

Relapsed Extramedullary Multiple Myeloma Presenting as Bilateral Solid Perirenal Masses

Thomas Rau and Aya Kamaya, M.D.

We present a patient with IgA myeloma who responded well to chemo-radiation therapy. The patient subsequently underwent autologous followed by nonmyeloablative allogenic bone marrow transplant and relapsed after six years in an unusual manner with extensive extramedullary disease with bilateral perirenal involvement. The highly variable expression of myeloma at relapse highlights the importance of individualized follow-up and periodic imaging for early detection of relapse.

Introduction

Multiple myeloma is a neoplastic disorder caused by proliferation of B lymphocyte plasma cells that gives rise to a clone of immunoglobulin-secreting cells. Renal failure, osteolytic lesions, and hypercalcemia are typical and the result of overproduction of immunoglobulins and osteoclast activating factors by tumor cells. No curative treatment currently exists. Current trials with autologous hematopoietic cell transplantation followed by nonmyeloablative allogeneic hematopoietic cell transplantation have been shown to reduce transplant related mortalities and provide longer disease free remissions [1]. Relapse typically mani-

festes as impairment of bone marrow function and increases in monoclonal antibodies (M-protein). However, relapse without a concomitant increase in M-protein has been reported and associated with poorly differentiated plasma cells and an aggressive clinical course [2]. Extramedullary plasmacytoma as a mode of relapse is highly unusual. To our knowledge, this is the first reported case of myeloma recurrence with extramedullary plasmacytoma and bilateral perirenal involvement after having undergone autologous and nonmyeloablative allogeneic hematopoietic cell transplantation.

Case Report

A previously healthy 54-year-old man presented with a two-month history of low back pain which started after mild lifting. A work-up revealed an elevated total protein of 11.7 g/dL and serum protein electrophoresis with a beta-2 spike of 6.6 g/dL. A quantitative immunoglobulin test returned abnormal with an IgA of 6350, IgD of 404, and an IgM of 15 mg/dL. Diffuse osteopenia, multiple skull lucencies and one mid-humeral right 5 mm lucency were revealed by a metastatic bone survey. Further work-up included an MRI that demonstrated T5, T12, and L2 compression fractures and a bone marrow biopsy showed hypercellular marrow, trilineage hematopoiesis, and 50%

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Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging

Thomas Rau (Email: tomjrau@gmail.com) is at the Rosalind Franklin University of Medicine and Science, Chicago Medical School, North Chicago, IL 60064, United States of America.

Aya Kamaya, M.D. (Email: kamaya@stanford.edu), is in the Department of Radiology, Stanford University Medical Center, Stanford University, Palo Alto, CA 94305, United States of America.

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involvement with myeloma cells. The work up supported a diagnosis of stage IIIa IgA multiple myeloma.

Radiation therapy was instituted for vertebral lesions T12 through L2. Afterwards, he completed six cycles of vincristine, adriamycin, and dexamethasone chemotherapy and received thalidomide resulting in a reduction of his M-protein from 3.6 to 0.2 grams. A year later the patient underwent an autologous hematopoietic stem cell followed by nonmyeloablative allogeneic cell transplant. His course following transplant was complicated by chronic graft-versus-host disease involving his mouth, eyes, skin, nails and esophagus. Symptoms were managed well with immunosuppressive therapy though his course was complicated by steroid induced diabetes, cataracts, and episodes of cytomegalovirus esophagitis. A bone marrow biopsy two years post-transplant confirmed that his myeloma was in remission.

After a six-and-a-half year disease-free period the patient re-presented at age 60 years with low back pain and increasing fatigue. He was found to be anemic and physical exam revealed a subcutaneous skin nodule on his back. A fine needle aspiration of the mass revealed plasma cells consistent with extramedullary plasmacytoma which was diagnostic for multiple myeloma relapse. CT showed bilateral perirenal masses (Fig. 1) not seen on previous imaging two years prior (Fig. 2). Paraspinal masses, a small mass anterior to the stomach, and subcutaneous masses with heterogeneous attenuation similar to the perirenal masses were also seen (Fig. 1). Given the biopsy results of the subcutaneous mass, its imaging similarities to the other masses, and their simultaneous appearance, the new lesions

most likely represented extramedullary lesions rather than primary neoplasms and no further biopsies were performed.

