CMV Pneumonitis following Bendamustine containing Chemotherapy

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Abstract

Bendamustine has been increasingly used for treatment of indolent lymphoma due to its comparable efficacy and side effect profile. As the drug is getting used more, specific adverse effects related to its use are also emerging particularly prolonged lymphopenia. Here we present a case of CMV reactivation following bendamustine containing chemotherapy.

Introduction

There has been an increasing trend for the use of Bendamustine in low grade lymphoma due to its comparable efficacy and side effect profile. As the drug is getting used more, specific adverse effects related to its use are also emerging particularly prolonged lymphopenia. Here we present a case of CMV reactivation following bendamustine containing chemotherapy.

Case Report

A 72-year lady was referred to our pulmonary clinic with complaints of fever of 2 weeks duration and dry cough along with shortness of breath for last two days. She had been diagnosed with low grade B cell non Hodgkin lymphoma 6 months ago and was treated with 6 cycles of Rituximab (600 mg on day 1), Bendamustine (100 mg on day 1,2) and dexamethasone (8 mg daily for 3 days post each chemotherapy cycle). She had completed her last (6th) cycle just over 2 weeks ago. She had a history of hypertension, osteoarthritis, hyperthyroidism and an episode of pneumonia one year ago. She was not known to have any other cardio respiratory illnesses in the past. Her complete blood counts showed grade 3 lymphopenia. Renal and liver profiles were normal. Dengue and Malaria screens were negative. She had already received 5 day course of oral amoxicillin and clavulanic acid and despite that the fever was persistent.

On arrival to chest clinic, her room oxygen saturation was 92% at rest and dipped down to 84% on walking 50 meters. Chest was clear on auscultation. She had undergone a PET scan 2 days earlier for response assessment following completion of chemotherapy. It showed diffuse ground glass opacities in both lungs with no evidence of metabolically active disease within the body. Bronchoscopy and lavage was done the next day. Bronchoscopy findings were normal. BAL aerobic culture, AFB stain, AFB gene Xpert and PCP-PCR were all negative. Bronchial lavage showed presence of inclusion bodies and BAL qualitative CMV PCR was positive. Blood CMV PCR showed 6680 copies/ml. She was treated for CMV pneumonitis with Inj Ganciclovir 5mg/kg twice a day for 2 weeks. The fever resolved and hypoxia settled. The patient became completely asymptomatic within 7 days of treatment and on completion of antiviral treatment her repeat Blood CMV PCR was <1000 copies/ml. The patient remained asymptomatic and was discharged from chest clinic a month later.

Discussion

Bendamustine has shown a favourable risk profile and comparable efficacy as compared to standard R-CHOP regimen for indolent lymphoma in particular there is decrease incidence of alopecia. However bendamustine is known to cause more severe CD4 lymphopenia which can predispose patients to opportunistic infections like CMV. Our patient had grade 3 lymphopenia at the time of clinical presentation. Isono et al conducted a prospective study on reactivation of CMV following bendamustine chemotherapy and showed median CD4+ lymphocyte count prior to treatment of 218/µL which fell down to 75/µL by the end of treatment. The incidence of CMV reactivation in this study was approximately 15% of patients. However the actual risk of symptomatic CMV disease, which would require medical intervention was not much clear. This is in contrast to various earlier studies showed the incidences of CMV infection ranged from 0 to 5.0% and 0 to 1.5% in Bendamustine alone or in combination with Rituximab respectively. Ken Ohmachi et al found an incidence of 10.2% in their multicenter trial and recommended that the lowest threshold for CMV antigenemia assay needs to be examined in patients who develop a fever of unknown origin without neutropenia, and preemptive therapy with ganciclovir should be initiated in CMV-positive patients. A more recent study from Japan shows the risk of symptomatic CMV antigenemia as high as 20% and predominantly involving patients who were on long...
term steroids and had baseline lower absolute lymphocyte count. There is therefore a clear trend of increasing incidence of CMV reactivation reports on Bendamustine chemotherapy over last two years.

It is not clear whether bendamustine, rituximab, dexamethasone, or the combination thereof is responsible for the relatively high incidence of CMV infection with this regimen. However Rituximab leading to CMV reactivation is very rarely reported and Kroll et al found that there were no episodes of CMV viremia in patients taking rituximab. Also the steroid therapy in standard chemotherapy is only for 5 days in each cycle. Our patient developed symptomatic CMV infection after the 6th cycle of chemotherapy which could reflect increase in the risk with increasing duration of bendamustine therapy as observed in various other case reports.

**Conclusion**

This case report adds to the increasing reports of CMV reactivation following Bendamustine chemotherapy. A high index of suspicion should be kept for CMV reactivation in these patient should they develop fever without a clear focus of infection or have focal symptoms consistent with CMV reactivation. Further studies are needed to stratify higher risk patient population and to determine the need for prophylactic antiviral medications in high risk group.

**References**


