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Case Report

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Uncommon Presentation of Multiple Myeloma: Pleural Effusion and Extensive Extramedullary Involvement

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ABSTRACT

A 60-year-old female presented with abdominal pain, weight loss, and fatigue. Imaging revealed a pancreatic mass, bilateral pleural effusion, ascites, and lytic bony lesions. Investigations confirmed multiple myeloma with lambda light chain disease. Positron emission tomography-computed tomography (PET-CT) scan demonstrated extensive metabolically active soft tissue masses involving the pancreatic region, retroperitoneum, mediastinum, paravertebral regions, and multiple skeletal lesions with extraosseous soft tissue involvement, along with bilateral pleural effusions with metabolically active pleural and extrapleural deposits. The patient was initiated on a bortezomib, cyclophosphamide, and dexamethasone chemotherapy regimen with therapeutic thoracentesis for pleural effusion management. After two cycles, the patient showed remarkable clinical improvement. A repeat PET-CT scan revealed significant interval regression of soft tissue masses, metabolic activity resolution, and regression of pleural and extrapleural deposits. The extensive skeletal lytic lesions showed morphological stability but regression of associated metabolic activity and extraosseous soft tissue. This case highlights the potential of novel agent-based regimens in achieving exceptional responses in multiple myeloma patients with extensive extramedullary disease (EMD), including uncommon manifestations like pleural effusion. Early recognition and prompt initiation of appropriate therapy are crucial for improving outcomes in such cases.

Keywords: Multiple myeloma; Extramedullary disease; Pleural effusion; Bortezomib; Positron emission tomography-computed tomography (PET-CT)

INTRODUCTION

Multiple myeloma is a plasma cell neoplasm characterized by the proliferation of monoclonal plasma cells in the bone marrow and extramedullary sites. Extramedullary disease (EMD) is an uncommon manifestation of multiple myeloma, occurring in approximately 7-18% of patients during the disease course[1,2]. Pleural effusion, an infrequent manifestation of EMD, occurs in approximately 6% of multiple myeloma cases[2]. The presence of pleural effusion in multiple myeloma can significantly complicate the clinical course, often necessitating additional interventions such as therapeutic thoracentesis[3].

EMD is associated with more aggressive clinical behaviour and poorer prognosis compared to medullary myeloma[4]. This case report aims to address this gap by providing a detailed account of a

rare instance of multiple myeloma with extensive extramedullary involvement, including pleural effusion, at the initial diagnosis. The current report underscores the importance of early recognition and prompt initiation of appropriate therapy in such cases to improve patient outcomes.

Case presentation

A 60-year-old female presented with a two-month history of abdominal pain, vomiting, constipation, significant weight loss (5-6 kg), loss of appetite, and progressive fatigue and weakness. On physical examination, the patient appeared cachectic and pale. Vital signs revealed tachycardia (pulse rate 100/min), tachypnea (respiratory rate 28/min), blood pressure 110/70 mmHg, and a temperature of 37.2°C. Bilateral pedal oedema was noted. Respiratory examination showed dullness on percussion and reduced breath sounds in bilateral infrascapular and infraaxillary areas. Abdominal examination revealed mild distension with diffuse tenderness, more pronounced in the epigastric region, but no palpable masses.

Laboratory investigations demonstrated normocytic normochromic anaemia (Hb 11.3 g/dL), normal white blood cell (6.5 × 109/L) and platelet (180 × 109/L) counts, mildly elevated serum creatinine (1.3 mg/dL), and hypercalcemia (11.2 mg/dL). Serum protein electrophoresis revealed an M-spike of 2.8 g/dL. The serum-free light chain assay showed significantly elevated lambda chains (1200 mg/L) with a markedly decreased kappa/lambda ratio (0.0125). Beta-2 microglobulin was elevated at 5.8 mg/L. Bone marrow aspiration and biopsy demonstrated 70% plasma cells.

Imaging studies were crucial in establishing the extent of the disease. Chest X-ray showed bilateral pleural effusion, more pronounced on the right side, without prominent lung masses. CT of the abdomen and pelvis revealed a pancreatic mass (4.5 × 3.2 cm) in the body and tail, bilateral pleural effusion, moderate ascites, and multiple lytic bony lesions in the vertebrae, pelvis, and proximal femora. A PET-CT scan demonstrated a large metabolically active soft tissue mass (SUVmax 12.5) in the pancreatic region, extending to the periportal, retroperitoneal, mediastinal, and paravertebral regions. Extensive metabolically active marrow deposits and lytic lesions were noted throughout the axial and appendicular skeleton, with significant spinal cord compression at the T11-T12 level. Bilateral pleural effusions with metabolically active pleural and extrapleural soft tissue (SUVmax 8.2) were also observed (Figure 1).

