

Skull Mass as the First Manifestation of Recurrent Multiple Myeloma in a Renal Transplant Patient

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Abstract

Background: Although there are a few reports of recurrence of multiple myeloma in the transplanted kidney, recurrence of multiple myeloma (MM) presenting, as an isolated lesion in the brain, has been reported rarely.

Case Report: Here we present a 60-year-old woman who underwent a kidney transplantation following a rise in her BUN and creatinine, having shown advanced tubulo-interstitial nephritis in her native kidney microscopic biopsy examination. Two years following her renal transplantation, she presented with a skull mass which was regarded as a possible meningioma. A biopsy of her transplanted kidney was performed due to her constantly raised BUN/Cr which revealed "Myeloma cast nephropathy".

Conclusion: We describe an unusual presentation of recurrent multiple myeloma, as a brain mass mimicking meningioma and simultaneously in the transplanted kidney, and discuss the differential diagnosis of the patient's primary disease.

Keywords: Renal pathology, Multiple myeloma, Kidney transplantation.

Introduction

Multiple myeloma (MM) is a malignant disorder of plasma cells that produce monoclonal immunoglobulin. The disease is characterized by anemia and monoclonal gammopathy.^{1,2} about 20-50% of patients with MM show some degrees of renal insufficiency and "cast nephropathy" is the major cause of renal failure in these patients.^{3,4} Aggregation of free light chain (FLC), which filtrated into glomerule and Tamm-Horsfall protein (THP) in renal tubules, is the cause of FLC toxicity in "cast nephropathy" caused by MM.⁵ Herein, we report the case of a 60-year-old white woman presenting MM who initially underwent renal transplantation by misdiagnosis and finally a rare recurrence of primary disease, making the proper disease management clear.

Case Report

A 60-year-old white woman was admitted to Alzahra

hospital (Isfahan, Iran) with the chief complaint of vomiting accompanied by nausea and flank pain. In her history, she had undergone renal transplantation due to "Advanced tubulo-interstitial nephritis" two years ago, and after transplantation she was started on cyclosporine, cellcept and prednisolone.

In her recent body status, renal function was evaluated by measuring BUN/Cr and both were elevated (BUN: 80 mg/dl, Cr: 1.8 mg/dl) while plasma cyclosporine level and the electrolyte levels were all in the normal range. The patient's serum albumin was 3.1 g/dl and she had a 2+ protein in her urine sample. Ultrasonography revealed enhanced parenchymal echogenicity, diminished corticomedullary differentiation, and a solitary upper pole cortical cyst.

She felt the sensation of a foreign object in her brain; so a consultant neurologist suggested a radiological investigation of her skull, which revealed an extra-axial mass. The MRI report revealed a diagnosis of possible meningioma, which would warrant a craniotomy and resection of the tumor (Figure-1).

A biopsy of the transplanted kidney was undertaken and

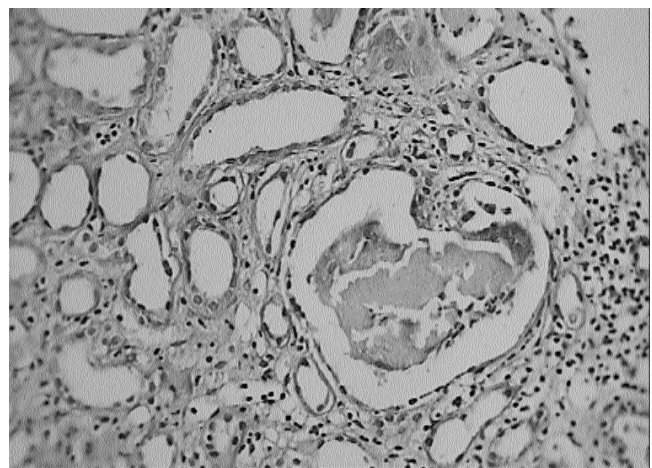


Figure-1: Tubular cast, containing neutrophils, lymphoplasmacytic infiltration in the interstitium and a multinucleated giant cell.

