, including BK virus nephropathy, cytomegalovirus infection, and pyelonephritis. Moreover, there was no evidence of monoclonal immunoglobulin deposition or plasma cell–related kidney infiltration.

Notably, focal calcium oxalate crystal deposition was identified, consistent with secondary oxalate nephropathy, and was considered a contributory factor to graft dysfunction. During this period, DSA levels remained stable, and tacrolimus trough concentrations were within the therapeutic range (5-8ng/mL). Long-term, tacrolimus trough levels were maintained within the same 5–8 ng/mL range to balance the risk of graft rejection with the ongoing oncologic risk related to her history of smoldering multiple myeloma progressing to symptomatic MM. Urine cultures, serum cytomegalovirus, and BK polyomavirus DNA tests were negative.

In October 2019, treatment with bortezomib, thalidomide, and dexamethasone (VTD protocol) was initiated. Therapy was discontinued after six cycles due to adverse effects, including bortezomib-induced peripheral neuropathy and new-onset diabetes mellitus attributed to corticosteroid use. Despite early treatment discontinuation, the patient achieved a very good partial response (VGPR) according to IMWG uniform response criteria, documented by: negative serum and urine immunofixation, with only a residual monoclonal band visible on serum protein electrophoresis; Normalization of FLC levels and kappa/lambda ratio; Resolution of Bence Jones proteinuria; Normalization of serum immunoglobulin levels; No clinical or radiological evidence of residual disease.

Kidney graft function improved concomitantly, with stabilization of serum creatinine and reduction of proteinuria.

From November 2019 to December 2024, the patient maintained VGPR and stable graft function. Trends in hematologic and renal parameters are illustrated in **(Figure 5)** and **(Figure 6)**. A full summary of post-transplant laboratory data is provided in **(Table 2)**.

Annual skeletal surveys consistently showed no evidence of end-organ involvement related to plasma cell dyscrasia. DSA levels remained stable over the 61-month post-transplant period. In December 2024, proteinuria had decreased to 130 mg/24 h, and serum creatinine was 1.9 mg/dL. In January 2023, surgical excision of a suspicious cutaneous lesion was performed, which was histologically confirmed as squamous cell carcinoma.

3. Discussion

KT is the best therapeutic option in ESKD for several reasons, including improved survival, better quality of life, and greater cost-effectiveness compared with dialysis therapy [13].

Certain pre-transplant conditions can delay or preclude access to KT, such as specific types of neoplasms or pre-neoplastic conditions. Additionally, in both the short- and long-term post-transplant periods, the presence and intensity of immunosuppressive therapy can influence, and potentially increase, the risk of neoplasm development. Currently, the presence of MGUS does not affect access to KT according to the Kidney Disease Improving Global Outcomes (KDIGO) 2020 [14, 15]. However, previous studies have demonstrated a benign course and low risk of progression in pre-transplant MGUS after KT. In a Mayo Clinic series, 42 cases of MGUS were identified among 3,518 patients who underwent KT, and 55% of these patients had MGUS before KT. Over a median follow-up of 8.5 years, only four patients progressed to hematologic malignancy: two developed SMM, and two developed lymphoproliferative disorders [14–16]. Similarly, retrospective studies from Spain and Italy reported low progression rates of MGUS post-KT [11–18].

Historically, KT has not been considered for patients with active MM and ESKD due to poor prognosis [14]. However, novel therapeutic agents developed over the past two decades have significantly improved both progression-free and overall survival in patients with MM. Consequently, KT may now be considered in selected patients,

typically after at least two years of treatment and in the absence of disease relapse [17].

