

# A Patient with Multiple Myeloma who Developed Severe Myoclonus after Stem Cell Transplantation

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## Abstract

There are various neurologic manifestations of Multiple Myeloma (MM) seen either at presentation or as a complication of various anti-myeloma agents administered during the course of the disease. These neurologic complications might occasionally be challenging to diagnose and treat. Peripheral nervous system is more commonly affected and peripheral neuropathy is the most common form of neurologic complications seen in MM. Here we report a gentleman with MM on regular renal replacement therapy developed severe myoclonus 3 days status post autologous stem cell (ASCT). Besides MM, he had Hypertension and Diabetes Mellitus as to his renal failure. He was also suffering from neuropathy for which gabapentin was commenced.

**Keywords:** Multiple myeloma; Neurological complications; Myoclonus; Gabapentin (GBP)

## Introduction

Neurologic manifestations of plasma cell disorders mainly involve peripheral nervous system, with peripheral neuropathy being the predominant form. Spinal cord compression, leptomeningeal involvement, intracranial plasmacytomas, and cranial palsies induced by electrolyte and metabolic derangements are among other neurological manifestations of MM [1]. Moreover anti-myeloma treatment might as well lead to emergence and/or exacerbation of the existing neuropathy. The subtype, incidence and reversibility of drug related across the multiple agent used to treat MM. We report here a patient with MM who developed myoclonus after high dose melphalan and autologous stem cell transplantation.

## Case Report

A 65-year-old gentleman with myeloma, diabetes, and chronic kidney disease (regular program three times a week) has developed sensory neuropathy right after receiving Bortezomib. He previously, was treated with 8 cycles of Bortezomib + and was admitted for autologous stem cell transplantation. His pretransplantation (EMG) showed sensorimotor neuropathy. Gabapentin was started with 300 mg/day and was 300 mg/day every other day up to 1200 mg/day to his , prior to conditioning regimen. A week after high doseMelphalan (140 mg/m<sup>2</sup>, 380 mg) and autologous stem cell rescue, he developed multifocal myoclonus, which severely impaired his normal daily activities. The Gabapentin dose was immediately reduced to 600 mg, however without any improvement in his multifocal myoclonus. Gabapentinblood level was measured to be 19,1U/mL (2-12u/mL). Gabapentin was discontinued and his symptoms resolved 2 days after discontinuation of Gabapentin.

## Discussion

Gabapentin is a commonly used antiepileptic agent that has also been used for controlling neuropathic pain. Diabetic and Bortezomib associated sensory neuropathy are among the indications of Gabapentin treatment [2,3]. Gabapentin is primarily excreted from the kidneys and does not have hepatic clearance, and as expected its' clearance is altered in patients with deranged renal function [4,5]. Myoclonus, sudden brief, shock-like involuntary movement can be caused by anoxic brain injury, metabolic derangement, focal brain lesions, medications and viral infections [6]. It is a movement disorder that typically affects the upper half of the body. Individuals with this condition experience quick, involuntary muscle jerking or twitching (myoclonus) that usually affects their arms, neck, and trunk. Less frequently, the legs are involved as well (restless legs syndrome). More than half of affected individuals also develop dystonia, which is a pattern of involuntary muscle contractions that causes twisting and pulling movements of specific body parts. The dystonia associated with myoclonus may affect a single part of the body, causing isolated problems such as a writer's cramp in the hand, or it may involve multiple areas of the body. High frequency myoclonus refers to twitches at more than one/minute [5]. Myoclonus is also reported in 0.1% to 12.5% of patients using Gabapentin [5,7] and also restless legs syndrome can be seen under Gabapentin treatment [5]. Hypoglycaemia, and altered sensorium are also among the manifestations of Gabapentin toxicity [7,8]. Gabapentinand its clearance is reduced in the elderly and patients with chronic renal failure (CRF) [8]. The of Gabapentinis prolonged to >20 hours in patients with CRF as compared to 5 to 8 hours with normal renal function[]

Gabapentinoverdose seems to be the most likely cause of the myoclonus in the presented as he has never had previous myoclonus, there was a clear temporal relationship between myoclonus andGabapentin, besides the elevated blood Gabapentin levels. As

expected his severe myoclonus improved completely after Gabapentin was withdrawn.

Melphalan might cause altered mental status in Myeloma patients with impaired renal functions [2]. However mental status of our patient was not affected. very rare with Gabapentin, only a report of a patient mentions the co- of and mental status changes [5].

Gabapentin may induce movement disorders at clinically recommended doses, and these disorders may develop within days of initiation and subside promptly after drug [9,10]. The incidence of myoclonus in patients with epilepsy taking Gabapentin during premarketing studies was 0.1%, higher incidence of 5 reported by [10]. However the myoclonus was mild and did not significantly interfere with daily activities in their series. The investigators suggested the risk factors for the development of myoclonus were myoclonus, mental retardation, chronic static encephalopathy, or diffuse brain damage [11].

The incidence and severity of Gabapentin related myoclonus in patients with impaired renal function or ESRD seems to be relatively higher. This higher incidence and more severe form is not surprising; as can also induce myoclonus, the drug is impaired in end stage renal disease (ESRD) and finally Gabapentin causes myoclonus through a mechanism different from that of -induced myoclonus [7,8,10].

Gabapentin provides a voltage-sensitive calcium channel modulation to protect the diabetic peripheral pain [5]. However the exact mechanisms of Gabapentin-induced myoclonus remain poorly understood. The serotonin neurotransmitter system claimed to be involved, as this system has been intimately linked to myoclonus [12]. Myeloma patients undergoing renal replacement therapy are not excluded from autologous stem cell transplant protocols, though a dose reduction to 140 mg/m<sup>2</sup> is required. However as the presented case indicates, they seem to be vulnerable to various toxicities including the drug induced ones. Patient's medication list should be carefully reviewed besides the other possible causes of the symptoms.

## Conclusion

The presented patient with no signs and symptoms of encephalopathy had severe multifocal myoclonus that interfered with his daily activities. The high serum level of GBP, the temporal

relationship between Gabapentin and development of myoclonus and resolving of symptoms after Gabapentin discontinuation, highly suggests Gabapentin as the cause of myoclonus. Gabapentin toxicity should be considered in the differential diagnosis of neurological symptoms in patients with MM particularly the ones on renal replacement therapy [13].

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