Sequential, Autologous Hematopoietic Stem Cell Transplant Followed by Renal Transplant in Multiple Myeloma

Abstract

A 30-year-old female was symptomatic with headache, fatigue, and weakness since October 2011 and was told to have anemia. In January 2012, she was admitted outside with pulmonary edema. Investigations revealed advanced azotemia, anemia, and hypercalcemia. Urine showed 2 + proteins and 30–35 red blood cells. There was no history of oral ulcers, rash, Raynaud's phenomenon, or hemoptysis. She was evaluated for causes of rapidly progressive "renal failure." Hemolytic work-up; antinuclear antibody, double-stranded DNA, and anti-neutrophil cytoplasmic antibody were negative. Kidney biopsy was done and interpreted as acute interstitial nephritis with hyaline casts. She was started on hemodialysis and treated with steroids and cyclophosphamide. She came to our institute in January 2012. Investigations showed evidence of paraproteinemia with kappa restriction. Bone marrow showed 15% plasma cells. Kidney biopsy was reviewed and was diagnostic of cast nephropathy. She was treated with 6 monthly cycles of dexamethasone and bortezomib. She achieved complete remission in July 2012. Maintenance doses of bortezomib were continued until May 2014. Autologous bone marrow transplantation was performed on June 06, 2014. Monthly, bortezomib was continued till April 2015. Subsequently, workup for renal transplantation was started with her father as her donor. Test for sensitization was negative. Renal transplantation was done on January 1, 2016, with prednisolone, mycophenolate, and tacrolimus. She achieved a serum creatinine of 0.6 mg% on the 4th postoperative day. Thereafter, she continues to remain stable.

Keywords: *Bone marrow transplant, plasma cell dyscrasia, renal transplant, sequential transplant*

D. Bhowmik, S. Yadav, L. Kumar[1], S. Agarwal[2], S. K. Agarwal, S. Gupta

Departments of Nephrology, [1]Medical Oncology and [2]Surgical Disciplines, All India Institute of Medical Sciences, New Delhi, India

Introduction

Plasma cell dyscrasia is one of the common malignancies, especially in the elderly, although it may also afflict the young adults. About half of these patients have some renal dysfunction at presentation and about 10% require hemodialysis.[1] Occasionally, patients present to the nephrologist for evaluation of unexplained renal failure and investigations reveal plasma cell dyscrasia. We present a similar clinical scenario in a female who had hypertension, pulmonary edema and presented with rapidly progressive renal failure (RPRF). Investigations revealed cast nephropathy. She underwent autologous hematopoietic stem cell transplant while on maintenance hemodialysis and subsequently successful live related renal transplantation. To the best of our knowledge, this is the first such reported case from India.

Case Report

A 30-year-old female presented to the Renal Clinic of our hospital in January 2012 for the investigation of rapidly progressive renal failure (RPRF). Her illness started in October 2011 with headache and weakness. Subsequently, she developed exertional dyspnea and orthopnea. She was detected to have anemia and increased blood pressure of 160/90 mmHg. She was initially admitted to a private hospital, with features suggestive of pulmonary edema. Investigations there revealed hemoglobin (Hb) 9 g%, total leukocyte count 13,100, blood urea 253 mg%, creatinine 13.9 mg%, Na 131 mEq/L, K 6.2 mEq/L, calcium 11.9 mg%, phosphate 6.8 mEq/L, uric acid 9.5 mEq/L, intact parathyroid hormone 27.6 pg/ml. Urine routine revealed 2+ proteins, 30–35 red blood cells (RBCs), and 10–12 white blood cell. Urine protein-creatinine ratio was 3.9. There was no history of reduced urine output, hematuria, dysuria, fever, nonsteroidal anti-inflammatory drug use, alternative drug use, calcium supplementation, oral ulcers, skin rash, Raynaud's phenomenon, photosensitivity, hemoptysis, or epistaxis.

