Muscle disease in medical and systemic disorder

Thanes Termglinchan M.D.

Hand out last version!!!

Myopathy in systemic disease

Clinical: Myopathy are 1st presentation of systemic diseases

Systemic disease→ muscle involvement

Causes: disease progression, complication from systemic disease or complication from treatment

Investigation: Identify systemic disease, auto abs, Electrophysiologic study, muscle imaging and muscle biopsy

Treatment: Rx underlying, symptomatic Rx, rehabilitation and immunosuppressive therapy

Systemic and medical diseases

Definition:

- Generalized or focal diseases
- Affecting a systems: CNS, vascular system, blood
- **Example**: leukemia, anemia, CNS disease, vasculitis, DM, endocrine, hemochromatosis, rheumatological disorder, sarcoidosis, SLE, scleroderma, CKD, inflammatory bowel diseases

Myopathy due to systemic diseases

- **Endocrine disorders**
- **Infectious disease: bacterial, viral, parasite**
- **Immunological disease**
- *Vascular diseases: rare*
- **Critical illness neuromyopathy**
- **Drug/toxic induced myopathy**
- **Malignancies**
- *Hematological disorders: rare*
- *Renal related*
- *Inflammatory bowel disease*
- *Metabolic disorders:*

Diabetes myopathy

Diseases	Muscle involvement	Pathophysiology	Treatment
Diabetes myopathy	Wasting, muscle inflammation, ischemia, infarction, hemorrhage, necrosis, fibrosis, or fatty atrophy	Many	Symptomatic, steroid
1. Diabetes amyotrophy	**Clinical**: Painless muscle wasting	Plexopathy or affecting satellite cell	Symptomatic
2. Diabetic myonecrosis	Acute onset of swelling and severe muscle pain, normal CBC, ESR but ↑CRP. Dx: muscle MRI	Poor control DM	bed rest and analgesics Self-limiting
3. **Diabetic muscle infarction**	Acute onset local pain, together with a focal, palpable mass lesion. Dx: Muscle MRI Avoid MPx due to risk of hemorrhage.	Related poor control DM.	Immobilization and pain control. A short course of prednisolone.

Hypothyroidism

Hypothyroid myopathy:

Clinical: proximal weakness, myalgia, cramp and generalized fatigue. hyperCKemia, sometime rhabdomyolysis, pain and muscle swollen, myoedema, slow relaxation and myasthenia.

- Autoimmune thyroid disease associated DM or PM.
- Hoffmann's syndrome, characterized by muscle stiffness and muscle pseudo-hypertrophy.

Pathogenesis: anaerobic and mitochondrial aerobic metabolism

Lab: ↑ CK, ↓T3&T4 and ↑TSH.

Muscle pathology: non specific, atrophy type2, hypertrophic muscle fibers.

Rx hypothyroid, improve myopathy ~1 year

Hyperthyroidism

Hyperthyroidism:

- Severity of the myopathy not relate to severity of the thyrotoxicosis
- Thyrotoxic myopathy: common in male

Clinical: Nervousness, anxiety, psychosis, tremor, heat intolerance, insomnia, diarrhea and weight loss.

NMJ

MG associated Grave disease

Myopathy

Mild and usually painless proximal weakness or as idiopathic ocular myositis.

Severe shoulder girdle atrophy or 20% distal weakness

- Thyrotoxic periodic paralysis
- Acute or chronic bulbar muscle dysfunction (bulbar myopathy)
- Thyroid orbitopathy (Grave dz)

Neuropathy

Rare

- Myokymia or fasciculation caused by irritability to anterior horn cell
- Demyelinating polyneuropathy

Hyperthyroidism

Lab: ←→ or ↑ CK level, NCS normal, EMG: may be fasciculation.

↑ fT3 or fT4, ↓TSH.

Muscle pathology: non-specific e.g. type 1 or 2 atrophy, scatter necrotic fibers, Vacuoles (in thyrotoxic periodic paralysis)

Pathogenesis:

- **Thyrotoxic myopathy**: enhance muscle metabolism (Thyroid R -> type 1>2), ↓ protein synthesis (insulin anabolic of aa and protein metabolism)
- **Thyrotoxic periodic paralysis(TPP)**: membrane inexcitability, thyroid→ ↑ K efflux from muscle→partial depolarization.

Treatment:

- Rx hyperthyroid, propranolol prevent attack of TPP.
- Thyroid orbitopathy: corticosteroid and immunosuppressive may be benefit?

Hyper-/hypoparathyroidism

- Myopathy related calcium and phosphate metabolism.
- PTH regulation of serum Ca2+ levels by promoting bone resorption, ↑ renal calcium absorption and phosphate excretion, and enhancing 1,25-vitamin D conversion.

Hyperparathyroidism

- Dropped head syndrome, muscle pain, or ischemic, calcifying myopathy.
- Spontaneous rupture of the Achilles tendon.
- Dysphagia.

Hypoparathyroidism

- myopathy, neuromyotonia, or rhabdomyolysis

Hyperparathyroidism

- ↑ 1.25-dihydroxy-vit D, hypercalcemia and hypophosphatemia.

PTH: Stimulate proteolysis in muscle

Clinical:

- Muscle weakness is very common in osteomalacia if untreated.
- Lower proximal limb weakness, atrophy, bone pain (microfracture)
- Dropped head syndrome
- Hyperreflexia, cramp and paresthesia (~50%)

Others non myopathy

- Peripheral neuropathy or cognitive impairment (caused by hyperCa2+)
- 2^{o} hyperPTH (CKD): myopathy, myonecrosis or rhabdomyolysis (calcifiphylaxis = calcification of arteries).

Hyperparathyroidism

Lab: normal CK, osteomalacia,

1^{o} PTH: ↑Ca2+, ↓ Po_4^{2}, ↑serum PTH and ↑1,25 dihydroxy-vit D

2^{o} PTH: ↓ 1,25 dihydroxy-vit D due to CKD.

- NCS and EMG: normal
- **MPX**: non specific, type 2 fiber atrophy.
- Ca^{2+} and PO_4^{2}- level correlate severity of muscle weakness

Treatment: medical Rx and surgery.

- 1^{o} PTH : Parathyroidectomy,
- 2^{o} PTH : vit D, calcium or renal transplantation

Hypoparathyroidism

- Uncommon for muscle weakness

Clinical

- 2^{o} hypocalcemia: A hand, paresthesia, tetany
- Chovestek's sign and trousseau's sign

Lab: normo CK, ↓ serum PTH, ↓ Ca2+, 1,25-dihydroxyvit D, ↑ Po_4^{2} .

NCS and EMG: normal.

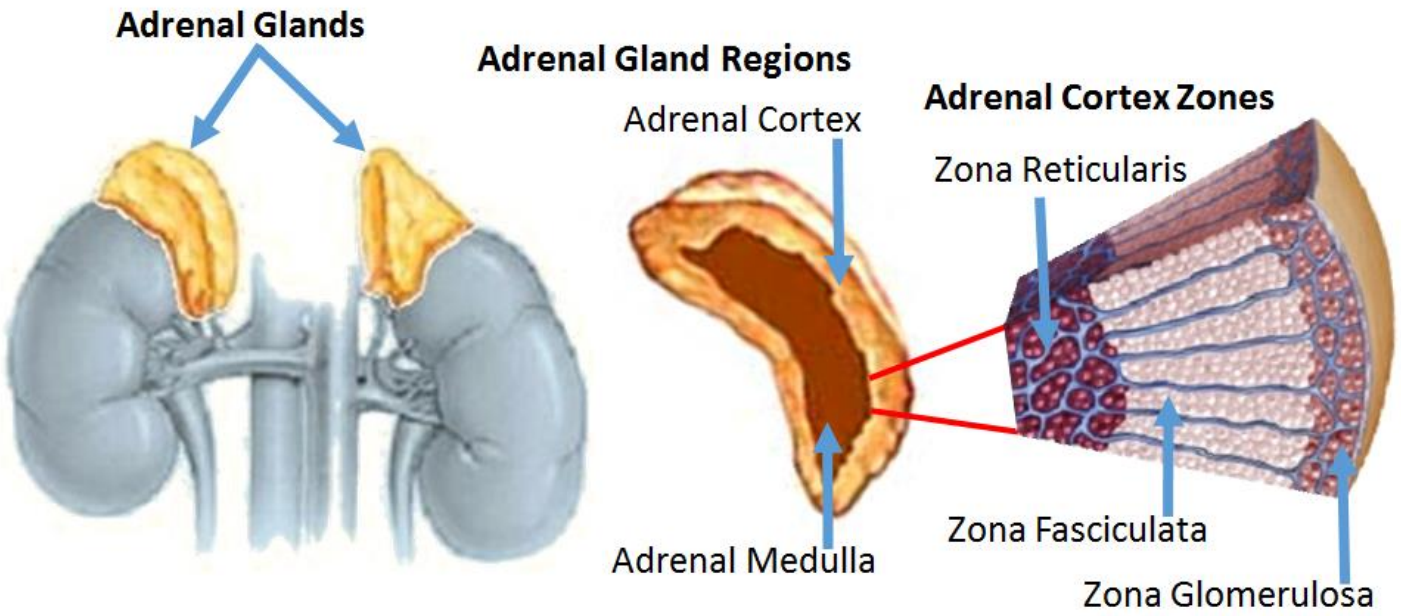
- fasciculation (2^{o} hypocalcemia = n. hyperexcitability)

Rx: Ca2+ and vit D administration.

Disorder of adrenal gland

3 regions:

- Zona fasciculate (glucocorticoid): ↑ excretion →steroid myopathy
- Zona glomerulosa (mineralocorticoid): ↑ excretion → hypokalemia
- Zona reticularis (androgens hormone):no weakness



Steroid myopathy

- ↑Glucocorticoids (pituitary, adrenal tumor and iatrogenic)
- Prednisolone ≥ 30 mg/day, chronic administration
- **Risk of myopathy**: fluorinated >non-fluorinated, Triam > beta > dexa)

Clinical:

- Proximal muscle weakness (spare distal extremity, oculobulbar, facial muscles)
- Cushingoid appearance.

