



## EMG Case No. 85, February 2007

**Presenting Symptom(s):** 61 year old female complains of a five day history of bilateral lower extremity weakness and inability to ambulate.

### This case is no longer available for CME Credit.

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**Disclosures:** WC Scott, None; S Kishner, None.

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**Appropriate Audience:** Residents and practicing physicians.

**Learning Objectives:** After completing this educational activity, participant will be able to: (1) Effectively evaluate an adult patient who complains of weakness and formulate a differential diagnosis for this presenting symptom; (2) Working through patient history, physical exam, and electrodiagnostic findings, an algorithm is described to help identify the differential diagnosis of acute weakness; and (3) Identify a medication commonly used in practice, which may account for an iatrogenic cause of acute myopathic derived weakness.

**Level of Difficulty:** Intermediate.

### *History*

A sixty-one year old African-American female with a past medical history of coronary artery disease, myocardial infarction, hypertension, and chronic renal insufficiency presented with complaints of an inability to ambulate over the past four days secondary to weakness.

One month prior to this she was admitted with acute on chronic renal insufficiency and evaluated for her severe low back pain. CT scan of the lumbar spine revealed erosive arthritic changes involving the sacroiliac joints bilaterally and the facet joints of the entire lumbar spine with bony expansion. This was most consistent with gouty or psoriatic arthritis. A fluoroscopically guided left sacroiliac joint and pubic joint biopsy was performed. This revealed uric acid crystals. She was placed on colchicine, and allopurinol with subsequent decline of serum uric acid from 11.10 to 9.3.

Two and a half weeks after her last discharge, she was readmitted with complaints of a profound bilateral lower extremity weakness that began rapidly and progressively approximately four days ago. Prior to this she performed her home exercise program and was able to ambulate household distances with her walker, but then declined



functionally to non-ambulatory status. Her weakness was not related to trauma or any exacerbation of her low back pain. She denied numbness, tingling, or any other changes in sensation.

1. Prior to continuing, please develop a differential diagnosis and list each possible diagnosis in order of likelihood.
2. Is there any additional information regarding the clinical history that might be helpful in clarifying your differential list or changing its order of priority?

### **Commentary I**

At this juncture the differential diagnosis is broad. The differential diagnosis can be categorized into neurologic and non-neurologic and subdivide the former into upper motor neuron, lower motor neuron, neuromuscular junction, and myopathic disease processes.

The lower extremity weakness is bilateral and symmetric. The acuity of the patients' weakness points to a diagnosis that could evoke rapid change in symptomatology. The recent diagnosis of gout affecting the sacroiliac joints, lumbar spine and pubic symphysis is interesting and an obvious clue, but it should not cloud unrelated possibilities.

With this information, possible upper motor neuron diagnosis could include stroke; multiple sclerosis; parasagittal meningioma affecting the bilateral motor cortex; transverse myelitis; epidural hematoma; spinal cord injury due to compression (perhaps a gouty tophus), infarct, disc herniation; amyotrophic lateral sclerosis; poliomyelitis; uremia induced encephalopathy; West Nile encephalitis; tumor; seizure; and paraneoplastic syndromes. Bilateral symmetric lower motor neuron diseases include polyneuropathies such as Guillain-Barre; tick paralysis; chronic renal failure induced peripheral neuropathy; gouty neuropathy; and lumbar plexopathy. Neuromuscular junction disorders may include myasthenia gravis, Eaton Lambert, and iatrogenic causes. Primary acute myopathies may include polymyositis, dermatomyositis, metabolic myopathies, electrolyte abnormalities; and toxic myopathies including thyroid disorders, and iatrogenic causes. Examples of non-neuromuscular etiologies may include deconditioning, or psychiatric diagnoses. More information is required to narrow this differential diagnosis.

### ***History, continued***

She denied any family history that may be connected to her weakness. She has no allergies. She has not had any recent immunizations. She denied any recent travel. She denied a history of alcoholism or use of tobacco and recreational drugs. She lives in Louisiana and is happily married with two children, both of who are in good health. She was employed as a manager of a clothing store and reports satisfaction with her work. Her current medications include allopurinol 150mg daily, colchicine 0.6mg twice daily, aspirin 325mg daily, amlodipine 5mg daily, metoprolol 150mg twice daily, clonidine 0.1mg twice daily, famotidine 20mg daily, gabapentin 300mg three times daily, lidocaine patch to her low back, and simvastatin 40mg at night.

