CASE REPORT

Inflammatory myopathy as the initial presentation of cryoglobulinaemic vasculitis

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SUMMARY

Cryoglobulinaemic vasculitis is characterised by immunoglobulin deposition at low temperatures. The most common manifestations are cutaneous involvement, arthralgias, Raynaud's phenomenon, peripheral neuropathy and renal disease. Myopathy is unusual and only a few cases have been reported. Here, we present a 31-year-old woman who developed progressive muscle weakness involving upper and lower extremities, dysphagia, paraesthesias and palpable purpura. Diagnostic studies revealed elevated creatine kinase, diffuse myopathic and sensorimotor axonal neuropathy on electromyography and nerve conduction studies, and inflammatory myopathy on muscle biopsy. Cryoglobulin levels were elevated on two occasions. She responded favourably to cyclophosphamide and high-dose corticosteroids. Cyclophosphamide was continued for 1 year followed by methotrexate. Prednisone was gradually tapered and discontinued 1 year later. She remained in clinical remission after 4 years of follow-up. This case suggests that cryoglobulinaemia should be considered in the differential diagnosis of a patient presenting with inflammatory myopathy.

BACKGROUND

Cryoglobulinaemic vasculitis is characterised by the deposition of immunoglobulins that precipitate at low temperatures. This condition is associated with a variety of disorders including haematological diseases (eg, Waldenström's macroglobulinaemia and multiple myeloma), chronic infections (eg, hepatitis B and C, and HIV) and autoimmune disorders.¹ Among the most common clinical manifestations are cutaneous involvement, arthralgias, Raynaud's phenomenon, peripheral neuropathy and renal disease. Treatment varies according to the underlying disease, but high-dose corticosteroids together with other immunosuppressive and/or immunomodulatory therapies are recommended for severe cases.²

Inflammatory myopathy is characterised by proximal weakness, elevated serum muscle enzymes, myopathic changes on electromyography studies and muscle biopsy showing muscle fibre necrosis with mononuclear cells infiltrates.³ Inflammatory muscle disease occurs as a primary disorder or in association with other autoimmune connective tissues diseases or malignancies.³ The association of inflammatory myopathy with cryoglobulinaemia is rare. Here, we present a 31-year-old woman with cryoglobulinaemic vasculitis who initially presented with inflammatory myopathy.

CASE PRESENTATION

A 31-year-old previously healthy woman presented with a 4-month history of myalgias and progressive upper and lower extremities muscle weakness. Other symptoms included dysphagia to solids and liquids, paraesthesias and skin rash in lower extremities. The patient was found with elevated muscle enzymes (creatinine kinase (CK) = 12 170 U/L) for which a clinical diagnosis of inflammatory myopathy was made. Initially, she was treated with high-dose corticosteroids (prednisone 60 mg daily) for 2 months, but her symptoms worsened despite therapy. She was hospitalised, and on admission she was found with severe proximal muscle weakness in upper (3/5) and lower extremities (2/5). She had a marked swelling and tenderness of both legs. Palpable purpuras were noted in lower extremities. The rest of the physical examination was unremarkable.

INVESTIGATIONS

White cell count, haemoglobin level, platelet count, erythrocyte sedimentation rate, serum creatine and blood urea nitrogen levels were normal. Serum CK was elevated at 1677 U/L. Liver enzymes were mildly elevated. Urine analysis showed haematuria (15–20 RBC/HPF), but no proteinuria or cellular casts. Thyroid function tests were normal. Serum protein electrophoresis did not disclose a monoclonal or polyclonal gammopathy. Cryoglobulins were detected in two different occasions. Hepatitis B surface antibodies were detected, but there was no serological evidence of chronic disease. Hepatitis C and HIV tests were negative. C3 and C4 complement levels were normal. Rheumatoid factor and antinuclear, anti-dsDNA, anti-Smith, anti-RNP, anti-Ro, anti-La antibodies and antineutrophil cytoplasmic antibodies were negative. The electromyography and nerve conduction tests showed a diffuse myopathic process with overimposed sensorimotor axonal neuropathy. Muscle biopsy revealed a diffuse endomysial inflammation with muscle fibre necrosis and regeneration (figure 1). Skin biopsy of a purpuric lesion showed perivascular lymphocytic infiltrates. Chest radiographs were normal.

