Rapid Progression of Solitary Plasmacytoma to Multiple Myeloma in Lumbar Vertebra

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The prognosis of solitary plasmacytoma varies greatly, with some patients recovering after surgical removal or local fractional radiation therapy, and others progressing to multiple myeloma years later. Primary detection of progression to multiple myeloma is important in the treatment of solitary plasmacytoma. There have been several analyses of the risk factors involved in the early progression to multiple myeloma. We describe one case of solitary plasmacytoma of the lumbar vertebra that was treated with surgical decompression with stabilization and additional radiotherapy. The patient had no factors associated with rapid progression to multiple myeloma such as age, size, immunologic results, pathological findings, and serum free light chain ratio at the time of diagnosis. However, his condition progressed to multiple myeloma less than two months after the initial diagnosis of solitary plasmacytoma. We suggest that surgeons should be vigilant in watching for rapid progression to multiple myeloma even in case that the patient with solitary plasmacytoma has no risk factors for rapid progression to multiple myeloma.

Key Words : Solitary plasmacytoma · Serum free light chain · Multiple myeloma · Lumbar vertebrae.

INTRODUCTION

Solitary plasmacytoma (SP) is defined as a solitary mass of neoplastic plasma cells, and can be classified into 2 types according to location: skeletal and non-skeletal plasmacytoma. The clinical outcome of SP varies greatly; many patients are cured with the appropriate therapy but some patients develop disseminated multiple myeloma (MM) years later. Radical radiotherapy and alternative surgery are treatment modalities producing sufficient local control. However, despite these treatments, 50-60% of patients with SP progresses to MM. Regarding time to progression, Knobel et al. reported that median time to MM development from skeletal SP was 21 months with a 5-year probability of 51% and Bertanha et al. analyzed the average time was 41 months. Thus, identifying the predictors associated with plasma cell malignant proliferation, in addition to the primary detection of aggravation of the SP are crucial in the management and survival of patient. In general, clinicians assume that patients with SP who do not have profiles consistent with progression to multiple myeloma will be eventually cured, or will progress to MM only slowly.

This report describes a case of SP of the lumbar vertebra without progression factors, which developed into MM less than two months after initial diagnosis despite appropriate treatment. We also review previous reports on the related factors involved in disseminated MM.

CASE REPORT

A 48-year-old man visited the neurosurgery department for right leg pain. He had experienced low back pain and hyperesthesia in the right leg for six weeks without a trauma history. One week prior to presentation, he experienced right hip flexion weakness. Neurological evaluation revealed right hip flexion (G3/5) and extension weakness (G4/5), and the patient showed an abnormal increased sensitivity in the right leg L3 dermatome, and he had continuous lower back pain with tenderness.

Computed tomography (CT) scanning and magnetic resonance imaging (MRI) showed a geographic osteolytic lesion in the right mid-posterior element of the L3 vertebra and the right psoas muscle, and an epidural mass with dural sac compression (Fig. 1A, B). Subsequently, the patient underwent...
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We performed a total corpectomy of L3 to remove the destructive column and dural sac mass and stabilized the vertebrae with an expandable interbody cage (Synex System®, SYNTHES, USA) and posterior pedicle screw fixation L1/2/4 (Varian medical system®, VARI-ANS, USA) (Fig. 2). The patient’s neurologic symptoms were improved to normal neurologic function after surgery.

Histological diagnosis of the resected tumor was plasmacytoma. The immunohistochemical (IHC) staining of the neoplastic plasma cells revealed only weak Immunoglobulin (Ig) kappa chain restriction and CD138 positive expression (Fig. 3A). Bone marrow aspiration biopsy was performed when the plasmacytoma was diagnosed, and normal marrow proliferation was observed. Serologic studies of immunofixation and protein electrophoresis revealed weak monoclonal gammopathy, IgG-kappa type. The serum free light chain (SFLC) ratio was 1.16 (normal reference range; 0.26-1.65). The patient had no rapid progression factors and underwent local fractional radiotherapy (RT) at a dose of 45 Gy.

Less than two months after pathologic diagnosis, he noted a painful, soft mass, 3×3 cm in diameter in the left wrist. There was also a palpable right inguinal mass. A repeat PET/CT also demonstrated multiple bony masses with moderately increased FDG uptake in the left distal ulna, right parietal skull, right and left clavicle, right and left humerus, sternum, left 8th rib, right and left ilium, left acetabulum, and left proximal femur, due to spread of malignant tumor. A soft tissue mass with increased FDG uptake was noted in the right proximal thigh with lymph node enlargement seen in the right and left external iliac, left pericolic, and right inguinal lymph nodes (Fig. 4). The right inguinal mass was excised for evaluation for multiple myeloma, and IHC staining of the mass revealed a strong kappa chain positive reaction. The mass was CD138 positive and there was high proliferative activity of Ki-67 detected. The SFLC ratio was elevated to 32.3.