On review of systems, she denied fever, chills, changes in weight or appetite, headaches, history of seizures, changes in vision, hearing, or recent changes in sensation. She denied nausea or vomiting, or abdominal pain, but admitted to 3-4 episodes of diarrhea daily for the past 3 days. She denied any skin changes, respiratory problems, gynecologic problems, bowel or bladder incontinence, or any other urinary problems. Her thyroid was checked recently and was normal. She complained of symmetric bilateral lower extremity weakness and is non-ambulatory, but denied spasms, cramping, swelling of the extremities, or muscle pain. She continued to complain of moderate low back pain, but this was stable. She denied any serious symptoms leading to psychiatric diagnoses. All other review of systems was unremarkable.

1. If necessary, revise your differential diagnosis based on the additional clinical history.
2. On which details of the physical examination should you focus at this point?

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## Commentary II

The additional history narrows the differential diagnosis. Without concomitant neurological symptoms a localized CNS lesion causing pure motor deficits in the bilateral lower extremities was unlikely to be identified. For this reason and others, the diagnosis of stroke, multiple sclerosis, ALS, encephalopathy, intracranial hemorrhage, and tumor were very unlikely, although a parasagittal meningioma affecting the motor cortex alone was remotely possible. Chronic renal failure induced peripheral neuropathy and gouty neuropathy have been described as sensory motor neuropathies. Spinal cord injury due to disc herniation, compression, infarct, myelopathy, or myelitis; and lumbosacral plexopathies, could also likely manifest with a sensory component to her symptoms, but she denied changes in sensation. The patient's denial of constitutional symptoms, seizures, thyroid disorder, or a family history of a disease related to weakness also eliminated a lot of possibilities. Her interview revealed no overt psychiatric pathology that would explain her symptoms. Iatrogenic statin induced myopathy was possible, but she had been on the same dose of simvastatin for several years. Although it is still quite possible that simvastatin was still be responsible, we were curious why her symptoms occurred on this occasion. Simvastatin's known myopathic side effect may have been potentiated by an interaction with a medication that was recently initiated. Colchicine induced myopathy has also been described in the literature and may have been the culprit given the temporal relationship between the recent prescription of colchicine and her onset of weakness two weeks later. The patients' history of acute on chronic renal insufficiency may have also impaired clearance of this medication resulting in toxic levels.

### *Physical Examination*

The patient had normal vital signs. She was anxious, but alert, pleasant, cooperative, and fully oriented. Her cranial nerves were fully intact. Mental status exam was normal. With good effort, manual muscle testing of the upper extremities was 4/5 bilaterally throughout. Her hips were 2/5 bilaterally in all planes. Knee flexion and extension were also 2/5 bilaterally. Ankle plantar and dorsiflexion were both 4/5 bilaterally. Her strength did not appear to weaken with repetitive activity. Her tone was flaccid in the lower extremities and normal in the upper extremities bilaterally, and there was no evidence of fasciculations or spasms. Palpation of her muscles and range of motion of her joints did not elicit pain. There was no appreciable atrophy of the lower extremities. Active and passive range of motion was within normal limits for all joints in the four extremities. Sensation was normal to pinprick and light touch throughout her body. Proprioception was also intact. She was slightly hyporeflexic in the bilateral lower extremities with no clonus or Hoffman's sign. Plantar responses were down going bilaterally. Neural tension signs were negative. There were no skin lesions or rashes. Pulses were normal in all four extremities.

1. At this point, review your differential diagnosis and revise as appropriate.
2. Are there additional observations on physical examination that might be helpful in narrowing your differential list?

## Commentary III

Findings on physical exam re-confirmed many of the conclusions drawn from the information gathered in the history. The neurological exam was particularly helpful. Hypotonia in the proximal musculature and slight hyporeflexia coupled with an absence of cranial nerve and sensory findings likely ruled-out an upper-motor neuron process. The lack of observed fasciculations made the diagnosis of ALS unlikely, but did not rule it out. The lack of myalgia or arthralgia also made several rheumatologic etiologies less likely. The absence of neural tension signs in the lower extremities, the lack of sensory findings, and the bilateral nature of the process made the diagnosis of radiculopathy, along with several other pathologies affecting peripheral nerves less likely. The absence of a significant difference in strength testing after repetitive activities and presence of her normal facial appearance and function made diagnoses associated with the neuromuscular junction less likely. However, the history and physical exam may have still been consistent with a non-inflammatory or painless myopathic process. The previously mentioned possibility of colchicine-induced myopathy was in line with this clinical scenario.



