Prevalence of clinical and laboratory manifestations and comorbidities in polymyositis according to gender

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ABSTRACT

Objective: To assess gender distribution in polymyositis (PM) and its influence on disease, regarding clinical and laboratory manifestations, outcome and comorbidities. **Methods:** Retrospective single-center cohort study assessing 75 consecutive patients with PM (Bohan and Peter, 1975) from 1990 to 2010. Complementary tests were related to early diagnosis of PM. **Results:** The study assessed 52 women and 23 men (ratio 2.3:1), most of whom white (84.0%), with a mean age of 42.7 ± 13.7 years (16 to 67 years), and mean disease duration of 6.9 ± 5.5 years (0 to 20 years). Approximately 50% experienced disease relapse during follow-up. Nevertheless, two thirds were in remission at the end of this study, with 4.0% of deaths. There was no difference between genders regarding demographic, clinical and laboratory characteristics, clinical outcome and the drug therapy instituted. Regarding comorbidities, there was a high prevalence of hypertension (38.7%) and diabetes mellitus (17.3%), equally distributed between genders. There was also a high prevalence of depression and fibromyalgia, which were only observed among females. **Conclusions:** The prevalence of PM was higher among women than among men (2.3:1). Because the prevalence of comorbidities was high in the case series studied, it is worth emphasizing the need for their control to provide better quality of life for patients with PM.

Keywords: polymyositis, comorbidity, depression, gender and health, myositis.

INTRODUCTION

Systemic autoimmune diseases are usually most common among women, with an incidence ranging from 2:1 to 10:1. Systemic lupus erythematosus (SLE) and Sjögren's syndrome, for example, have a female/male ratio of 7-10:1, while for rheumatoid arthritis (RA) and systemic sclerosis that ratio is 2-3:1.[1]

The male gender is considered a good prognostic factor regarding remission in patients with RA on anti-TNF,[2] with better disease activity indices.[3] In Behçet's disease and primary Sjögren's syndrome, the male gender is related with higher frequency of neurological manifestations[4] and pulmonary impairment,[5] respectively.

Polymyositis (PM) is a chronic systemic inflammatory myopathy of unknown cause, often affecting women[6-8] and individuals aged between 30 and 50 years.[8] So far, there is no study comparing the profile of PM manifestations between genders, except for a general and indirect impression obtained in epidemiological studies.[9,10] For example, interstitial pulmonary disease in PM/dermatomyositis (DM) is associated with arthritis and/or arthralgia, anti-Jo-1 antibody, and the male gender.[9] Chen et al.[10] have primarily assessed neoplasia predictive factors in PM/DM, and have reported that the male gender was an independent risk factor.

Therefore, this study aimed at assessing the gender distribution in PM and its influence on disease, regarding clinical and laboratory manifestations, clinical outcome, and comorbidities.

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PATIENTS AND METHODS

This study assessed 75 consecutive patients with PM followed-up at the Unit of Myopathies of our tertiary service from 1990 to 2010. All patients met the Bohan and Peter classification criteria.[11,12] The study was approved by the local Ethics Committee (HC nº 0039/10), and demographic data and information regarding the clinical and laboratory manifestations were obtained from medical records.

The laboratory data were those routinely requested at the early PM diagnosis investigation. Creatine kinase (normal range: 24-173 U/L), aldolase (normal range: 1.0-7.5 U/L), aspartate aminotransferase (reference value: up to 37 U/L) and alanine aminotransferase (reference value: up to 41 U/L) measurements were obtained using the automated kinetic method. Autoantibodies against cell components were investigated by indirect immunofluorescence using Hep-2 cells as substrate. The anti-Jo-1 antibody was measured by immunoblotting; the erythrocyte sedimentation rate was determined by the Westergren method; and C-reactive protein was quantitatively determined in the serum by turbidimetry. Complementary tests, such as electroneuromyography, muscle biopsy of the biceps (upper limb), and chest computed tomography, were routinely requested at the first medical visits. Once excluded the possibilities of infection and neoplasia, disease relapse was defined as the recurrence of clinical and laboratory activity consequent to a reduction in the dose of corticosteroid and/or withdrawal of immunosuppressive drugs between the medical visits, due to clinical stability.

