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Research Article

Dyslipidemia in Adult Dermatomyositis and Polymyositisis not Associated with Anti-Lipoprotein Lipase

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Abstract

Dyslipidemia has been observed in many systemic autoimmune diseases, including systemic lupus erythematosus, Dermatomyositis (DM) and Polymyositis (PM). In systemic lupus erythematosus, the mechanism of dyslipidemia has been attributed to the presence of Anti-Lipoprotein Lipase (anti-LPL) antibodies. A similar pattern of dyslipidemia can also be observed in patients with DM and PM. Therefore, the aim of this study was to determine the possible presence of anti-LPL antibodies in 69 consecutive patients with DM and PM. The IgG anti-LPL was detected by a standard ELISA. The lipoprotein risk levels were evaluated according to National Cholesterol Education Program-Adult Treatment Panel III (NCEP/ATPIII). The mean age of patients with DM and PM was 31.6±10.2 and 29.4±9.1 years, respectively. There was a predominance of female gender and white ethnicity. Lipoprotein NCEP risk levels were observed in 69.8% of DM and 68.8% of PM patients. Despite the high frequency of dyslipidemia in these patients, no anti-LPL antibodies were detected. Our data suggest that a distinct physiopathogenicity is involved in dyslipidemia. Additional studies are necessary to elucidate the dyslipidemic mechanisms in these inflammatory myopathic diseases.

Keywords: Anti-lipoprotein lipase; Dermatomyositis; Dyslipidemia; Inflammatory myopathies; Polymyositis

Abbreviations

DM: Dermatomyositis; ELISA: Enzyme-Linked Immunosorbent Assay; HAQ: Health Assessment Questionnaire; HDL-c: High Density Lipoprotein Cholesterol; LDL-c: Density Lipoprotein Cholesterol; LPL: Lipoprotein Lipase; MMT: Manual Muscle Testing; NCEP low /ATPIII: National Cholesterol Education Program-Adult Treatment Panel III; PM: Dolymyositis

Introduction

Dermatomyositis (DM) and polymyositis (PM) are rare autoimmune diseases that are associated with high morbidity and functional disabilities [1]. These diseases are characterized by a progressive and insidious proximal muscular weakness of the limbs. Moreover, there are cutaneous involvements in DM, such as heliotrope and/or Gottron's papules [1]. Recent studies have shown a high prevalence of metabolic syndrome in patients with DM (41.7%) [2] and PM (45.7%) [3]. This high prevalence, along with the chronic use of corticosteroids, functional disabilities and the tendency towards a sedentary lifestyle or even complete bed rest by some patients, may increase cardiovascular risk and mortality in the population with DM and PM. In particular, dyslipidemia was present in 67.9% and 71.4% of patients with DM [2] and PM [3], respectively, and was characterized by high and low serum levels of triglycerides and High Density Lipoprotein Cholesterol (HDL-c), respectively. The alterations found in the triglyceride and HDL-c levels may be associated with the decrease in activity of Lipoprotein Lipase (LPL) [4], which is responsible for the hydrolysis of triglycerides located in lipoprotein particles [5,6]. Another hypothesis is that the presence of anti-LPL antibodies is the primary contributor, which has been demonstrated in other systemic autoimmune diseases such as systemic lupus erythematosus [7,8], systemic sclerosis and rheumatoid arthritis [9]. This would establish a link between the immune/ inflammatory response and the triglyceride levels and would suggest that systemic autoimmune diseases favor the development of dyslipidemia [10]. Thus, it is relevant to evaluate the presence of anti-LPL antibodies in patients with DM and PM, because these diseases present with a high frequency of dyslipidemia.

Materials and Methods

Patients

This cross-sectional single center study analyzed 69 consecutive adult patients with DM (N=53) and PM (N=16) who were enrolled from 2012 to 2014. All patients fulfilled at least four of the five classification criteria of outlined by Bohan and Peter [11]. Conditions that could interfere with the lipid profile were excluded, such as patients with diabetes mellitus, hepatopathies, thyroidopathies, the use of lipid lowering drugs, pregnant women, and post-menopausal women. Patients who had associations with other systemic autoimmune diseases as well as neoplasia and other myopathies (metabolic, stat in induced necrotizing myopathies, inclusion body myositis and muscular dystrophies) were also excluded.