**Physical Examination, Continued**

The remainder of the physical exam is normal for her age.

1. If necessary, revise your differential diagnosis based on the additional physical findings.
2. Design your approach to the electrophysiologic examination based on the existing data.

**Commentary IV**

A thorough history and physical exam had significantly narrowed the differential diagnosis in this complicated case. Electrodiagnostic testing helped to provide further evidence to eliminate possibilities from our differential diagnosis.

**Electrophysiologic Data**

SENSORY NERVE CONDUCTION STUDIES							
NERVE	SIDE	STIM SITE	RECORD	cm	AMPL	LAT	CV
Sural	Right	Calf	Lateral Malleolus	14	12	3.77	50.7
Ulnar	Right	Wrist	Little finger	14	38	3.38	57.4
Ulnar	Left	Wrist	Little finger	14	27	3.38	56.3
Median	Right	Wrist	Middle finger	14	38	4.34	50.4
Median	Left	Wrist	Middle finger	14	29	4.70	49.7

MOTOR NERVE CONDUCTION STUDIES							
NERVE	SIDE	STIM SITE	RECORD	cm	AMPL	LAT	CV
Median	Left	Wrist	Abductor Pollicis Brevis	8	7.8	5.04	
Median	Left	Elbow	Abductor Pollicis Brevis	22	7.6	8.60	50.6
Ulnar	Left	Wrist	Abductor Digiti Minimi	8	6.9	3.08	
Ulnar	Left	Elbow	Abductor Digiti Minimi	24	6.9	5.72	64.4
Median	Right	Wrist	Abductor Pollicis Brevis	8	6.9	4.96	
Median	Right	Elbow	Abductor Pollicis Brevis	20	6.5	8.28	46.7
Ulnar	Right	Wrist	Abductor Digiti Minimi	8	7.8	3.04	
Ulnar	Right	Elbow	Abductor Digiti Minimi	22	7.3	5.92	59.0
Peroneal	Right	Ankle	Extensor Digitorum Brevis	8	3.5	4.76	
Peroneal	Right	Head of Fibula	Extensor Digitorum Brevis	32	3.2	12.62	47.1



Peroneal	Left	Ankle	Extensor Digitorum Brevis	8	4.1	5.28	
Peroneal	Left	Head of Fibula	Extensor Digitorum Brevis	32	3.8	11.52	48.9

<b>NEEDLE ELECTROMYOGRAPHY</b>									
INSERtional activity: N, sust, unsust									
FIB: 0, 1+, 2+, 3+, 4+									
OTHer: 0 or fascic, myotonia, myokymia									
EFFort: N, decr									
RECRuitment: N, inc or dec 1+, 2+, 3+, 4+									
AMPlitude: N, inc or dec 1+, 2+, 3+, 4+									
DURation: N, inc or dec 1+, 2+, 3+, 4+									
POLyphasia: N, inc or dec 1+, 2+, 3+, 4+									
R/L	MUSCLE	INSER	FIB	PSW	EFF	REC	AMP	DUR	POL
R	Deltoid	N	0	0	N	Full	N	N	N
R	Biceps Brachii	N	0	0	N	Full	N	N	N
R	Triceps	N	0	0	N	Full	N	N	N
R	Brachioradialis	N	0	0	N	Full	N	N	N
R	Extensor Indicis Proprius	N	0	0	N	Full	N	N	N
R	1 <sup>st</sup> dorsal Interosseous	N	0	0	N	Full	N	N	N
R	Abductor Pollicis Brevis	N	0	0	N	Full	N	N	N
R	Paraspinals, Cervical	N	0	0	N	Full	N	N	N
L	Vastus Medialis	N	3+	2+	N	Inc 2+	N	Dec 2+	N
L	Medial Gastrocnemius	N	0	0	N	Full	N	N	N
L	Tibialis Anterior	unsust	3+	2+	N	Inc 3+	Dec 4+	Dec 2+	Inc 3+
L	Peroneus Longus	unsust	2+	2+	N	Inc 1+	N	N	Inc 2+
L	Gluteus Medius	unsust	0	0	N	Inc 2+	Dec 3+	Dec 1+	N
L	Gluteus Maximus	unsust	3+	2+	N	Inc 3+	Dec 4+	Dec 2+	Inc 3+
L	Paraspinals, Lumbar	unsust	1+	2+	N	Inc 1+	N	N	Inc 2+
R	Vastus Medialis	N	3+	2+	N	Inc 2+	N	Dec 2=	N
R	Medial Gastrocnemius	normal	0	0	N	Full	N	N	N
R	Tibialis Anterior	unsust	3+	2+	N	Inc 3+	Dec 4+	Dec 2+	Inc 3+
R	Peroneus Longus	N	0	0	N	Full	N	N	N
R	Gluteus Medius	unsust	0	0	N	Inc 2+	Dec 3+	Dec 1+	N
R	Gluteus Maximus	unsust	1+	2+	N	Inc 1+	N	N	Inc 2+
R	Paraspinals, Lumbar	unsust	1+	2+	N	Inc 1+	N	N	Inc 2+