The patient was diagnosed with MM and underwent adjuvant chemotherapy, and thalidomide and dexamethasone were administered.

**DISCUSSION**

Solitary plasmacytoma of bone (SPB) represents only 5% of all plasma cell malignancies and is a heterogenous condition. Some patients have only solitary bone lesion, while others progress to MM. The usual presentation of this is with bone pain; however, 25% develop neurological dysfunction in the form of cord or nerve root compression. The diagnosis of SPB requires the presence of a solitary bone lesion confirmed by skeletal survey including bone scan or PET/CT, abnormal plasma cell proliferation proven by bone marrow or tissue biopsy and lack of proof of organ dysfunction.

Radiotherapy is considered the treatment of choice for SPB. Knobel et al. confirmed favorable local disease control with radiotherapy alone in their review of 206 patients with SPB.
cal relapse occurred in 21 (14%) out of 148 patients who received radiotherapy alone compared with 4 (80%) out of 5 patients who were treated with surgery and chemotherapy. Previous studies recommend radiotherapy for SPB encompassing the tumor volume shown on MRI with a margin of at least 2 cm and treating to a dose of 40 Gy in 20 fractions with a higher dose of 50 Gy in 25 fractions being considered for SPB>5 cm40.

Recently researchers evaluated the outcomes of over 125 patients with SP receiving only radiation therapy as initial treatment. Radiation controlled the local plasmacytoma in over 90% of the patients. Recurrences occurred in only 20% of patients who showed a disappearance of immunoglobulin (M-protein) following treatment with radiation. Patients who did not show a decrease in M-protein levels following radiation therapy had a 60% chance of recurrence. This result was compared to other reports evaluating the outcome of patients with SP who received both chemotherapy and radiation as initial treatment. The addition of chemotherapy to radiation therapy revealed no overall benefit regarding the rate of progression to MM40.

Surgery (“radiotherapy” versus “surgery and radiotherapy”) did not affect the 10-year probability of local control40. Therefore, surgical resection is not indicated for SPB, but some patients may require neural decompression, spinal stabilization because of their neurologic compromise or structural instability41,24. This patient complained of right leg monoparesis with difficulty in ambulation and lumbar MRI revealed epidural mass with dural sac compression of L3. He underwent surgical decompression with stabilization of L1/2/4 using pedicle screws.

According to the mostly used Durie and Salmon (DS) staging system, SPB is regarded as Stage I myeloma. In 2005, the international myeloma staging system (ISS) was announced which divides DS stage I patients into three further stages41. This patient belonged to DS Stage IA and ISS Stage I: this stage is defined as showing mildly increased serum beta 2-microglobulin and normal serum albumin. The natural course of Stage I when traced over a 10-year follow-up period demonstrates four patterns of prognosis. These are development of MM (65%), local recurrence (12%), dissemination to a new solitary lesion (15%), and cured. Regarding times to progression to MM, there is a wide month range. The average median time is 24 to 36 months9,13,16,20. Knobel et al.13 reported it was 21 months (range : 2-135), and Bertanha et al.19 announced it is 41 months (range: 1.5-120). Less than two months, rapid progression to MM in SP of DS stage IA and ISS stage I without potential dissemination factors is a rare condition.

For the difficulty in predicting prognosis, most patients need further follow-up to detect possible progression of SP and monitoring with regular serum or urine immunologic studies. There are several reports on the potential risk factors that influence the frequency of progression to MM.

Knobel et al.13 found that younger patients, especially with vertebral localization, had the better outcome when treated with moderate-dose (30 Gy) RT. Kilciaksiz et al.12 reported that younger age was an independent good prognostic factor for progression to MM. Lesion size was reported as one of the prognostic features for conversion of SPB into MM. Tsang et al.27 showed that patients with a mass size <5 cm had a local control rate of 100%, while for patients with larger tumors, the rate reached was almost 40%. In this case, the disrupted soft mass was about 4 cm in diameter. The optimum RT dose of treatment of SPB has not been established20 but local failure has not been observed in the patients who received 45 Gy or more to the isolated lesion15,27. Following RT application, persistent myeloma protein was an adverse prognostic factor. In most SPB patients, the myeloma protein level has a key role in the primary detection of MM13,16,19,20. Pathological factors have been investigated in some studies. The existence of a high level of angiogenesis is linked to a poor outcome. Kumar et al.16 examined whether increased angiogenesis may help to identify the patients likely to progress to myeloma.

