

# Polymyositis: support for an immunogenetic basis

*Polimiosite: contribuição para uma hipótese imunogenética*

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## ABSTRACT

We present a follow-up study on a case of polymyositis affecting two sisters of one same parenthood. Their cases have been documented in a previous report concerning an almost two decades history including the diagnostic protocol as well as laboratorial, histopathological and image tests. The degree of relatedness between their parents suggests that genetic factors may contribute to the development of the disease. The immunogenetic findings disclosed in the present study corroborate such an association.

**Keywords.** Myositis, HLA Antigens, Brazil.

**Citation.** Nóbrega OT, Karnikowski MGO. Polymyositis: support for an immunogenetic basis.

## RESUMO

Apresentamos a continuação da investigação sobre dois casos de polimiosite ocorridos entre irmãs de uma mesma filiação. Seus casos foram documentados em uma publicação anterior acerca de quase duas décadas de acompanhamento clínico, que incluiu o protocolo diagnóstico assim como exames laboratoriais, histopatológicos e por imagem. O grau de parentesco entre os genitores das pacientes sugere que fatores de herdabilidade podem predispor ao desenvolvimento da doença. Os achados imunogenéticos revelados pela presente investigação reforçam tal associação.

**Unitermos.** Miosite, Antígenos HLA, Brasil.

**Citação.** Nóbrega OT, Karnikowski MGO. Polimiosite: contribuição para uma hipótese imunogenética.

**This study was performed at the Catholic University of Brasilia, Brasilia-DF, Brasil.**

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Relato de Caso  
Recebido em: 08/09/08  
Aceito em: 11/03/09  
Conflito de interesses: não

## INTRODUCTION

Polymyositis (PM) comprises an inflammatory process that results in a myopathy due to an abnormal immune response to skeletal muscle fibers and to the connective tissues circunvinate<sup>1</sup>. PM is characterized by high levels of auto-antibodies to membrane and nuclear constituents in the serum of patients diagnosed with this condition<sup>2,3</sup>. Moreover, activation of T-cytolytic lymphocytes reactive to self-antigens is a possible mechanism underlining the pathology<sup>4</sup>. The diagnosis procedure in polymyositis is performed by means of clinical findings such as proximal muscle weakness, elevated dosages of enzymatic markers of muscular integrity, abnormalities in electromyographic exams and infiltrates in muscle biopsy<sup>5</sup>. Even though causes for PM remain undefined, an increasing awareness that genetic factors are implicated has evolved from studies that reveal an association of the disease with certain human leukocyte antigens (HLA)<sup>6</sup>. The augmented frequency of the HLA-B8 and -DR3 serological phenotypes among patients diagnosed with this pathology suggests a genetic profile that may predispose to its onset<sup>7</sup>. A study implicated the DRB1\*0301 and DQA1\*0501 alleles as risk factor for PM in the Causasian population, but not in other ethnic group<sup>8</sup>. In the other hand, it was found that patients with PM had significantly increased frequency of the DQB1 and DRB1 alleles in the Chinese population<sup>9,10</sup>. Despite the ethnicity, the occurrence of more than one case within the same family still consists in a rare finding<sup>11-13</sup>.

This work has the purpose to describe a follow-up study performed with two patients with PM which are sisters from one same parenthood and whose an almost two-decade medical records have been described previously<sup>14</sup> and summarized in Table 1. The purpose of this study was to determine the HLA phenotypes implicated with the cases identified.

## METHOD

The class I (A and B) and class II HLA (DQ and DR) phenotypes of each of the five members of the

family in study were determined using a routine serological method performed worldwide for HLA typing. Briefly, 30 ml blood samples were collected from each individual in ACD tubes after a 12-hour fasting period, being each sample immediately processed according to the standard NIH complement-dependent microcytotoxicity assay, as described elsewhere<sup>15</sup>. This work has been approved by the University's Ethics Committee (# 04/2002) and conducted in accordance to provisions of the Helsinki's Declaration. Each subject provided a written consent.

**Table 1.** Biochemical dosage of specific muscular enzymes from the serum of each patient at the onset of the disease, expressed as international units per liter (IU/l).

