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CASE REPORT

Guillain-Barr Syndrome Caused by Cytomegalovirus after Multiple Myeloma Treatment

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SUMMARY

Background: **Both humoral and cell-mediated immunity of the patient affected by multiple myeloma (MM) are impaired; thus, infection is the main cause of the onset of symptoms and death caused by MM. Bortezomib is a first-line drug approved for patients with multiple myeloma (MM) and has significantly increased their overall survival. However, bortezomib-induced peripheral neuropathy (PN) remains a significant side effect that has led to its discontinuation in some patients. Guillain-Barre syndrome (GBS) is thought to be related to immune damage, and most patients have cytomegalovirus (CMV), Epstein-Barr virus (EBV), or mycoplasma infection before onset. Cases of GBS secondary to MM are rare.**
Methods: **We provide a case of GBS caused by cytomegalovirus infection after MM treatment, and briefly review the existing literature.**
Results: **Secondary GBS after MM. This patient received active treatment. The clinical symptoms are gradually improving.**
Conclusions: **The use of bortezomib has the risk of reactivating the virus. It is more about the reactivation of hepatitis B virus. Nonetheless, cytomegalovirus and Epstein-Barr virus shall have our attention. Patients with MM need to monitor CMV, regularly, especially during the treatment of bortezomib. At the same time, they also need to closely monitor the symptoms and signs of the nervous system to guard against the occurrence of GBS.**
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KEYWORDS

multiple myeloma (MM), Guillain-Barre syndrome (GBS), cytomegalovirus (CMV), immunocompromised

INTRODUCTION

Multiple myeloma (MM) is a hematological malignancy characterized by the accumulation of monoclonal plasma cells. This is a slow-progressing disease with a median survival of 5 years [1]. Chemotherapy and autotransplantation are the main methods to treat MM [2]. Because of immune deficiency, MM can cause a variety of infections, such as bacteria, viruses, fungi, etc. The increased infection rate is not only due to the decrease in neutrophils caused by disease or chemotherapy [3], but also related to MM-related immunosuppression and MM-related treatment. Guillain-Barre Syndrome (GBS)

is an autoimmune disease that affects the surrounding nervous system and is usually caused by a viral infection in the respiratory or gastrointestinal tract. Plasma exchange or intravenous immunoglobulin and supportive treatment have significantly improved the outcome of GBS, reducing mortality from 30% to 5% [4]. Bortezomib has demonstrated significant activity in clinical trials, mainly against recurrent or newly diagnosed multiple myeloma (MM). Peripheral neuropathy is a significant toxicity of bortezomib, requiring dose modification and potential changes in the treatment plan when it occurs [5]. About 10% of patients had to stop the bortezomib treatment because they cannot tolerate PN [6]. We introduced a patient with MM who was considered for GBS caused by CMV infection secondary to 4 courses of bortezomib.

CASE REPORT

A 50-year-old female patient was diagnosed with foam urine in the First Affiliated Hospital of Zhejiang University in June 2019; blood free light chain LAM 472 mg/L, free KAP/LAM light chain ratio 0.01, bone marrow morphology: promyelocytic cells 53%, bone marrow biopsy: massive plasma cell growth, FISH: 1q21 positive, confirmed as: multiple myeloma lambda light chain type, followed by 4 courses of PRD chemotherapy (bortezomib 1.3 mg/m^2 on days 1, 4, 8, 11, lenalidomide 10 mg, on days 1 to 21, and dexamethasone 40 mg, on days 1, 4, 8, 11) , were accompanied by mild peripheral nerve numbness, and the primary disease was evaluated by sCR.

