ORIGINAL RESEARCH PAPER

General Medicine

MULTIPLE MYELOMA: A CASE REPORT

KEY WORDS: Multiple myeloma, plasma cells, Immunocompromised.

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ABSTRACT

Here we are presenting a case of 46-year-old male patient who presented with complaints of musculoskeletal pain, loss of appetite, weight loss, headache and generalised weakness. Biochemical investigations revealed microcytic hypochromic anemia and hyperglobulinemia. Bone marrow biopsy examination revealed multiple myeloma.

INTRODUCTION

Plasma cell neoplasia is a lymphoid neoplastic proliferation of B cells. This denomination encloses multiple myeloma (MM), solitary bone plasmacytoma and extramedullary plasmacytoma. MM consists of a clonal proliferation of plasma cells based in the bone marrow, with various degrees of differentiation. Neoplastic cells usually produce monoclonal immune globulins, most commonly Immunoglobulin G (IgG) or Immunoglobulin A (IgA) that can be detected in serum or urine. The tumour & it's products & host response ultimately led to a variety of symptoms like anaemia, bone pain, increased incidence of fracture, hyper calcaemia, renal failure & increased susceptibility to infections. The peak incidence of Multiple myeloma is in the seventh decade of life. Treatment involves mainly irradiation and chemotherapy and the prognosis is generally poor.

Case Report

A 46-year-old male, farmer by occupation of low socioeconomic status, and recently diagnosed with hypertension presented with c/o bilateral tingling and numbness in lower limb for 2 months which was sudden in onset and present in all 4 limbs simultaneously, symptoms aggravated over exertion and exposure to cold weather and are present continuously and not relieved by rest.

He also c/o headache for 10-12 days which was gradual in onset, dull aching, holocranial and associated with 2-3 episodes of vomiting containing food particles, non-bilious, non-blood tinged.

Patient also c/o high grade fever for 10-12 days associated with chills and rigors and perspiration relieved on taking antipyretics. Patient also c/o generalized weakness and loss of appetite for 2 months, and cough with expectoration since 4- 5 months.

On examination patient was febrile with a temperature of 101.6F, PR of 136 bpm, BP of 166/104 mmhg. His chest sounds were clear with no added sounds. He had no murmur or rub. On per abdomen examination his abdomen was soft and non-tender. He was conscious and oriented; pupils were reactive and bilateral plantar reflex were flexor. Patient had bilateral positive nystagmus and rombergs test was positive towards right side, subsequently MRI brain was done which was normal.

His laboratory investigations during the course of treatment in hospital were, Hb was 9.0gm/dl dropped to 6.6gm/dl, total counts were 13500cells/cu.mm and platelet were 2.17lakhs/cu.mm which dropped to 60000/cu.mm, with raised C- reactive protein value of 199mg/L with microcytic hypochromic anemia on peripheral smear. Patients fever profile was done it turned out to be negative.

He presented with serum calcium 11.3mg/dl, phosphorus 2.0mg/dl, uric acid levels 4.5mg/dl and magnesium 2.1mg/dl. On urine examination he had albumin +2, trace sugar and negative Bence jones proteins. His serum creatinine was 2.2mg/dl which progressively deteriorated to 7.1mg/dl on 5th day of admission. His albumin was 2.4mg/dl and globulin were 5.6mg/dl which gave a A/G ratio of <1. His 2decho revealed concentric lvh, lvef-55%, mild MR. X ray skull revealed few well circumscribed punched out lytic lesion with no sclerotic rim (giving rain drop appearance of the skull) suggests p/o multiple myeloma.

Serum electrophoresis showed monoclonal band seen in gamma region. Free light chain assay was also significantly raised. Renal biopsy showed acute tubular necrosis with features consistent with cast nephropathy.

Patient had dyspnea, decreased urine output, desaturation, tachycardia and began to deteriorate symptomatically from 5th day of admission. Blood gas analysis showed severe metabolic acidosis and patient was shifted to ICU. Nephrology advice was sought which suggested hemodialysis. Patient underwent three cycles of hemodialysis. During the course of patient developed severe acute respiratory distress syndrome and was intubated in view of falling GCS score and saturation.