PACIENTS TESTS	Maximum Reference Values		
	G.R.V.C.	M.R.V.C.	
oxalacetic transaminase	145	24.5	30
pyruvate transaminase	186	29	37
lactate dehydrogenase	419	273	240
creatin kinase (CK)	2,600	1,580	70
aldolase	26.3	19.7	7.6

## RESULTS AND DISCUSSION

In the present study, both patients are sisters from the same parenthood, where the parents are first degree cousins. Such relatedness can be inferred from the sets of HLA phenotypes determined (Table 2), since both parents share 5 out of the 8 alleles investigated. Interestingly, each patient possesses leucocyte antigens of the B8 and DR3 serological groups, considered to be the major risk factors for the onset of PM<sup>7</sup>. Nonetheless, our results show that such background can not be considered its sole triggering factor since every other family members display a similar antigen pattern without any

**Table 2.** Class I and class II HLA phenotypes of each member of family in study.

	HLA-A		HLA-B		HLA-DR		HLA-DQ	
<b>Father</b>	A1	A28	B8	B15	DR2	DR3	DQ1	DQ2
<b>Mother</b>	A1	A11	B8	B21	DR1	DR3	DQ1	DQ2
<b>Brother</b>	A1	A36	B8	Y	---	DR3	---	DQ2
<b>M.R.V.C.</b>	A1	A11	B8	B21	DR1	DR3	DQ1	DQ2
<b>G.R.V.C.</b>	A1	A28	B8	B15	DR2	DR3	DQ1	DQ2

Y : unknown; --- : bad reaction or homozygote

sign of the disease. Thus, even though a definitive relationship between immunogenetic factors and polymyositis has not been established, we consider that the cases reported here corroborate such an association between B8+/DR3+ serology and the myopathyc condition. Moreover, our results suggest that concurrent homozygosis for alleles elsewhere in the genome may account to the onset of the disease.

## ACKNOWLEDGMENTS

The authors gratefully thank both patients and their family for the consent on this study. The authors also thank Dr. Hugo Mendonça Mundin, Chief of the Transplant Immunology Laboratory of the Hospital de Base do Distrito Federal, for providing the means for the serological tests presented in this study.

## REFERENCES

- Dalakas MC. Polymyositis, dermatomyositis and inclusion-body myositis. *N Engl J Med* 1991;325:1487-98.
- Miller FW. Myositis-specific antibodies: touchstones for understanding the inflammatory myopathies. *JAMA* 1993;270:1846-9.
- Bluthner M, Bautz FA. Cloning and characterization of the cDNA coding for a polymyositis-scleroderma overlap syndrome-related nucleolar 100 kDa protein. *J Exp Med* 1992;176:973-80.
- Miller FW, Love LA, Barbieri SA, Balow JW, Plotz PH. Lymphocyte activation markers in idiopathic myositis: changes with disease activity and differences among clinical and auto-antibodies subgroups. *Clin Exp Immunol* 1990;81:373-9.
- Greenberg SA. Inflammatory myopathies: evaluation and management. *Semin Neurol* 2008;28:241-9.
- Rider LG, Gurley RC, Pandey JP, Garcia de la Torre I, Kalovidouris AE, O'Hanlon TP, et al. Clinical, Serological, and Immunogenetic features of familial idiopathic inflammatory myopathy. *Arthritis Rheum* 1998;41:710-9.
- Garlepp MJ. Genetics of the idiopathic inflammatory myopathies. *Curr Opin Rheumatol* 1996;8:514-20.
- Rider LG, Shamim E, Okada S, Pandey JP, Targoff IN, O'Hanlon TP, et al. Genetic risks and protective factors for idiopathic inflammatory myopathy in koreans and american whites: a tale of two loci. *Arthritis Rheum* 1999;42:1285-90.
- Han X, Zhai N, Zhang Q, Li J, Liu J, Du J, et al. Association of HLA-DQB1 alleles and dermatomyositis/polymyositis. *Zhonghua Yi Xue Yi Chuan Xue Za Zhi*. 2002;19:322-3.
- Zhai N, Zhang Q, Han X, Song F. Association of HLA-DRB1 alleles with polymyositis/dermatomyositis in northern Chinese Hans. *Chin Med Sci J* 2002;17:198.
- Lewkonja RM, Buxton PH. Myositis in father and daughter. *J Neurosurg Psychiatr* 1973;36:820-5.
- Hokezu Y, Higuchi I, Yanai S, Nagai M, Nagamatsu K. A family case of HAM and HTLV-I carrier including two sisters presenting with myositis. *Rinsho Shinkeigaku* 1994;34:563-8.
- Scola RH, Werneck LC, Prevedello DMS, Toderke EL, Iwamoto FM. Diagnosis of polymyositis and dermatomyositis: a study of 102 cases. *Arq Neuropsiquiatr* 2000; 58(3-B):789-99.
- Karnikowski MGO, Costa BRV, Osella OFS, Nóbrega OT. Polymyositis: clinical investigation in two sisters. *Arq Neuropsiquiatr* 2002;60(3A):624-7.
- Terasaki PI, Bernoco D, Park MS, Ozturk G, Iwaki Y. Microdroplet testing for HLA-A, -B, -C, and -D antigens. *Am J Clin Pathol* 1978;69:103-20.