An elevated M-protein of 1.5 gms was measured and a bone marrow aspirate revealed trilineage hematopoiesis and left shifted myelopoiesis. Bone marrow biopsy showed less than 5% plasma cells but kappa light chain restriction. These findings were consistent with relapsed multiple myeloma with progression to multiple extramedullary plasmacytomas.



Figure 1A. 60-year-old man with relapsed multiple myeloma. CT demonstrates a small mass (short arrow) anterior to the stomach.



Figure 1B. CT demonstrates new perirenal mass (long arrow) and subcutaneous mass (arrowhead).



Figure 1C. CT demonstrates bilateral perirenal masses (long arrows) with heterogeneous attenuation.

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Discussion

The case described is of a patient with IgA multiple myeloma who responded well to radio-chemotherapy and underwent autologous followed by nonmyeloablative allogeneic bone marrow transplant. He relapsed after six years with progression to multiple extramedullary plasmacytomas. Despite minimal clinical symptoms, the patient had developed widespread soft tissue tumors affecting both kidneys, abdomen, and subcutaneous space.

The development of gross extraosseous soft tissue masses is highly unusual except in the rare variant of IgD myeloma and is most striking in our patient's mode of relapse [8]. An extensive literature search found only a few case reports of multiple myeloma progressing with similar features. Foucar, Davies, and Suchman each reported cases of multiple myeloma which progressed to extensive extramedullary disease at multiple sites and maintained anaplastic histologic features [2,4,5]. In our case, relapse was associated with widespread extramedullary mass lesions including bilateral perirenal masses and an immature plasma cell differentiation supporting the theory that an aggressive anaplastic variant of multiple myeloma may exist [2]. Interestingly, our patient was largely asymptomatic at the time of relapse. Despite impressive widespread mass lesions affecting both kidneys, our patient only complained of back pain and fatigue, and he denied any urinary symptoms. However, histologic grading has not always predicted the aggressiveness of the disease. Jowitt reported a case of multiple myeloma that relapsed

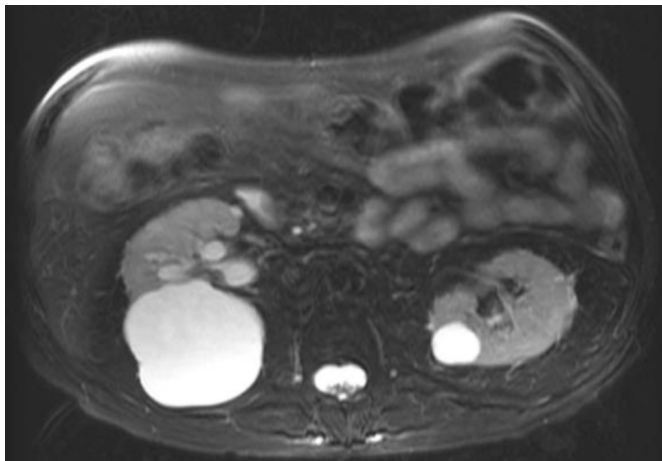


Figure 2. MRI from two years prior to relapse showed only simple cysts bilaterally but no masses in the perirenal spaces.

with prominent extramedullary abdominal tumors and a fulminant course despite maintaining a well differentiated plasmacytoid form [6]. Thus, other factors that do not manifest histopathologically may determine the aggressiveness of the disease.

Extramedullary plasmacytoma is a rare variant of plasma cell tumors constituting about 3% of all cases as a primary lesion. It is distinguished from multiple myeloma by the absence of bone marrow infiltration, osteolytic lesions, hypercalcemia, renal insufficiency, and a urinary or serum M-protein level less than 2 g/dL. About 80% of lesions occur in the head and neck with localized disease whereas those occurring elsewhere including the gastrointestinal tract tend to present in a disseminated manner [3,10]. Though the plasma cell dyscrasias are related, the clinical course and prognosis differ. This unusual variant tends to proceed with a more benign course with rare progression to multiple myeloma and a median survival of 10 years. The extramedullary lesions also tend to be controllable with surgical resection and local irradiation [7].