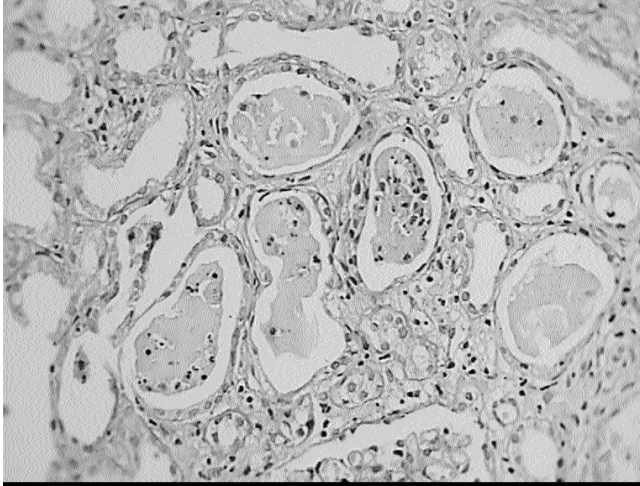


Figure-2: Tubular casts, containing neutrophils, lymphoplasmacytic infiltration in the interstitium.

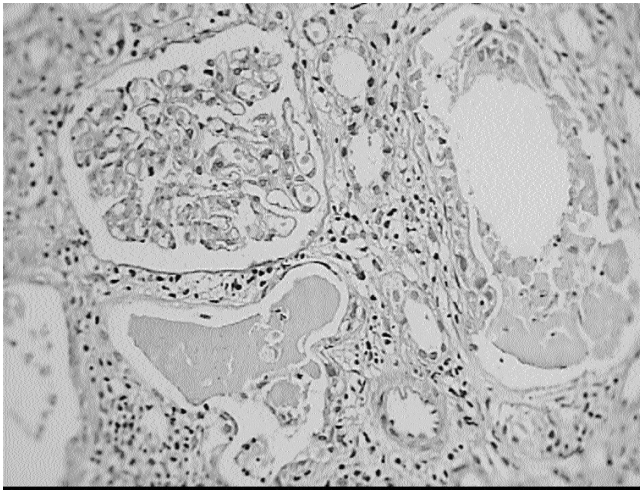


Fig 3: Tubular cast, containing neutrophils, lymphoplasmacytic infiltration in the interstitium. The glomerulus is intact.

we reviewed paraffin embedded formalin fixed sections, stained with Hematoxylin and Eosin (H&E), Periodic acid Schiff (PAS), Jones and Masson trichrome in which, 46 glomeruli were present with no conspicuous changes by light microscopy. There was patchy mild to moderate interstitial fibrosis and mild edema with an accompanying diffuse moderate lymphoplasmacytic cells and neutrophil infiltration. Some tubules contained typical large/elongated brittle casts with fractures and giant cells at both ends and some casts contained neutrophils. Occasionally multinucleated giant cell reaction was seen in the interstitium (Figures 2-4).

Immunofluorescence for IgG, IgA, IgM, C3, C4, C1q and fibrin showed no significant staining and the diagnosis of "Myeloma cast nephropathy" was made by nephro-pathologist. Soon after, bone marrow aspiration and vertebral bone biopsies

