Inclusion Body Myositis

Idiopathic inflammatory myopathies are a group of chronic, autoimmune conditions affecting primarily the proximal muscles. The most common types are dermatomyositis, polymyositis, necrotising autoimmune myopathy and sporadic inclusion body myositis (IBM). It seems that inclusion body myositis has a prominent degenerative component.

IBM is the most common age-related muscle disease in the elderly and is an incurable disorder leading to severe disability. It is a slowly progressive inflammatory myopathy characterised by:

- Weakness of the proximal parts of the limbs.
- Diminished deep tendon reflexes.
- Dysphagia.
- Mixed myopathic and neurogenic changes on electromyography.

It is an underdiagnosed condition as it occurs mainly in the elderly, with multiple comorbidities, and is frequently misdiagnosed as polymyositis and wrongly treated with steroids. Treatment-resistant 'polymyositis' in the over-50s is often IBM.

Histologically, features include:

- Inflammatory infiltrate.
- Cytoplasmic vacuolation.
- Characteristic tubo-filamentous inclusions within the cytoplasm and nuclei of muscle cells.

It occurs in both sporadic and inherited form (s-IBM and i-IBM, respectively). iIBM has autosomal recessive and dominant variants. Genetic susceptibility factors are thought to influence who develops s-IBM but this is poorly understood currently. Familial and sporadic types share the same clinical, biological, MRI and histological features.

The aetiology of IBM is largely unknown. There is debate as to whether it is primarily a T cell-mediated inflammatory myopathy or a myodegenerative disease. Interest has been stimulated by the finding that substances deposited in muscle are similar to those found in the brain in Alzheimer's disease - e.g., amyloid precursor proteins.

Epidemiology

- Most cases present in patients aged over 50 years but it can occur much earlier, at any time between the 20s and 80s.
- Population studies from the Netherlands and Sweden suggest a population prevalence of 2.2-4.9 per million, with age-adjusted rates of 16 per million in the over-50s.

Risk factors

- Co-existent disease is quite common but this reflects the disease's association with ageing.
- It is found in men more often than in women with a ratio of between 1.4:1 and 3:1.

Presentation

Muscle weakness is the usual presenting feature. It usually presents after the age of 50. The distribution is variable and can be both proximal and distal. It typically presents with distal upper extremity weakness accompanied by proximal lower extremity muscle weakness. Associated clinical findings include asymmetric weakness, foot drop and dysphagia.

- Weakness is often asymmetrical in contrast to polymyositis.
- Fatigue and exercise intolerance are common but not with shortness of breath and the respiratory muscles are usually spared.
- Dysphagia is problematic in 40-50% of patients.
- Limb weakness is not inevitable and weakness of erector spinae and 'droopy neck' can be the presentation.
- Muscle pain and cramps are uncommon but may occur. Sensory or autonomic changes only tend to occur if there is also a concurrent polyneuropathy, such as may occur with diabetes.

Examination

Strong indicators of IBM:

- Weakness of flexion of the wrist and fingers is disproportionate compared with any weakness of extension.
- Extension of the knee is weak compared with flexion of the hip.

Important negative findings to exclude differential diagnoses:
Tendon reflexes are usually suppressed in myopathy and in this condition it is most marked at the knee. Sensation should be intact unless there is also a polyneuropathy. There should be no cognitive impairment, no abnormality in co-ordination and no evidence of upper motor neurone disease. Look for the rash of dermatomyositis to exclude it.

**Differential diagnosis**
- Inherited and sporadic forms are differentiated by family history. Incomplete penetrance, death of a relative who died before the age of onset of the disease or incorrect diagnosis can make pedigrees misleading.
- Dermatomyositis and polymyositis may show skin lesions and the creatine kinase level may be markedly elevated. It is rarely normal in active disease. In IBM it is normal or mildly elevated only.
- Oculopharyngeal dystrophy affects the external ocular muscles that are spared in this condition.
- Chronic atrophic sarcoid myopathy can be difficult to differentiate.
- *Myasthenia gravis* affects the external ocular muscles, and muscle fatigability is a key feature.
- *Motor neurone disease* usually shows features of upper motor neurone lesions.

**Investigations**

Standard routine investigations should include:
- FBC.
- Calcium and phosphate.
- Creatine kinase.
- ESR.
- Fasting glucose.
- TFTs.

Specialist investigations include:
- Nerve conduction tests - these should be normal.
- Electromyography - this may show a myopathic process. It may be necessary to test several muscles.
- Muscle biopsy as the final diagnostic procedure - biopsy should be taken from a muscle that is moderately but not severely affected. Histological processing may require immunohistochemical staining (for beta-amyloid and ubiquitin) and electron microscopy.

**Management**

There is no effective treatment for the disease and few high-quality randomised controlled trials. Treatment is challenging as the disease is typically resistant to standard immunotherapy.

Prednisone is usually not effective and may lead to more rapid progression. However, some patients may experience at least a temporary improvement.

Some treat newly diagnosed patients with immunosuppression on the basis that early suppression of the inflammatory cascade may prevent downstream effects leading to muscle degeneration.

Studies with methotrexate, anti-T-lymphocyte globulin, etanercept, oxandrolone or beta interferon failed to identify clinical efficiency. Although intravenous immunoglobulin can help with dysphagia, it was not found effective for muscle strength.

The most encouraging study used alemtuzumab, a monoclonal antibody that depletes peripheral lymphocytes. It seemed to delay the disease progression for up to six months and improved muscle strength in some patients.

Without effective treatment, the role of the multidisciplinary team to support and optimise function is critical:
- Speech and language therapy for assessment of dysphagia. A gastrostomy may be required if severe.
- Dietary support.
- Physiotherapy and occupational therapy may help to make the best of limited ability.

**Prognosis**

Progressive muscle weakness of the finger flexors and quadriceps muscles results in loss of independence with activities of daily living and eventual wheelchair dependence.

The mean or median loss of independent ambulation ranges between 7 and 14 years from the date of diagnosis.

Progressive dysphagia is associated with a poorer prognosis and a poorer quality of life.

**Further reading & references**
- *Inclusion Body Myositis*, Online Mendelian Inheritance in Man (OMIM)
- *Inclusion Body Myositis*, National Institute of Neurological Disorders and Stroke


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