

# Localized extramedullary relapse after autologous hematopoietic stem cell transplantation in multiple myeloma

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## ABSTRACT

Extramedullary plasmacytomas are rare manifestation of plasma cell malignancies. After hematopoietic stem cell transplantation (HSCT), presentation of localized plasmacytoma with extramedullary growth is very unusual. We report a case of a 56-year-old woman with Dune-Salmon stage IIIA immunoglobulin A-kappa multiple myeloma, which presented 120 days after autologous HSCT with extramedullary plasmacytoma arising from a lymph node in supraclavicular region. The patient had no pretransplant-history related with extramedullary disease. There was no increase of plasma cells in bone marrow or monoclonal protein in urine or serum. Aspiration smears of lymph node revealed a population of plasmacytoid cells at various stages of maturation. The patient was successfully treated with local radiotherapy and has remained progression-free for more than 20 months.

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**E**xtramedullary plasmacytomas (EMP) represent 3% of all plasma cell neoplasm.<sup>1</sup> They occur in the respiratory system, cavernous sinus, lymph node, thyroid, lung, parotid, breast, esophagus, liver, spleen, pancreas, adrenal gland, eyes, bladder, extremities, spinal canal and peritoneal cavity.<sup>2</sup> Treatment of multiple myeloma (MM) with chemotherapeutic drugs, complete remission is less 5%, the median survival is less than 3 years and may reach 5 years only in selected responder patients.<sup>3</sup> In patients with MM, high dose therapy followed by autologous peripheral blood stem cell transplantation (SCT) results in higher complete response (CR) rates and prolonged overall survival compared to conventional chemotherapy treatment. The SCT inpatients with MM may constitute high response rates with 20-50% of apparent CR.<sup>4</sup> But, only a small group of patients may achieve durable

remissions and usually most of cases relapsed median of 25-40 months after SCT.<sup>5</sup> The patterns of relapse in MM, after SCT are very heterogeneous and may be differ from the clinical presentation of the disease at diagnosis.<sup>6</sup> Extramedullary relapse, usually occur in subcutaneous tissue, lymph node, soft tissue and central nervous system.<sup>7</sup>

Here, we report EMP of lymph node in a patient who had hematological complete remission of multiple myeloma after autologous hematopoietic SCT.

**Case Report.** A 56-year-old woman was admitted to hematology department with complaint of low back and left leg pain, 15 months ago. On admission, her blood pressure was 130/80 mm Hg, pulse rate was 84 beats/min (regular) and respiratory

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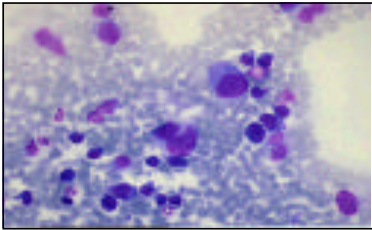


Figure 1 - Fine needle aspiration of the right axillary mass illustrates atypical plasma cells, May-Grunwald-Giemsa x 400.

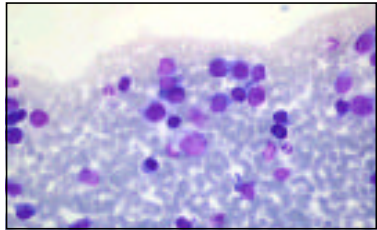


Figure 2 - The infiltrate primarily composed of atypical and immature plasma cells with occasional Russell bodies, May-Grunwald-Giemsa x 400.

