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Double transplant in a patient with multiple myeloma: Bone marrow and kidney

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ABSTRACT

Multiple myeloma (MM) is described as a clonal plasma B-cell hematological malignancy. The proliferation of plasma cells produces monoclonal heavy or light chain proteins. The lytic lesions (also known as salt and pepper pattern) in skull X-Ray are pathognomonic for MM, and can also be found in vertebrae, ribs, pelvis and long bones. This paper reports the case of a 54-year-old female patient with MM initially diagnosed with renal failure, years later multiple myeloma was identified as the etiology of the renal failure. The patient received an autologous hematopoietic stem cell transplant (HSCT) followed by a renal transplant one year later. After 3 years of the HSCT the patient is in complete remission with improved renal function.

Key words: multiple myeloma, renal failure, transplantation.

Trasplante doble en una paciente con mieloma múltiple: médula ósea y riñón

RESUMEN

El mieloma múltiple es una neoplasia hematológica clonal de las células B. La proliferación de las células plasmáticas produce proteínas monoclonales de cadenas pesadas o ligeras. Las lesiones líticas que se encuentran comúnmente en las radiografías de cráneo son patognomónicas de mieloma múltiple, conocidas como lesiones en sal y pimienta que también pueden encontrarse en vértebras, costillas, pelvis y huesos largos. Este artículo comunica el caso de una paciente de 54 años de edad con mieloma múltiple, inicialmente diagnosticada con insuficiencia renal y posteriormente se identificó mieloma múltiple como causante del daño renal. La paciente recibió trasplante autólogo de células madre hematopoyéticas. Un año después se le realizó un trasplante renal. Tres años después del trasplante hematopoyético, la paciente está en remisión completa y con mejoría de la función renal.

Palabras clave: mieloma múltiple, insuficiencia renal, trasplante.

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INTRODUCTION

Multiple myeloma (MM) is defined as a malignant neoplastic B-cell disorder, caused by the proliferation of clonal plasma-cells, which are accumulated in the bone marrow microenvironment.[1,2] Clinically it is characterized with anemia, bone lesions, hypercalcemia and renal dysfunction.[3] Annually the incidence of MM is 4 to 6 cases per 100,000 population.[4] In Mexico, MM represents 4% to 8% of the hematological malignancies. Ninety percent of the patients with this disease are above 50 years.[5]

CASE REPORT

A 54-year-old woman with multiple myeloma was seen in our center to be evaluated and treated. The patient had been well until November of 2010 when kidney disease was developed. Since then, hemodialysis was started. She sought for a second medical opinion because of lack of improvement in renal function, presenting the following clinical picture: nausea, colic pain, constipation, tachycardia, dyspnea, cephalalgia, vertigo, irritability, hematuria, arthralgia and weight loss.

Lytic lesions were found in skull x-ray, MM was suspected (Figure 1). A bone marrow biopsy showed plasma cell neoplasm with expression of CD38, CD138, CD138 and D1 cyclin; with light chain kappa restriction. She went to another medical center where treatment with thalidomide, dexamethasone, allopurinol and sodium bicarbonate was started. Then she was referred to our center. The blood count showed anemia with hemoglobin of 8.9 g/dL. Rouleaux was found in the peripheral blood. Erythrocyte sedimentation rate was elevated. The serum calcium was within normal parameters, and the serum phosphorus value was elevated (3.1 mEq/L). The lactate dehydrogenase showed a value of 215 IU/L. Renal function was normal.

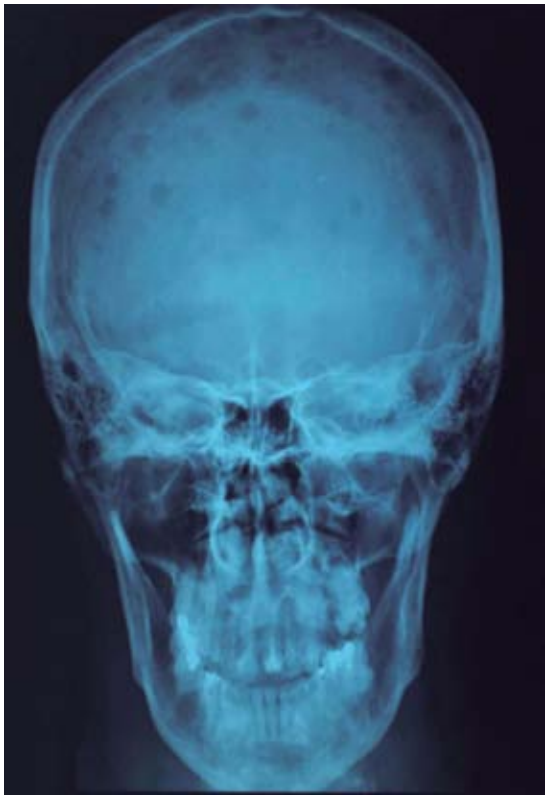

Figura 1. Lytic lesions in skull x-ray.

