

A case of progressive leg weakness

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Case presentation

- A 75 year old man with past medical history of lumbar spinal stenosis s/p surgery in 2007 was referred to neurology clinic for evaluation of muscle weakness.
- Patient reported leg weakness that started seven years ago. The weakness initially started in left leg and later progressed to involve right leg.
- His weakness was characterized by difficulty in standing up from sitting position, difficulty raising the thigh and trouble climbing the stairs.
- He also noticed that he was choking occasionally and voice had become weak.

Physical examination

	R	L		R	L
O.Occli	5	5	O.Oris	4	4
Neck flexion		5	Neck extension		5
Deltoid /Biceps	5	5	Tricep	5	5
Wrist flexion	5	5	Wrist Extension	5	5
Finger flexion	3	3	Finger extension	4	4
Hip adduction	3	2	Hip abduction.	4	3
Hip flexion	3	3	Hip extension	4	3
Knee flexion	3	3	Knee extension	4	4
Plantar flexion	4	4	Dorsiflexion	4	4

Physical exam cont.

- atrophy of bilateral quadriceps, left biceps and forearm flexors.
- Reflexes are 2+ and symmetric in UEs, 1 + at knees and absent at ankles.
- PP and vibratory sensations are reduced in distal LEs; proprioception was intact.
- Needed support while getting up from chair , could walk only with support.
- Voice was weak

Diagnostic testing's

creatinine kinase – 664 IU/L

Serum aldolase was high 12.5 U/L.