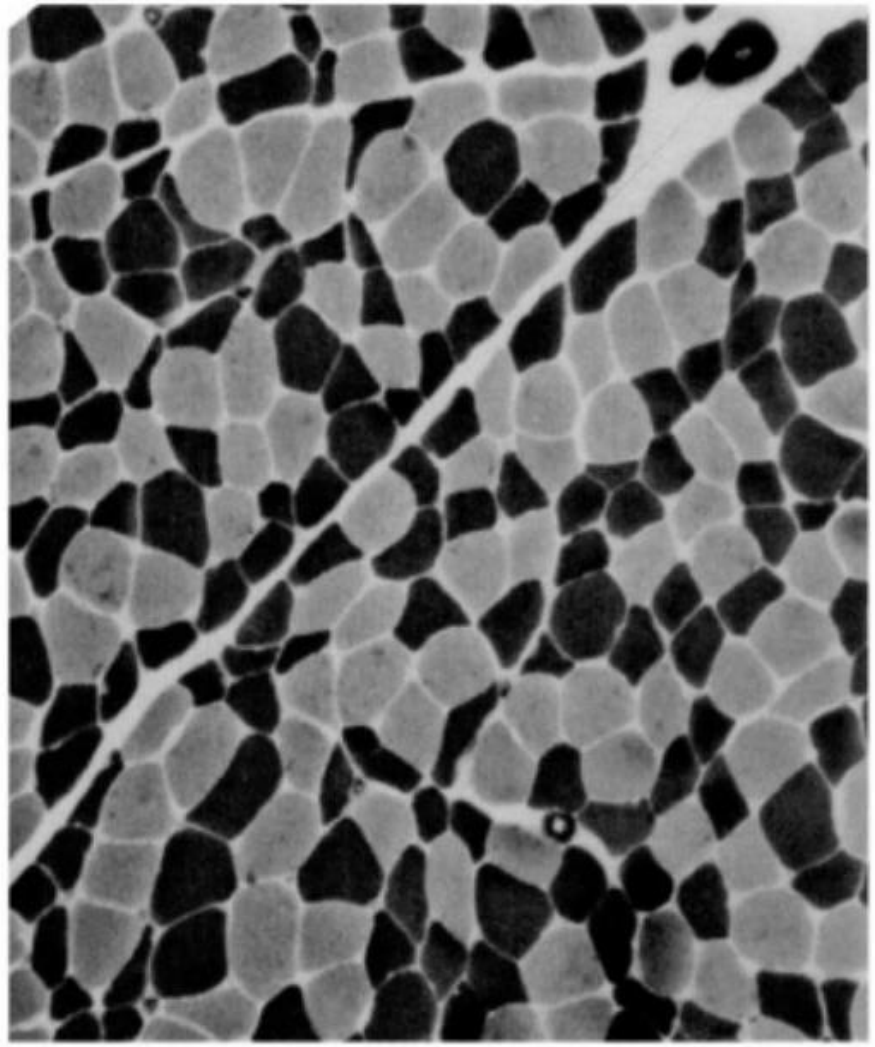
Lab: normo CK, low K, high Na.

NCS and EMG: normal

MPX: type 2 fiber atrophy

Rx: Rx underlying disease. Taper steroid.

Type II fiber atrophy



Muscular manifestations in systemic diseases

- **Acute**: pathogen-caused myositis, muscle infarction, or rhabdomyolysis.
- **Subacute and chronic**: secondary endocrine or secondary metabolic myopathy, myasthenia, immune-mediated myositis, muscle abscess, or vasculitis with secondary myopathy.

Infectious diseases

Viral infections:

- myositis, rhabdomyolysis.
- Self limiting.

Myositis: few data for in detail.

- The calves pain(80%), lower limb weakness (71%), impaired ambulation (57%), and gait disturbance (40%)
- Duration : 3.6 days

J Pediatr (Rio J) 2015;91:442–7

Viral infections: pathogens

- **Reported virus**: influenza-B, influenza-A, parainfluenza-1, parvoviruses, HTLV-1 , Epstein-Barr virus, arboviruses (e.g., dengue myositis), adenovirus, coxsackie, herpes, HIV-1, or chickenpox.

Report muscle involvement:

- Influenza-B in pediatric : 17.9% developed myositis
- HTLV-1: axial myositis
- The chickenpox virus: orbital myositis
- Chronic HCV infection: DM or IBM
- HIV-1: PM, DM or IBM or abscess

Viral infections

Rhabdomyolysis: benign course

- dengue and influenza-A
- **Risk factors**: myalgia, arterial hypertension, and acute renal failure

HIV-related myopathy

Myopathy in HIV infections: common in adult, early-late stage of HIV.

- Sometime combine with HIV-related neuropathy

Type of myopathy:

- Inflammatory myopathy: HIV related myositis: NAM, PM, IBM
- Zidovudine (AZT) myotoxicity
- HIV wasting syndrome
- Opportunistic infection e.g. toxoplasmosis,

Pathogenesis: HIV trigger a T cell mediated and MHC class 1 restricted immune response.

HIV-related myopathy

Investigations:

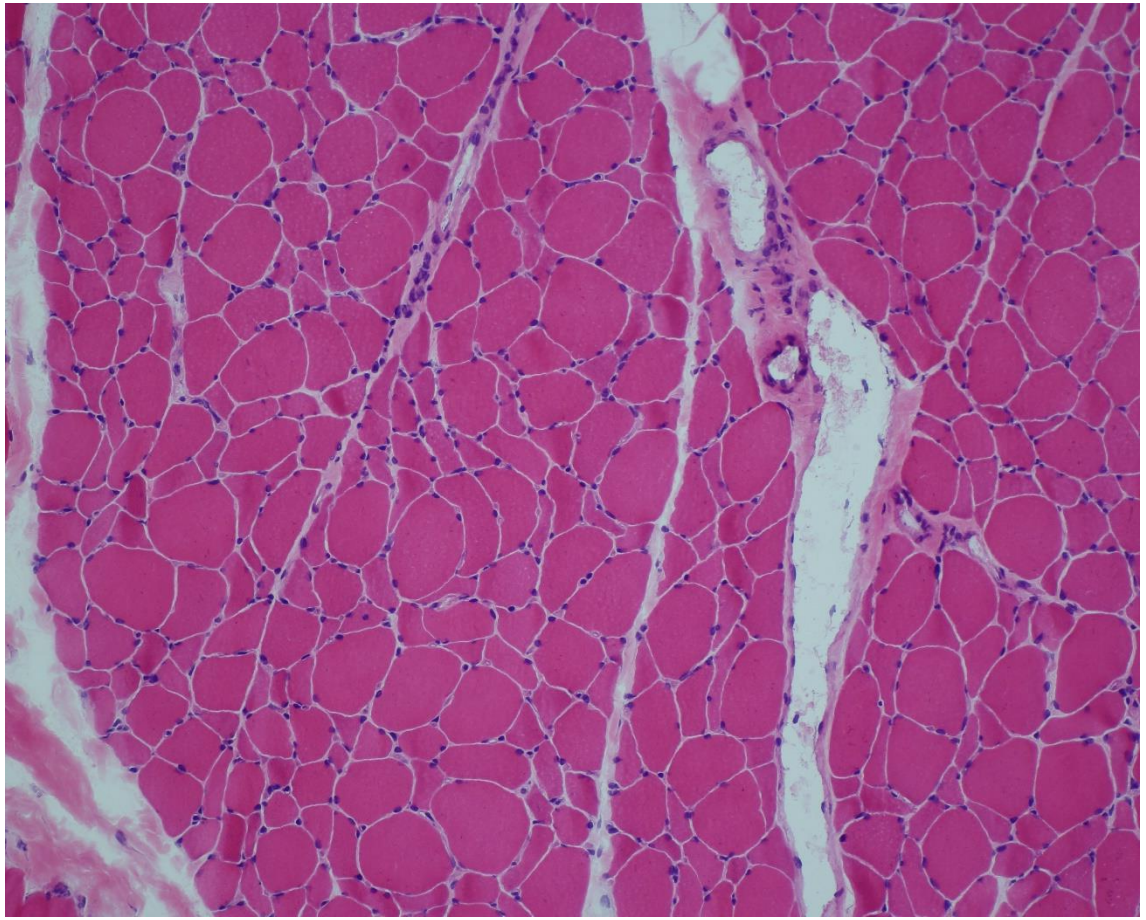
- ↑ CK, membrane instability myopathy
- **MPX**: perivascular inflammation (but non specific, no necrotizing vasculitis), PM

  sometime: RRFs, nemaline rod, cytoplasmic bodies.

