CASE REPORT

Efficacy of immunosuppressive treatment in a systemic lupus erythematosus patient presenting with inclusion body myositis

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SUMMARY
Inclusion body myositis (IBM) is an inflammatory myopathy that is generally unresponsive to immunosuppressive drugs. The coexistence of IBM with other autoimmune connective tissue diseases is rare. We present a case of a 76-year-old woman with systemic lupus erythematosus (SLE) who developed proximal muscle weakness of lower extremities and mild elevation of serum creatine kinase (CK) at 495 U/L. Muscle biopsy showed changes of endomysial inflammation and rimmed vacuoles consistent with IBM. She was treated with prednisone 40 mg daily and methotrexate 12.5 mg weekly. One month later, her physical examination showed minimal proximal weakness of lower extremities. CK levels decreased to 44 U/L. Prednisone dose was gradually decreased to 5.0 mg daily. She remained stable with normal CK levels during a follow-up period of 10 months. This case, together with other reports, suggests that IBM in the setting of SLE represents a different subtype that can benefit from immunosuppressive treatment.

BACKGROUND
Inclusion body myositis (IBM) is a rare presentation of inflammatory myopathy with clinical features that clearly separate it from the other inflammatory myopathies such as polymyositis and dermatomyositis. One of the characteristic features of IBM is the presence of proximal and distal muscle weakness. The underlying pathology driving the disease is unknown. IBM tends to more frequently affect males over the age of 50 years and carries a poor prognosis. IBM is considered to be, in most cases, refractory to treatment with conventional immunosuppressive medications and those who respond, subsequently have a progressive slow decay in function. IBM usually presents as an isolated disease but there are some reports of IBM occurring in patients with autoimmune connective tissue diseases, including systemic lupus erythematosus (SLE). We present a case of a 76-year-old woman with SLE who developed IBM and experienced a remarkable clinical response to immunosuppressive therapy.

CASE PRESENTATION
A 76-year-old woman with SLE since September 2003 presented with non-erosive inflammatory polyarthritis, prolonged morning stiffness (>1 h), lymphopenia, leukopenia, mild thrombocytopenia, elevated erythrocyte sedimentation rate (130 mm/h), elevated C reactive protein (6.0 mg/L), positive antinuclear antibodies (1:320, speckled pattern) and C3 hypocomplementemia. She met the Systemic Lupus International Collaborating Clinics classification criteria for SLE. She was treated with hydroxychloroquine 400 mg daily and prednisone 20 mg daily. She responded well to this treatment and prednisone dose was gradually decreased until discontinued in July 2004. She remained in complete clinical remission until October 2011, when she developed severe inflammatory polyarthritis. Prednisone 10 mg daily was started and synovitis resolved. However, multiple attempts to decrease prednisone dose below 10 mg daily were unsuccessful due to recurrent polyarthritis.

In December 2013, the patient developed mild difficulty getting up from a chair or bed. On examination, she had mild proximal muscle weakness (4/5) of lower extremities. Electromyography showed a mixed pattern of myopathic and neurogenic changes. Serum creatine kinase (CK) was mildly elevated at 484 U/L (normal range 30–223 U/L) but aldolase levels were normal. The possibility of corticosteroid-induced myopathy was considered, for which prednisone dose was gradually decreased until discontinued in December 2014. After discontinuation of prednisone, she had worsening of muscle weakness requiring assistance while standing up or climbing stairs. She had no other associated symptoms. On examination, she had proximal muscle weakness (3–4/5) of lower extremities, including knee extensors and hip flexors. She had normal strength in the upper extremities and distal lower extremities. The rest of the examination was unremarkable.

INVESTIGATIONS
Laboratory tests showed normal white cell count, haemoglobin, platelet count, urine analysis, liver enzymes, blood urea nitrogen, serum creatinine, thyroid tests and serum protein electrophoresis. Westergren sedimentation rate was normal at 19 mm/h. CK was elevated at 495 U/L. Serum aldolase level was normal. Anti-double stranded DNA, anti-Smith, anti-ribonucleoprotein (RNP), anti-Ro, anti-La and anti-Jo-1 antibodies were not elevated. C3 and C4 levels were normal. Malignancy screening tests including chest X-rays, mammography, pelvic examination and colonoscopy were unremarkable. A muscle biopsy of the left thigh,
performed in March 2015, revealed endomysial inflammation and rimmed vacuoles with deposits of P62 (figures 1 and 2). The microscopic description and histochemistry and immunohistochemistry analyses of the examined tissue are shown in box 1. The patient met the clinicopathological criteria for defined IBM according to the 2011 European Neuromuscular Centre IBM Research Diagnostic Criteria.