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Address for correspondence:
Dr. D. Bhowmik, Department of Nephrology, All India Institute of Medical Sciences, New Delhi - 100 029, India.
E-mail: dmbhowmik@yahoo.co.in

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She was initiated there on hemodialysis and stabilized. Further evaluation of RPRF was done. The hemogram showed no schistocytes, and serum lactate dehydrogenase was 872 U/L (normal for her renal function). Serum antinuclear antibody, double-stranded DNA, and anti-neutrophil cytoplasmic antibody were negative; C_3 was 98 mg/dL. Serum protein electrophoresis was normal. Serum immunofixation electrophoresis (IFE) revealed a monoclonal gammopathy, with elevated kappa chain. Urine IFE too showed kappa light chains. Serum β2 microglobulin was 38.72 mcg/ml. X-rays of the skull, pelvis, and dorsolumbar spine were normal.

Kidney biopsy was done there and reported as prominent tubular hyaline casts with mild to moderate acute interstitial nephritis. She was given intravenous pulses of steroid and cyclophosphamide. Subsequently, she came to Renal Clinic at our hospital. The serum free light chain assay revealed kappa 381.14 mg/dl, lambda 58.31 mg/dl, with a kappa/lambda ratio 6.54 (0.26–1.65). Bone marrow examination revealed 15% plasma cells. The kidney biopsy slides were reviewed. It showed five glomeruli, which were unremarkable. The tubules showed fractured casts with giant cell reaction. There was significant interstitial atrophy. The pathologic diagnosis was myeloma cast nephropathy (kappa light-chain restricted), with chronic kidney disease.

Maintenance hemodialysis was continued and she was referred to medical oncology. There, she received induction therapy with bortezomib and dexamethasone. Six cycles were given from January to June 2012. She achieved complete remission. The serum and urine protein electrophoresis became negative for gammopathy. Bone marrow aspiration showed 1%–2% plasma cells. Maintenance bortezomib was continued till May 2014 when she was planned for autologous bone marrow transplantation. Autologous hematopoietic stem cell transplantation was performed on June 6, 2014. Melphalan was administered at the dose of 100 mg/m^2; total of 150 mg; and CD34+ 4.34 × 10^6/kg cells were infused. Posttransplant complications included febrile neutropenia and gastrointestinal (GI) toxicity, which settled down with time.

On follow-up, serum protein electrophoresis (SPEP) and bone marrow were normal. The free light chain ratio was 2.9 (WNL for her renal functions). After bone marrow transplant, monthly, bortezomib was continued until April 2015 when it was stopped in view of thrombocytopenia. It was treated with steroids for 2 months. Throughout the period, maintenance hemodialysis through arteriovenous fistula in the right forearm was continued. Hb was maintained at around 10 g% with injection erythropoietin 6000 units/week. In December 2014, renal transplantation was planned with father (59 years) as donor. Sensitization history included two units packed RBC infusion in June 2014 and two pregnancies. The complement-dependent cytotoxicity and flow cross-matches were negative. Her Hb was 10.9 g%, total leukocyte count 3700/mm^3, and platelets 98,000/mm^3. Hence, pretransplant mycophenolate was withheld. No induction therapy was given. Renal transplant was performed on January 4, 2016, with immunosuppression consisting of prednisolone and tacrolimus. Subsequently, mycophenolate was added. She achieved a serum creatinine of 0.6 mg% on day 4. Posttransplantation course was uneventful. Currently, she was 4½ months postrenal transplant. She was receiving tablet prednisolone 7.5 mg, mycophenolate 500 mg TDS, and tacrolimus 5.5 mg BD (tacrolimus level 5.5 ng/ml).

Discussion

Renal dysfunction is very common in patients with plasma cell dyscrasia. It affects the kidney by three mechanisms: cast nephropathy, also called myeloma kidney, is most common (40%–63%), followed by monoclonal immunodeposition disease (19%–26%) and amyloid light-chain amyloidosis (7%–30%).[2] Renal dysfunction with multiple myeloma is associated with increased morbidity and mortality.[3] In the period, before novel agents and stem cell transplantation, the median survival of patients of cast nephropathy on dialysis was dismal 6 months.[2] There has been significant improvement in survival of patients with renal dysfunction in the past decade due to the use of thalidomide and bortezomib.[4] Currently, the initial aim is to achieve remission with chemotherapy, followed by high-dose melphalan therapy and autologous stem cell transplantation (ASCT) in suitable patients. However, patients on dialysis are usually not considered for stem cell transplantation.[5,6] Dosage of the conditioning agents is problematic: under-dosing increases the risk of recurrent disease, while overdosing can cause toxicity to the GI mucosa, heart, and lungs, besides infection.[7] Subsequent renal transplantation is even rarer but has been reported from few centers in younger patients with good performance status.[8-10]