  Rimmed vacuoles (pathology compatible IBM)

Treatment:

- Antiretroviral medications
- Corticosteroid rx (myositis)



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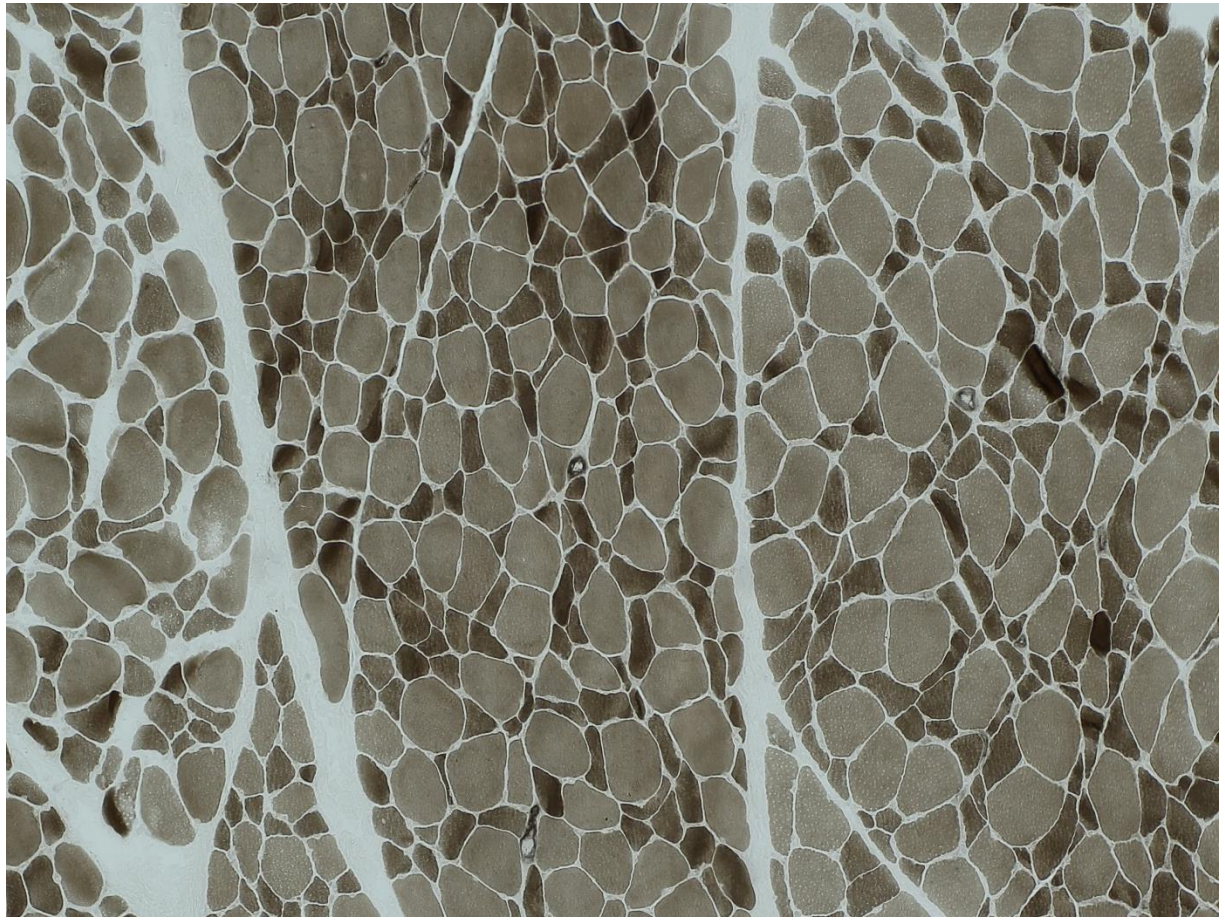


ATPase9.9

ชาย 29 ปี มาด้วยอาการปวดต้นขาด้านใน ๒ ข้าง ไม่มีไข้ ตรวจร่างกายปกติ ไม่มีอ่อนแรง new diagnosis HIV infection
Lab: **CK** normal, muscle MRI showed edema at adductor group of both thigh
MPX at left adductor magnus

Bacterial infections

Myositis or rhabdomyolysis

Myositis

- Bacterial polymyositis: pyomyositis (MC: S. aureus)
- **Source**: arthritis, sacroilitis, a spinal abscess from bacteremia or sepsis.
- Pyomyositis of the iliopsoas muscle may be complicated by septic pulmonary embolism.
- Sepsis from streptococcus group-G originating from arthritis may cause diffuse polymyositis

Bacterial infections

- streptococcal necrotizing myositis: fatal !!!
- Others: Klebsiella pneumoniae or mycobacterium tuberculosis.
- C.jejuni: systemic myositis (Host: HIV or skin penetration).

Rhabdomyolysis

Pathogen

- Staphylococcus aureus, Salmonella, brucella, mycoplasma pneumoniae, tuberculosis, tetanus,

Protozoal infections

Clinical: myositis or rhabdomyositis.

Causative agent: include sarcocystis, plasmodium falciparum, toxoplasma gondi, neospora, microspore.

Rhabdomyolysis: malaria

Cysticercosis

Taenia solium involve skeletal muscles.

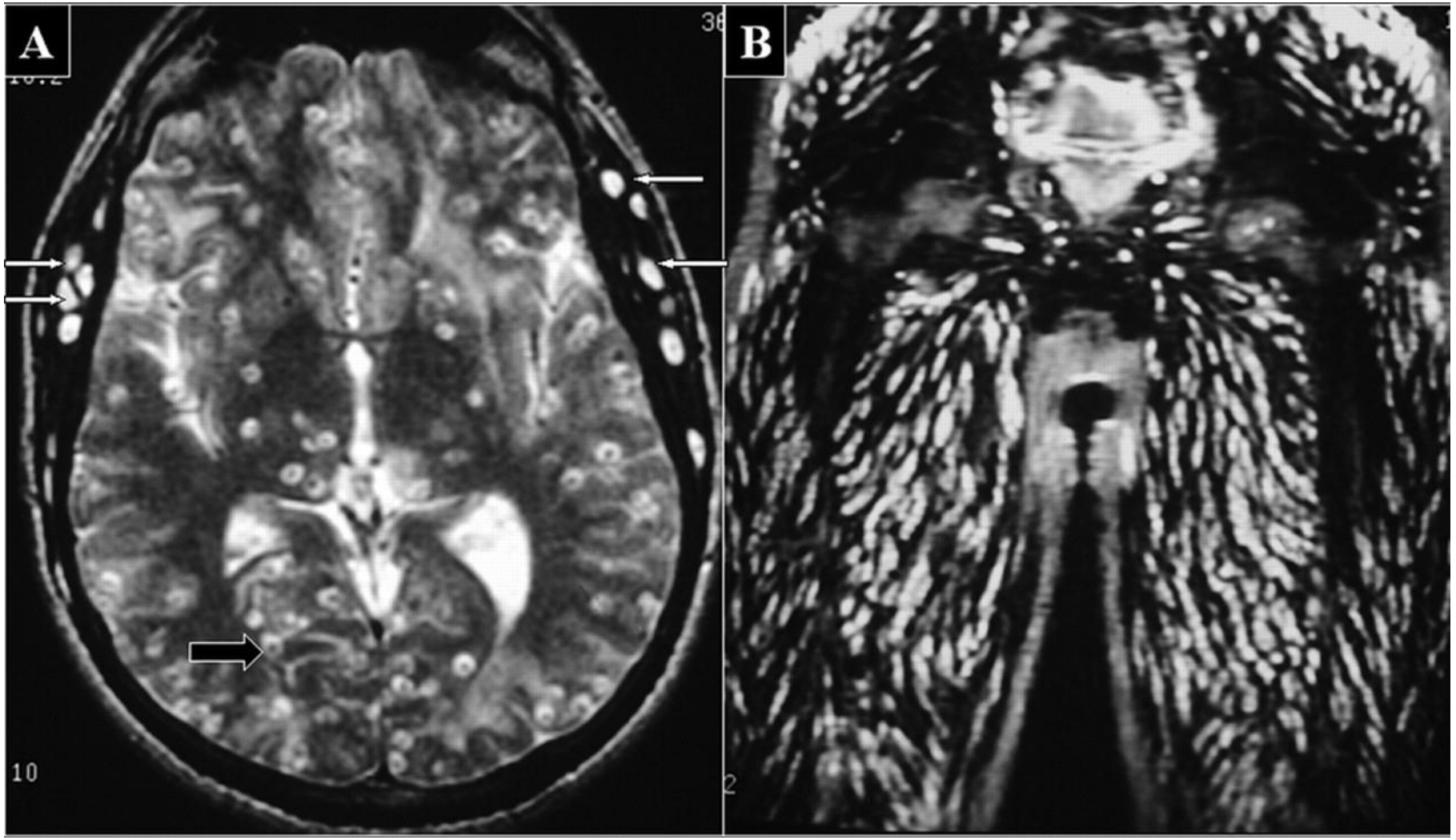
Contaminate larva from food or water→hematogenous spreading

Clinical: myalgia**,** tenderness, pseudohypertrophy of infected muscles (tongue and calves), mild weakness

Lab: high CK, eosinophilia

Treatment:

- Praziquantel for myositis?
- Niclosamide and paromycin for adult tapeworm
- **Steroid:** reduced reaction from degenerate parasite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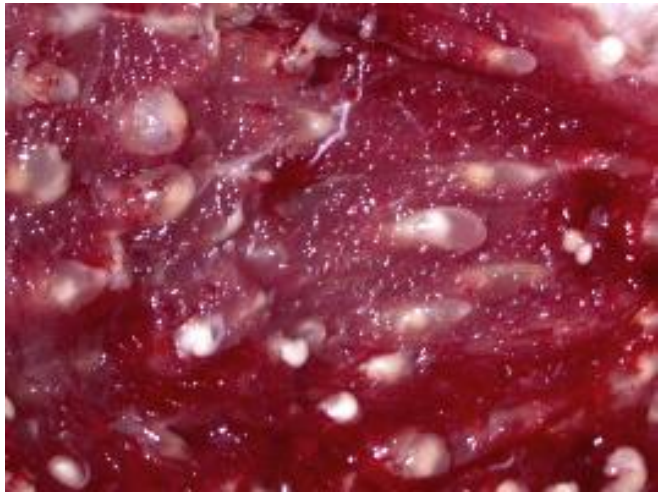


Immunological disorders

Inflammatory myopathy: DM, PM, IBM and NAM

Overlap syndromes: DM or PM or necrotizing myopathy associated with well-defined MCTD.

Diseases: SLE, Sjogren syndrome, rheumatoid arthritis, systemic sclerosis, the anti-synthetase syndrome.

Overlap syndrome

- DM or PM associated with Scleroderma, MCTD, Sjogren syndrome, SLE or RA.
- Muscle pathology: non specific e.g. perivascular or perimysial inflammation.
- More response to immunosuppressive Rx.