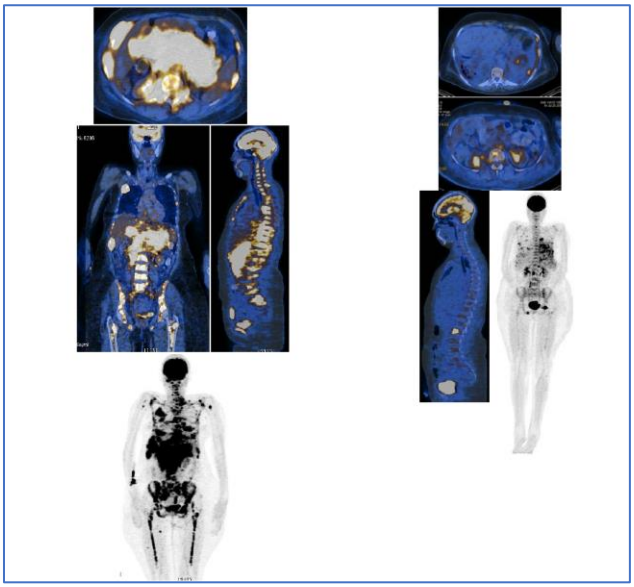

Figure 1. PET-CT scans comparing Multiple Myeloma before and after chemotherapy

Based on these findings, a diagnosis of multiple myeloma with lambda light chain disease, extensive extramedullary involvement, and myelomatous pleural effusion was established. The patient was classified as International Staging System (ISS) stage III.

Treatment

The patient was initiated on a comprehensive treatment regimen tailored to address the extensive disease involvement and associated complications. The backbone of the treatment was the Bortezomib, Cyclophosphamide, and Dexamethasone (VCD) chemotherapy regimen. This consisted of Bortezomib 1.3 mg/m^2 subcutaneously on days 1, 4, 8, and 11, Cyclophosphamide 300 mg/m^2 orally on days 1, 8, and 15, and Dexamethasone 40 mg orally on days 1, 2, 4, 5, 8, 9, 11, and 12. The cycle was repeated every 21 days.

Supportive care measures were implemented concurrently. These included Zoledronic acid 4 mg intravenously every 4 weeks for bone disease management, prophylactic acyclovir for herpes zoster prevention, and thromboprophylaxis with low molecular weight heparin.

The symptomatic pleural effusion was managed with therapeutic thoracentesis. Under ultrasound guidance, 1.2 L of pleural fluid was drained from the right side, providing significant symptomatic relief. Analysis of the pleural fluid confirmed an exudative effusion with the presence of atypical plasma cells, consistent with myelomatous involvement.

To address the spinal cord compression at T11-T12, the patient received high-dose Dexamethasone (40 mg daily for 4 days) and underwent radiation therapy to the affected vertebrae (30 Gy in 10 fractions).

Outcome and follow-up

The patient was closely monitored and followed up for six months after initiating treatment. The response to therapy was evaluated across multiple clinical, imaging, and biochemical parameters.

Clinically, after two cycles of VCD, the patient showed significant improvement. Her respiratory symptoms markedly decreased, and she experienced a resolution of abdominal pain and constipation. A weight gain of 3 kg was noted, and her performance status improved from an initial ECOG 3 to ECOG 1.

Imaging response was assessed by a repeat PET-CT scan at 2 months, demonstrating marked interval regression of soft tissue masses. The pancreatic region mass had reduced to 1.8 × 1.2 cm with a decreased SUVmax of 3.2. Near-total resolution of periportal deposits and significant retroperitoneal, mediastinal, and paravertebral deposit regression were observed. While the skeletal lytic lesions showed morphological stability, there was a notable regression in their associated metabolic activity, with the mean SUVmax decreasing from 9.8 to 3.5. Pleural and extrapleural deposits showed significant regression, though bilateral pleural effusions persisted but with reduced volume (Figure 1).

Biochemically, after 3 cycles of VCD, serum-free lambda light chains decreased dramatically to 80 mg/L. M-protein was no longer detectable on serum protein electrophoresis, and serum calcium levels had normalized.

The treatment was not without complications. The patient developed Grade 2 peripheral neuropathy, which was managed with gabapentin and a dose reduction of bortezomib. She also experienced one episode of neutropenic fever, which resolved with intravenous antibiotics.

According to the International Myeloma Working Group criteria, the patient achieved a very good partial response (VGPR). She continued on the VCD regimen for a total of 6 cycles, after which she was transitioned to maintenance therapy with lenalidomide.

DISCUSSION

This case highlights the potential of novel agent-based regimens, such as the VCD regimen used in this case, in achieving remarkable responses in multiple myeloma patients with extensive extramedullary involvement, including uncommon manifestations like pleural effusion.