DISCUSSION

MM is a malignancy involving the abnormal proliferation of plasma cells with incidence that has notably increased over the past decades. While the primary focus of the management lies in establishing optimal treatment strategies to achieve symptom control, the potential for immunocompromising-related complications should not be overlooked. As illustrated with an example of this case report, patients who have been diagnosed with MM and treated for an extended period of time with immunotherapies, might face a risk of developing rare, potentially life-threatening infections, such as due to *Cryptococcus* species. The most likely mechanism behind the increased susceptibility of these patients involves the combination of pathophysiology of MM itself that is furthered by the immunosuppressive nature of therapies used. While the advances in therapies transformed a previously lethal disease into a chronic condition with relapses, they have also increased the risk for other comorbidities. As explained in Nucci et al (2009), type of

infection risk depends on the specific therapy used. The most common infections affecting patients who have been started on the induction therapy with melphalan plus prednisone include pneumonia and bacteraemia caused by *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Escherichia coli* [1]. However, it should be noted that this treatment regimen has become a rare choice in clinical settings in the US recently. Use of high-dose dexamethasone regimens has been associated with mucosal candidiasis, herpes simplex virus (HSV) or varicella zoster virus (VZV) infections. Prophylactic use of either acyclovir or valacyclovir is recommended for prophylaxis against VZV reactivation to all patients receiving immunotherapy [2]. Thalidomide however was not associated with increased risk of infections. Bortezomib was found to be raising the risk for VZV infection, while lenalidomide was not conclusively linked to any particular infection [1]. Notably, autologous transplantation, which is another mode of treatment effective in managing MM, does increase infection risk through associated neutrophilia and mucositis pre-engraftment, as well as through depression of cell-mediated immunity post-engraftment. Associated infections include *Clostridium difficile*, VZV, cytomegalovirus (CMV) and *Pneumocystis jirovecii* [1].

While bacterial and viral infections tend to occur during the first year and again between years 4 and 9 after MM diagnosis, invasive fungal infections have been found to occur at much later stages in association with cumulative immunodeficiency [3]. Aspergillosis is the most common of this category of infection and most likely occurs due to neutropenia following administration of high-dose corticosteroids. Presentation with cryptococcosis is much more rare and related data are limited. A literature review performed by Chastain et al (2022) revealed that infections due to *Cryptococcus* species were mainly present in MM patients treated with corticosteroids, lenalidomide, pomalidomide, cyclophosphamide, and bortezomib [3]. The best form of primary management is dependent on the severity of the cryptococcal infection, and usually involves IV amphotericin B, flucytosine and oral fluconazole; however, other agents might be indicated.

Infection prevention prophylaxis in severely immunocom promised myeloma patients is of paramount importance to providing proper care for this population. In order to mitigate the risk, a multifaceted approach to infection prevention is crucial. An important first step is patient risk stratification based on tumor and host-related factors, through detailed past medical history, physical examination and organ function evaluation [1]. The mainstay of complication prevention is antimicrobial prophylaxis. Specific indications depend on particular disease indicators and risks. Agents used include but are not limited to trimethoprim-sulfamethoxazole in case of *P. jirovecii* prevention. CMV prophylaxis should be primarily based on the appropriate prophylactic combination of ganciclovir and valganciclovir [4].

Candidiasis infection is recommended to be pretreated with either topical or oral clotrimazole. In addition to antimicrobial prophylaxis, immune enhancement through vaccination is another facet of myeloma patient care. Vaccinations against influenza A and B, *S. pneumoniae*, *H. influenzae* and VZV remain as available options. Remaining measures revolve around lifestyle modifications including but not limited to smoking cessation, high personal hygiene standards, and broadly defined exposure avoidance, such as environmental, food preparation, travel, pets contact and recreational activities [1].

Future directions in the management of patients with MM with respect to immunocompromised state are imperative to prevent infectious complications such as those with *Cryptococcus* species. In addition to continuously enhancing supportive care measures, additional avenues can be explored. Personalized medicine with specific emphasis on immune profiling could enable more tailored treatment strategies, potentially minimizing immunosuppression-related complications. This approach still awaits validation but holds great promise [5]. Ongoing research is required to further determine the value of approaches such as CAR-T cell therapy, monoclonal antibodies, bispecific antibodies or ADCs [6]. The goal of refining future approaches is to enhance patients' immune responses while minimizing the risks associated with conventional treatments. These efforts collectively underscore the importance of a multifaceted management of immunocompromised patients with MM. Future research in these areas is anticipated to come to develop and expand our understanding of effective strategies for this complex patient population.

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