Nerve conduction data reveals prolonged distal latency for bilateral median sensory and motor responses, with responses from all other nerves and muscles tested within normal limits. On EMG, abnormal spontaneous activity is noted in several lower extremity muscles bilaterally with small, polyphasic motor units with short duration, appearing with early recruitment. EMG of the right upper extremity was normal.

1. On the basis of both the clinical and electrophysiologic evaluations, formulate your diagnostic impression.



List the most likely diagnosis first and follow in order with the other possibilities that are not excluded by the data. Eliminate those diagnoses not supported by the data.

2. Are there additional electrophysiologic data that you feel would further delineate the diagnosis? (Remember, collecting data that are not needed for the diagnosis is costly and uncomfortable for the patient.)

### ***Electrophysiologic Data, continued***

No further electrodiagnostic testing is necessary to confirm the diagnosis.

1. Make the final revisions of your diagnostic impression(s)

### **Go to Diagnostic Impression**

1. What other diagnostic procedures (laboratory tests, etc.), if any, are needed?
2. What treatment would you recommend?

The patient had the following lab tests done prior to this evaluation: basic metabolic profile (creatinine 1.8, AST 84, ALT 46, otherwise normal), CBC with differential (within normal limits), thyroid profile (within normal limits), creatinine kinase (4,852- elevated), GFR (29- depressed), urine analysis (+ urate crystals, otherwise within normal limits), random urine myoglobin (6 – elevated), rheumatologic and inflammatory markers were within normal limits.

### ***Diagnostic Impression***

In the proximal bilateral lower extremities, the motor units on needle exam appeared polyphasic with low amplitude, decreased duration, and early myopathic recruitment. Coupled with the spontaneous activity of positive sharp waves and fibrillations, the EMG results are consistent with an active myopathic process revealed in the proximal muscles tested in the bilateral lower extremities. In addition, prolonged distal latencies in median sensory and motor responses in the absence of findings in distal segments of other peripheral nerves, suggests a diagnosis of bilateral median neuropathy at the wrist.

In this complicated and unusual case presentation of gout followed by treatment with colchicine and subsequent weakness in a patient with a history of renal insufficiency, the diagnosis was made of colchicine-induced myopathy affecting the proximal bilateral lower extremities.

Colchicine myopathy has been sporadically reported by case studies in the literature and the diagnosis is consistent with the findings in this case. Largely, colchicine myopathy is a clinical diagnosis with confirmatory findings seen on electrodiagnostic exam and muscle biopsy, although the definitive diagnosis is made by withdrawal of colchicine resulting in resolution of symptoms. Patients typically present with a history of renal insufficiency; and painless, symmetric, and progressive proximal weakness, as well as, hypotonia and hyporeflexia, and lack of sensory symptoms