Immune diseases	Muscle pathology	Clinical and lab
Scleroderma	Type 2 fiber atrophy Perimysial fibrosis	Weakness is common CK, NCS and EMG: normal
	SS or CREST: 5-15% have **myositis**	↑CK, irritable on EMG Anti-Scl-70 in SS Anticentromere ab in CREST
SLE	Disuse atrophy Myositis like DM (↑IFN-1 inducible gene), MxA +ve in blood vessel.	Weakness is common (usually disuse atrophy)
Sjogren syndrome: **Sicca syndrome**	Non-specific Rare showed muscle inflammation	Myalgia Disuse atrophy: arthritis and pain Myositis: rare, ocular myositis, PM, IBM
Rheumatoid arthritis	Type 2 fiber atrophy	Myositis is rare, ocular or myositis
MCTD	DM > PM NAM	MSA or MAA

Systemic lupus erythematosus (SLE)

Clinical: 9% developed myositis

Disease:

- PM: mixed connective tissue disease e.g. SLE, scleroderma, and polymyositis along with high titers of anti-U1 and anti-U2-nRNP antibodies.
- NAM or rhabdomyolysis.
- Type 2 fiber atrophy.
- Ocular myositis - rare

Systemic sclerosis

= arthralgia, synovitis, contractures, tendon friction rubs, tenosynovitis, and muscle disease (5.6% high CK).

Clinical: myositis with myalgia and weakness e.g. dropped head syndrome.

Response to IVIg !!

Sarcoid myopathy

Sarcoidosis: pulmonary symptom and lymphadenopathy. Erythema nodosum and arthralgia.

- Incidental granulomas can be seen in muscle biopsy.
- Palpated granuloma within muscle.

Clinical: focal myalgia, tenderness, atrophy, weakness.

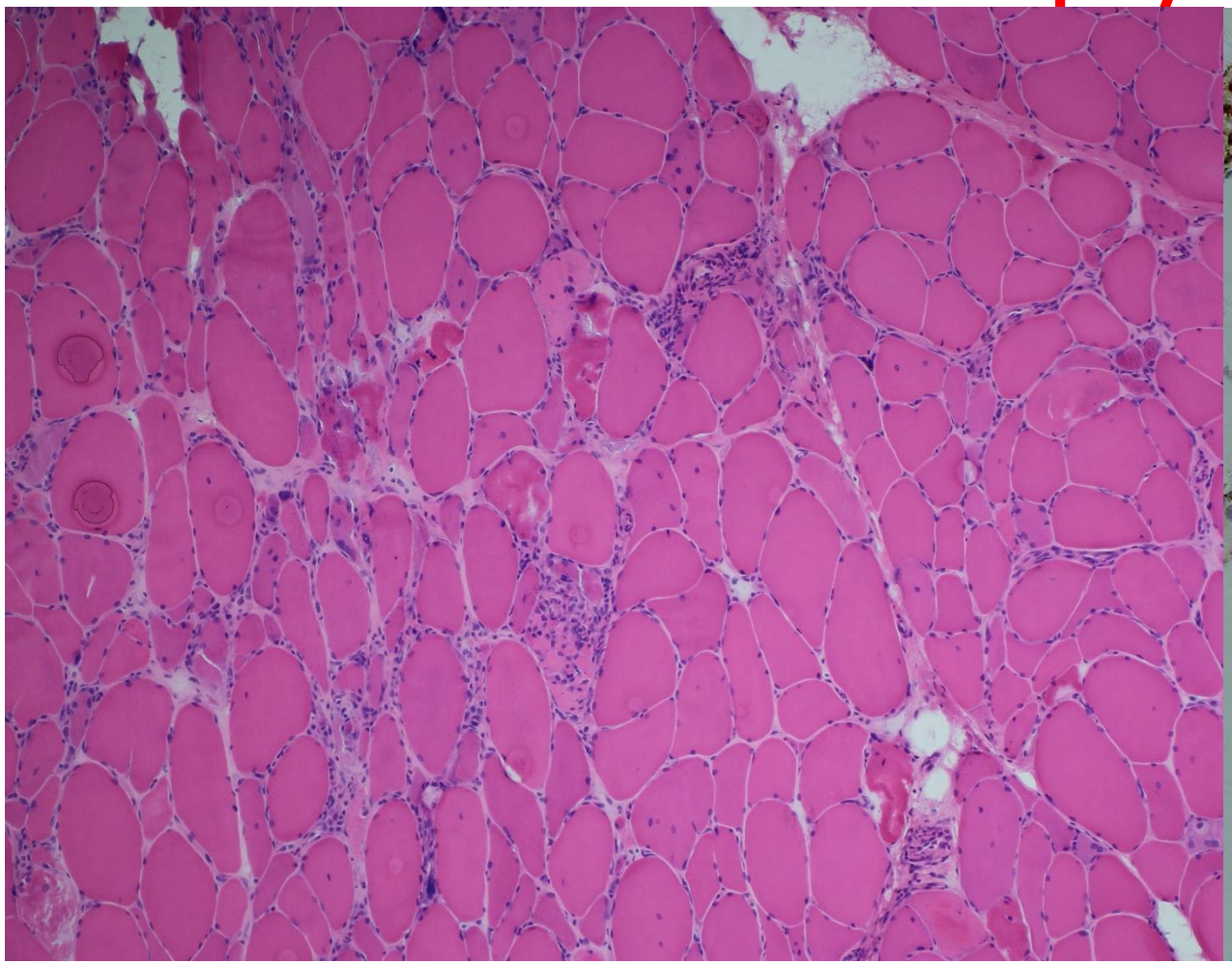
Lab: CK ↔ or ↑ , serum ACE ↔ or ↑ , CXR: hilar lymphadenopathy and parenchyma involvement.

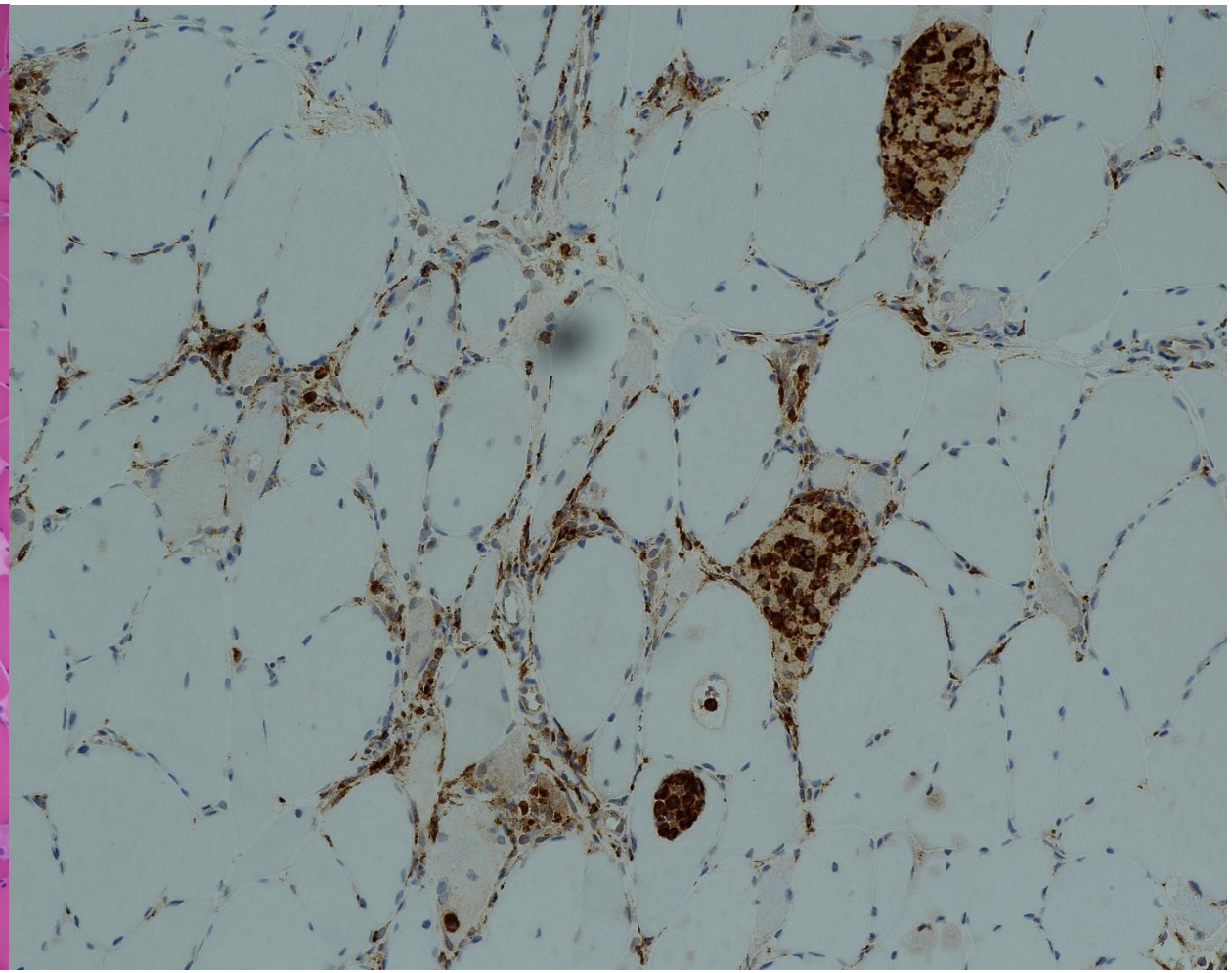
EMG: normal, myopathic or mixed neurogenic/myopathy.

Treatment: Focus on other systemic manifestation, myositis is typical asymptomatic.