Thyroid stimulating hormone was high -6.47 mIU/L

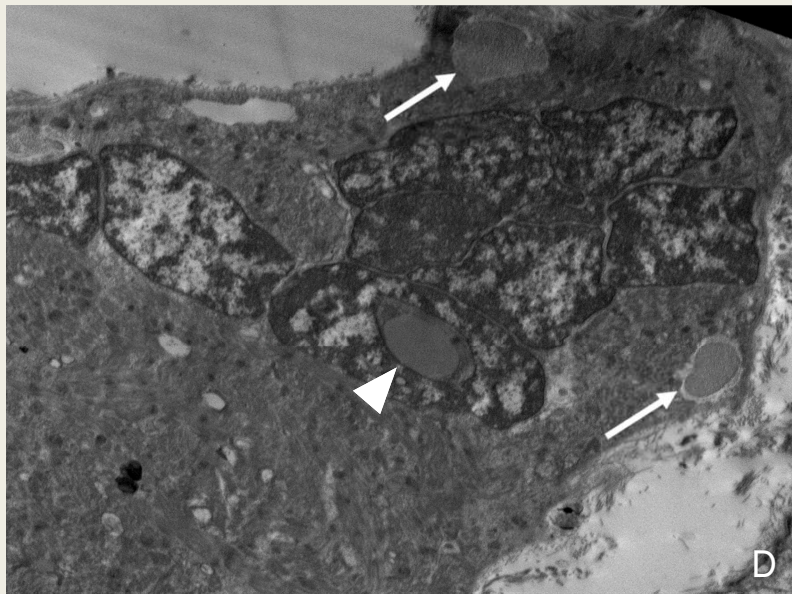
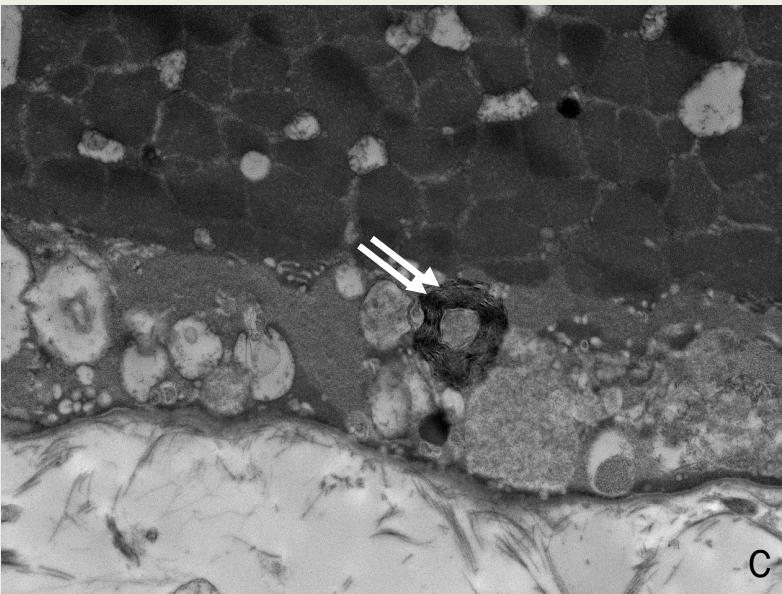
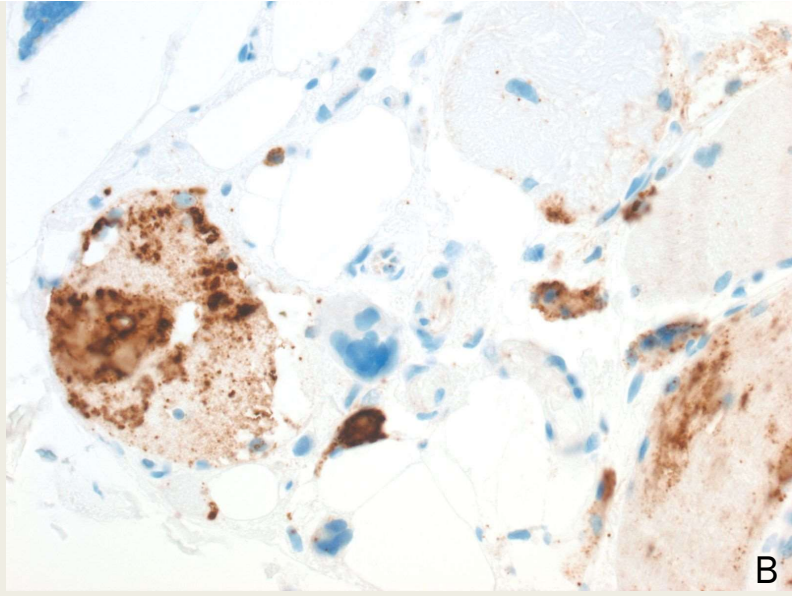
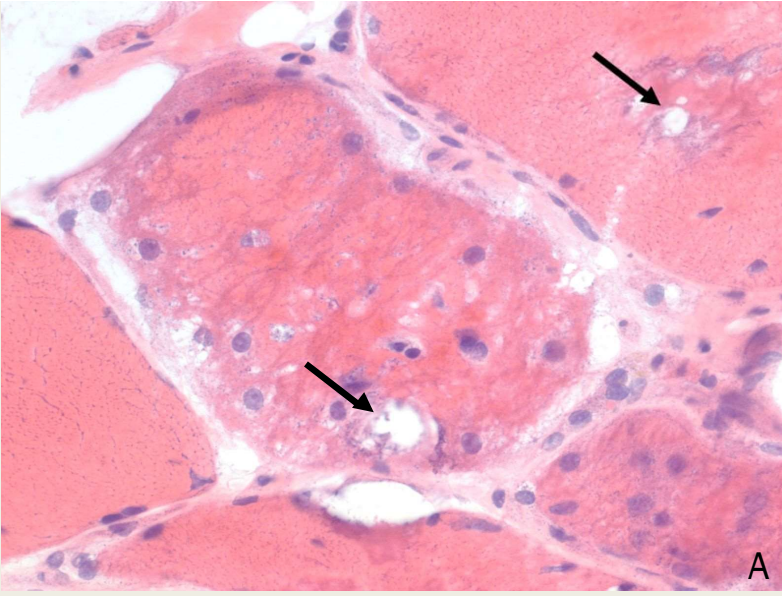
HMGCOA reductase antibody was negative,

ESR,CRP negative.

Acetylcholine receptor antibody panel negative

CT Scan of lumbar spine showed multilevel degenerative changes of the lumbar spine along with prior right-sided L4-5 and L5-S1 laminectomy changes.

EMG/NCS study showed electrophysiological evidence of chronic lumbosacral radiculopathy primarily affecting the L5 nerve root level and evidence of a myopathic process based on the presence of early full recruitment in the left upper extremity.