Recently, an abnormal SFLC ratio has been shown to be a powerful prognostic factor in determining the risk of progression to MM at the time of the initial diagnosis in patients with SP12,23. To assess clonality, Dingli et al.23 used the ratio of kappa-lambda light chain levels and reported that patients with an abnormal FLC had a higher incidence of monoclonal protein in the urine and a larger se-

Fig. 4. A repeated PET/CT reveals disseminated multiple bony lytic lesions with increased FDG uptake.

**Table 1.** Factors relating to early progression of solitary plasmacytoma to multiple myeloma

| Related factors          | Rapid progression | Non-rapid progression |
|-------------------------|-------------------|-----------------------|
| Age                     | Above 55 years old| Below 55 years old    |
| Lesion size             | >5 cm             | <5 cm                 |
| Radiotherapy dose       | Below 45 Gy       | Above 45 Gy           |
| Myeloma protein         | Spike             | Resolution            |
| Serum free light chain  | Increased         | Normal*               |
| Pathologic angiogenesis | High-grade        | Low-grade             |

*Normal reference of serum free light chain ratio : 0.28-1.65
rum M spike. We have summarized the generally accepted early progression factors (Table 1).

The likelihood of surgery-induced dissemination may be a considerable risk factor. The surgical procedure itself reduces progression factors (Table 1). We have summarized the generally accepted early progression factors.

CONCLUSION

Though patients presenting with solitary plasmacytoma may have no risk factors for developing MM, we suggest that surgeons should be always be aware of the potential for rapid progression to MM from the time of the initial diagnosis.

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References

1. Bertanha F, Boufelli G, de Camargo OP, Baptista AM, Caiero MT, de Oliveira CR, et al.: Oncologic progression of bone plasmacytomas to multiple myeloma. *Clinics (Sao Paulo)* 61 : 139-146, 2006

2. Brivio F, Gilardi R, Bucovec R, Ferrante R, Rescalani R, Vigoré L, et al.: Surgery-induced decline in circulating dendritic cells in operable cancer patients: a possible explanation of postoperative immunosuppression. *Hepatogastroenterology* 47 : 1337-1339, 2000

3. Cappuccio M, De Jure F, Gasbarriti A, Bandiera S, Boriani S: Solitary plasmacytoma of the spine: a 22 years follow-up case report. *Eur Rev Med Pharmacol Sci* 10 : 251-256, 2006

4. Chakraborti C, Miller KL: Multiple myeloma presenting as spinal cord compression: a case report. *J Med Case Rep* 4 : 251, 2010

5. Dimopoulos M, Kyle R, Fermund JP, Rajkumar SV, San Miguel J, Chan-an-Khan A, et al.: Consensus recommendations for standard investigative workup: report of the International Myeloma Workshop Consensus Panel 3. *Blood* 117 : 4701-4705, 2011

6. Dimopoulos MA, Moulopoulos LA, Maniatis A, Alexanian R: Solitary plasmacytoma of bone and asymptomatic multiple myeloma. *Blood* 96 : 2037-2044, 2000

7. Dingli D, Kyle RA, Rajkumar SV, Nowakowski GS, Larson DR, Bida JP, et al.: Immunoglobulin free light chains and solitary plasmacytoma of bone. *Blood* 108 : 1979-1983, 2006

8. Frassica DA, Frassica FJ, Schiray MF, Sim FH, Kyle RA: Solitary plasmacytoma of bone: Mayo Clinic experience. *Int J Radiat Oncol Biol Phys* 16 : 43-48, 1989

9. Greipp PR, San Miguel J, Durie BG, Crowley JJ, Barlogie B, Bladé J, et al.: International staging system for multiple myeloma. *J Clin Oncol* 23 : 3412-3420, 2005

10. Hogan BV, Peter MB, Shenoy HG, Horgan K, Hughes TA: Surgery-induced immunosuppression. *Surgeon* 9 : 38-43, 2011

11. Holland J, Trenkner DA, Wasserman TH, Fineberg B: Plasmacytoma. Treatment results and conversion to myeloma. *Cancer* 69 : 1513-1517, 1992

12. Kılıçkaş S, Celik OK, Pak Y, Demiral AN, Pehlivam M, Orhan O, et al.: Clinical and prognostic features of plasmacytomas: a multicenter study of Turkish Oncology Group-Sarcoma Working Party. *Am J Hematol* 83 : 702-707, 2008