The comorbidities assessed were as follows: systemic arterial hypertension (SAH), diabetes mellitus, depression, fibromyalgia (FM), neoplasias, acute myocardial infarction (AMI) and stroke. The diagnosis of FM was based on the American College of Rheumatology classification criteria.[13] Depression was defined according to Zimmerman et al.[14] The diagnosis of SAH was based on the V Brazilian Arterial Hypertension

Table 1
Demographic, clinical and laboratory profile of patients with polymyositis

	All patients (N = 75)	Men (N = 23)	Women (N = 52)	P
Mean age* ± SD (years)	42.7 ± 13.7 (16-67)	42.3 ± 14.7 (16-66)	42.9 ± 13.2 (19-67)	0.874
Duration of disease ± SD (years)	6.9 ± 5.1 (0-20)	6.8 ± 5.5 (1-20)	6.9 ± 4.9 (0-20)	0.993
Duration of symptoms at the time of diagnosis (months)	2.3 ± 4.4 (0-24)	1.9 ± 2.9 (0-12)	2.4 ± 5.0 (0-24)	0.580
White (%)	63 (84.0)	21 (91.7)	42 (80.8)	0.323
Clinical manifestation				
Constitutional symptoms (%)	35 (46.7)	12 (52.2)	23 (44.2)	0.618
Bedridden (%)	21 (28.0)	6 (26.1)	15 (28.9)	1.000
Articular involvement (%)	39 (52.0)	13 (56.5)	26 (50.0)	0.626
Pulmonary involvement				
Dyspnea (%)	20 (27.4)	6 (26.1)	14 (26.9)	1.000
Dysphonia (%)	5 (6.7)	0	5 (9.6)	0.315
Gastrointestinal involvement				
Dysphagia (%)	22 (29.3)	6 (26.1)	16 (30.8)	0.787
Dyspepsia (%)	21 (28.0)	7 (30.4)	14 (26.9)	0.785
Disease remission (%)	49 (65.3)	15 (65.2)	34 (65.4)	1.000
Disease relapse (%)	33 (44.0)	9 (39.1)	24 (46.2)	0.622
Follow-up (%)	59 (78.7)	17 (73.9)	42 (80.8)	0.549
Death (%)	3 (4.0)	1 (4.4)	2 (3.9)	1.000
Autoantibodies				
Antinuclear factor (%)	38 (50.7)	12 (52.2)	26 (50.0)	0.804
Anti-Jo-1 (%)	12 (16.0)	3 (13.0)	9 (17.3)	0.745
Muscle enzymes (beginning of disease)				
Creatine kinase ± SD (U/L)	4167.6 ± 4736.6	5023.0 ± 5481.3	3793.4 ± 4318.2	0.379
Aldolase ± SD (U/L)	62.6 ± 61.5	89.9 ± 89.7	52.3 ± 42.2	0.167
Aspartate aminotransferase (U/L)	186.6 ± 233.4	187.2 ± 255.6	186.5 ± 224.8	0.994
Alanine aminotransferase (U/L)	152.7 ± 180.5	160.1 ± 224.7	150.0 ± 160.8	0.893
C-reactive protein (mg/L)	19.7 ± 33.0	38.8 ± 49.8	10.1 ± 11.1	0.120
ESR (mm/1st hour)	24.7 ± 20.9	22.0 ± 20.9	25.5 ± 20.9	0.680
Computed tomography				
Basal pulmonary fibrosis (%)	7 (9.3)	2 (8.8)	5 (9.6)	1.000
Ground-glass lesion (%)	13 (17.3)	6 (26.1)	7 (13.5)	0.201

* Age at polymyositis diagnosis.
SD: standard deviation; ESR: erythrocyte sedimentation rate.
P value refers to men vs women.

Guidelines,[15] and that of diabetes mellitus on the American Diabetes Association guidelines.

The results were expressed as mean ± standard deviation (SD) or percentage. Student's *t* test was used for parametric data, and Fisher's exact test for non-parametric data. Statistical analysis was performed with the STATA software, version 7.0 (Stata, College Station, TX, USA), and P values < 0.05 were considered statistically significant.