Refractory weakness, sometime coincident with IBM (sometime share clinical and histology of IBM)

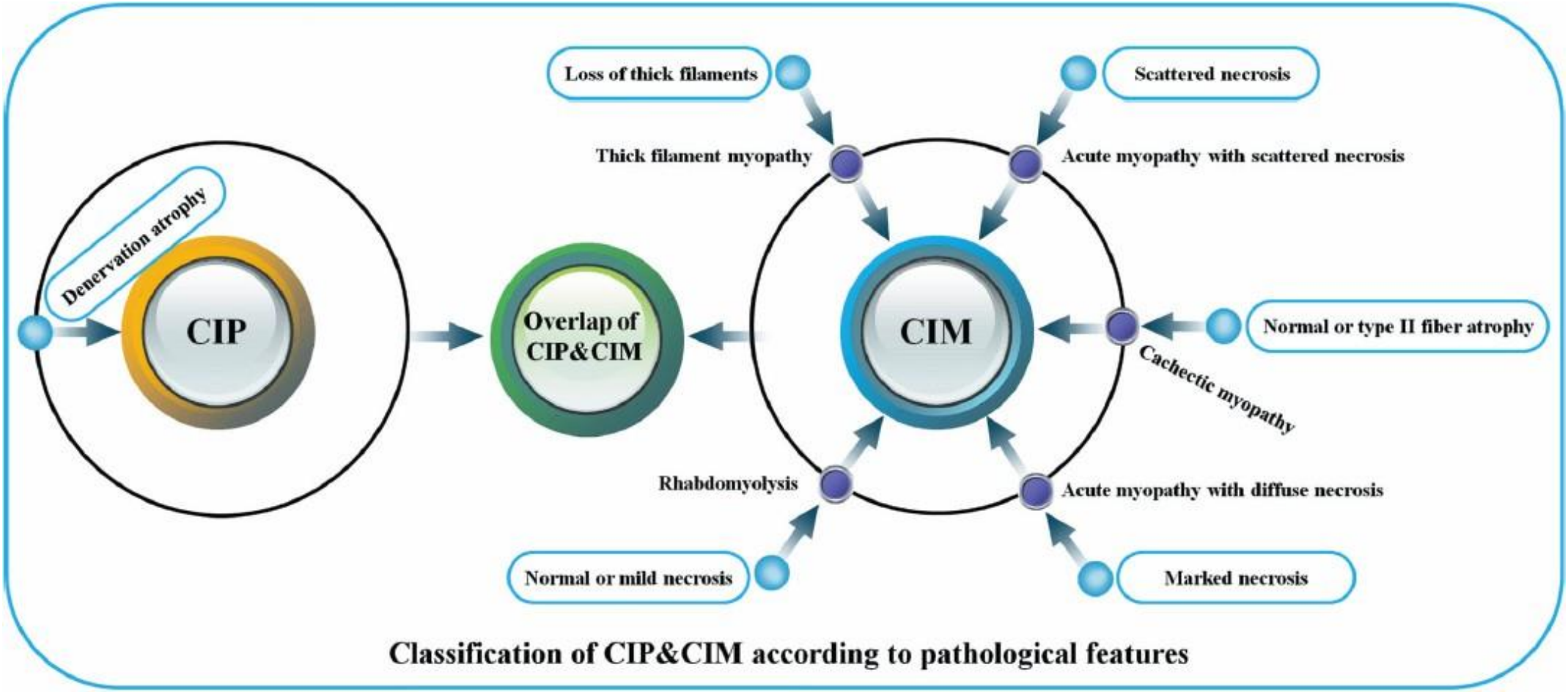
Muscle biopsy of Sarcoidosis



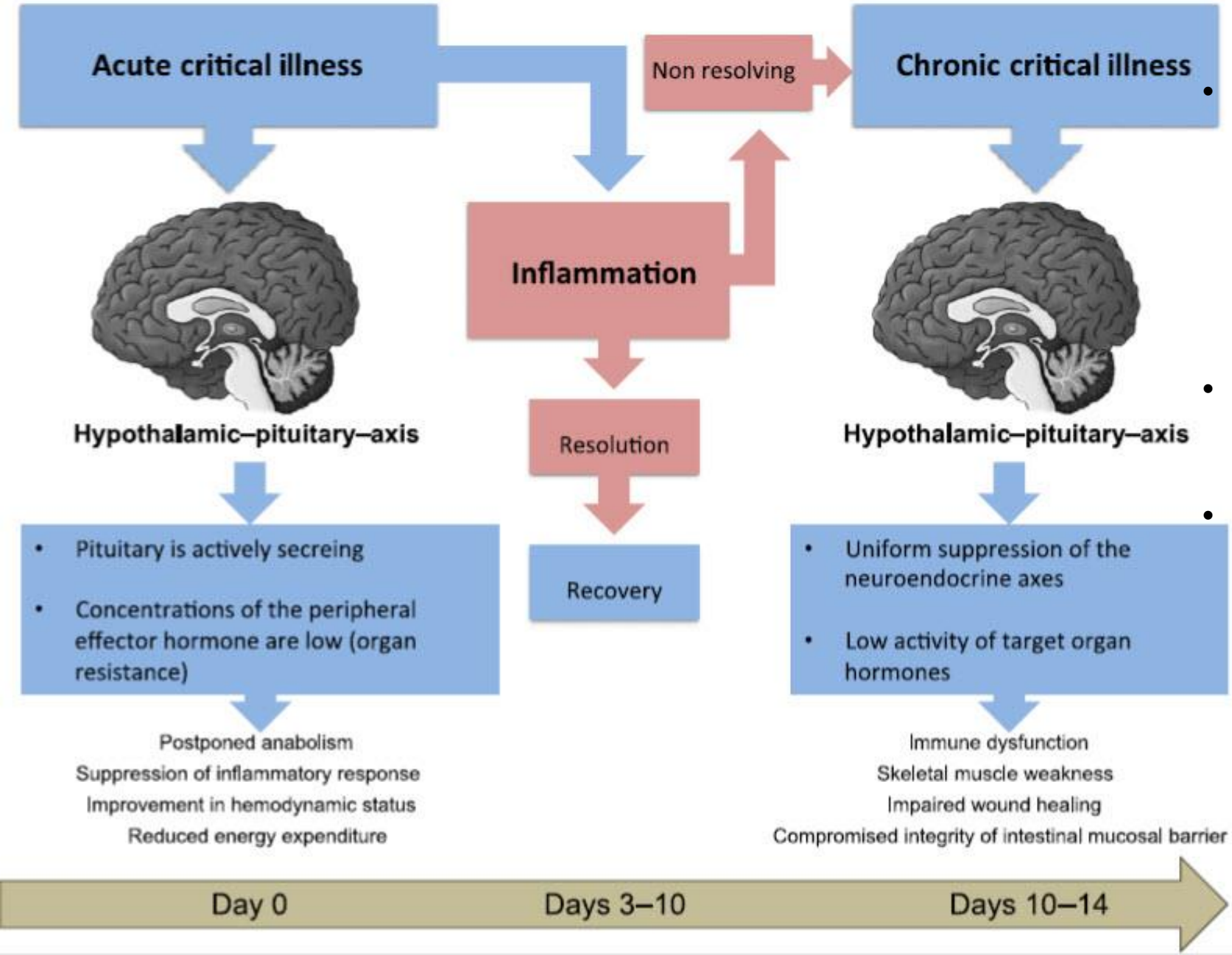


CD 68

Critical illness polyneuropathy and myopathy



Zhou CK, et al. / Neural Regeneration Research. 2014



- The acute disease is characterized by the presence of a significant inflammatory response and the activation of the hypothalamic–pituitary axis, with the purpose of delaying the anabolism and increase the catabolism to make available the energy substrates.
- The resolution of the inflammatory process results in healing and restoration of normal neuroendocrine activity.
- If inflammation fails to resolve, the persistent disease leads to the development of an exhaustion of the neuroendocrine response with the appearance of chronic critical illness.

Eur J Clin Invest 2015; 45 (12): 1341–1349

Critical illness neuromyopathy

- Muscle weakness + failure to wean from the ventilator.
- Structural changes associated with CIP and CIM include axonal nerve degeneration, muscle myosin loss, and muscle necrosis.
- Electrical inexcitability of nerves and muscles with reversible muscle weakness.
- An acquired sodium channelopathy causing reduced muscle membrane and nerve excitability is a possible unifying mechanism underlying CIP and CIM.
- **Diagnosis**: clinical, electrophysiological, and muscle biopsy investigations.
- **Treatment**: Control of hyperglycemia and early rehabilitation.

Critical illness myopathy

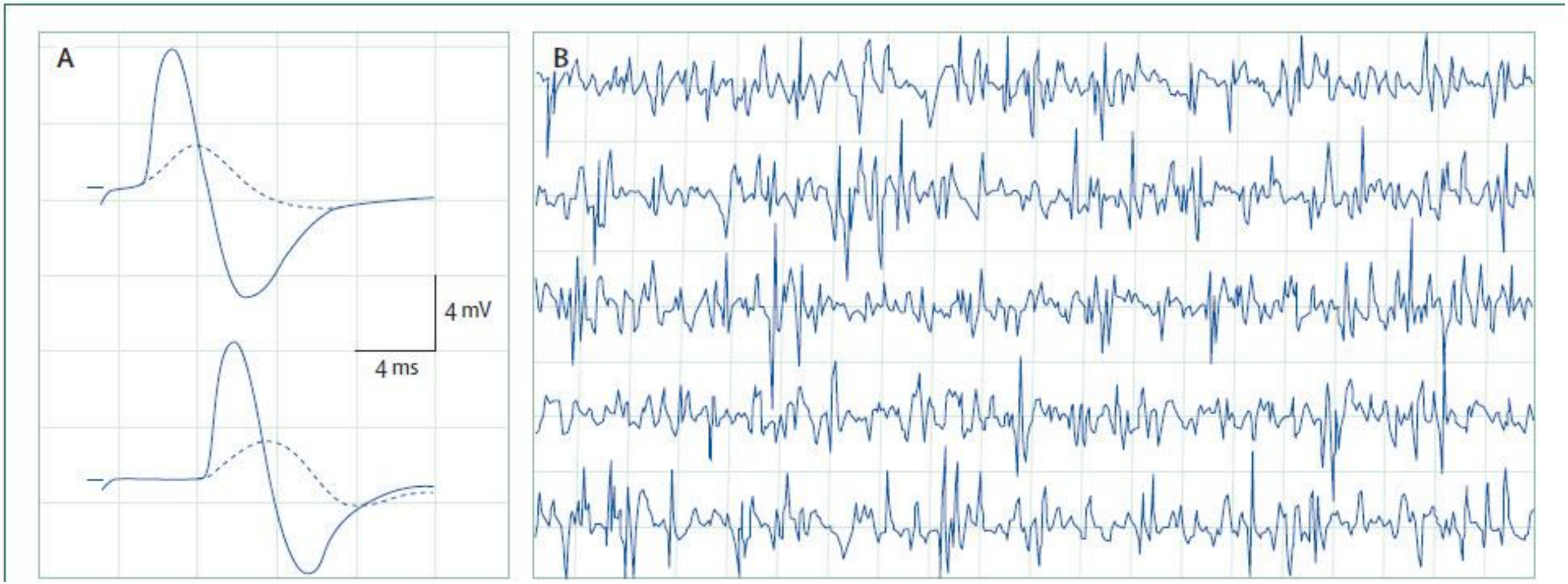
- A primary myopathy.
- Clinical same as CIP except normal sensation and frequent facial weakness.

