

# A Case of Multiple Myeloma with Triple Herpes Virus Infections

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## ABSTRACT

Multiple myeloma is rare B cell malignancy that affects elderly. Therapeutic regimens consist of high dose chemotherapy followed by haematopoietic stem cell transplantation (HSCT). Both humoral and cell mediated immunities are compromised in these patients, leading to increased susceptibility to infections. Here, we report a case of 62-year male with multiple myeloma who developed infection with three viruses from herpes family during the first cycle of chemotherapy.

**Key Words:** *Multiple myeloma. Chemotherapy. Herpes viruses.*

## INTRODUCTION

Multiple myeloma, a rare B cell malignancy is characterised by the presence of monoclonal proteins in serum and/or urine, lytic bone lesions and decreased serum immunoglobulin levels.<sup>1</sup> Both humoral and cell mediated immunities are compromised in patients receiving treatment for multiple myeloma.<sup>2</sup> Multiple myeloma is generally a disease of elderly; and therapeutic strategies include high dose chemotherapy with bortezomib and the immunomodulatory agents, thalidomide and Lenalidomide, followed by haematopoietic stem cell transplant (HSCT). Old age, anti-neoplastic drugs and disease-related complications increase the susceptibility to infections.<sup>3</sup>

We report a case of multiple myeloma in a 62-year male patient who developed triple herpes virus infection during the first cycle of treatment.

## CASE REPORT

A 62-year man presented with 10-month history of generalised skin itching, myalgias, weakness and bone pain to medical specialist in a renowned hospital in private sector. He consulted many physicians, thereafter; but complaints still persisted and his condition continued to deteriorate. Eventually, he was thoroughly investigated by medical specialists and found to have progressively increasing retic count, decreasing haemoglobin (Hb) levels and azotemia. He was referred to Armed Forces Bone Marrow Transplant Centre (AFBMT) for further workup for hemolytic anemia, where he underwent bone marrow aspiration along with trephine biopsy in August 2017. He was finally diagnosed as a case of multiple

myeloma. His skeletal survey revealed bilateral radio-lucent lesions in both pelvic and femoral bones. This further supported the diagnosis of multiple myeloma.

Over the period of time, there was progressive worsening of patient's condition with development of difficulty in walking, altered consciousness, weight loss, and anorexia. He was admitted in AFBMT and was started on triple regimen which consisted of bortezomib, lenalidomide and dexamethasone. On the 11th day of cycle, he developed generalised erythematous rash (Figure 1), followed by fever, bilateral pleural effusion, and oral leukoplakia on lateral side of tongue (Figure 2). Multiple specimens were sent to the laboratory to reach diagnosis. His blood culture did not yield growth of any bacteria, and skin biopsy was not suggestive of any histopathological lesion. An oral swab sample was collected from the site of lesion in the mouth and was sent in viral transport medium (VTM) to Virology Department, Armed Forces Institute of Pathology, Rawalpindi. The PCR testing was performed for three viruses belonging to herpesviridae family: EBV, CMV and HSV-1, due to their strong association with multiple myeloma and with the triple regime given for treatment of this disease. The sample was found to be positive for all of the three herpes viruses, simultaneously (Table I).

Chemotherapy was stopped and patient was given antiviral agents, i.e. acyclovir orally and ganciclovir



**Figure 1:** Generalised erythematous rash.



**Figure 2:** Oral leukoplakia due to EBV.

**Table I:** The herpes viruses positivity profile.

Herpes simplex virus PCR	HSV - TYPE 1 detected (Sacace Biotech, Italy)
Cytomegalo virus PCR	1005 Copies/ml (Sacace Biotech, Italy)
Epstein Barr virus PCR	32410 IU/ml (Sacace Biotech, Italy)

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intravenously 5 mg/kg 12-hourly induction dose followed by maintenance dose of 5 mg/kg once daily. The patient responded well with the generalised crusting of rash. With time, his respiratory signs improved and the oral lesions also disappeared. His conscious level got better and he started taking orally. With improvement in the generalised condition of the patient, the family requested for the patient to be discharged. The patient was discharged with advice about taking oral valganciclovir, 450 mg 2 tablets (900 mg) once daily. The condition of patient again worsened due to improper care facilities at home. He expired on 5th day of discharge from hospital. The cause of death could not be ascertained due to lack of follow-up; and was only narrated on telephone by the patient's relatives.

### DISCUSSION

The combination of lenalidomide, high dose dexamethasone and bortezomib is a novel treatment option for multiple myeloma, but studies showed that they increase the risk of infections.<sup>1,2</sup> The current therapies based on these agents have improved the outcome of patients with multiple myeloma as well as increased infection rate with CMV, *Aspergillus*, *Fusarium*, HSV and VZV.<sup>3</sup>

Jones *et al.* reported reactivation of EBV in patients treated with lenalidomide and its derivatives.<sup>4</sup> Taniguchi *et al.* reported a case of 68-year female with refractory multiple myeloma who developed fatal bilateral CMV pneumonia and *herpes simplex* esophagitis after treatment with bortezomib and dexamethasone.<sup>5</sup>

Another case of 68-year African-American male with multiple myeloma was reported by Harris *et al.* who developed pneumococcal meningitis along with HSV esophagitis after nine cycles of bortezomib and dexamethasone.<sup>6</sup>

Here, we have reported a case of multiple myeloma who developed co-infection with three members of herpesviridae family during the first cycle of chemotherapy. To the authors' knowledge, no such case of multiple myeloma with CMV, EBV and HSV co-infection has been reported in literature. A high degree of suspicion must always be kept in mind while treating patients of multiple myeloma on triple regimen; lenalidomide, high dose dexamethasone and bortezomib. Timely testing for viral infections with proper treatment is necessary in such cases to avoid fatal complications.

### REFERENCES

1. Hideshima T, Raje N, Richardson PG, Anderson KC. A review of lenalidomide in combination with dexamethasone for the treatment of multiple myeloma. *Ther Clin Risk Manag* 2008; **4**:129.
2. Vickrey E, Allen S, Mehta J, Singhal S. Acyclovir to prevent reactivation of varicella zoster virus (herpes zoster) in multiple myeloma patients receiving bortezomib therapy. *Cancer* 2009; **115**:229-32.
3. Nucci M, Anaissie E. Infections in patients with multiple myeloma in the era of high-dose therapy and novel agents. *Clin Infect Dis* 2009; **49**:1211-25.
4. Jones RJ, Iempridee T, Wang X, Lee HC, Mertz JE, Kenney SC, *et al.* Lenalidomide, thalidomide, and pomalidomide reactivate the Epstein-Barr virus lytic cycle through phosphoinositide 3-Kinase signaling and Ikaros expression. *Clin Cancer Res* 2016; **22**:4901-12.
5. Taniguchi D, Takahara O, Takasaki Y, Tawara M, Joh T, Tomonaga M. Fatal cytomegalovirus pneumonia and associated Herpes virus infection in a relapsed/refractory multiple myeloma patient treated with bortezomib plus dexamethasone. *Case Rep Oncol* 2009; **2**:140-3.
6. Harris J, Smith T, Preis J. Intractable hiccups due to herpetic esophagitis in an immunocompromised patient. *IDCases* 2016; **4**:34-7.