There were variations of fiber size with an increase in the number of myofibers with internal nuclei and a few splitting fibers. No segmental necrosis is identified; however, there were fibers with rimmed vacuoles (Path Fig. A). Immunohistochemically, they were variably positive for p62 and ubiquitin and, focally and weakly, for TDP-43 (Path Fig. B).

Electron microscopic examination identified these vacuoles to contain granular and membranous debris, some with a myelin figure (Path Fig C), as well as intra-sarcoplasmic and intra-nuclear filamentous inclusions (Path Fig. D). These findings were consistent with the diagnosis of inclusion body myopathy. Typical features of other inflammatory myopathies, namely polymyositis and dermatomyositis, were not seen.

Diagnosis

INCLUSION BODY MYOSITIS

Inclusion body myositis

- First described in 1971
- Epidemiology
 - *Prevalence 71 per million and incidence 7.9 per million in USA (Olmstead County, MN)*
 - *Europe: 4.3 – 33 per million prevalence*
 - *Male preponderance: 60% to 75%*
 - *Diagnosis of IBM is frequently delayed by 5-7 years.*

Clinical features

- Asymmetric
- distal and proximal muscle weakness
- slowly progressive course
- Involvement of the hip flexors, quadriceps, tibialis anterior with weakness of the ankle dorsiflexors, and forearm flexors with grip weakness are characteristic of IBM
- Facial muscles (especially muscle controlling eye closure) may be involved, but the oculomotor muscles are spared
- Dysphagia due to involvement of the cricopharyngeal muscle occurs in about one-third to one-half of patients
- Muscle atrophy progresses in parallel with the duration and severity of weakness



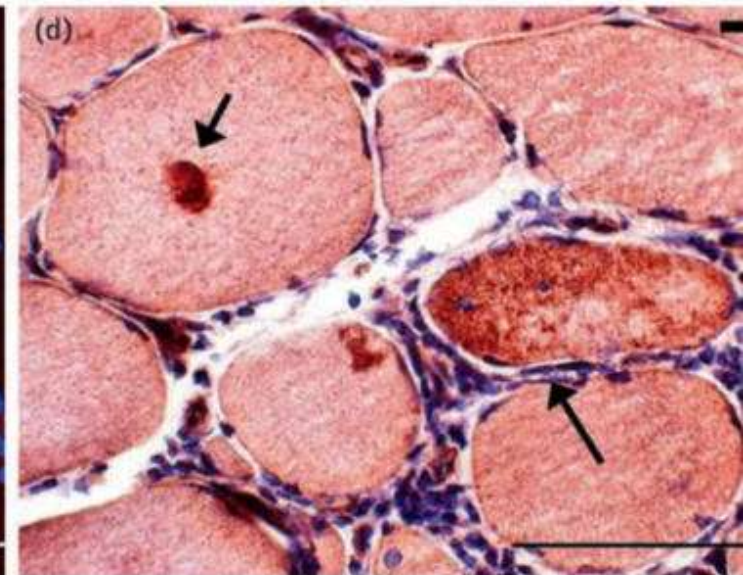
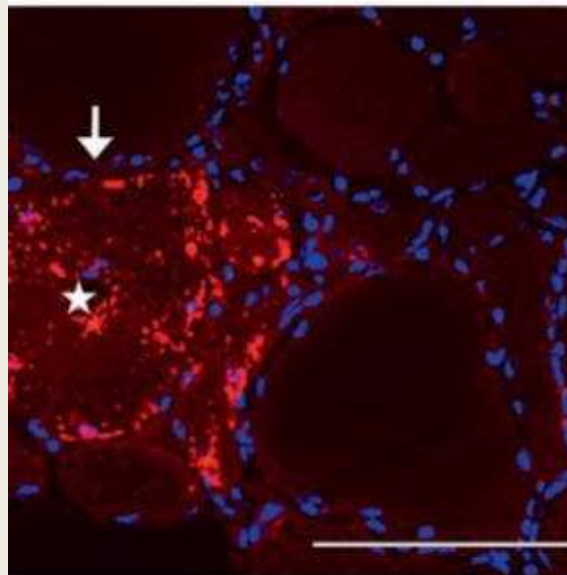
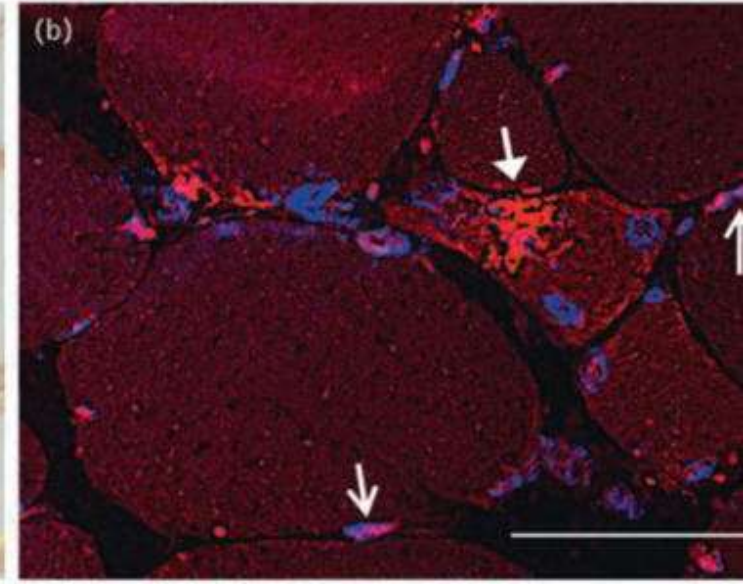
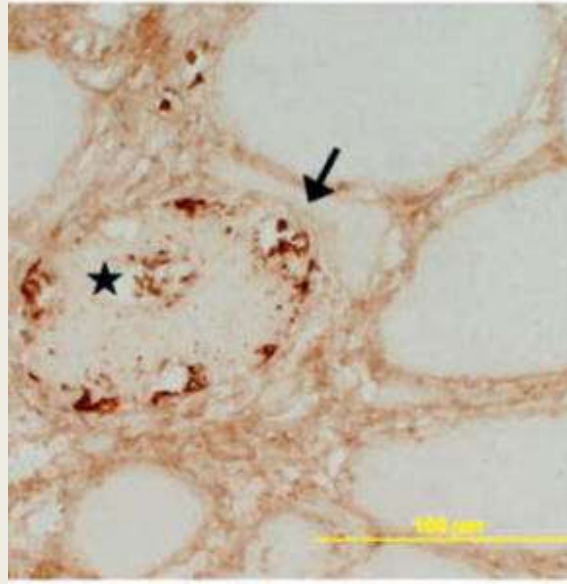
Diagnostic criteria