Electrodiagnosis: reduction CMAPs and an increase in their duration (both prox and distal)especially lower extremity, normal SNAPs, reduced muscle excitability on direct stimulation. CMAP duration can be two to three times longer than in healthy controls.

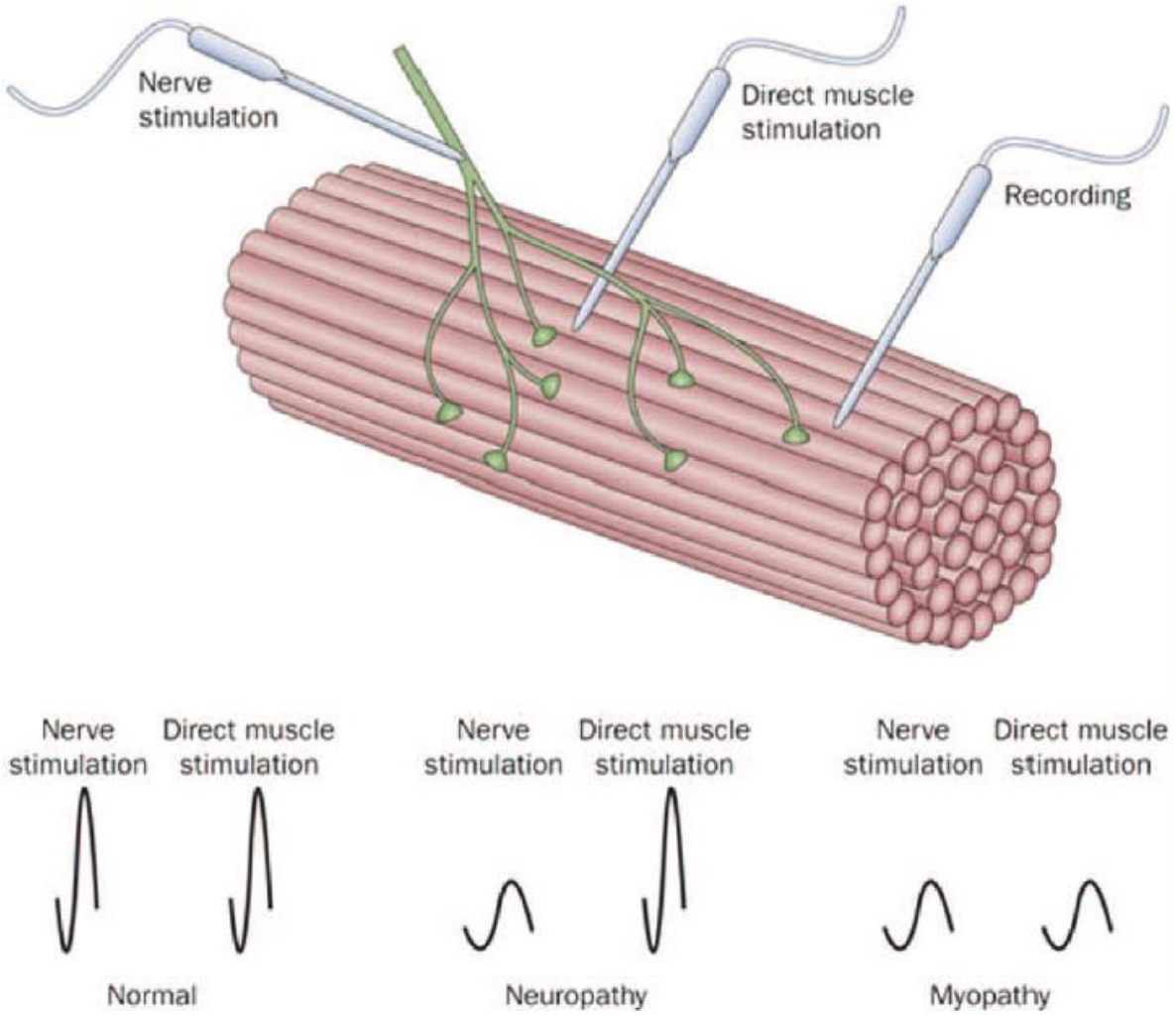
Direct muscle stimulation: indicate CIM

- Direct muscle stimulation ratio: $\frac{CMAP\ nerve\ stimulation}{CMAP\ direct\ m.stimulation}$ >0.5
- Direct muscle stimulation CMAP <3 mV.

NCS and EMG of sepsis patient with weaning difficulty



Direct muscle stimulation



- D irect muscle stimulation ratio: $\frac{CMAP\ nerve\ stimulation}{CMAP\ direct\ m.stimulation}$ <0.5
- Direct muscle stimulation CMAP <3 mV.

INVESTIGATION	CIP	CIM	CINM
EMG	Spontaneous fibrillation potentials and sharp waves; + long duration, high-amplitude polyphasic MUPs (reinnervation)	Spontaneous fibrillation potentials and sharp waves; short duration, low-amplitude MUPs with early recruitment	Features of both CIP and CIM
DIRECT MUSCLE STIMULATION	Nerve: muscle ratio <0.5; Normal direct muscle CMAP amplitude	Nerve:muscle ratio ≥0.5; Reduced direct muscle CMAP amplitude	Variable depending on the relative components of CIP and CIM

CIP and CIM

	Incidence	Clinical features	Electrophysiological findings	Serum creatine kinase	Muscle biopsy	Prognosis
Polyneuropathy						
Critical illness polyneuropathy	Common	Flaccid limbs, respiratory weakness	Axonal degeneration of motor and sensory fibres	Nearly normal	Denervation atrophy	Variable
Neuromuscular transmission defect						
Transient neuromuscular blockade	Common with neuromuscular blocking agents	Flaccid limbs, respiratory weakness	Abnormal repetitive nerve stimulation studies	Normal	Normal	Good
Critical illness myopathy						
Thick-filament myopathy	Common with steroids, neuromuscular blocking agents, and sepsis	Flaccid limbs, respiratory weakness	Abnormal spontaneous activity	Mildly elevated	Loss of thick (myosin) filaments	Good
Acute myopathy with scattered necrosis	Common	Flaccid limbs, respiratory weakness	Myopathy	Mildly or moderately raised	Scattered necrosis	Variable
Acute myopathy with diffuse necrosis (necrotising myopathy of intensive care)	Rare	Flaccid weakness, myoglobinuria	Severe myopathy	Greatly raised, myoglobinuria	Marked necrosis	Poor
Disuse (cachectic) myopathy	Common	Muscle wasting	Normal	Normal	Normal or type II fibre atrophy	Variable
Rhabdomyolysis	Rare	Flaccid limbs	Near normal	Markedly elevated (myoglobinuria)	Normal or mild necrosis	Good
Combined polyneuropathy and myopathy	Common	Flaccid limbs, respiratory weakness	Indicative of combined polyneuropathy and myopathy	Variable	Denervation atrophy and myopathy	Variable

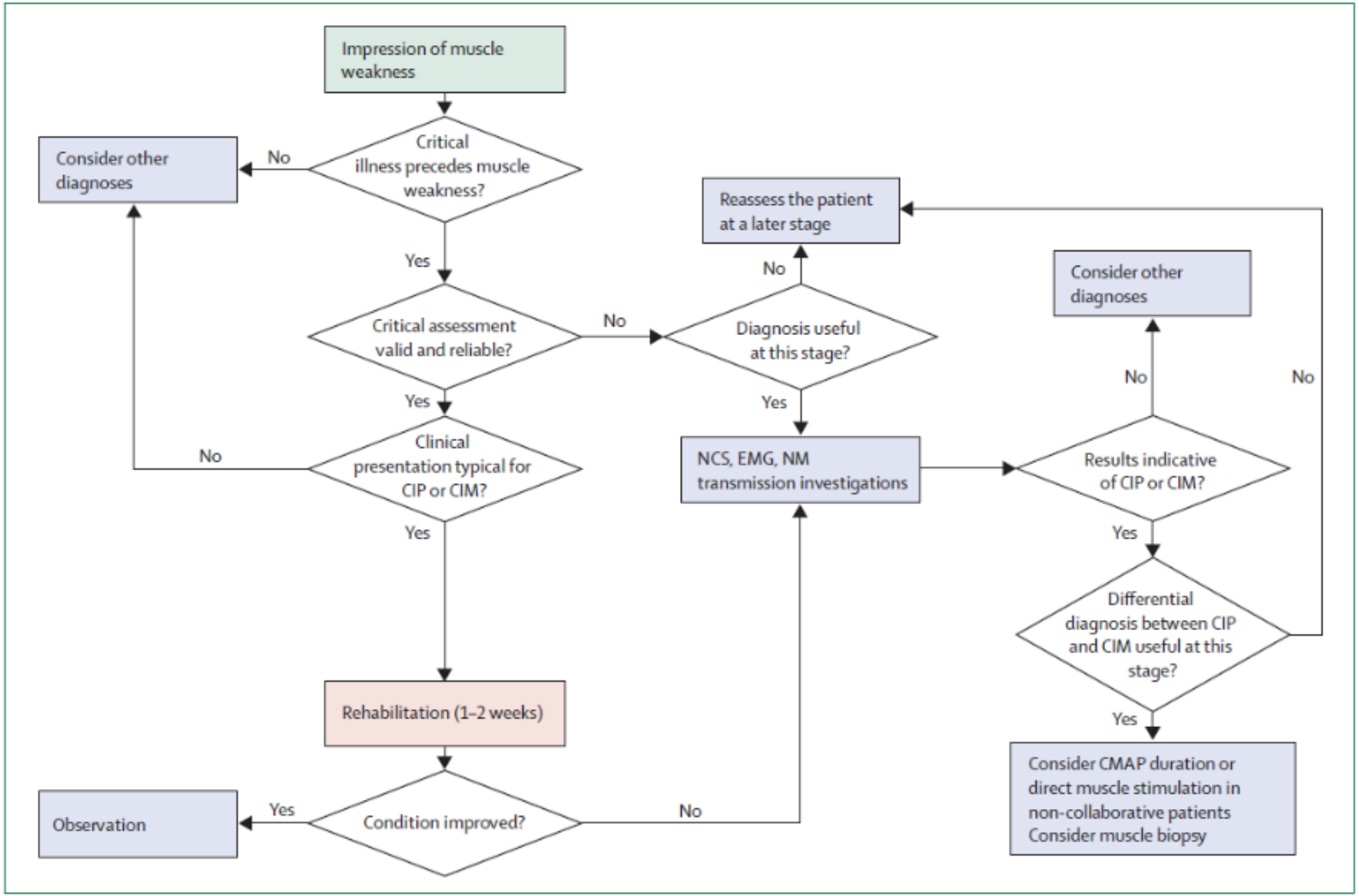
Modified from Bolton,[27] by permission of Springer.