TREATMENT

The patient was treated with high-dose intravenous corticosteroids (methylprednisolone 60 mg every 12 h for 3 days) and intravenous cyclophosphamide (750 mg), followed by prednisone 60 mg daily and cyclophosphamide 100 mg orally daily.

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Figure 1 High-power H&E stain of muscle biopsy specimen reveals an intense interstitial mononuclear infiltrate with myocyte degeneration.

OUTCOME AND FOLLOW-UP

She responded favourably to immunosuppressive treatment. Paraesthesias, palpable purpura and haematuria resolved within 1 month. Muscle strength improved after 2 months of therapy (4/5 in upper and lower extremities). She completed 1 year of treatment with cyclophosphamide. Prednisone was slowly tapered until it was discontinued 1 year later. Maintenance therapy with methotrexate 12.5 mg weekly was given. After 4 years of follow-up, she remained clinically stable with normal muscle strength, CPK levels below 500 U/L and undetectable cryoglobulins. She had no other manifestations of cryoglobulinaemic vasculitis.

DISCUSSION

Our patient had myopathy as the first clinical sign of a cryoglobulinaemic vasculitis. Symptoms were similar to those seen in inflammatory myopathy with proximal weakness, elevated muscle enzymes and muscle biopsy showing inflammatory changes. The diagnosis of cryoglobulinaemic vasculitis was supported by the presence of circulating cryoglobulins, palpable purpura, peripheral neuropathy, haematuria and a favourable response to cyclophosphamide. While musculoskeletal symptoms such as arthralgias and myalgias are common in cryoglobulinaemia, myositis is very unusual.

It is important to distinguish patients with asymptomatic cryoglobulinaemia and those with a cryoglobulinaemic syndrome or vasculitis in whom systemic manifestations occur. Patients with inflammatory muscle disease as well as others with autoimmune diseases frequently have detectable cryoglobulins, but few have associated clinical manifestations. For example, Lambie *et al*⁴ reported that 62.5% of patients with polymyositis and dermatomyositis had positive serum cryoglobulins, but none had clinical evidence of systemic vasculitis.

Only another case of coexistent polymyositis and cryoglobulinaemic vasculitis has been reported. Voll *et al*⁵ reported a 73-year-old man with a 1-year history of proximal muscle weakness, elevation of muscle enzymes and myopathic changes on electromyogram and having purpuric rashes in lower extremities and positive serum cryoglobulins. He had no other clinical manifestations of cryoglobulinic syndrome or vasculitis. Muscle biopsy showed necrotic and muscle fibre degeneration with a dense inflammatory cell infiltrate, predominantly composed of plasma cells. In contrast, our patient had a small proportion of

plasma cells on muscle biopsy with histopathological findings more consistent with those seen in patients with polymyositis.

Muscle weakness in patients with cryoglobulinaemia could also be caused by peripheral neuropathy which usually affects distal extremities and has a predominant sensory component.⁶ Muscle biopsy performed in 21 patients with essential mixed cryoglobulinaemia showed denervation, and vasculitis was observed in five patients.⁷ Our patient had both sensory and motor neuropathy, but muscle biopsy findings did not show denervation; therefore, muscle weakness was more likely related to inflammatory myopathy.

Our case, together with other reports, alerts physicians to consider cryoglobulinaemia in the differential diagnosis of inflammatory myopathy, particularly in patients who do not respond to conventional therapy. Furthermore, cyclophosphamide was very effective to control the inflammatory myopathy in our patient. Cyclophosphamide is not conventionally used for inflammatory muscle disease, rather reserved for patients who do not respond to standard therapy. Thus, cyclophosphamide may be considered as perhaps one of the first-line therapies for inflammatory myopathies.

Learning points

- ▶ Cryoglobulinaemic vasculitis usually presents with palpable purpura, arthralgias, Raynaud's phenomenon, peripheral neuropathy and renal disease.
- ▶ Muscle involvement is very uncommon in this disorder.
- ▶ We report a 31-year-old woman with cryoglobulinaemic vasculitis who initially presented with proximal muscle weakness, dysphagia and elevation of muscle enzymes.
- ▶ Cryoglobulinaemic vasculitis should be included in the differential diagnosis of a patient presenting with inflammatory myopathy.

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