TREATMENT
In April 2015, the patient was treated with prednisone 40 mg daily and methotrexate 12.5 mg orally weekly.

OUTCOME AND FOLLOW-UP
The patient had a remarkable clinical response to this therapy. One month later, she was able to stand up without assistance. Physical examination showed minimal proximal weakness of the lower extremities (4–5/5). CK decreased to normal levels (44 U/L). Muscle strength was fully recovered after 2 months of therapy. Prednisone dose was gradually decreased to 5.0 mg daily. The patient remained stable with normal CK levels during a follow-up period of 10 months.

DISCUSSION
We present a case of an elderly woman with SLE who developed IBM, and had a rapid and effective clinical response to corticosteroids and methotrexate. The frequency of IBM associated with a connective tissue disease is unknown although it appears to be very rare. There are few reports in the literature of patients developing IBM in association with other connective tissue diseases such as Sjögren’s syndrome, scleroderma, rheumatoid arthritis and SLE. In most of these cases, the patients had a favourable response to immunosuppressive treatment.

Previously, five cases of SLE have been reported in association with IBM (table 1). In these cases, the dominant presentation was proximal muscle weakness and all had a modest elevation of CK serum levels, normal or slightly elevated inflammatory markers, absence of myositis-specific antibodies and marked elevation of antinuclear antibody titres. As in sporadic

Box 1 Microscopic description and histochemistry and immunohistochemistry analyses of muscle biopsy

**MICROSCOPIC DESCRIPTION (H&E AND MODIFIED GOMORI TRICHOME STAINS)**
- Focal muscle fibre size variation and atrophy, with some angulated fibres
- Internal nucleation observed in 15–16% of fibres
- No fibre splitting observed
- Mild to moderate endomysial and perimysial fibrosis
- Fatty penetration/replacement
- Hyper basophilic regenerating fibres observed
- Moderate inflammatory infiltrate, predominantly endomysial
- No perifascicular pattern of atrophy or inflammation
- Focal fibre necrosis with phagocytosis present
- No ragged red fibres observed.
- Rimmed-like vacuoles focally present

**HISTOCHEMISTRY**
- Nicotinamide adenine dinucleotide (NADH) and ATPase: type 2 fibre predominance with no fibre type grouping; atrophic fibres are both type 1 and type 2
- Periodic acid-Schiff stain: no abnormal distribution of glycogen
- Oil red O stain: no abnormal size nor distribution of lipid droplets
- Congo red examined with polarised light: negative for amyloid

**IMMUNOHISTOCHEMISTRY**
- Myosin heavy chain immunohistochemistry: type 2 fibre predominance with no fibre type grouping
- Normal pattern of spectrin and dystrophin (1, 2 and 3) stains
- Human leucocyte antigen-Class 1 overexpression
- Infiltrate predominantly endomysial consisting of a lymphoid and monocytoid cell population, composed of T-cells, with a prominent expression of CD3, CD4 and CD8. The proportion of CD4:CD8 was 1:2.
- Numerous CD68 macrophages present, some associated to degenerating fibres and blood vessels.
- Tau protein positive in rimmed vacuoles
- P62 deposits present in rimmed vacuoles

Figure 1 Predominantly endomysial inflammatory infiltrate is present. Rimmed-like vacuoles are observed near the inflammatory area (H&E ×100).

Figure 2 Rimmed-like vacuoles stain strongly positive for P62 protein (P62 ×200).
Table 1 Demographic features, clinical manifestations, serological tests and clinical outcomes of patients with coexistent systemic lupus erythematosus and inclusion body myositis