Table: **Generalised neuromuscular disorders associated with critical illness**

Lancet Neurol 2011; 10: 931–41

Diagnosis

- Difficulty in weaning in unexplained others conditions: increased respiratory or cardiac load, metabolic disturbances.
- Limb weakness.
- EPS and muscle biopsy.
- Diagnosis: CIM, CIP and combine CIM and CIP.



Lancet Neurol 2011; 10: 931–41

Management

- **Intensive insulin therapy**: goal 80-110 mg/dl →↓ EPS of CIP and length of ventilator but increased mortality in adult ICU patients.
- **Early rehabilitation**: Repeated daily passive mobilization, early physical and occupational therapy → improved functional independence and prevent muscle atrophy.

A bedside ergometer

Neurology 2005; **64:** 1348–53.
Lancet 2009; **373:** 1874–82.

Management

- A protocol of coordinated daily interruption of sedatives with spontaneous awakening and interruption of mechanical ventilation with spontaneous breathing trials

1-year survival is improved; for every seven patients treated with this intervention, one life can be saved.

Girard TD, Kress JP, Fuchs BD, et al., : a randomised controlled trial. *Lancet* 2008; 371: 126–34.

Drug induced myopathies

- Well established myotoxic substances (table)
- Classified based on histologic features and/or presumed pathogenic mechanisms
- Emphasis on statin induced myopathy: clinical spectrum and management
- General mechanism : destabilize the lipophilic muscle membrane → myonecrosis→ "**NECROTIZING MYOPATHIES**" : High CK, irritable muscle membrane on EMG.
- Discontinuation of the offending agent usually leads to resolution of the myopathic process, except "**statin-associated immune-mediated**"

Potentially Myotoxic Substances

- **Adalimumab**
- **ϵ-Aminocaproic acid**
- ***Alcohol***
- **Amiodarone**
- **Apamin (bee venom)**
- **Barium**
- **Chlorophenoxy herbicides**
- **Chloroquine**
- **Ciguatoxin**
- **Clofibrate**
- **Colchicine**
- **Corticosteroids**
- **Crotamine**
- **Crotoxin**
- **Cyclosporine**
- **Daptomycin**
- 20,25-Diazacholesterol
- Emetine
- Ethanol
- Fibrates
- Gemcitabine
- Germanium
- Gold
- Gossypol
- Interferon-α
- Ipecac
- Isotretinoin
- Labetalol
- Lithium
- Minocycline
- Mojave toxin
- Nucleoside reverse-transcriptase Inhibitors (eg, azidothymidine[AZT])
- **D-Penicillamine**
- **Pentaborane**
- **Procainamide**
- **Propofol**
- **Snake venom**
- ***Statins***
- **Tacrolimus**
- **Taipoxin**
- **Tumor necrosis factor α antagonists**
- **Spanish toxic oil (myotoxic component not clearly identified)**
- **L-Tryptophan**
- **Valproate**
- **Vecuronium bromide**
- **Vinca alkaloids**

Drug induced myopathies

Dominant pathology	Mechanism	Drugs commonly implicated
Fibrosis, necrosis	Myotoxicity, fiber trauma, infection, lysosomal rupture	IM of opiates and antibiotics
Necrosis, macrophages	Myotoxicity Ischemia Hypokalemia (acute) Microvascular thrombosis Impaired protein and energy metabolism, myofibrillar myopathy	Alcohol, statin, fibrates Opiates, Amphetamines and derivatives Diuretics, liquorice derivatives EACA Emetine (ipecac), retinoids
Inflammation Lymphocytic Eosinophilic Macrophagic	Immune mediated	Statin D-penicillamine, procainamide L-Tryptophan Aluminium-based vaccines

Drug induced myopathies

Dominant pathology	Mechanism	Drugs commonly implicated
Mitochondrial damage or depletion (RRFs, COX-negative fibers)	Inhibition of mitochondrial gamma DNA polymerase	Zidovudine
Myosin heavy chain loss	Ionic imbalance leading to filament disaggregation	Steroids in association with neuromuscular blockade
Type 2 fiber atrophy	Reduced protein synthesis	Alcohol, drug-induced hypokalemia, steroids
Vacuoles Myeloid bodies Spheromembranous bodies Featureless	 Lysosomal inhibition Inhibition of microtubular polymerization Hypokalemia (chronic)	 Amiodarone, chloroquine,perhexiline Colchicine, vincristine Diuretics, liquorice, derivatives, amphotericin

Neoplasms

- A paraneoplastic phenomenon
- **Clinical**: focal or generalized myositis, polymyositis, dermatomyositis, or necrotizing myopathy.
- Tumors: leukemia, lymphomas, or other solid tumors.

Leukemia: rare, case report

- Acute myelocytic leukemia: PM, DM
- CLL: iBM

Lymphoma: frequent

- B-cell lymphoma, T-cell-lymphoma, and Hodgkin's lymphoma :PM or DM or EOM, isolated myositis.

Paraneoplastic myopathy

Solid tumor: Lung, gastrointestinal, and breast carcinomas.

- Necrotizing myopathy.

Waldenstrom’smacroglobulinemia:

- antidecorin (BJ) myopathy.

Thymoma

- Rippling muscle syndrome

Renal diseases and myopathy

2 major categories:

1. Conditions that affect both the kidney and the nervous system
2. Neurologic sequelae of renal disease (renal failure)

Hereditary CONDITIONS AFFECTING BOTH THE KIDNEY AND THE NERVOUS SYSTEM

Disease Type and Disease/ Syndrome	Inheritance	Genetic Mutation	Renal Manifestations	Neurologic Manifestations
Glomerular disease Pierson syndrome	AR	LAMB2	Congenital nephrotic syndrome	Anomalies of the retina and Neuromuscular junction
Distal tubular disorders Gitelman syndrome	AR	SLC12A3	Hypokalemia, metabolic alkalosis, hypomagnesemia, hypocalciuria	Intermittent muscle weakness and tetany
Distal (type 1) renal tubular acidosis	AD	SLC4A1	Nephrocalcinosis, nephrolithiasis, mild to moderate hypokalemia	Periodic paralysis
	AR	ATP6V0A4, ATP6V1B1	Hyperchloremic metabolic acidosis, moderate to severe hypokalemia, nephrocalcinosis	Periodic paralysis, sensorineural hearing loss

Continuum (Minneap Minn) 2017;23(3):722–743.

RENAL FAILURE AND myopathy

- Renal production and excretion of bicarbonate and pulmonary elimination of carbon dioxide.
- Neurologic complications through the development of acid-base imbalances, electrolyte disturbances, or toxin accumulation (uremia).
- Most common is alteration of consciousness.
- Myopathy can be related in metabolic alkalosis, hypo-/hyper kalemia, hypocalcemia, hypermagnesemia and hypophosphatemia

Uremia

- CNS complications (e.g. lethargy, encephalopathy, seizures, acute movement disorders and coma) and peripheral nervous system complications (e.g. neuropathy and myopathy).

Uremic myopathy: secondary ↑ PTH

- Correlate with renal function
- **Mechanism:** uremic toxins, altered vitamin D metabolism, carnitine deficiency, insulin resistance, ischemia, and malnutrition.
- **Clinical:** proximal limb weakness and muscle wasting with bone pain and tenderness.
- **Improved with renal transplantation.**

Major Electrolyte Disturbances and Their Corresponding Neurologic Manifestations

Electrolyte Disturbance	Definition	Neurologic Manifestations	Caution
Hypokalemia	Serum potassium <3.5 mmol/L	Weakness with normal reflexes, ascending weakness (sparing cranial nerves), paresthesia	Cardiac arrhythmias; hypocalcemic tetany with concurrent hypocalcemia
Hyperkalemia	Serum potassium >5 mmol/L	Weakness with hyporeflexia, ascending weakness (sparing cranial nerves), burning paresthesia	Cardiac arrhythmias especially without coadministration of calcium
Hypocalcemia	Serum calcium <8.2 mg/dL; ionized calcium <4.4 mg/dL	Tetany, trismus, opisthotonus, encephalopathy, seizures, Chvostek sign, Trousseau sign	Digitalis toxicity in patients on digoxin with rapid or aggressive correction
Hypophosphatemia	Serum magnesium <0.6 mmol/L	Acute areflexic paralysis with diaphragmatic, pharyngeal, facial, and extraocular muscle weakness preceded by perioral paresthesia	Hypocalcemia-related complications with rapid or aggressive correction

Major Electrolyte Disturbances and Their Corresponding Neurologic Manifestations

Electrolyte Disturbance	Definition	Neurologic Manifestations	Caution
Hypomagnesemia	Serum magnesium <0.6 mmol/L	Tetany with Chvostek and Trousseau signs, encephalopathy, seizures, hyperreflexia, tremor, chorea, myoclonus with startle	Weakness with rapid or aggressive correction
Hypermagnesemia	Serum magnesium >2 mmol/L	Acute flaccid areflexic paralysis with respiratory insufficiency (may mimic a midbrain syndrome)	Ischemic heart disease, arrhythmias, preeclampsia, or bronchial constriction with rapid or aggressive correction

Continuum (Minneap Minn) 2017;23(3):722–743.