rate was 20 breaths/min. Hemoglobin level was 9.6/gr/dL, white blood cell count  $4.4 \times 10^3/\mu\text{L}$ , platelet count  $270 \times 10^3/\mu\text{L}$ . Erythrocyte sedimentation rate was 95 mm/h and C-reactive protein was 14 mg (N:  $0 \pm 6$  mg). Albumin level was 2.5 gr/dL while globulin levels was 4.2 gr/dL in serum. There was increase in immunoglobulin A (IgA) and kappa light chain levels on urine and serum immune-electrophoresis. The IgA level was 6.2 gr/dL. Creatinine and 132-microglobulin levels were normal. Cranial x-ray revealed multiple lytic lesions. Bone marrow aspiration showed 73% plasma cell infiltration. The patient staged as stage IIIA and received 4 courses of ventricular assist device (VAD) combination chemotherapy with vincristine (0.4 mg/d on days 1-4), adriamycin (9 mg/m<sup>2</sup> on days 1-4), dexamethasone (40 mg/d on days 1-4, 9-12, 17-21). The patient was re-evaluated after 4 courses of VAD treatment. The M-protein was not detected on serum or urine. The plasma cell count was decreased to 5% in bone marrow and on x-ray survey of the bones, there was no progression of the lytic lesions. After the fourth cycle of VAD treatment, stem cell mobilization with 4 g/m<sup>2</sup> cyclophosphamide plus 4 g/m<sup>2</sup> MESNA plus 10 µg/kg granulocyte colony-stimulating factor (G-CSF) was performed. A total of  $6 \times 10^6/\text{kg}$  CD34+ cells were collected with apheresis (Dideco Excel). Then a high-dose melphalan (HDM) course (200 mg/m<sup>2</sup>) was administered. Stem cells were rein fused the following day. Neutrophil ( $>500/\mu\text{L}$ ) engraftments was observed on the 12th day while platelet ( $>20,000/\mu\text{L}$ ) engraftments was observed on the 15th day. At the first month, interferon-alpha 3x 5 MU 3 times per week as maintenance treatment was began. At the 2nd month of HSCT, plasma cell count was 3% and no monoclonal protein was detected in serum and urine. After 4 months, the patient was readmitted with complaint of right supraclavicular nodule while receiving

interferon-alpha. There was 3 x 2 cm mass lesion on the right supraclavicular area, noted by physical exam and computerized tomography. Cytological examination of the nodular mass showed atypical plasma cells infiltration and also premature plasma cells (Figure 1 & 2). Radiation therapy was applied to right supraclavicular region. Nodular mass disappeared following irradiation. After irradiation, the patient showed progression-free survival for more than 20 months and still free of disease.

**Discussion.** High-dose chemotherapy (HDT) supported by autologous hematopoietic SCT has produced both higher remission rates and longer overall and event-free survivals (EFS) than conventional dose chemotherapy.<sup>4,6</sup> Localized extramedullary relapse after autologous hematopoietic SCT in MM is very rare. The clinical presentation of these relapses is very heterogeneous and little research has focused on this area. Alegre et al<sup>8</sup> had evaluated the clinical characteristics of 280 patients with MM who relapsed after transplantation was assessed during the long-term post-transplantation follow-up. Extramedullary manifestations with single or multiple plasmacytomas had been estimated to occur in 40 of 180 patients (14%) after autologous hematopoietic SCT. Other relapse were insidious (18%), classical (66%) leukemic (2%). There has been no correlation given for the classical prognostic factors such as C-reactive protein and 2 microglobulin level with patterns of relapse in this study.<sup>8</sup>

Solitary primary extramedullary plasmacytoma is a neoplasm of the plasma cells arising in regions other than bone marrow in patients with no clinical or biochemical evidence of multiple myeloma.<sup>9</sup> Solitary primary extramedullary plasmacytomas are found principally in elderly people. They occur predominantly in the head and neck area with a tendency to involve the submucosal tissues of the

upper airway. There are some case reports regarding extramedullary relapse after autologous hematopoietic SCT in MM. The presentation of recurrent disease as localized plasmacytoma with extramedullary growth is unusual in the post-transplant setting and the patterns of relapse of MM after HDT and usually different from the clinical presentation of the disease at diagnosis.<sup>10</sup> Extramedullary plasmacytoma after SCT in MM may appear anywhere and related with trauma.<sup>7</sup> Clinical presentation could be unifocal or multifocal in subcutaneous tissue, involving leg, forearm or central nervous system.<sup>6</sup> After SCT, the patients may present with extramedullary plasmacytoma appearing as lymph node in supraclavicular region.<sup>8</sup> Fine needle aspiration cytology is often diagnostic for the diagnosis of plasmacytoma as in our case.

To the best of our knowledge, after hematopoietic SCT in MM, the presentation of solitary plasmacytoma as supraclavicular lymphadenopathy has not been reported. Solitary extramedullary plasmacytoma is usually treated by radiation therapy. Surgery, either alone in cases deemed unsuitable for radiation therapy as an adjunct with radiation has also been used.<sup>11</sup> Our patient was successfully treated with local radiation therapy of solitary plasmacytoma and has remained progression-free for more than 20 months and the treatment of interferon-alpha was continued in the patient during this period. In conclusion, after hematopoietic SCT, localized extramedullary plasmacytoma of the lymph node is of rare occurrence and it may appear as result of local recurrence. In patients with MM after hematopoietic SCT, solitary plasmacytoma should be remembered if there is a lymphadenopathy in anywhere of body.

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