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Bortezomib-Induced Myopathy in Multiple Myeloma : A Case Report

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Introduction

- Multiple myeloma is frequently associated with weakness due to both disease-related and treatment-related causes and this clinical complexity often makes it difficult to determine the exact etiology of muscle weakness in affected patients.
- Bortezomib is a proteasome inhibitor widely used as a first-line therapy for multiple myeloma. Peripheral neuropathy is a well-recognized adverse effect of bortezomib.
- In contrast, bortezomib-induced myopathy is rare and remains underrecognized in clinical practice.
- As a result, it can be easily misdiagnosed as peripheral neuropathy, steroid-induced myopathy, or general deconditioning.
- Early recognition of bortezomib-induced myopathy is important because discontinuation of the offending agent may lead to functional recovery.
- We report a case of biopsy-proven bortezomib-induced myopathy in a patient with multiple myeloma who presented with progressive proximal lower-extremity weakness.

Case report

- A 68-year-old woman with multiple myeloma presented with progressive proximal lower-extremity weakness. The symptoms developed approximately six weeks after initiation of bortezomib-based chemotherapy.
- She had received induction chemotherapy consisting of bortezomib, thalidomide, and dexamethasone.
- She underwent surgery for a left intertrochanteric femoral fracture, but remained unable to stand with a walker due to persistent bilateral lower-extremity weakness.
- Neurologic examination revealed predominant proximal weakness in the lower extremities with preserved distal muscle strength. No definite weakness was observed in the upper extremities. Sensory examination revealed no definite hypoesthesia.
- Electrophysiologic studies showed normal sensory nerve conduction findings. Motor nerve conduction studies demonstrated decreased CMAP amplitudes in the bilateral tibial, peroneal, and femoral nerves(Table 1).
- Needle electromyography revealed myopathic motor unit action potentials with early recruitment patterns. No abnormal spontaneous activity was observed at rest(Table 2).
- Serum creatine kinase level was within the normal range and serologic studies for autoimmune diseases were unremarkable.
- Muscle biopsy of the left vastus medialis showed myofiber size variation, lipid-laden microvacuoles, and degenerating and atrophic myofibers(Fig 1). These histopathologic findings were consistent with bortezomib-induced myopathy.
- Bortezomib and dexamethasone were discontinued. The patient showed gradual improvement in proximal muscle strength and functional status.
- Follow-up electrophysiologic studies demonstrated recovery of CMAP amplitudes, although femoral nerve responses remained partially reduced.

Table 1. Nerve Conduction Study Findings

		Initial study (R/L)			Follow-up study (R/L)		
Nerve	Stimulation	Latency	Amp	CV	Latency	Amp	CV
Motor							
Peroneal	Ankle	4.06/3.56	**0.4/0.4**	-	4.06/4.01	**1.1/1.2**	-
	Fibular head	10.90/10.35	**0.4/0.3**	46.8/47.1	11.15/12.46	**1.1/1.0**	42.4/**35.6**
Tibial	Ankle	3.56/3.98	**2.1/2.7**	-	3.75/4.11	5.9/6.0	-
	Popliteal fossa	12.23/12.29	**1.9/2.3**	42.7/45.7	12.50/12.86	4.3/4.3	42.3/42.3
Femoral	Inguinal	6.35/6.6	**1.1/0.4**	-	6.20/6.41	**3.0/2.7**	-
Sensory							
Sup. Peroneal	Foot	2.08/2.42	4.4/5.3	-	2.60/2.45	6.0/5.3	-
Sural	Lat. malleolus	2.23/1.79	8.2/8.5	-	2.19/1.88	8.4/8.8	-
LFCN	Lat. thigh	1.90/1.77	3.4/2.3	-	-	-	-

Bold values indicate measurements below the lower limit of normal.
R: Right, L: Left, CV: conduction velocity, Lat: Lateral, Sup: Superficial, LFCN: Lateral femoral cutaneous nerve

Table 2. Needle Electromyographic Findings

	Initial study			Follow-up study		
Muscle (Left side)	ASA	MUAP	Recruitment	ASA	MUAP	Recruitment
Rectus femoris	None	Myopathic	Early	None	Myopathic	Early
Iliopsoas	None	Myopathic	Early	None	Myopathic	Early
Adductor longus	None	Myopathic	Early	None	Myopathic	Early
Vastus medialis	None	Normal	Normal	None	Normal	Normal
Tibialis anterior	None	Normal	Normal	None	Normal	Normal
Peroneus longus	None	Normal	Normal	None	Normal	Normal
GCM	None	Normal	Normal	None	Normal	Normal
Mid lumbar PSP	None	-	-	-	-	-
Lower lumbar PSP	None	-	-	-	-	-

ASA: abnormal spontaneous activity, MUAP: motor unit action potential,
GCM: gastrocnemius, PSP: paraspinalis.