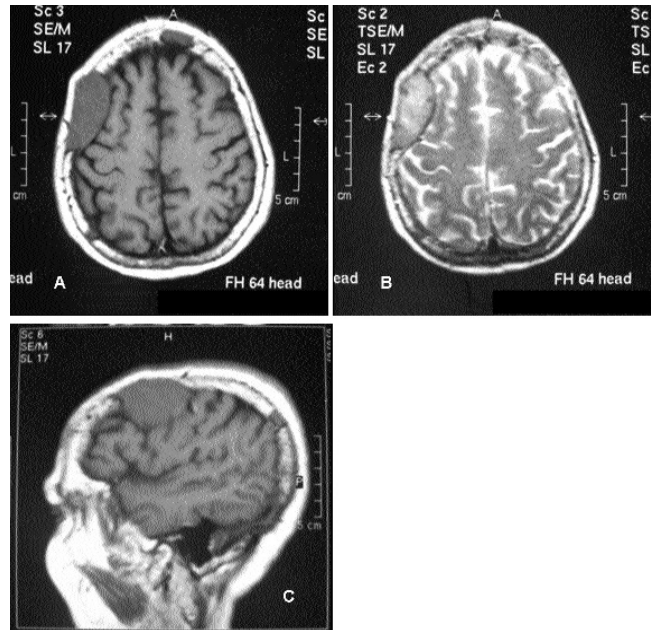


Figure-4: Axial T1 and T2 weighted (A, B), and sagittal T1 weighted (C) MRI images: There is a frontal high convexity, extra-axial lesion at the right side. It is isosignal with the gray matter in T1 and T2 weighted sequences. No adjacent gliosis is noted. One may presume it as meningioma.

were performed and during microscopic evaluation, diffuse neoplastic proliferation of plasma cells was observed. These cells had a scanty cytoplasm with moderately large and peripherally located nucleus. In immunohistochemical (IHC) staining, these cells showed diffuse positivity for CD 138. Serum protein electrophoresis showed monoclonal proteins (M proteins) in the blood.

Rouleaux formation was clearly seen in her peripheral blood smear (PBS). The previous sections of her native kidney biopsy (which was initially reported on 2 years before this episode) was reviewed again which suggested the main differential diagnosis of "Myeloma cast nephropathy".

The patient was referred to the oncology team and she was started on dexamethasone, underwent plasma pheresis, and because of the advanced stage of the disease, the immunosuppressive agents were discontinued. Thalidomide was also added to the treatment regimen and the brain lesion began to regress. The patient was scheduled for permanent dialysis (three times a week). Three-year follow-up patient did not show any similar condition or recurrence of disease.

Discussion

Management of myeloma cast nephropathy is a medical emergency, because of its poor prognosis, when a patient become dialysis dependent (about 3.5 months).⁶

Renal failure, caused by "FLC and THP cast", may be the first and sometimes the only clinical manifestation of MM. These casts are surrounded by macrophage and multinucleated

giant cells in tubules which may lead to tubular rupture and finally results in tubulointerstitial nephritis.^{7,8}

Saline volume expansion, alkalization of urine, treatment of hypercalcemia and hyperviscosity, dialysis as indicated, and chemotherapy are the treatments of choice for "cast nephropathy".⁹

There are few reports of MM recurrence after transplantation.⁴ In patients, who has renal insufficiency due to high-grade MM, renal transplantation is not a good choice of therapy because of impaired immune surveillance, susceptibility to viral infection (especially Epstein Barr virus), chronic antigenic stimulation due to the presence of foreign allograft antigens, cytokines such as IL-6 and IL-10, and direct effect by immunosuppressants like azathioprine.¹⁰ At present, renal transplantation is recommended for MM patients who are in complete remission or for those with a low-grade disease.^{11,12}

Plasmacytomas involving the skull are rare¹³ and in our search of literature, only one case of recurrent multiple myeloma, presenting as a skull base mass was found,¹⁴ and there is no report of recurrent MM after transplantation as a skull mass.

Several years ago, renal transplantation was done in MM patients because of limited data on outcome of transplantation and suggestion of Sammett et al. was a reference for physicians to do transplantation¹⁵ but Husein et al., presented recurrence of MM in a patient who was undergone renal transplantation and allograft function was deteriorated by myeloma cast nephropathy which showed the original face of myeloma cast nephropathy and its risk of recurrence.¹⁴ Another report of transplantation in a MM patient showed recurrence of MM¹⁰ and these days transplantation is not a fine therapy for MM patients who are not at the complete remission.

Conclusion

We report a case of MM whom initially diagnosed as tubulointerstitial nephritis and renal transplantation was done for her; but recurrence of MM (that did not diagnosed before transplantation) as a skull mass and also deterioration of kidney

graft function clear the original pathologic process of her disease. This is the first case of recurrent multiple myeloma after transplantation presenting as a skull mass. So, we would like to emphasize that pathologists should consider "myeloma cast nephropathy" as a differential diagnosis in patients with "tubulointerstitial nephritis".

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