On November 4, 2019, a sudden diarrhea occurred, followed by fever, and the platelet count (which was always in the normal range) suddenly dropped to 6 x 10^9/L, so she was admitted to the hospital. Check for CMV DNA 5.75 x 10^2 copies/mL, CMV antigen (IE + E) 8/50,000 leukocytes, CMV antigen (PP65) 7/50,000 leukocytes, and after the therapy of methylprednisolone impact and anti-infective, platelets returned to normal. But the patient experienced numbness in both lower limbs and neuralgia gradually worsened, dysuria occured, and the level of sensory disturbances gradually increased, followed by chest tightness, accompanied by chest distress, and muscle strength was assessed as grade IV. However, she was unable to walk, showed ataxia, and was mentally weak. The knee-tibia test and finger-nose test resulted in inaccuracy, the tendon reflex had disappeared, and the abduction of the right eye was limited. Number of nucleated cells measured in cerebrospinal fluid showed 1 unit/μL, protein 1.12 g/L, albuminocytologic dissociation in cerebrospinal fluid (CSF) tests. Also, an electromyogram showed that peripheral nerve in upper and lower limbs are damaged, severe sensory fiber damaged, lower limb damaged compared to upper limbs, left tibial nerve F response was mildly abnormal. According to the above symptoms, we finally diagnosed her as Guillain-Barre syndrome. The patient was treated with high-dose immunoglobulin (IVIG) (400 mg/kg/d for five days), hormone shock (10 mg/d every day), ganciclovir injection antiviral, nutritional nerve, etc. After half a month or so the clinical symptoms gradually improved.

DISCUSSION

The case we have reported is a MM with a well-defined diagnosis. Secondary GBS after MM is rarely reported, according to current literature.

The main characteristics of GBS are progressive, symmetrical, gradually decreasing sensation and muscle strength, weakening or disappearing reflexes [7]. GBS is considered to be an immune-mediated PN. The pathogenesis of GBS is mainly related to immune-mediated demyelinating or axonal mutation [8,9], which is characterized by multiple nerve roots and surrounding nerve involvement and protein-cell separation in cerebrospinal fluid (CSF) tests, intravenous IVIG and plasma exchange therapy are effective. Studies have shown that there is usually one infection event before the onset of GBS, and about two-thirds of patients reported having respiratory or gastrointestinal symptoms in the weeks before onset [10]. This patient also had gastrointestinal symptoms before the onset of the disease, sudden platelet decline, and a high cytomegalovirus detection, and secondary cytomegalovirus infection is clear. Cytomegalovirus infection may be the main cause of GBS. However, some scholars believe that the secondary GBS consideration in patients with MM is related to the use of bortezomib. In 1987, Mactier RA reported the first GBS secondary to MM patients with kappa light chain type [11]. Xingbin Dai et al. [12] and Yu-Ling Xu et al. [13] each reported a case of MM patients with GBS following the first and second courses of bortezomib. They ruled out other reasons thought to be cause the GBS. They believe that the use of bortezomib in patients with MM has a risk of inducing GBS. Sharpley FA et al. [14] reported 57 patients diagnosed with multiple myeloma or AL amyloidosis. After treatment with bortezomib, 39% (n = 12/31) of patients with serum CMV virus were detected to have CMV reactivation, while CMV sero-negative patients are 0%, which indicates that the secondary GBS in MM patients may be related to virus reactivation. Therefore, patients who use bortezomib in clinical practice should pay attention to cytomegalovirus and EB monitoring and intervene as early as possible. The effect of receiving high-dose gamma globulin shock treatment in the early stage of the disease is positive. Our patients also achieved control over the disease after receiving high-dose IVIG in the early stage.

In conclusion with the example of our patients, the patient was diagnosed as MM, MM with low immune function and susceptible to viral infection. It is clear that there is cytomegalovirus infection, thus GBS in this patient was probably due to cytomegalovirus infection. Meanwhile, the use of bortezomib has the risk of reacti-

vating the virus. It is more about the reactivation of hepatitis B virus. Nonetheless, cytomegalovirus and Epstein-Barr virus shall have our attention. Patients with MM need to monitor CMV regularly, especially during the treatment with bortezomib. At the same time, they also need to closely monitor the symptoms and signs of the nervous system to guard against the occurrence of GBS.

Declaration of Interest:
The authors declare that there is no conflict of interest regarding the publication of this paper.

Informed Consent:
Informed consent was obtained for this case report.

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