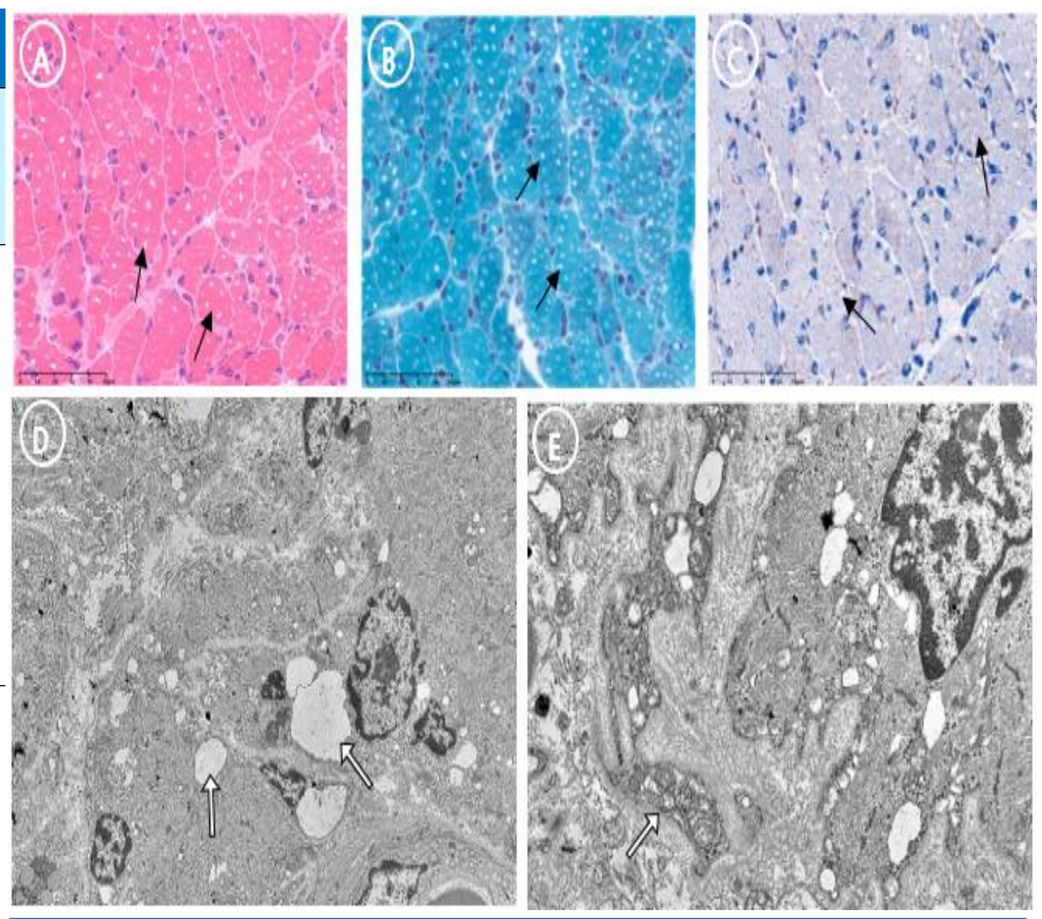

Figure 1. Histopathologic and electron microscopic findings of a muscle biopsy obtained from the left vastus medialis

(A) Hematoxylin and eosin staining and (B) modified Gomori trichrome staining show moderate size variation of myofibers with microvacuoles within muscle fibers (arrows). (C) Oil Red O staining shows increased lipid droplet accumulation within muscle fibers (arrows).

Conclusion

- This case demonstrates bortezomib-induced myopathy presenting as progressive proximal muscle weakness in a patient with multiple myeloma. Bortezomib-induced myopathy is a rare but clinically important adverse effect that may be underrecognized.
- It typically presents with proximal weakness, normal CK levels, and myopathic findings on electromyography without abnormal spontaneous activity. These features may lead to misdiagnosis as peripheral neuropathy or steroid-induced myopathy.
- Early recognition of this condition is important because discontinuation of bortezomib may result in clinical and electrophysiologic recovery.