Our patient's disease evolution is interesting in that its relapse was associated with bilateral solid perirenal masses as well as other solid masses, a pattern of spread usually seen in primary extramedullary plasmacytoma. However, the relatively benign nature of primary extramedullary plasmacytoma compared to that seen in extramedullary plasmacytoma during relapse of multiple myeloma suggests that these are different clinical entities.

Indeed, the pattern of relapse following treatment for multiple myeloma portends a different clinical course and prognosis. A recent study by Alegre et al studied 280 patients with relapse after autologous peripheral stem cell transplant for multiple myeloma and found a very heterogeneous pattern of relapse [9]. Fourteen percent progressed with one or more extramedullary plasmacytomas, 18% were associated with an insidious rise in M-protein, 2% with plasmacytic leukemia, while the remaining 66% relapsed with classic myeloma with new osteolytic lesions. The authors speculate that these different modes of expression could be due to clonal selection following intensification therapy and the persistence of a resistant clone.

The highly variable modes of relapse following treatment for multiple myeloma highlights the importance for an individualized approach for follow up monitoring. Since the elevation of M-protein and presence of clinical symptoms are unreliable indicators of disease remission, the need for periodic imaging may be necessary to detect early relapse.

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References

1. Maloney DG, Molina AJ, Sahebi F, et. al. Allografting with nonmyeloablative conditioning following cytoreductive autografts for the treatment of patients with multiple myeloma. *Blood*. 2003 Nov 1;102(9):3447-54. [PubMed]
2. Davies SV, Jones B, Starkie CM, Murray JA. Bulky extramedullary plasmacytomata: rare mode of relapse in myelomatosis. *J Clin Pathol*. 1989 Mar;42(3):246-9. [PubMed]
3. Wiltshaw E: The natural history of extramedullary plasmacytoma and its relation to solitary myeloma of bone and myelomatosis. *Medicine (Baltimore)*. 1976 May;55(3):217-38. [PubMed]
4. Suchman AL, Coleman M, Mouradian JA, Wolf DJ, Saletan S. Aggressive plasma cell myeloma. A terminal phase. *Arch Intern Med*. 1981 Sep;141(10):1315-20. [PubMed]
5. Foucar K, Raber M, Foucar E, et. al. Anaplastic myeloma with massive extramedullary involvement: Report of two cases. *Cancer*. 1983 Jan 1;51(1):166-74. [PubMed]
6. Jowitt SN, Jacobs A, Batman PA, Sapherson DA. Atypical progression of multiple myeloma with extensive extramedullary disease. *J Clin Pathol*. 1994 March; 47(3): 269-271. [PubMed]
7. Knowling MA, Harwood AR, Bergsagel DE. Comparison of extramedullary plasmacytomas with solitary and multiple plasma cell tumors of bone. *Journal of Clinical Oncology*. 1983 Apr;1(4):255-62. [PubMed].
8. Jancelewicz Z, Takatsuki K, Susai S. IgD multiple myeloma. Review of 133 cases. *Arch Intern Med*. 1975 Jan;135(1):87-93. [PubMed]
9. Alegre A, Granda A, Martnezchamorro C, et. al. Different patterns of relapse after autologous peripheral blood stem cell transplantation in multiple myeloma: Clinical results of 280 cases from the Spanish Registry. *Haematologica*. 2002 Jun;87(6):609-14. [PubMed]
10. Tong D, Griffin TW, Laramore GE, et. al. Solitary plasmacytoma of bone and soft tissues. *Radiology*. 1980 Apr;135(1):195-8. [PubMed]
11. Maslovsky I, Lugassy G, Blumental R, Ducach A, Yehuda O, Abeliovich D. Multiple chromosomal abnormalities in fulminant anaplastic myeloma. *Clin. Lab. Haem.* 1999 Jun;21(3):207-10. [PubMed]
12. Ooi GC, Chim JC, Au WY, Khong PL. Radiologic manifestations of primary solitary extramedullary and multiple solitary plasmacytomas. *AJR*. 2006 Mar;186(3):821-7. [PubMed]