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Kidney Transplant in Multiple Myeloma: A Clinical Case

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1. Abstract

In this new era of novel Multiple Myeloma (MM) therapies, disease-free survival and especially overall survival of these patients has increased. Although historically considered as a contraindication for kidney transplant, the efficacy of these new drugs is changing this paradigm. Some case reports of MM patients with good hematologic outcomes and low or intermediate risk of relapse have described good results after successful kidney transplantation.

We report a case of a 39-year-old woman, from Cape Verde, presented with rapidly progressive renal failure needing dialysis induction. Etiological study revealed proteinuria of 4.6g/day, hypogammaglobulinemia, serum immunofixation with a monoclonal band in Kappa light chain, Bence Jones Kappa protein, elevated free light chain ratio and beta 2-microglobulin, 10% plasma cells in bone marrow aspirate and bone biopsy with monoclonal plasma cells with Kappa chain restriction. Kidney biopsy revealed nodular glomerulosclerosis with Kappa chain deposition on immunofluorescence on tubular cells' basement membranes – Monoclonal Immunoglobulin Deposition Disease. Shortly after the patient was treated with dexamethasone, cyclophosphamide and bortezomib with complete response and submitted to haematopoietic stem cell transplantation eight months after the initial therapy with a very good partial response. Although she remained dialysis-dependent, the patient maintained in clinical remission. Seven years after the initial diagnosis, the patient was submitted to a standard criteria deceased donor kidney transplant with low immunological risk (three mismatches, panel reactive antibody of 0% and no donor-specific antibodies). Induction immunosuppression was with basiliximab, tacrolimus, mycophenolate mofetil and methylprednisolone. Cold ischaemia time was 5h37 and warm ischaemia time 31 minutes. There was immediate graft function and the patient was discharged seven days after the transplant with a serum creatinine of 0.8mg/dL. She was on maintenance immunosuppression with tacrolimus, mycophenolate mofetil and prednisolone with stable renal function (serum creatinine 0.8-1.1mg/dL) and very good partial response of MM 12 months after kidney transplant.

The authors present a case of a MM patient submitted to kidney transplantation with good outcomes. This highlights that nowadays kidney transplant should be considered and offered to selected patients according to their clinical characteristics and MM treatment response.

2. Introduction

Multiple Myeloma (MM) is a neoplasm characterized by a proliferation of clonal plasma cells that produce a monoclonal immunoglobulin [1]. Kidney injury is a common feature in this disease, affecting up to 50% of these patients at diagnosis and, although current treatment has increased renal function recovery in up to 80 of patients, MM still remains an important cause of end-stage kidney disease [1].

There are several known mechanisms of MM renal injury that range from prerenal causes, such as volume depletion and renal flow obstruction associated with calculi, to cast nephropathy, Monoclonal Immunoglobulin Deposition Disease (MIDD) and amyloidosis [1,2].

Although MM was historically a contraindication for kidney transplant due to high recurrence rates and poor graft survival, the efficacy of new disease-directed drugs is changing this paradigm [2,3]. In the last 15 years, disease-free survival and especially overall survival have increased exponentially due to novel MM therapies [2,3].

There is already some evidence of MM patients with good hematologic outcomes, low or intermediate risk of relapse and otherwise eligible for kidney transplantation, that have been transplanted with good results [2-6].

We present a case report of a patient with MM that was submitted to kidney transplantation with good renal and haematological outcomes.

3. Case Report

We report a case of a 39-year-old woman of African descendance, with irrelevant past medical history, that was evacuated from her home country (Cape Verde) to the Nephrology Department of Centro Hospitalar Universitário Lisboa Norte in Lisbon, Portugal because of a rapidly progressive renal failure requiring dialysis induction in March of 2015.

The aetiological study performed revealed nephrotic-range proteinuria (4.6g/day), hypogammaglobulinemia, serum immunofixation with a monoclonal band in the Kappa light chain lane, Bence Jones Kappa protein on urine immunofixation, elevated free light chain ratio (288.19mg/L) and beta 2-microglobulin (32.51mg/L), 10% plasma cells in bone marrow aspirate and bone biopsy with monoclonal plasma cells with Kappa chain restriction. Kidney biopsy revealed nodular glomerulosclerosis in a non-diabetic patient. Since the frozen section of the renal biopsy specimen sent for immunofluorescence analysis had no glomeruli, immunofluorescence was performed in the paraffin fragment that showed Kappa chain deposition on the tubular cells' basement membranes. Therefore, MIDD Kappa subsequent to Kappa light chain MM was assumed.

On April 2015, she started VCD (dexamethasone, cyclophosphamide and bortezomib) chemotherapy, which was followed by a complete haematologic response. Consequently, on December 2015 she was submitted to autologous haematopoietic stem cell transplantation with a very good partial response, even though she remained haemodialysis-dependent.

As she remained relapse-free from the time of the stem cell transplant, after a multidisciplinary discussion involving the renal transplantation team, the haematology department and, ultimately, the patient, she was wait-listed for deceased donor kidney transplantation in November 2021.

The patient was submitted to standard criteria deceased donor kidney transplant on February 2nd of 2022. Relevant immunological characteristics were the presence of three HLA mismatches, a panel reactive antibody of 0% and no donor-specific antibodies. Induction was performed with basiliximab, tacrolimus, mycophenolate mofetil and methylprednisolone, as per our kidney transplant unit protocol. The cold ischaemia time was 5 hours and 37 minutes and the warm ischaemia time was 31 minutes. There was immediate graft function and the patient was discharged seven days after the surgery with a serum creatinine of 0.8mg/dL.