### **Commentary V**

Colchicine, derived from *Colchicum autumnale*, has been used for over five hundred years to treat gout.<sup>1</sup> The recommended dosage for treatment of acute gouty attacks starts with colchicine 1.0-1.2 mg, followed by 0.5-0.6 mg every 2 hours as needed until either pain is relieved or gastrointestinal symptoms occur. Colchicine is readily absorbed and a peak serum level is reached 30 to 120 minutes after ingestion with a serum half-life of 20 minutes. When given orally or intravenously, colchicine enters hepatic circulation and is partially demethylated in the liver by the cytochrome P450 system and then accumulates in the liver, bone marrow, leukocytes, intestines, spleen, and



testes; or is excreted unchanged in the urine or feces. Normally 15-40% of colchicine is excreted unchanged and 4-15 percent is excreted as metabolites within the first 48 hours. As such, with normal recommended dosage plasma levels may become elevated with either hepatic or renal compromise.<sup>2</sup> The risk of myopathy is predominantly related to the presence of renal insufficiency as indicated by a serum creatinine level greater than 140umol/L.<sup>4</sup> End stage renal disease precludes the administration of colchicine since it cannot be removed by dialysis.<sup>6</sup> An apparent high volume of distribution, implies extensive tissue binding.<sup>7</sup> However, colchicine in doses of 0.5mg once daily has rarely induced myotoxicity even in patients with impaired renal function.<sup>8</sup> In a literature review by Wilbur et al, the duration of colchicine therapy in patients who experienced myopathy ranged from 4 days to 11 years with a cumulative daily dose of 1.4 +/- 0.96 grams.<sup>5</sup>

Drug interactions may also impact the development of colchicine myopathy. Acute myopathy has been attributed to the concomitant use of colchicine and HMG-CoA reductase inhibitors in patients with renal insufficiency via interactions within the cytochrome P450 system. This mechanism has been implicated in case reports with both simvastatin,<sup>12</sup> and pravastatin.<sup>13</sup> Because of the profound cardiac risk in our patient, we decided pursue a trial of discontinuing the colchicine while continuing treatment with simvastatin. In this case, this decision resulted in resolution of the patient's weakness without losing the cardioprotection of the statin medication. However, if the patient's weakness had not resolved, then it would have been prudent to stop both medications.

Although it is typical for neurotoxins to cause direct axonal destruction, colchicine induces damage to microtubules. Microtubules are involved with cell mobility and also intracellular transport operations. Colchicine binds to tubulin reversibly with a high affinity and prevents polymerization of tubulin into microtubules, thereby impairing axoplasmic transport in peripheral nerves.<sup>3</sup> Colchicine also affects skeletal muscle by altering the microtubular network that allows the normal extrusion of lysosomes in skeletal muscle cells.<sup>4</sup> Overdevelopment of autophagic vacuoles may subsequently injure the lysosomal membrane permeability causing its release of proteolytic enzymes into the cytoplasm and resulting in myofibril degenerative changes.<sup>2</sup>

Other than gastrointestinal side effects, acute toxic side effects of colchicine, such as bone marrow failure or reversible azoospermia, are rare but well recognized. Given the frequency of colchicine administration and concomitant hepatorenal insufficiency, evidence supports this authors opinion that colchicine myopathy is under reported. In a database search by Wilbur et al., only seventy-five cases of colchicine-induced myopathy were identified from 1966-2003.<sup>5</sup> Furthermore, despite the historical use of colchicine, only since 1996 has the adverse reaction of myopathy been reported in the British National Formulary.<sup>2</sup>

Although, colchicine may affect the microstructure involved with axoplasmic flow and thereby affect the peripheral nerves; myopathic features predominate in both the physical exam and electrodiagnostic findings.<sup>5</sup> The presenting symptoms and clinical findings are variable to some degree. Patients typically have proximal symmetric muscle weakness and areflexia and at times mild sensory changes.<sup>5</sup> Choi et al. report marked proximal weakness and atrophy, distributed symmetrically more in the legs than in the upper limbs, with absent deep tendon reflexes in the legs and weak reflexes in the arms. Tanios et al. reported on a patient with a history of primary biliary cirrhosis, who took colchicine and developed an initial chief complaint of severe respiratory muscle dysfunction. EMG evidence confirmed a proximal myopathy and symptoms resolved shortly after discontinuation of colchicine. Although colchicine myopathy usually presents as painless muscle weakness, Tapal et al. described a patient on colchicine for seven years, whose myalgia and weakness was relieved after discontinuation of colchicine. Not all cases involve concomitant renal insufficiency. Kissen et al described a patient with normal renal function who took a routine dose of colchicine for treatment of familial Mediterranean fever and developed colchicine induced myopathy. Of note, onset of myopathy does not apparently correlate with gastrointestinal symptoms.<sup>5</sup>

Electrodiagnostic findings in patients with colchicine myopathy typically demonstrate increased insertional activity with fibrillations and positive sharp waves, and normal conduction velocities. Motor unit potentials in the proximal musculature have the usual myopathic polyphasic appearance with short durations, small amplitudes, and early



recruitment.<sup>13,14</sup> In addition, Choi et al and other case reports have also shown abnormalities on nerve conduction studies consistent with axonal polyneuropathy.