- Muscle biopsy provides diagnosis – more than 1 biopsy may be required.
- Clinical criteria:
 - *Most recent 2011 ENMC criteria:*
 - 77-84% sensitivity; 98-100% specificity
 - Combination of finger flexor or quadriceps weakness and endomysial inflammation with invasion of nonnecrotic muscle fibers or rimmed vacuoles has 90% sensitivity and 96% specificity

Investigations

- Serum CK less than 10-fold higher than normal are common with IBM, while levels greater than 15-fold suggest other causes.
- EMG typically reveals an “irritable myopathy” with increased insertional activity, fibrillations, positive waves, and early recruitment of short-duration, small-amplitude polyphasic motor unit action potentials (MUAPs).
- Muscle biopsy- more than one biopsy is required
 - *Muscle biopsy findings that are highly specific for IBM include the presence of rimmed vacuoles, mononuclear cell inflammatory infiltrate of non-necrotic muscle fibers, and the presence of either amyloid deposits or tubulofilaments by electron microscopy.*
- Testing for autoantibodies directed against cytoplasmic 5'-nucleotidase 1A (cN1A) may be helpful for distinguishing IBM from other forms of myositis.
 - *However, anti-cN1A antibodies are also detected in about 20 percent of patients with SLE and Sjögren's syndrome in the absence of muscle disease*

TDP-43 AND P62
IMMUNOSTAINING
IN SIBM



Treatment

- No optimal therapy
- Refractory to steroids , immunosuppressive therapy, IVIG , beta interferon.
- Etanercept, Alemtuzumab improved some muscle strength but were not useful over few months.
- Bimagrumab - human monoclonal antibody was initially thought to be a breakthrough but it failed phase II b/III trial in 2016.
- gene therapy and some more research studies are going on.

Goals of care





THANK YOU

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