Paraproteinemia was detected by electrophoresis. Light kappa chains of monoclonal type were quantified by immunofixation in serum and urine. Molecular analysis demonstrate deletion of 13q by FISH, β_2-microglobulin 25.76 mg/L. Urinalysis showed proteinuria and was detected light kappa chain of monoclonal type in the protein electrophoresis urine analysis.

The patient was transfused in 1988 due to a complication in birth labor. In February 2011 she was diagnosed with hepatitis C virus (HCV). No treatment was recommended, because of the low viral load. She had no other abnormalities in the physical exam.

The diagnosis of multiple myeloma was confirmed. The treatment was modified to thalidomide, dexamethasone and bortezomib. The patient was stable during a year with this scheme plus the hemodialysis program mentioned.

One year later, an autologous hematopoietic stem cell transplant (HSCT) was performed. One dose of 200 mg/m^2 IV of melphalan was administrated. The autologous transplant was performed, under the protocol of our hematological center.[6] The patient received 0.8 x 10^6 CD34 cells/kg. Recovering platelets and granulocytes on day +12.

She continued the hemodialysis scheme of two sessions per week. Fifteen days after the graft eritropoyetin was administrated for six weeks. Seven months after the HSCT, it was necessary to administrate intravenous iron due to iron deficiency anemia. In March of 2015 a renal transplant was performed from her sibling.

DISCUSSION

About 20-40% of MM patients are commonly affected by renal failure at diagnosis and 20% of the patients have already kidney damage.[7] In this patient renal failure was diagnosed before MM diagnosis and she had been in hemodialysis during 7 months. There are several variables described in the literature that predict renal recovery after HSCT, among others a requirement of hemodialysis for less than six months and prior autologous HSCT.[8]

Renal failure in patients with MM is a result of damage caused by the toxic effects that monoclonal light chains produce to renal structures, mainly in tubules and glomeruli. Also hypercalcemia is a cause of renal damage. It is remarkable in this case because it was found that the patient had hyperphosphatemia which is a pathologic effect related to renal failure, and this produce a depletion of calcium. This could be the reason why the patient did not have hypercalcemia.

Renal biopsy was performed before the diagnosis of MM and before the arrival of the patient to the hematology center. Patients whom proteinuria consists mainly of light chains, renal biopsy is not justified.[7] The histopathological findings in the pathology report of the renal biopsy were not compatible with myeloma nephropathy. Light chain depositions or amyloidosis were not detected.

The treatment of MM depends on the age and physical status. In patients under 65 years autologous HSCT is considered a consolidation treatment after obtaining a complete remission with chemotherapy. For the patient described here, the induction therapy was selected to have the best results as possible and included bortezomib, thalidomide and dexamethasone.[2] It has been described that a high dose melphalan, plus autologous stem-cell transplantation, prolong progression free and overall survival in MM.[9]

For the maintenance during 2 years before the renal transplant, the patient received thalidomide combined with a glucocorticoid (in this case dexamethasone), because it has shown to improve the progression free survival.[10] Thalidomide has shown to improve the rates of remission and also the progression-free survival.[4] Bortezomib was considered maintenance treatment. This agent was selected because of the evidence that using bortezomib as maintenance is the best choice when renal failure is present.[10]

In the literature there are several positions and points of view regarding the timing in which the renal transplant and the HSCT are performed. The renal allograft usually is not the first choice, due to the limited number of donors available. Leung et al reported a study based on 6 patients with renal failure due to primary amyloidosis

on whom renal allografts were performed before the HSCT, 5 of those patients had a positive outcome with no complications. Some authors state that there are better results when the renal transplant is performed before the HSCT, the main argument supporting this hypothesis is that with this approach the introduction of a healthy kidney prior to HSCT is more resistant to injury from chemotherapy and facilitates appropriate medication dosage to the patient.[11]

On the majority of patients with MM treated with both HSCT and kidney transplant, the renal transplant was performed first, followed by the HSCT.[12-14]

HSCT followed by kidney transplantation was first described in 2006 by Khoriaty and coworkers.[15] In that case the authors decided to start treatment with stem cell transplantation and follow-up the patient to seek for renal function improvement. Then they proceeded with a renal transplantation that achieved a better renal function with no complications. To our knowledge, this patient represents the 8th case reported with MM treated with autologous HSCT followed by kidney transplant.[16]

In this case, the HSCT was performed initially in order to treat the MM. Since the patient was already on hemodialysis and the HSCT could represent a potential damage for the renal function, the kidney transplantation was decided to be done after the possible kidney injury induced by chemotherapy and immunosuppression, as reported on a similar case by Beitinjaneh et al (2009).[17] It was also decided to be done after to assess for regression of renal damage that has been previously reported.[8]

Currently the patient is in complete remission, the renal function remains stable without renal graft rejection. She is receiving tacrolimus, prednisone and thalidomide.

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