The presence of extramedullary disease (EMD) is associated with a more aggressive disease course and poorer prognosis in multiple myeloma(5,6). However, recent studies have demonstrated the efficacy of bortezomib-based therapies in managing EMD, leading to improved outcomes[7,8]. Bortezomib is a proteasome inhibitor that induces apoptosis in cancer cells by disrupting the ubiquitin-proteasome pathway, accumulating misfolded proteins and subsequent cell death[9]. Cyclophosphamide, an alkylating agent, interferes with DNA replication and transcription, causing cytotoxicity in rapidly dividing cells[10].

Dexamethasone, a corticosteroid, exerts anti-inflammatory and immunosuppressive effects, enhancing the cytotoxic effects of chemotherapy and inducing apoptosis in plasma cells[11]. Together, these agents provide a multi-pronged attack on myeloma cells, contributing to significant clinical improvements.

The efficacy of bortezomib-based regimens in treating extramedullary disease (EMD) in multiple myeloma has been supported by various studies. For instance, Cavo et al. reported that patients with EMD who underwent bortezomib-based therapies

showed improved progression-free and overall survival [12]. This case adds to the existing evidence by demonstrating a remarkable response to the VCD regimen in a patient with extensive EMD, including pleural effusion, corroborating findings from similar case reports and studies[13].

The limitations of this case report include the short follow-up duration, which restricts the ability to assess long-term outcomes and potential late-onset side effects of the treatment. Additionally, the case report focuses on a single patient, limiting the generalizability of the findings. More extensive studies with extended follow-up periods are needed to validate the efficacy and safety of the VCD regimen in patients with multiple myeloma and extensive EMD.

CONCLUSION

This report illustrates a rare case of multiple myeloma with extensive extramedullary involvement, including pleural effusion, at the initial diagnosis, which showed a remarkable response to bortezomib-based chemotherapy. Early recognition and prompt initiation of effective treatment regimens are crucial for improving outcomes in such cases.

REFERENCES

1. Bladé J, Fernández de Larrea C, Rosiñol L, et al. Soft-tissue plasmacytomas in multiple myeloma: incidence, mechanisms of extramedullary spread, and treatment approach. J Clin Oncol. 2011;29(28):3805-12.

2. Iqbal N, Tariq MU, Shaikh MU, et al. Pleural effusion as a manifestation of multiple myeloma. BMJ Case Rep. 2016;2016:bcr2016215433.

3. Ramos AL, Trindade M, Santos Pinto A, et al. Pleural effusion and multiple myeloma - more than meets the eye: A case report. Mol Clin Oncol. 2021;15(5):238.

4. Bansal R, Rakshit S, Kumar S. Extramedullary disease in multiple myeloma. Blood Cancer J. 2021;11(9):161.

5. Miller J, Alton PA. Myelomatous pleural effusion-A case report. Respir Med Case Rep. 2012;5:59–61.

6. Varettoni M, Corso A, Pica G, et al. Incidence, presenting features and outcome of extramedullary disease in multiple myeloma: a longitudinal study on 1003 consecutive patients. Ann Oncol. 2010;21(2):325–330.

7. Reddy PV, Singh V, Roy R, et al. Multiple myeloma presenting as clival mass: a diagnostic delimma. BMJ Case Rep . 2021;14(3):e240670.

8. Alkan O, Tiryaki TO , Kalayoglu-Besisik S. Myelomatous Pleural Effusion: A Rare Involvement in Myeloma. J Med Cases. 2020 Mar;11(3):55-56.

9. Weinstock M, Aljawai Y, Morgan EA, et al. Incidence and clinical features of extramedullary multiple myeloma in patients who underwent stem cell transplantation. Br J Haematol. 2015;169(6):851–8.

10. Chen D, Frezza M, Schmitt S, et al. Bortezomib as the First Proteasome Inhibitor Anticancer Drug: Current Status and Future Perspectives. Curr Cancer Drug Targets. 2011;11(3):239–53.

11. Alkylating Agent - an overview | ScienceDirect Topics [Internet]. [cited 2024 Jul 25]. Available from: https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/alkylating-agent.

12. Giles AJ, Hutchinson MKND, Sonnemann HM, et al. Dexamethasone-induced immunosuppression: mechanisms and implications for immunotherapy. J Immunother Cancer. 2018; 6: 51.

13. Cavo M, Gay F, Beksac M, et al. Upfront Autologous Hematopoietic Stem-Cell Transplantation Improves Overall Survival in Comparison with Bortezomib-Based Intensification Therapy in Newly Diagnosed Multiple Myeloma: Long-Term Follow-up Analysis of the Randomized Phase 3 EMN02/HO95 Study. Blood. 2020;136(Supplement 1):37–8.