RESULTS

This study assessed 75 consecutive patients with PM in the period between 1990 and 2010, including 52 women and 23 men with a 2.3:1 ratio, respectively. Their mean follow-up time at our service was 6.9 ± 5.5 years. Most patients were white (84.0%), their mean age at the time of diagnosis was 42.7 ± 13.7 years (16 to 67 years), and the mean duration of disease was 6.9 ± 5.5 years (0 to 20 years). The time between PM symptom onset and diagnosis in the general sample was 2.3 ± 4.4 months (0 to 24 months). Table 1 shows the clinical and laboratory characteristics of the patients. Approximately half of the patients experienced a PM relapse during follow-up. Nevertheless, two thirds of the patients showed disease remission at the end of this study. Death occurred in 4.0%.

The initial drug therapy consisted of corticosteroid (oral prednisone, 1 mg/kg/day), with gradual dose reduction during one to two months after clinical and laboratory stability. When the disease was more severe, pulse therapy with methylprednisolone (1 g/day, parenteral route, three consecutive days) was administered. The following corticosteroid sparing agents

Table 2
Drug therapy instituted in patients with polymyositis

Drug therapy	All patients (N = 75)	Men (N = 23)	Women (N = 52)	P
Corticosteroid				
Prednisone (1 mg/kg/day) (%)	73 (100.0)	23 (100.0)	52 (100.0)	1.000
Methylprednisolone (%)	35 (46.7)	13 (56.5)	22 (42.3)	0.323
Methotrexate (%)	49 (65.3)	13 (56.5)	36 (69.2)	0.305
Azathioprine (%)	40 (53.3)	12 (52.2)	29 (53.9)	1.000
Cyclophosphamide (%)	15 (20.0)	4 (17.4)	11 (21.2)	1.000
Cyclosporine (%)	15 (20.0)	4 (17.4)	10 (19.2)	1.000
Mycophenolate mofetil (%)	3 (4.0)	1 (4.4)	2 (3.9)	1.000

P value refers to men vs women.

Table 3
Comorbidities diagnosed after polymyositis onset

Comorbidities	All patients (N = 75)	Men (N = 23)	Women (N = 52)	P
Systemic arterial hypertension (%)	29 (38.7)	10 (43.5)	19 (37.3)	0.618
Pre-polymyositis (%)	18 (24.0)	5 (21.7)	13 (25.0)	1.000
Post-polymyositis (%)	11 (14.7)	5 (21.7)	6 (11.5)	0.306
Diabetes mellitus (%)	13 (17.3)	6 (26.1)	7 (13.5)	0.201
Pre-polymyositis (%)	7 (9.3)	3 (13.0)	4 (7.7)	0.669
Post-polymyositis (%)	6 (8.0)	3 (13.0)	3 (5.8)	0.363
Major depression (%)	11 (14.7)	0	11 (21.2)	0.028
Fibromyalgia (%)	6 (8.0)	0	6 (11.5)	0.169
Neoplasia (%)	4 (5.3)	1 (4.4)	3 (5.8)	1.000
Acute myocardial infarction (%)	3 (4.0)	1 (4.4)	2 (3.9)	1.000
Stroke (%)	0	0	0	1.000

P value refers to men vs women.

were used in monotherapy or association, depending on tolerance, adverse effects, and disease refractoriness: azathioprine (2-3 mg/kg/day), methotrexate (20-25 mg/week), cyclosporine (3-5 mg/kg/day), mycophenolate mofetil (2-3 g/day), leflunomide (20 mg/day) and cyclophosphamide (0.5-1.0 g/m^2 of body surface) (Table 2). All patients received prednisone (1 mg/kg/day), and approximately half of them underwent additional pulse therapy with methylprednisolone (1 g/day, three consecutive days). Parenteral use of cyclophosphamide was indicated for pulmonary impairment, which was characterized by progression of dyspnea and compatible images on computed tomography. No difference was observed between women and men regarding the distribution of demographic, clinical and laboratory characteristics, clinical outcome, and the drug therapy instituted (Tables 1 and 2).

Regarding comorbidities (Table 3), depression and FM occurred only among women, but only depression had a statistically significant prevalence in the female gender (P = 0.028). None of the female patients had bipolar disorder. The prevalence of SAH in our case series was high (38.7%), and that was evident even before the PM symptom onset and diagnosis (24.0%), increasing approximately 50% after myopathy establishment. Diabetes mellitus had a prevalence of 9.3% prior to PM establishment, but after that the prevalence increased to 17.3%, with the same distribution in both genders. Neoplasia and AMI occurred in 5.3% and 4% of the patients, respectively. Regarding neoplasias, one man was diagnosed with femoral osteoid osteoma one year after the diagnosis of PM, and three women were diagnosed with the following neoplasias: thyroid follicular carcinoma (one year after PM); metastatic epidermoid carcinoma (three years after PM); and renal neoplasia (15 years after PM). No stroke was identified.