Hypokalemia

Clinical : similar to HOPP

- Symmetrical or generalized weakness, myalgia and cramps.

Lab:

- K <2 mEq/L, high CK.
- NCS normal, EMG: irritable myopathy.
- EKG: bradycardia, flattened T wave, prolong PR and QT interval, U wave.

MPX: vacuolated fibers and scattered necrotic.

Rx: correct hypokalemia, work up causes

Hyperkalemia

- Generalized muscle weakness.
- Chvostek's sign, myotonic lid lag. (membrane excitability)

Lab:

- K > 7mEq/L
- Renal insufficient and acidosis.
- Tall, peaked T
- **Rx:** correct hyperkalemia, Rx underlying diseases

Etiologies of secondary hypokalemic and hyperkalemic paralyses

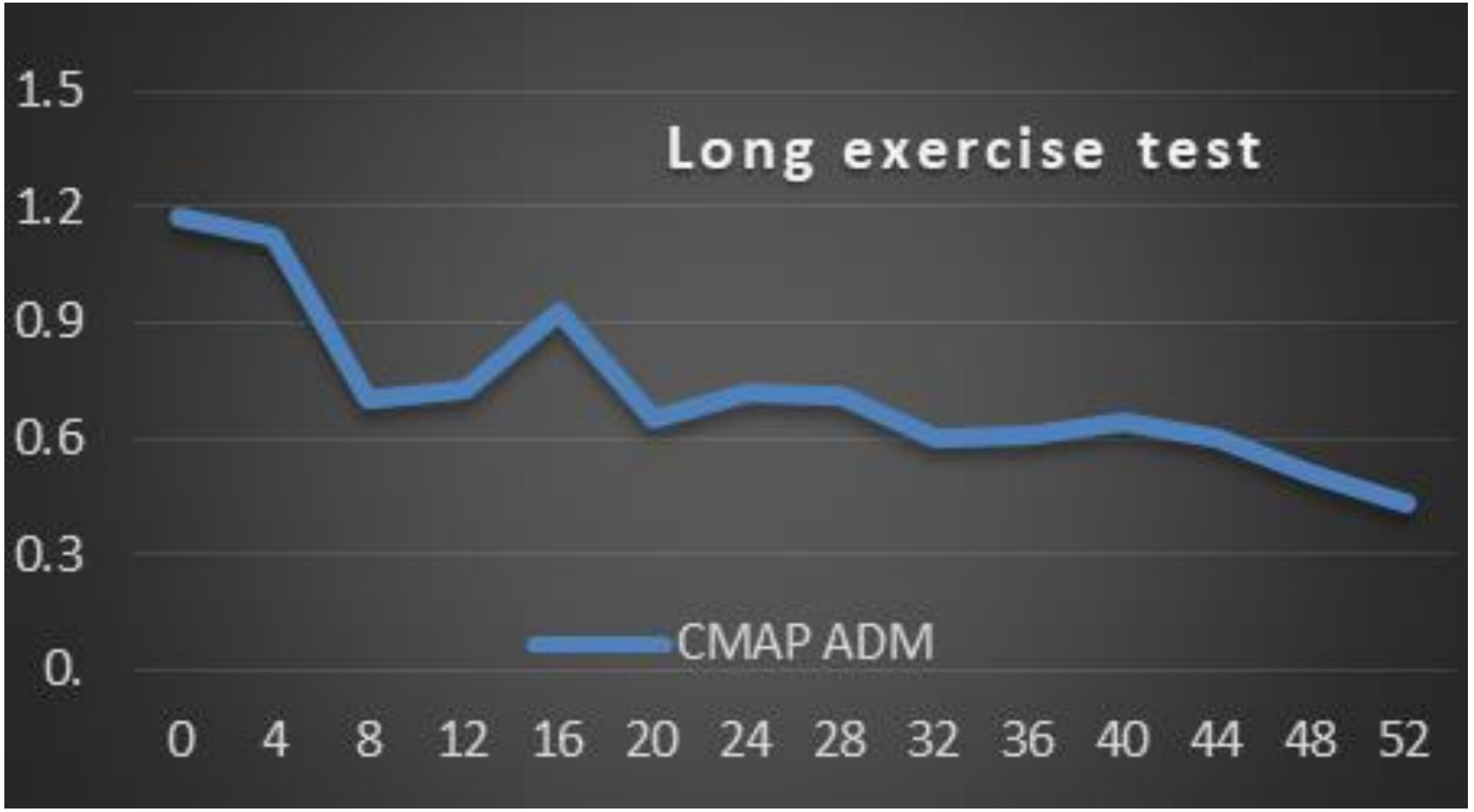
Hypokalemic paralysis

- Thyrotoxic periodic paralysis
- Renal tubular acidosis
- Villous adenomas
- Bartter's syndrome
- Hyperaldosteronism
- Chronic or excessive use of diuretics, corticosteroids
- Amphotericin B toxicity
- Alcoholism
- Toluene toxicity
- Barium poisoning

Hyperkalemic Paralysis

Addison disease
Hypoaldosteronism
Isolated aldosterone deficiency
Excessive potassium supplementation
Potassium-sparing diuretics
Chronic renal failure
Rhabdomyolysis

Long exercise test



decrease CMAP 51%

Hypophosphatemia

- Serum Phosphate <0.4 mM/L : generalized muscle weakness, rhabdomyolysis and myoglobinuria.
- Some cases have paresthesia and decreased DTR.

Etiologies of hypophosphatemia:

- Diabetic ketoacidosis, acute alcoholic intoxication, hyperalimentation with phosphate-poor preparations, severe diarrhea, taking phosphate-binding antacids.

Rx:

Correction of serum phosphate levels.

Disorder of magnesium

Hypermagnesemia (may be with hypocalcemia)

Clinical: Severe generalized and ventilator muscle weakness

Chovstek's and Trousseau's sign and tetany

Etiology: 2^{o} over usage of magnesium-containing laxatives + renal insufficiency.

Rx: correct serum magnesium.

Disorder	Myopathy	Focal myositis	Polymyositis	Dermatomyositis	IBM	MG	Rhabdomyolysis
Infectious disease							
• Viral infections	+	+ (om)	+	+	+	+	+
• Bacterial infections	–	+ (om)	+	–	–	–	+
• Protozoal infections	–	+ (om)	+	+	–	–	+
• Helminthic infections	–	+ (om)	+	+	–	–	–
Endocrinological disorders							
• Diabetes	+	–	–	–	–	–	–
• Hypothyroid dysfunction	+	–	+	+	–	–	+
• Hyperthyroid dysfunction	+	+(om)	+	+	–	–	–
• Hyperparathyroidism	+	–	–	–	–	–	+
• Hypoparathyroidism	+	–	–	–	–	–	–
• Hypo-/hyperadrenalism	+	–	–	–	–	–	–
Metabolic diseases							
• Hemochromatosis	+	+	+	–	–	–	–
• Amyloidosis	+	–	+	–	–	–	–
• Porphyria	+	+	–	–	–	–	+

Disorder	Myopathy	Focal myositis	Polymyositis	Dermatomyositis	IBM	MG	Rhabdomyolysis NAM
Immunological disorder							
• SLE	–	+ (om)	+	–	–	–	+
• Sjogren syndrome	+	+ (om)	+	+	+	–	–
• Rheumatoid arthritis	–	+	+	–	–	–	–
• Systemic sclerosis	–	+	+	+	–	–	–
• Psoriasis	+	+ (om)	+	+	–	–	–
• Antisynthetase syndrome	–	+ (om)	+	–	+	–	–
• Sarcoidosis							
Vascular diseases							
• Behcet disease	–	+ (om)	+	–	–	–	–
• Wegener	–	+ (om)	–	–	–	–	–
• Churg–Strauss syndrome	–	+ (om)	+	–	–	–	–
Neoplasms							
• Leukemia	–	–	+	+	+	–	–
• Lymphoma	–	+	+	+	–	–	–
• Breast, lung, gastrointestinal	+	–	–	–	–	–	–
• Bladder tumor	+	–	–	–	–	–	–

Diagnose muscle manifestations of systemic disease

Etiology	**Investigations**
Suspected muscle involvement	CK, EMG, Muscle imaging, muscle biopsy
Myositis or tumor	FDG-PET
Infections	Ab to virus or PCR Bacteria: aspirate, gram stain, culture
Muscle inflammations	Muscle specific autoantibodies e.g. anti-Jo1, anti-PL7, anti-PL12 (ASS) (166), anti-EJ, anti-OJ, anti-SRP, antiMi-2, anti-PM-Scl75, anti-PM-Scl100, and anti-Ku
SLE, scleroderma, or polymyositis overlap syndrome.	U1-nRNP antibodies
Waldenstrom's macroglobulinemia	Antidecorin antibodies (BJ antigen)
systemic sclerosis	Topo1 and RNP antibodies
Antidecorin antibodies (BJ antigen)	

Treatment

	Symptoms	Treatment
Specific Rx:	Rx related systemic dz activity	Treatment underlying disease
Symptomatic Rx:	Muscle cramps, muscle stiffness, myalgia	NSAIDs, steroids, immunoglobulin, or immunosuppressants
Diabetic myonecrosis	Myalgia, muscle swelling	bed rest and analgesics.
Vasculitis-related myopathy, immune	Weakness, myalgia, fever	**Immuno-suppression**
Infectious myositis	Focal myalgia, fever	Antibiotic, antihelmintics, drainage, debridement or resection

Conclusion
myopathy in systemic disease

Clinical: generalized, focal, regional weakness

Etiology: immune, drug/toxic, dz progression, complication from diseases and complication from Rx

Investigation: general, dz specific work up, imaging and muscle biopsy.

Treatment:

- Rx underlying disease
- Symptomatic Rx
- Immunosuppressive

Reference

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