13. Knobel D, Zouhair A, Tsang RW, Poortmans P, Belkacemí J, Bolla M, et al.: Prognostic factors in solitary plasmacytoma of the bone: a multicenter Rare Cancer Network study. *BMC Cancer* 6 : 118, 2006

14. Knowling MA, Harwood AR, Bergsagel DE: Comparison of extramedullary plasmacytomas with solitary and multiple plasma cell tumors of bone. *J Clin Oncol* 1 : 255-262, 1983

15. Kumar S: Solitary plasmacytoma: is radiation therapy sufficient? *Am J Hematol* 83 : 695-696, 2008

16. Kumar S, Fonseca R, Dispenzieri A, Lacy MQ, Lust JA, Wellick L, et al.: Prognostic value of angio genesis in solitary bone plasmacytoma. *Blood* 101 : 1715-1717, 2003

17. Liebross RH, Ha CS, Cox JD, Weber D, Delassale K, Alexanian R: Clinical course of solitary extramedullary plasmacytoma. *Radiother Oncol* 52 : 245-249, 1999

18. Liebross RH, Ha CS, Cox JD, Weber D, Delassale K, Alexanian R: Solitary bone plasmacytoma: outcome and prognostic factors following radiotherapy. *Int J Radiat Oncol Biol Phys* 41 : 1063-1067, 1998

19. Liu HY, Luo XM, Zhou SH, Zheng ZJ: Prognosis and expression of lambda light chains in solitary extramedullary plasmacytoma of the head and neck: two case reports and a literature review. *J Int Med Res* 38 : 282-288, 2010

20. Mayr NA, Wen BC, Hussey DH, Burns CP, Staples JJ, Doornbos JE, et al.: The role of radiation therapy in the treatment of solitary plasmacytomas. *Radiother Oncol* 17 : 293-303, 1990

21. Mendoza S, Urrutia J, Fuentes D: Surgical treatment of solitary plasmacytoma of the spine: case series. *Iowa Orthop J* 24 : 86-94, 2004

22. Rajkumar SV, Kyle RA, Therneau TM, Melton LJ 3rd, Bradwell AR, Clark RJ, et al.: Serum free light chain ratio is an independent risk factor for progression in monoclonal gammapathy of undetermined significance. *Blood* 106 : 812-817, 2005

23. Snezek CI, Katzmann JA, Kyle RA, Dispenzieri A, Larson DR, Therneau TM, et al.: Prognostic value of the serum free light chain ratio in newly diagnosed myeloma: proposed incorporation into the international staging system. *Cancer* 69 : 38-43, 2008

24. Soutar R, Urrutia J, Fuentes D: Surgical treatment of solitary plasmacytoma of the spine: case series. *Israel Orthop J* 24 : 86-94, 2004

25. Rajkumar SV, Kyle RA, Therneau TM, Melton LJ 3rd, Bradwell AR, Clark RJ, et al.: Serum free light chain ratio is an independent risk factor for progression in monoclonal gammapathy of undetermined significance. *Blood* 106 : 812-817, 2005

26. Snezek CI, Katzmann JA, Kyle RA, Dispenzieri A, Larson DR, Therneau TM, et al.: Prognostic value of the serum free light chain ratio in newly diagnosed myeloma: proposed incorporation into the international staging system. *Cancer* 69 : 38-43, 2008

27. Trezorowski G, Pewsey JR, Stern M: Natural killer cell immunity after transplantation. *Swiss Med Wkly* 142 : w13700, 2012

28. Tsang RW, Gospodorowicz MK, Pintilee M, Bezjak A, Wells W, Hodgson DC, et al.: Solitary plasmacytoma treated with radiotherapy: impact
of tumor size on outcome. Int J Radiat Oncol Biol Phys 50 : 113-210, 2001
28. van der Bij GJ, Oosterling SL, Beelen RH, Meijer S, Coffey JC, van Egmond M : The perioperative period is an underutilized window of therapeutic opportunity in patients with colorectal cancer. Ann Surg 249 : 727-734, 2009
29. Wilder RB, Ha CS, Cox JD, Weber D, Delasalle K, Alexanian R : Persistence of myeloma protein for more than one year after radiotherapy is an adverse prognostic factor in solitary plasmacytoma of bone. Cancer 94 : 1532-1537, 2002
30. Zazpe I, Caballero C, Cabada T, Guerrero D, Gallo-Ruiz A, Portillo E : Solitary thoracic intradural extramedullary plasmacytoma. Acta Neurochir (Wien) 149 : 529-532; discussion 532, 2007