DISCUSSION

This study comprised a large case series and assessed gender distribution in PM and its influence on disease. The following characteristics were observed in our case series: most patients affected were women (2.3:1), similar clinical and laboratory characteristics and comorbidities in both genders, high prevalence of SAH and diabetes mellitus, with emphasis on major depression, present only among women.

In this study, the mean age at disease onset was 40 years, similar to that reported in the literature,[16-33] differing only from the mean age reported for Senegal and Singapore (50 years).[24,25]

Usually, autoimmune diseases, including idiopathic inflammatory myopathies, affect mostly the female gender,[1,15,18-25] fact reinforced by the findings of the present study. SLE and Sjögren's syndrome, for example, have female:male ratios of 7-10:1, while for RA, systemic sclerosis and idiopathic inflammatory myopathies that ratio is 2.3:1.[1,16,18-25] That difference in distribution might reflect the influence of endogenous sexual hormones and genetic factors.[17-24]

Our data show that the outcome and demographic, clinical, and laboratory characteristics of PM were similar in both genders, differently from that occurring in other systemic autoimmune diseases, in which gender can influence the course of disease. SLE, for example, tends to have a worse prognosis in men, although that is controversial in the literature.[26-29]

Approximately half of the patients had constitutional symptoms or articular involvement at the beginning of disease. All patients had proximal muscle weakness in four limbs, and one fourth was bedridden despite the short time of disease onset (approximately two months). In addition, pulmonary (dyspnea) and gastrointestinal (dysphagia or dyspepsia) involvements were observed in approximately one third of the patients, reinforcing the need for assessing individuals with PM more comprehensively, not only from the viewpoint of exclusive musculoskeletal involvement.

Depression is a frequent finding in chronic systemic diseases, such as RA (13%-20% of the cases),[30-33] FM (39%)[33] and SLE (34%).[29] In the general community and primary care, depression occurs in 2%-4% and 5%-10% of female patients, respectively,[34] differently from this study findings, in which depression was seen in 21.2% of the women. Depression, particularly in RA, is associated with higher frequency of hospitalization, greater number of medical visits, worse quality of life, lower adherence to drug therapy, and increased risk of mortality.[34-37] Depression is twice more frequent in women as compared with men,[38] while FM is approximately ten times more prevalent.[39] Our patients with depression showed neither greater disease relapse nor higher incidence of death. Although the association between depression and FM is relatively common, in the present study those two comorbidities coexisted only in women, being simultaneous in only one female patient.

High prevalence of SAH and diabetes mellitus was observed, as compared with that of the Brazilian population, 20% and 9%, respectively.[40,41] After the diagnosis of PM, the incidence of SAH and diabetes mellitus increased by 50% and 100%, respectively, which can reflect the use of corticosteroids. Recently, based on an epidemiological data base, Limaye et al.[42] have shown a high incidence of cardiovascular events after the diagnosis of all idiopathic inflammatory myopathies (dermatomyositis, PM, and inclusion body myositis). In the

present study, neoplasias occurred in approximately 5% of the patients, with no gender distinction, and that index is in accordance with those reported in the literature: 3.3% and 7.7%.[43-45]

The present study showed a low prevalence of cardiovascular events (AMI and stroke), with no distinction between genders, which can be partially justified by the short-term follow-up (approximately eight years), different from the indices reported in the literature, 6%-75%.[46,47]

Regarding the course of disease, two thirds of the patients were in remission due to corticotherapy and/or immunosuppressive drugs. Half of the patients, with no gender distinction, experienced disease relapse, emphasizing the need for regular medical follow-up of those patients. Death occurred in 4.0% of the patients, with no gender distinction.

In conclusion, PM affected women at the ratio of 2.3:1, with a high prevalence of comorbidities, both in men and women. Major depression affected exclusively the female gender. When assessing patients with PM, we should pay close attention to comorbidities, aiming at their rapid control and, thus, better quality of life for patients.

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