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Review

Sjögren's syndrome-associated myositis with germinal centre-like structures

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ABSTRACT

Objective: Muscular impairment is a rare systemic manifestation of SS that is rarely described in the literature and classically non-specific, both clinically and histologically. We reviewed the cases of 4 patients with primary SS presenting with myositis and a common histologic pattern on muscular biopsy with germinal centre-like structures resembling that which occurs in salivary glands.
Methods: We analysed the data files of patients with SS who had muscular manifestations and underwent a muscular biopsy. Among 23 patients with SS who had muscle biopsies, 13 had non-specific myositis and 10 (4 primary and 6 secondary SS) had a common histologic pattern consisting of germinal centre-like structures. We analysed the data files of the 4 patients with primary SS presenting with myositis with muscular germinal-centre like structures.
Results: The 4 patients had an unspecific clinical presentation, with myalgias, muscular weakness and normal or elevated values of CPK. In the four patients, SS-associated myositis had common histologic characteristics, with endomysial and perimysial inflammatory infiltrate. The cellular infiltrate was composed predominantly of CD4+ T lymphocytes and B lymphocytes. The B and T CD4+ cells infiltrates may gather into masses, even forming lymphoid follicles. Three patients were treated with corticosteroids and/or hydroxychloroquine with improvement of myositis and 1 patient was lost to follow-up.
Conclusions: We describe four patients with a common histologic appearance of myositis with lymphoid follicles associated with primary SS. The clinical presentation was non-specific and non-severe, with favorable outcome with corticosteroids and/or hydroxycholoroquine. The discovery of this particular histologic appearance in a muscle biopsy independent of the final diagnosis should indicate the possibility of SS.

Contents

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1. Introduction

Sjögren's syndrome (SS) is an autoimmune disease characterized by a lymphocytic and plasmocytic infiltration of the exocrine glands. SS is responsible for a syndrome involving dryness of the mouth and eyes. SS can be complicated by various extra-glandular effects, particularly in the early stages. SS can also be associated to another autoimmune disease, such as systemic lupus erythematosus, rheumatoid arthritis, or scleroderma. The American-European Consensus Group criteria associate the dryness syndrome with an objective immunologic anomaly (anti-SSA or anti-SSB antibodies and/or an inflammatory infiltrate on biopsy of the accessory salivary glands [stage 3 or 4 in the Chisholm and Mason classification or a Focus score ≥ 1]) [1]. Muscular impairment is a rare systemic manifestation of SS that is rarely described in the literature and classically non-specific, both clinically and histologically. Salivary gland biopsy in patients with SS has yielded inconsistent, but reliable results. Indeed, the histologic demonstration of germinal centre-like structures is predictive of more severe disease and the development of lymphoma [2,3].

Herein, we report four cases of primary SS presenting with myositis and a common histologic pattern on muscular biopsy with germinal centre-like structures resembling that which occurs in salivary glands.

2. Patients and methods

The data files of all patients with SS who fulfilled American-European Consensus Group criteria and ACR 2012 criteria and were followed at Nantes University Hospital between 1984 and 2015 were reviewed. We analysed the data files of patients with SS who had muscular manifestations and underwent a muscular biopsy. All histopathologic muscle biopsy assessments were performed by the same pathologist (JMM).

Among 23 patients with SS who had muscle biopsies, 13 had non-specific myositis and 10 (4 primary and 6 secondary SS) had a common histologic pattern consisting of germinal centre-like structures. Among the 6 patients with secondary SS, 4 had dermatomyositis and 2 had overlap myositis syndrome with systemic lupus erythematosus and mixed connective tissue disease (MTCD).

We describe the clinical and histopathological data of the 4 patients with primary SS and myositis with muscular germinal centre-like structures.