Table 1: Baseline and pre-KT laboratory data

Time /lab data	Reference range	May 2015 (Baseline)	January 2016	July 2016	January 2017	July 2017	January 2018	April 2018 pre-KT
WBC (/mm3)	4000-8000	7300	4700	5000	4500	4300	4700	5500
Hb (g/dl)	12.5-16.0	8.6	10.9	13.0	11.8	12.0	11.4	10.2
PTL(/mm3)	150000-400000	231000	242000	276000	217000	306000	290000	293000
Protidemia (g/dl)	6.4-8.3	8.9	7.9	7.9	8.0	7.6	7.5	7.5
s-FLCs-Kappa (mg/l)	3.3-19.4	580.0	370.44	580.43	727.40	754.00	730.34	690.50
s-FLCs -Lambda (mg/l)	5.7-26.3	377.0	279.42	337.29	125.40	378.00	365.50	363.00
s-FLCs ratio	0.26-1.65	1.73	1.32	1.72	5.8	1.99	1.99	1.8
s-QFE	Negative	IgG- K	IgG- K	IgG- K	IgG- K and IgA- L	IgG- K and IgA- L	IgG- K and IgA- L	-
u-QFE	Negative	Negative	Negative	Negative	IgG- K and IgA- L	IgG- K and IgA- L	IgG- K and IgA- L	-
s-IFE	Negative	IgG- K	IgG- K	IgG-K	IgG- K and IgA- L	IgG- K and IgA- L	IgG- K and IgA- L	-
u-IFE	Negative	Negative	Negative	Negative	IgG- K and IgA- L	IgG- K and IgA- L	IgG- K and IgA- L	-
IgG (mg/dl)	660-1400	1470	1600	1830	2050	2170	2090	1570
IgA (mg/dl)	70-400	263	272	275	245	217	238	160
IgM (mg/dl)	40-230	55	39	38	31	32	30	55
Creatinine (mg/dl)	<1.10	5.3	HD	HD	HD	HD	HD	HD
BUN (mg/dl)	10-50	153	HD	HD	HD	HD	HD	HD
Uric acid (mg/dl)	2.6-6.0	4.5	4.7	3.5	4.5	4.0	4.1	4.3
Calcium (mg/dl)	8.1-10.4	9.0	8.4	8.9	9.6	8.8	9.3	9.0
Phosphorus (mg/dl)	2.6-4.5	5.1	5.2	4.2	4.8	5.7	5.1	3.2
Natrium (mmol/l)	137-147	143	141	138	137	134	139	138
Kalium (mmol/l)	3.6-5.4	5.0	5.5	5.3	4.7	4.1	4.8	4.7
PTH (pg/ml)	6-36	157	66	90	156	-	-	-
25-OH-vit D(ng/ml)	30-100	11	13	-	31	-	-	-
PU mg/24h	10-150	1130	-	-	-	-	-	-
Urine exam (pto) (mg/dl)	<20	30	-	30	30	-	-	-
HIV	Negative/Positive	Negative	-	-	Negative	-	-	-
HBV	Negative/Positive	Negative	-	-	Negative	-	-	-
HCV	Negative/Positive	Negative	-	-	Negative	-	-	-
Ab-anti-ds-DNA	Negative/Positive	Negative	-	-	-	-	-	-
ANA	>/=1: 80	Negative	-	-	Negative	-	-	-
ANCA	Negative/Positive	Negative	-	-	-	-	-	-
ENA	Negative/Positive	Negative	-	-	-	-	-	-
ESR (mm/sec)	0-15	35	-	-	-	-	-	-
RF (Ui/ml)	0-30	23	-	-	-	-	-	-
HbA1C (%)	4-6	5.7	-	-	5.6	-	-	-
Glucose (mg/dl)	70-100	76	-	-	78	-	-	-
Urine culture	Negative	Negative	Negative	Negative	Negative	Negative	Negative	-

WBC, white blood cells; Hb, hemoglobin; PTL, platelets; s-FLCs, serum free light chains; K, kappa; L, lambda; SPEB, serum electrophoresis; UPEB, urine electrophoresis; s-IFE, serum immunofixation; u-IFE, urine immunofixation; IgG, immunoglobulin G; IgA, immunoglobulin A; IgM, immunoglobulin M; BUN, blood urea nitrogen; PTH, parathormon; 25-OH vit D, 25-idrossicolecalciferolo; PU, proteinuria; HIV, human immunodeficency virus; HBV, hepatit B virus; HCV, hepatit C virus; ab-anti-ds-DNA, antibody against double strand DNA; ANA, Anti-nuclear antibodies; ENA, extractable nuclear antigens; ESR, erythrocyte sedimentation rate; RF, rheumatoid factor; HbA1C, glycosylated hemoglobin; Ucol., urinalysis; HD, hemodialysis.