Additional work up may include laboratory studies that typically show elevated CK, and possibly liver enzymes, all of which were evident in our patient, but resolved after cessation of colchicine administration. Although not required to make the diagnosis, muscle biopsy reveals vacuolar changes characterized by acid phosphatase-positive vacuoles and myofibrillar disorganization with lesions selective for type I fibers. Selective type I involvement is likely due to higher tubular concentration in type I fibers.<sup>12</sup> In our patient, as is often the case, the clinical suspicion was sufficient enough to discontinue colchicine without the need for muscle biopsy.

Treatment of patients with colchicine myopathy is discontinuation of colchicine, as well as, physical and occupational therapy to regain strength, endurance, ambulation, and function with activities of daily living. Prognosis is excellent after cessation of colchicine, with patients typically regaining strength and function after several weeks of therapy. Our patient progressed well during therapy and after three weeks in the rehabilitation unit, she regained independent status with functional mobility before she was discharged.

Given the frequent concomitant appearance of hepatorenal insufficiency and gout, or other disease processes treated with colchicine, it is important to recognize the debilitating, but reversible side effect of colchicine myopathy in patients who present with proximal muscle weakness, with or without, sensory changes and myalgia.

### **Bibliography**

- 1) Lascaratos J. Arthritis in Byzantine (AD 342-1453): *Ann Rheum Dis* 1995; 54:951-7.
- 2) SSL Choi et al: Colchicine induced Myopathy and neuropathy. *HKMJ* 1999; 5:204-7
- 3) Paulson JC, McClure WO. Inhibition of axoplasmic transport by colchicine. Podophyllotoxin and vinblastine: an effect on microtubules. *Ann NY Acad Sci* 1975; 253:517-27
- 4) Kunel RW, Duncan G, Watson D, Alderson K, Rogawski MA, Peper M. Colchicine myopathy and neuropathy. *N Engl J Med* 1987; 316:1562-8
- 5) Wilbur K, Makowski M. Colchicine myotoxicity: case reports and literature review, *Pharmacotherapy*; 2004 Dec; 24(12) 1784-92.
- 6) Bennett WM, Aronoff GR, Berns JS, et al Eds. Miscellaneous agents: In: *Drug prescribing in renal failure: dosing guidelines for adults*, 4<sup>th</sup> ed Philadelphia: American College of Physicians, 1999:77.
- 7) Lange U, Schumann C, Schmidt KL. Current aspects of colchicine therapy: classical indication and new therapeutic uses. *Eur J Med Res* 2001; 6:150-60
- 8) Wallace SL, Singer JZ, Duncan GJ, Wigley FM, Kunel RW. Renal function predicts colchicine toxicity: guidelines for the prophylactic use of colchicine in gout. *J Rheumatol* 1991; 18:264-9
- 9) Tanios et al. Severe respiratory muscle weakness related to long-term colchicine therapy. *Respiratory Care*, 2004 Vol 49 No2 189-91
- 10) Tapal et al. Colchicine Myopathy. *Scand J Rheumatol* 1996; 25(2): 105-6



- 11) Kissen EY, Corbo JC, Farraye FA, Merkel P. Colchicine Myopathy in a patient with familial Mediterranean fever and normal renal function. *Arthritis and Rheumatism*, Vol 49 No.4 2003 614-16
- 12) Fernandez C, Figarella-Branger D, Alla P, Harle JR, Pellisier JF. Colchicine myopathy: a vacuolar myopathy with selective type I muscle fiber involvement. An immunohistochemical and electron microscopic study of two cases. *Act Neuropathol (Berl)* 2002 Feb; 103(2): 100-6
- 13) Neuss MN, McCallum et al. Long-term colchicine administration leading to colchicine toxicity and death. *Arthritis Rheum* 1986;29:448-9
- 14) Rieger EH, Halasz NA, Wahlstrom HE Colchicine neuromyopathy after renal transplantation. *Transplantation* 1990; 49:1196-8
- 15) Dumitru D. *Electrodiagnostic Medicine*. 1995 Hanley & Belfus INC. Philadelphia, PA