Our patient presented with RPRF. Laboratory investigations showed anemia, hypercalcemia, and hyperuricemia. There was no evidence of hemolysis or vasculitis. The screening tests for multiple myeloma, viz., SPEP and skeletal survey, were negative. However, serum IFE revealed monoclonal gammopathy with elevated kappa chain, and kidney biopsy showed classic cast nephropathy. She achieved complete hematologic remission, with the induction treatment consisting of bortezomib and dexamethasone. However, her renal function did not improve with chemotherapy and she continued to remain dialysis dependent. After remaining in remission for about 2 years, she underwent successful autologous hematopoietic stem cell transplantation. A sustained remission is advised before renal transplantation as there are chances of recurrence of multiple myeloma postrenal transplant due to the effect

of immunosuppression.[11] In our patient, the total waiting period after remission was about 2½ years. The major issue before renal transplant was thrombocytopenia, which was thought to be due to immune thrombocytopenia, and was treated with steroids. Mycophenolate was introduced after the renal transplant. There were no problems in the posttransplant period.

Every patient of multiple myeloma with end-stage renal failure is not a candidate for ASCT; ASCT is indicated in patients with <65 years of age with no severe comorbidities. Although ASCT is feasible with renal failure, toxicities of high-dose chemotherapy are more frequent and more severe. The dose of melphalan should be reduced to 100 mg/m^2 instead of 200 mg/m^2. To the best of our knowledge, this is the first such case reported from India. This case highlights appropriate evaluation of RPRF, followed by close interaction of medical oncology and nephrology. We feel that sequential ASCT followed by renal transplantation is an appropriate modality of care of patients, with plasma cell dyscrasia with renal failure in young and otherwise fit patients.

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Conflicts of interest

There are no conflicts of interest.

References

1. Katagiri D, Noiri E, Hinoshita F. Multiple myeloma and kidney disease. Scientific World J 2013;2013:487285.
2. Bansal T, Garg A, Snowden JA, McKane W. Defining the role of renal transplantation in the modern management of multiple myeloma and other plasma cell dyscrasias. Nephron Clin Pract 2012;120:c228-35.
3. Baraldi O, Grandinetti V, Donati G, Comai G, Battaglino G, Cuna V, *et al.* Hematopoietic cell and renal transplantation in plasma cell dyscrasia patients. Cell Transplant 2016;25:995-1005.
4. Dimopoulos MA, Delimpasi S, Katodritou E, Vassou A, Kyrtsonis MC, Repousis P, *et al.* Significant improvement in the survival of patients with multiple myeloma presenting with severe renal impairment after the introduction of novel agents. Ann Oncol 2014;25:195-200.
5. Dimopoulos MA, Sonneveld P, Leung N, Merlini G, Ludwig H, Kastritis E, *et al.* International myeloma working group recommendations for the diagnosis and management of myeloma-related renal impairment. J Clin Oncol 2016;34:1544-57.
6. Terpos E, Kleber M, Engelhardt M, Zweegman S, Gay F, Kastritis E, *et al.* European Myeloma Network guidelines for the management of multiple myeloma-related complications. Haematologica 2015;100:1254-66.
7. Heher EC, Spitzer TR. Hematopoietic stem cell transplantation in patients with chronic kidney disease. Semin Nephrol 2010;30:602-14.
8. Beitinjaneh A, Burns LJ, Majhail NS. Solid organ transplantation in survivors of hematopoietic cell transplantation: A single institution case series and literature review. Clin Transplant 2010;24:E94-102.
9. Khoriaty R, Otrock ZK, Medawar WA, Khauli RB, Bazarbachi A. A case of successful double sequential bone marrow and kidney transplantations in a patient with multiple myeloma. Nephrol Dial Transplant 2006;21:3585-8.
10. Sánchez Quintana A, Rull PR, Atienza JB, McDonnell CN. Renal transplant in plasma cell dyscrasias with lenalidomide treatment after autologous stem cell transplantation. Nephrology (Carlton) 2013;18:641-3.
11. Heher EC, Rennke HG, Laubach JP, Richardson PG. Kidney disease and multiple myeloma. Clin J Am Soc Nephrol 2013;8:2007-17.