Table 2: Post -Kidney Transplant hematologic course and trend of graft function

Time /lab data	Reference range	5/2018	12/ 2018	6/ 2019	9/ 2019	10/2019	11/ 2019	12/2019	1/2020	6/ 2020	11/ 2020	6/ 2021	11/ 2021	3/ 2022	12/2022	1/2023	6/ 2023	1/2024	6/ 2024	12/2024
WBC (/mm3)	4000-8000	6700	5800	4700	4530	4800	4900	5500	6100	5800	4760	6800	6900	6600	6500	6700	6300	6500	7400	6500
Hb (g/dl)	12.5-16.0	11.0	11.3	12.0	10.0	11.5	12.2	12.8	12.8	11.8	11.2	11.4	11.2	11.6	12.0	11.9	11.5	10.8	11.6	10.7
PTL(/mm3)	150000-400000	301000	256000	232000	210000	234000	272000	217000	199000	258000	240000	259000	240000	235000	240000	272000	232000	284000	263000	219000
Protidemia (g/dl)	6.4-8.3	6.9	7.1	7.4	9.4	6.1	7.0	6.8	6.6	6.7	6.5	6.7	6.6	7.0	6.8	7.2	6.9	6.9	7.0	6.9
s-FLC-Kappa(mg/l)	3.3-19.40	680.10	670.50	642.0	642.0	-	26.90	-	26.50	27.6	30.4	32.1	30.40	40.70	63.90	-	97.70	106.0	117.0	178.0
s-FLC -Lambda (mg/l)	5.7-26.3	363.00	360.0	354.0	119.0	-	25.8	-	27.90	22.7	40.5	37.0	35.90	36.10	44.0	-	52.90	75.10	92.30	133.0
s-FLC ratio	0.26-1.65	1.8	1.8	1.8	5.4	-	1.04	-	0.95	1.2	0.88	0.87	0.85	1.13	1.45	1.6	1.85	1.41	1.27	1.34
IgG (mg/dl)	660-1400	1490	-	1430	3820	-	1140	924	877	901	898	1000	898	992	1110	1117	1240	1480	1784	1998
IgA (mg/dl)	70-400	154	-	147	92	-	77	71	68	77	76	93	76	103	117	116	119	189	235	257
IgM (mg/dl)	40-230	52	-	49	25	-	80	72	71	75	73	89	73	79	68	101	63	63	53	50
Creatinine (mg/dl)	<1.10	1.7	1.81	1.77	2.35	1.9	1.45	1.70	1.58	1.63	1.61	1.7	1.61	1.67	1.8	1.71	1.9	1.9	1.9	1.9
BUN (mg/dl)	10-50	84	96	86	130	70	70	84	70	98	89	99	78	92	82	83	94	96	110	113
Uric acid (mg/dl)	2, 6-6, 0	3.6	4.0	4.3	4.5	2.9	3.7	3.6	4.0	4.3	4.7	4.3	3.8	3.7	2.4	2.4	2.7	2.5	2.4	2.4
Calcium (mg/dl)	8.1-10.4	9.6	9.6	9.5	10.5	8.7	9.3	9.6	9.6	9.4	9.5	9.6	9.5	9.7	9.5	9.7	9.7	9.5	9.9	10.3
Phosphorus (mg/dl)	2.6-4.5	4.0	4.0	3.3	3.3	3.2	3.7	4.0	4.0	3.7	5.0	4.0	4.1	4.0	3.5	4.0	3.7	4.0	3.7	3.8
PU mg/24h	10-150	-	130	110	1100	1000	500	100	100	98	118	98	100	150	70	-	90	120	110	150
TL FK ng/ml	based on the physician's indication	7.8	6.9	6.7	6.7	7.2	6.8	6.9	5.9	5.5	6.4	5.5	6.0	5.8	6.0	-	5.7	5.9	6.5	6.7

WBC,white blood cells;Hb,hemoglobin;PTL,platelets;s-FLCs,serum free light chains;IgG,immunoglobulin G;IgA,immunoglobulin A;IgM,immunoglobulin M;BUN,blood urea nitrogen;PU,proteinuria;TL FK,though levels tacrolimus

The eligibility strategy becomes more challenging in patients with SMM. The potential benefits of KT in this population must be carefully weighed against the risk of graft loss due to disease progression. Current evidence is limited, mostly retrospective, and primarily concerns MGUS rather than SMM [7, 10, 17, 18].

In addition to hematological characteristics, the presence and intensity of immunosuppressive therapy, both in the short and long term, may increase the risk of SMM progression to MM following KT [15].