<table>
<thead>
<tr>
<th>Authors/publication year</th>
<th>Age and gender</th>
<th>Time interval between SLE and IBM</th>
<th>Clinical manifestations of SLE</th>
<th>Clinical manifestations of IBM</th>
<th>Autoantibodies</th>
<th>EMG and NCS</th>
<th>Biopsy</th>
<th>Treatment</th>
<th>Clinical outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yood and Smith12/1985</td>
<td>60-year-old woman</td>
<td>7 years</td>
<td>Malar rash Arthralgia Myalgia Proteinuria</td>
<td>Symmetric proximal UE and LE weakness; Symmetric distal LE weakness</td>
<td>CK=270 U/L</td>
<td>Positive Ab: ANA ENA RF Neg Ab: Anti-Pm-1</td>
<td>Pos. sharp waves, fibrillation and small polyphasic units</td>
<td>Chronic inflammatory myopathy, presence of rimmed vacuoles</td>
<td>Prednisone 60 mg daily for 3 months, then 40 mg every other day for 3 months</td>
</tr>
<tr>
<td>Limaye et al11/2000</td>
<td>51-year-old man</td>
<td>20 years</td>
<td>Malar rash Arthritis Myalgia Raynaud’s SLE myositis (prior to IBM)</td>
<td>Symmetric Proximal LE weakness</td>
<td>CK=2192 U/L</td>
<td>Positive Ab: ANA Anti-dsDNA</td>
<td>Not performed</td>
<td>Inflammatory myopathy, presence of rimmed vacuoles</td>
<td>Methotrexate 25 mg IM weekly, azathioprine 50 mg daily and prednisolone</td>
</tr>
<tr>
<td>Wenzel et al13/2001</td>
<td>71-year-old man</td>
<td>2 years</td>
<td>Subacute cutaneous lupus Leukopenia Lymphopenia Thrombocytopenia</td>
<td>Symmetric LE weakness</td>
<td>CK=16 U/L</td>
<td>Positive Ab: ANA Anti-SSA Anti-SSB RF Neg Ab: Anti-Ku Anti-Jo1 Anti-Mi-2 Anti PM-Scl anti-Ku</td>
<td>Mixed sensorimotor neuropathy, acute denervation</td>
<td>Atrophic muscle fibres, presence of rimmed vacuoles</td>
<td>Methotrexate 25 mg IV weekly and prednisolone (initial dose 100 mg, then 20 mg daily)</td>
</tr>
<tr>
<td>Derk et al9/2003</td>
<td>57-year-old woman</td>
<td>16 years</td>
<td>Oral ulcers Arthritis Sjögren’s syndrome</td>
<td>Symmetric proximal UE and LE weakness</td>
<td>CK=529 U/L</td>
<td>Positive Ab: ANA anti-dsDNA Neg Ab: Anti-Jo1 Anti-SRP Anti-Mi-2 Anti PM-Scl anti-Ku</td>
<td>Polyphasic units without fibrillation or positive waves</td>
<td>Variation in muscle fibre diameter, perivascular lymphocytic and interstitial infiltrates, presence of rimmed vacuoles</td>
<td>Methotrexate 25 mg PO weekly and prednisolone 40 mg daily tapered over 4 months</td>
</tr>
<tr>
<td>Massawi et al10/2003</td>
<td>73-year-old woman</td>
<td>15 years</td>
<td>Arthralgia Sjögren’s syndrome Leukopenia SLE myositis</td>
<td>Symmetric UE and LE distal muscle weakness</td>
<td>CK=190 U/L</td>
<td>Positive Ab: ANA Anti-dsDNA Anti-SSA Anti-SSB Neg Ab: Anti-Jo1</td>
<td>Not done</td>
<td>Chronic myopathic changes, prominent fibrosis, rimmed vacuoles</td>
<td>Intravenous immunoglobulins Failed methotrexate PO 25 mg weekly</td>
</tr>
<tr>
<td>Current case</td>
<td>76-year-old woman</td>
<td>11 years</td>
<td>Arthritis Leukopenia Lymphopenia Thrombocytopenia</td>
<td>Symmetric LE weakness</td>
<td>CK=495 U/L</td>
<td>Positive Ab: ANA Anti-dsDNA Anti-SSA Anti-SSB Anti-Jo1</td>
<td>Mixed myopathic and neurogenic changes</td>
<td>Muscle fibres variations, moderate inflammatory infiltrate, rimmed vacuoles</td>
<td>Methotrexate 12.5 mg PO weekly and prednisone 40 mg daily tapered to 5 mg daily over 5 months</td>
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Ab, antibodies; ANA, antinuclear antibodies; CK, creatine kinase; dsDNA, double stranded DNA; ENA, extractable nuclear antigens; IBM, inclusion body myositis; IM, intramuscular; IV, intravenous; Jo1, histidyl tRNA synthetase; LE, lower extremities; Mi-2, chromodomain helicase DNA binding protein; Pm1, antipolymyositis 1; PM-Scl, polymyositis-scleroderma; PO, orally; RF, rheumatoid factor; SLE, systemic lupus erythematosus; SRF, signal recognition particle; SSA Ab, Sjögren’s syndrome antigen A; SSB Ab, Sjögren’s syndrome antigen B; UE, upper extremities.
Inclusion body myositis (IBM) is an inflammatory myopathy that is generally unresponsive to corticosteroids and immunosuppressive drugs.

IBM usually presents as an isolated disease but there are reports in the literature of patients developing IBM in association with other connective tissue diseases such as systemic lupus erythematosus (SLE).

The case presented here and other reports suggest that, in the scenario of patients with SLE, IBM may present as a different entity with favourable outcome when treated with immunosuppressive therapy.

Competing interests None declared.

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REFERENCES