A singular case of dropped-head syndrome associated with anti-Pm-Scl myositis

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Introduction

There are very few case reports of isolated dropped-head syndrome revealing myositis. We describe a patient fulfilling diagnostic criteria for polymyositis, with dropped-head syndrome at onset, anti-Pm-Scl positivity and no signs of connective tissue disease.

Case Report

In 2012, at the age of 47 years old, the patient developed hypophonia, rinolalia, disphagia, progressive diffuse hypostenia, in particular of neck-extensor muscles. In 12 months, she had a complete drop-head syndrome with chin-to-chest sign. She could not climb the stairs, she walked with a cane and fell down several times. She even lost weight (10 Kg). Anamnesis was negative for hereditary diseases, past diseases and chronic therapies.

She was admitted at Neurology department in 2013 (Table 1). A complete electrophysiological study revealed a severe diffuse denervation, with myopathic potentials and early interferential recruitment, suggesting an inflammatory myopathy. Single-fibre EMG showed no signs of neuromuscular junction pathology. Brain MRI resulted negative. A complete blood examination revealed high serum CK levels (over 500 U/l). The search of anti-AChR and anti-MuSK antibodies, the cerebral spinal fluid examination and the screening for anti-gangliosyde antibodies were negative. Autoimmunity test revealed a high-titer positivity for anti-nuclear antibodies (1:1280), with presence of anti-Pm-Scl 100 antibodies. Other autoantibodies, including Sm, U1RNP, SSA, SSB, Scl70, Jo1, CENPB and dsDNA were negative.

We performed a muscle biopsy from left vastus lateralis. The histological examination revealed many atrophic fibres with necrosis and signs of regeneration. There were inflammatory lymphocytic infiltrates and endomysial fibrosis. Staining with Sudan black and PAS was normal. Immunochemistry showed MHC I complex exposed on many fibers.

The patient was negative for Raynaud syndrome, calcinosis, respiratory difficulties, oesophageal or pulmonar involvement and other signs of systemic connective tissue disease involvement.

No signs of hidden neoplasms were found. Total body CT scan, total body PET, EGDS, colonscopy and blood tests for neoplastic markers (CA 19.9, CA125, CEA, AFP and onco-neural antigens). Lymphocyte count and typing was normal. The screening for viral, bacterial or fungal infections, including HIV, HBV and HCV, was negative.

The patient was treated with a cycle of intra-venous immunoglobulins (IVIG) and high-dose Prednisone (1 mg/Kg/day), with progressive decrease, but no improvement was achieved.

In September 2013, the patient was newly admitted in Neurology because of generalized seizures, hypertension and MRI findings suggestive of Posterior Reversible Encephalopathy (PRESS). She was treated with anti-hypertensive and anti-epileptic drugs, with resolution of symptoms. In that occasion, the patient was treated with another cycle of IVIG, with no benefit on muscular weakness.

During the successive follow up, a trial with Azathioprine was attempted, but the patient developed severe anaemia. We performed other two cycles of IVIG, without benefit. Actually, the patient is treated with steroids in chronic, but still needs a Philadelphia collar to keep her head extended and uses a wheelchair to cover long distance.

Table 1: Summary of clinical features

Age at onset		47 years old
Clinics		Dropped-head sign, diffuse hypostenia with predominant bulbar involvement
Blood tests		Constantly elevated (> 500 U/l)
Electrophysiology	EMG	Severe diffuse denervation, myopathic potentials, early interferential recruitment
	SFEMG	No signs of NMJ pathology
Brain MRI		Normal
Autoimmunity	ANA	Positive with high titer (1:1280)
	ENA	Anti-Pm-Scl
	AChR, MuSK	Negative
	Gangliosydes	Negative
Muscle biopsy		Atrophic fibers, necrosis, regeneration, lymphocytic infiltrates, endomysial fibrosis, diffuse exposition of MHC I complex
Neoplastic screening		Negative
Infective diseases		Negative
Therapy		IVIG, Steroids, Azathioprine

Table 2: Our case in relation to different diagnostic criteria

Bohan and Peter (1975)	Definite Polymyositis
Tanimoto (1995)	Polymyositis
Dalakas and Hohlfeld (2003)	Definite Polymyositis
ENMC (2004)	Partially satisfied for Polymyositis
Troyanov (2005)	Overlap Polymyositis

Table 3: Characteristics of anti-Pm-Scl autoantibodies

Myositis-Associated Autoantibodies (MAA)

4-12% of patients with myositis

All age and ethnic groups

Associated with Polymyositis-Scleroderma overlap syndrome

Prognosis: 10% remission, 70% improvement, 20% worsening

Discussion and conclusions

We describe the complex case of a patient with diagnosis of polymyositis according to most of the diagnostic criteria proposed by now (Table 2). Nevertheless, according to recent classifications that define the range of myositis on the basis of antibody status, our patient presents the serological characteristic of overlap myositis or polymyositis-scleroderma (Table 2,3). However, she has no clinical sign of scleroderma or other connective tissue diseases, differently from the only other case described in literature with dropped-head and anti-Pm-Scl positivity (Garcin et al). Furthermore, our case is refractory to immunotherapy with steroids, Azathioprine and IVIG, which is another uncommon characteristic in immune-mediated myositis. Finally, the limited number of described cases prevents to prove the effective pathogenic role of anti-Pm-Scl Abs in myositis. In conclusion, we need more specific diagnostic criteria togheter with more extended surveys of immunological patterns to define more precisely the pathogenesis of autoimmune myositis.

References

- Dalakas MC, Hohlfeld R. Polymyositis and dermatomyositis. *Lancet* 2003; 362:971-982.
- Troyanov Y, Targoff IN, Tremblay J, et al. Novel classification of idiopathic inflammatory myopathies based on overlap syndrome features and autoantibodies: analysis of 100 French Canadian patients. *Medicine (Baltimore)* 2005; 84(4):231-249.
- Garcin B, Lenglet T, Dubourg O, et al. Dropped head syndrome as a presenting sign of scleromyositis. *J Neurol Sci* 2010; 292:101-103.
- Lundberg IE, Miller FW, Tjarlund A. Diagnosis and classification of idiopathic inflammatory myopathies. *J Int Med* 2016; 280:39-51.
- Betteridge Z, McHugh N. Myositis-specific autoantibodies: an important tool to support diagnosis of myositis. *J Int Med* 2016; 280:8-23.
- Clark KEN, Isenberg DA. A review of inflammatory idiopathic myopathy focusing on polymyositis. *Eur J Neurol* 2017; 0:1-11.
- Findlay AR, Goyal NA, Mozaffar T. An overview of polymyositis and dermatomyositis. *Muscle Nerve* 2015; 51(5):638-656.
- Dalakas MC. Inflammatory muscle diseases. *N Eng J Med* 2015; 372:1734-1747.
- Bohan A, Peter JB. Polymyositis and dermatomyositis. *N Eng J Med* 1975; 292(7):344-347; 292(8):403-407.
- Hoogendijk JE, Amato AA, Lecky BR, et al. 119th ENMC international workshop: Trial design in adult idiopathic inflammatory myopathies, with the exception of inclusion body myositis. *Neuromusc Dis* 2004; 14:337-345.