

Can Lenalidomide Protect against Severe COVID-19 Symptoms in Multiple Myeloma Patients? A Case Series and Review of the Literature

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ABSTRACT

We present a case series of three multiple myeloma (MM) patients on lenalidomide for maintenance therapy who were at high risk of coronavirus disease 2019 (COVID-19) complications and mortality. However, our patients had minor symptoms after testing positive for COVID-19 although they were unvaccinated. We think that lenalidomide might have a protective effect against severe COVID-19 symptoms.

KEYWORDS

COVID-19, multiple myeloma, lenalidomide

LEARNING POINTS

- Multiple myeloma (MM) patients with active disease need treatment to avoid morbidity and mortality; the risk of relapse is also higher without treatment.
- Our three unvaccinated patients had mild COVID-19 infection while being treated with lenalidomide despite having high-risk comorbidities generally associated with severe COVID-19.
- Some small studies have reported that lenalidomide is protective against severe COVID-19, but larger clinical trials are required to determine whether or not to continue lenalidomide in MM patients with COVID-19.

INTRODUCTION

COVID-19 infection is a global pandemic that has affected millions of people. Multiple myeloma (MM) is a mature B-cell lineage cancer that is associated with cellular and humoral immune dysfunction which renders patients susceptible to infection. Lenalidomide is an immunomodulatory agent currently used for MM treatment. Recently, the hypothesis that lenalidomide may provide protection against severe COVID-19 infection has been under study.

CASE DESCRIPTION

Case 1

A 61-year-old Caucasian man with heart failure with a reduced ejection fraction and morbid obesity was diagnosed with IgA kappa MM approximately 3 years ago. He completed six cycles of a lenalidomide, bortezomib and dexamethasone (RVd) regimen. He was on maintenance lenalidomide 10 mg daily for 3 weeks each month. The patient tested positive for COVID-19 and had mild symptoms

despite being unvaccinated. Laboratory tests were completely within normal limits. He self-quarantined at home and continued to take lenalidomide during that time.

On his most recent follow-up, the patient denied any new complaints and continued to be haemodynamically stable; his physical examination was unremarkable. He is closely follow-up by haematology and cardiology every 3 months.

Case 2

A 71-year-old Caucasian man with IgG kappa MM had finished an Rvd regimen and had twice undergone an autologous stem cell transplant (ASCT). He is currently on maintenance lenalidomide 10 mg daily for the last few months with a few interruptions due to neutropenia. He tested positive for COVID-19 after having a mild sore throat; he did not require oxygen supplementation or hospitalization. He completely recovered after self-quarantine without any complications. He was unvaccinated.

Laboratory tests showed mildly elevated kappa free light chains of 2.96 mg/dl (0.33–1.94), haemoglobin 10.5 g/dl (14–17), mean corpuscular volume (MCV) 116.6 fl (80–100), platelets 97,000/ μ l (150,000 and 400,000), WBC count 2100 cells/ μ l (3500–10,600), and absolute neutrophil count (ANC) 700 cells/ μ l (1580–7130).

On his most recent visit, the patient was doing well. His lenalidomide dose was reduced to 5 mg daily with 3 weeks on and 1 week off due to fatigue. He is closely followed up in our haematology clinic every 6 months.

Case 3

An 85-year-old African-American man was diagnosed with IgG lambda MM 3 years ago. He finished an Rvd regimen with denosumab for lytic lesions that was complicated by jaw necrosis and abscess. He was switched to maintenance lenalidomide 10 mg daily as he was not an ASCT candidate due to his poor performance status. He recently had a mild COVID-19 infection but did not require oxygen supplementation. He was also unvaccinated.

Laboratory tests showed mildly elevated kappa free light chains of 4.64 mg/dl (0.33–1.94), lambda free light chains 2.85 mg/dl (0.57–2.63) and haemoglobin 11.1 g/dl. Serum and urine immunofixation showed normal results.

After he had finished self-quarantining, he complained only of right-sided jaw pain. Lenalidomide was held until jaw debridement surgery and the antibiotic course had been finished. He continues to be in a stable condition.

DISCUSSION

Solid and haematological cancer patients who develop concurrent COVID-19 infection usually have poor outcomes^[1]. A large study at Memorial Sloan Kettering Cancer Center in the USA was conducted on 423 cancer patients with COVID-19 and reported that 40% of the patients were hospitalized, 20% had severe respiratory illness, 9% needed mechanical ventilation, and 12% died within 1 month. The study emphasizes that cancer patients have worse outcomes than other patients with COVID-19^[2].

COVID-19 in MM is an important topic because MM is currently the second most common haematological malignancy^[3]. Lenalidomide is an immunomodulatory drug used in various stages of MM management. It works by inhibiting the production of proinflammatory cytokines such as tumour necrosis factor-alpha (TNF- α), IL-1, IL-6 and IL-12, and stimulating the production of anti-inflammatory cytokine IL-10. These mechanisms combined result in effective MM management [4], and also suggest that lenalidomide may help to prevent the cytokine storm leading to immune inhibition that could be helpful against severe COVID-19 infection and its complications^[5–7].

The results of a single-centre study that included 60 MM patients with COVID-19 (42 patients were on lenalidomide, 18 were not) showed that lenalidomide maintenance treatment was safe for MM patients with COVID-19. The mortality rate was 23.8% in patients who had COVID-19 and were on lenalidomide in comparison with 33.3% in patients who were not on it. The recovery rates in both groups were 76.2% and 66.7%, respectively^[8, 9].

Another small observation of three patients with MM and COVID-19 in a tertiary centre in Saudi Arabia showed better outcomes with lenalidomide. All three patients were relatively young, and two had significant medical comorbidities and had previously undergone ASCT. All three patients recovered with no complications^[10].

Although our series only includes three patients, all were unvaccinated, elderly, and had multiple comorbidities that could have rendered them susceptible to severe COVID-19 complications. We think that lenalidomide's immunomodulatory effects might explain the minimal symptoms experienced by our three patients. However, further large studies are needed.

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