3. Results

3.1. Patient 1

A 72-year-old woman presented with a deterioration in general health, a 12-kg weight loss, fever for 3 months, bilateral steppage gait, and myalgias. She had complained of a sicca syndrome for 1 year. The physical examination demonstrated edema in the lower extremities and motor and sensory loss in the sural and peroneal nerve territories (Table 1). She had no skin lesions, and no peripheral lymphadenopathy or splenomegaly. A urinalysis revealed no proteinuria. Venous Doppler ultrasonography disclosed a deep vein thrombosis in the left lower extremity. Electromyography documented a peripheral axonal neuropathy. Laboratory testing was significant for an inflammatory syndrome with an increased CRP (71 mg/l), hypocomplementaemia, and positive rheumatoid factor with cryoglobulinemia; CPK was not tested. Antinuclear antibodies were negative. The laboratory tests are summarized in Table 2. A muscle biopsy was performed, identifying denervation, muscular ischemic lesions, and an interstitial inflammatory infiltrate with a pseudo-follicular pattern. A labial salivary gland biopsy was consistent with SS. She received initial treatment with corticosteroids and hydroxychloroquine (Table 3). After 9 years of follow-up, she remained stable on low-dose corticosteroids.

Table 1
Initial clinical features of 4 patients.

Feature	Case 1	Case 2	Case 3	Case 4
Epidemiologic features				
Sex, male/female	F	M	F	F
Age at diagnosis of SS, years	72	62	52	64
Age at diagnosis of myositis, years	72	62	52	39
Diagnosis criteria for SS				
Dry eyes	+	+	−	+
Dry mouth	+	−	+	+
Shirmer's test	+	NA	−	+
Decreased salivary flow	NA	NA	NA	+
Parotid swelling	−	−	−	+
Anti-SSA	−	−	+	+
Anti SSA-52 kDa	−	−	+	NA
Anti-SSA-60 kDa	−	−	+	NA
Anti-SSB	−	−	−	+
Pathologic salivary gland biopsy (Chisolm and Mason staging III or IV)	+	+	+	+
Extraglandular features of SS				
Cutaneous	−	−	−	−
Central nervous system	−	−	−	−
Peripheral nervous system	+	−	+	−
Renal	−	−	−	−
Arthritis	−	−	+	−
Pulmonary	−	−	−	−
Vascular	−	−	−	−
Haematological	−	−	−	−
Raynaud's phenomena	NA	−	−	+
Characteristics of myositis				
Muscular weakness	−	+	+	+
Proximal	−	+	+	+
Distal	−	+	+	−
Myalgias	+	−	+	−
Severity of muscular weakness	NA			Moderate
Moderate				Moderate
Electromyography			NA	
Neuropathy	+	−		−
Myopathy	−	+		+

SS: Sjögren's syndrome; NA: non-available.

3.2. Patient 2

A 62-year-old man complained of muscle weakness with progression over several years. Physical examination revealed muscle impairment in the upper and lower extremities with a predominant muscle deficiency in the left hand and a proximal amyotrophy. There was no sensory deficit, no cutaneous signs, and no sicca syndrome at the time of the initial clinical examination (Table 1). Electromyography documented muscular involvement. Laboratory testing showed positivity of anti-nuclear antibodies (1:640) without specificity, no CPK elevation, and no inflammatory syndrome (Table 2). Muscular biopsy revealed an inflammatory infiltrate with two patterns: an interstitial diffuse manifestation composed mainly of TCD8 cells; and nodular clusters with a pseudo-follicular pattern composed of central T CD4 + cells and numerous B cells. A labial salivary gland biopsy showed a grade 3 lymphocytic

Table 2
Initial biological features at diagnosis of 4 patients.

Biological feature	Case 1	Case 2	Case 3	Case 4
Increased CPK (×normal)	NA	−	+ (24)	−
Increased CRP (mg/l)	+ (71)	−	−	−
Rheumatoid factor	+	−	NA	+
Cryoglobulinemia	+	NA	NA	−
Complement		N	N	N
Hypergammaglobulinemia (g/l)	−	−	+ (26)	+ (NA)
Monoclonal gammopathy	+ (IgM)	−	−	−
ANA other than anti-SSA or -SSB	−	1/640 (no specificity)	−	−

SS: Sjögren's syndrome; NA: non-available; ANA: anti-nuclear antibodies; N: normal.