

Abstract

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Bortezomib-induced peripheral neuropathy (BIPN) has a profound impact on quality of life, which is an important issue considering the growing number of survivors of multiple myeloma and amyloidosis. BIPN is typically symmetric, distal, "stocking and glove" distribution and predominantly consists of sensory rather than motor symptoms. In this case series, we report an acute neurotoxicity syndrome induced by bortezomib, which is clinically distinct from BIPN by not being peripheral and distal. We describe 6 patients that developed unilateral or bilateral foot drop attributed to bortezomib. With bortezomib discontinuation symptoms improved gradually over months to years

Background

- # Bortezomib is a proteasome inhibitor that is highly effective in the treatment of multiple myeloma (MM) and light chain (AL) amyloidosis
- # PN is the main dose-limiting toxicity associated with bortezomib therapy
- # Motor neuropathy induced by bortezomib is uncommon and has been addressed specifically in case reports and small case series
- # Foot drop (sometimes referred to as "drop foot") is the inability to lift the forefoot due to motor weakness of the dorsiflexors
- # The differential diagnosis of foot drop in cancer patients includes local infiltrating tumor, lumbosacral radiculopathies, compressive peroneal neuropathy, infection, and medications

Objective

Describe the characteristics and natural history of 6 patients that had foot drop while on bortezomib

Materials & Methods

We reviewed the hospital records of 6 patients who developed foot drop while on bortezomib therapy for MM or AL amyloidosis

Pt Nu	Age	Gender	Amyloidosis or MM	Route pf bortezomib administration	Once vs twice weekly Maximal bortezomib dose	Preexisting sensory neuropathy	Type of LC involved	No of cycle that foot drop presented	Time to improvement or resolution	Legl
1	63	Male	AL amyloidosis	SQ	Once weekly 1.3	yes	lambda	1	1 month to resolution	Rt
2	65	Female	MM	SQ	Once weekly 1.3	yes	kappa	4	1 year to resolution	Rt
3	74	Male	AL amyloidosis	SQ	Once weekly 1.3	no	lambda	1	3 years with gradual improvement but no resolution	Lt
4	68	Male	MM	IV	Twice weekly 1.3	yes	kappa	One month after bortezomib was discontinued	Resolved after 3 years	Complete left partial right
5	63	Male	MM	IV and switched to SQ	Twice weekly 1.3	yes	lambda	8	Resolved after 1 year	Rt
6	46	Male	AL amyloidosis	SQ	Once weekly 1.5	no	lambda	3	Improved but not resolved after 4 years	Lt

Summary

Clinicians need to be aware of the likely risk for “non-classical” rare neuropathies associated with bortezomib and should monitor for these toxicities and promptly discontinue bortezomib to prevent irreversible nerve damage. Other possible reasons for drop foot such as compressions due to tumor infiltration or weight loss should be considered.

Discussion

Two patients developed the foot drop in the first cycle, suggesting the adverse effect is not dose-dependent but rather idiosyncratic. One patient was retreated with bortezomib, and the foot drop recurred and resolved upon discontinuation of the treatment. The two patients that did not discontinue bortezomib after the foot drop developed did not experience resolution of their symptoms but did experience improvement over a time course of years. In all six cases, we could not find alternate reasons for the symptoms.

References

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