Historically, the standard of care for SMM has been observation. However, IMWG revised diagnostic criteria, enabling early treatment for a subset of patients previously classified as SMM but exhibiting early malignant features [19].

In KT candidates with high-risk SMM, pre-transplant treatment may be considered 3-6 months prior to transplantation in living donor settings to reduce tumor burden. Conversely, routine pre-treatment is not recommended for patients awaiting deceased donor transplantation due to unpredictable organ availability and potential attenuation of therapeutic benefit over time [20].

Accurate pre-transplant risk stratification is essential. The IMWG 2/20/20 risk model and the Spanish Myeloma Group criteria provide precise assessments of progression risk [19, 21]. This allows individualized evaluation of KT candidates, whereby low-risk patients may proceed to transplantation, whereas high-risk patients may be deferred or receive preemptive treatment. Ultimately, these decisions remain complex and require a multidisciplinary approach. In our patient, close hematologic surveillance during the pre-transplant period demonstrated a stable SMM clinical course, which represents a key predictor of KT eligibility.

At the time of transplantation, ATG was used for immunosuppressive induction therapy due to a high immunological risk (four HLA mismatches and a positive PRA), in accordance with the local protocol. The use of ATG in induction immunosuppressive therapy, as reported by Passweg et al. [22], represents an increased risk of 10.4% for gammopathy development after solid organ transplantation. After the progression from SMM to MM in September 2019, the immunosuppressive regimen was maintained at therapeutic doses due to the patient's high immunological risk (elevated number of HLA mismatches and positive PRA at transplantation time) and prior history of acute antibody-mediated rejection and blood transfusion. Decisions were made in a multidisciplinary setting, carefully balancing the risk of graft rejection against potential acceleration of MM. The patient was closely monitored with frequent laboratory and clinical evaluations, allowing timely initiation of MM therapy without compromising graft function.

The progression of SMM to symptomatic MM after KT has been reported by Kormann et al. [15], who described three KT recipients with pre-transplant SMM; two of these patients (66.6%) developed MM with cast nephropathy within 2–4 months post-KT. In contrast, our patient progressed in 17 months after transplantation, likely reflecting a more indolent disease course. Both the cases reported by Kormann et al. and our patient underscore that transplantation in SMM patients carries a substantial risk of disease progression.

In our patient, progression to symptomatic MM necessitated initiation of VTD therapy, resulting in very good hematologic remission according to IMWG criteria. Importantly, although the outcome was favorable, this case illustrates that even carefully selected SMM patients may require post-transplant chemotherapy. Therefore, these experiences validate concerns regarding KT in SMM and highlight the critical importance of careful pre-transplant risk stratification, multidisciplinary management, and vigilant post-transplant hematologic surveillance to promptly identify and treat MM progression while preserving graft function.

Our patient also developed cutaneous squamous cell carcinoma approximately three years after MM evolution, which was successfully managed surgically. The increased risk of cutaneous squamous cell carcinoma in KT recipients and MM patients is well documented, underscoring the importance of regular dermatologic surveillance [15, 23]. During 61 months of follow-up, our patient maintained a stable hematologic status and graft function.

4. Conclusions

This case demonstrates that KT can be feasible in a carefully selected patient with SMM. However, the patient experienced progression to symptomatic MM post-transplant, highlighting that SMM carries a real risk of disease progression. These findings emphasize the importance of individualized patient selection, multidisciplinary management, and vigilant post-transplant hematologic monitoring to optimize outcomes. While KT may be considered in selected SMM patients, these results cannot be generalized to all patients with SMM.

Conflicts of Interest

The authors declare no competing interests that could have influenced the objectivity or outcome of this research

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Informed Consent

Informed consent for treatment and open access publication was obtained or waived by all participants in this study.

Large Language Model

None.

Authors Contribution

SM contributed to conceptualization, writing original draft, data collection, literature review, and patient follow up while SF contributed to review and editing, supervision, and interpretation of nephrology data, MT contributed to data curation, figure preparation, and literature review, CR contributed to histopathology analysis, interpretation of biopsy data, and figure preparation, and AP contributed to data collection, literature review, and interpretation of nephrology data.

Data Availability

The data supporting the findings of this study are not publicly available due to privacy and ethical restrictions related to patient

confidentiality, but are available from the corresponding author upon reasonable request.

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