She remained on maintenance immunosuppression with tacrolimus, mycophenolate mofetil and prednisolone with a stable renal function (serum creatinine 0.8-1.1mg/dL) and a very good partial response of MM even 12 months after kidney transplant.

Figure 1 illustrates the timeline of events from MIDD diagnosis to present day.

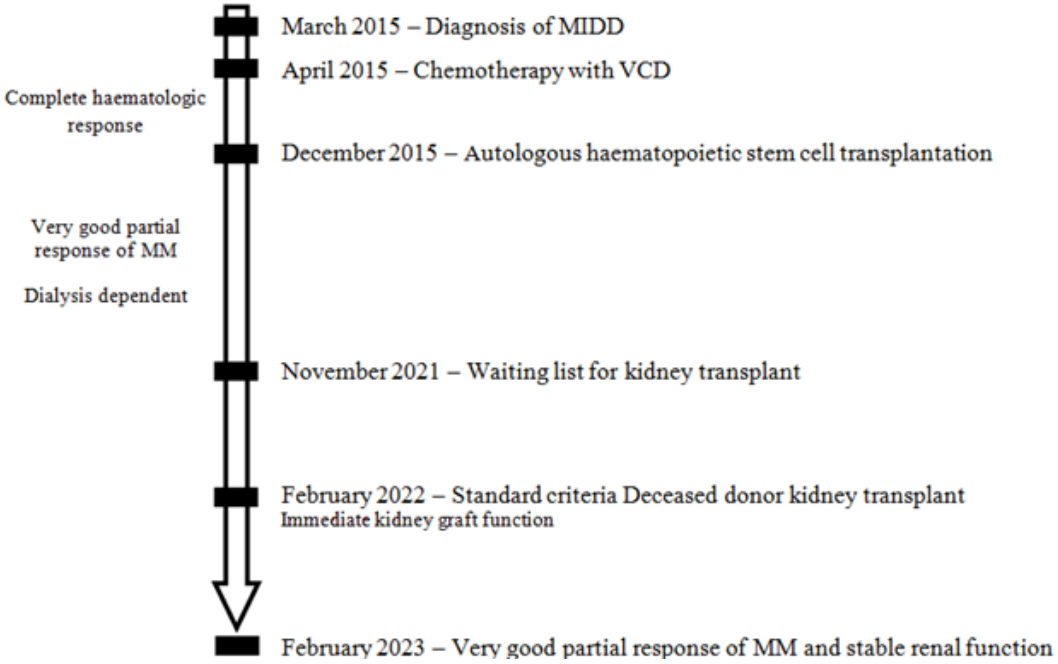

Figure 1: Timeline of events from MIDD diagnosis until present day

4. Discussion

MIDD is the second most common glomerulopathy in MM patients and its treatment, as in several other causes of MM renal injury, is based on the management of the underlying plasma cell neoplasm [1,5].

Modern bortezomib-based regimens followed by autologous stem cell transplantation have revolutionized MM outcomes with significantly better overall survival rates and better kidney outcomes [5]. These results have shifted the paradigm regarding eligibility for kidney transplantation in these patients, from previously contraindicated to now possible in selected patients with good haematological outcomes [2,3].

A retrospective analysis of the Organ Procurement and Transplantation Network/National United Network for Organ Sharing database by Dykes et al. which included 218 kidney transplant patients with MM revealed that these individuals had similar graft and age-matched overall survival compared to the "control" kidney transplanted population [4].

Recent evidence suggests two main strategies to transplant MM patients: 1) non marrow ablative treatment with HLA identical stem cell transplant and kidney transplant from the same donor, and 2) chemotherapy and stem cell transplantation to achieve MM remission followed by kidney transplant [2].

Spitzer's group has treated 13 MM patients using the first strategy, nine of which attained complete remission, however this requires the availability of an HLA-identical donor, thereby limiting its general application [2]. Another caveat of this strategy is that allogeneic bone marrow transplantation is not recommended as first-line treatment for MM [2].

Huskey et al. summarized a series of 14 patients with MIDD treated employing the second strategy, in which 11 had achieved and maintained a complete response of the MM [2]. This approach seems more feasible in the general practice as it does not require an HLA-identical donor and is based on the standard treatment for MM. Molina-Andújar et al. also described six cases of MIDD submitted to kidney transplant after MM treatment (Bortezomib-based, melphalan and autologous bone marrow transplant). Of these, one had a haematologic relapse and two haematologic progression, but only one with MIDD relapse in the graft [4]. The others sustained functional grafts.4 Huskey's group also presented its own experience with four MM patients (three with MIDD) of which three were treated with bortezomib-based schemes [2]. Although they also had recurrence of their MM, one has been in complete remission for three years and has normal renal function, another (that was in partial remission before the kidney transplant) had a kidney graft rejection ten months after the kidney transplant and the last died five and a half years later due to disease recurrence [2].

The authors present a case of a MM patient previously submitted to a bortezomib-based scheme of chemotherapy and autologous stem cell transplant (second strategy) with a very good partial response submitted to kidney transplantation with good renal and haematologic outcomes 12 months after.

Even though there is still a short follow-up, our case is in line with recent evidence regarding this subject. Furthermore, it highlights that nowadays kidney transplantation should be considered in selected MM patients considering not only their clinical characteristics, but also the MM response to the newer treatments that include bortezomib and stem cell transplantation. This emphasizes the fact

that in patients with MM and kidney disease (especially end-stage kidney disease) treatment should warrant a multidisciplinary approach including haematologists.

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