The present project was approved by the Ethics Committee of our Institution.

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Table 1: General features of patients with dermatomyositis and polymyositis.

	DM (N=53)	PM (N=16)
Age at disease onset (years)	31.6±10.2	29.4±9.1
Current age (years)	35.4±9.4	33.7±7.9
Duration: diagnosis - symptom onset (months)	6.0 (3.0-12.0)	3.5 (2.0-0.6)
Female gender	40 (75.5)	14 (87.5)
White ethnicity	40 (75.5)	10 (62.5)
Body mass index (kg/m^2)	26.7 (22.8-32.1)	28.3 (24.7-32.7)
Systemic arterial hypertension	12 (22.6)	5 (31.3)
Prednisolone usage	35 (66.0)	7 (43.8)
Prednisolonedoses (mg/day)	10.0 (0-38.0)	2.5 (0-10.0)
Global patient's visual analogue scale (0-10 mm)	2.0 (0.0-5.5)	2.0 (0.0-5.5)
Global physician's visual analogue scale (0-10 mm)	2.0 (0.3-5.5)	5.5 (0-5.8)
MMT8 (0-80)	80 (72-80)	74 (62-80)
HAQ (0.00-3.00)	0.43 (0.0-1.86)	0.93 (0.22-2.11)
Creatine phosphokinase (U/L)	155 (86-345)	918 (165-1641)
Aldolase (U/L)	5.1 (4.0-7.4)	8.2 (6.2-25.6)
Total cholesterol (mg/dL)	187 (156-215)	190 (167-238)
HDL-c (mg/dL)	49 (40-62)	50 (30-71)
LDL-c (mg/dL)	108 (156-215)	106 (67-149)
Triglyceride (mg/dL)	131 (79-187)	122 (75-177)

Data are expressed as the mean ± standard deviation, median (25th- 75th interquartile) or percentage (%).
DM: dermatomyositis; HAQ: health assessment questionnaire; HDL-c: high density lipoprotein cholesterol; LDL-c: low density lipoprotein cholesterol; MMT8: manual muscle testing; PM: polymyositis.

Eligible patients were interviewed, and the obtained demographic and clinical data were supplemented by a systematic review of the patient´s records. The disease status was obtained using the following questionnaires and scores: manual muscle testing (MMT8), global evaluation of the disease by doctor and patient through the visual analog scale, and a Health Assessment Questionnaire (HAQ) [12-16]. Serum samples were obtained from all patients after a 12-hour overnight fast after inclusion. Immunological and biochemical analyses were performed in the same serum samples.

Assay for antibody for LPL detection

The anti-LPL reactivity of the IgG isotype was measured by enzyme-linked immunosorbent assay (ELISA) as previously described [7]. Briefly, wells of Costar polystyrene plates were coated overnight with commercially available LPL from bovine milk (5µg/ml) (Sigma Chem. Co, St Louis, MO, USA). The test was performed with serum samples that were diluted 1/100 in Tris buffered-saline containing adult bovine serum. Anti-LPL IgG isotype antibodies were determined with alkaline-phosphatase conjugated goat antihuman IgG (Sigma Chem. Co, St Louis, MO, USA). The reaction was developed with p-nitrophenyl phosphate and the optical density was read at 408 nm with a Lab system Multiskan MS (Helsinki, Finland). IgG anti-LPL positivity was defined as serum samples with an optical density values ≥ 3 standard deviations above the mean optical density of 20 adult healthy control serum samples included in each assay.

Table 2: Lipid features in patients with dermatomyositis and polymyositis, according to the NCEP/ATPIII.

Parameters	DM (N=53)	PM (N=16)
Total cholesterol > 200 mg/dL	20 (37.7)	6 (37.5)
HDL-c< 40 mg/dL	12 (22.6)	4 (25.0)
LDL-c> 130 mg/dL	15 (28.3)	4 (25.0)
Triglyceride> 150 mg/dL	22 (41.5)	6 (37.5)
At least one of the previous parameters	37 (69.8)	11 (68.8)

Data are expressed as a percentage (%).
DM: dermatomyositis; HDL-c: high density lipoprotein cholesterol; LDL-c: low density lipoprotein cholesterol; PM: polymyositis.

Lipid profiles

Total cholesterol and triglycerides, HDL-c and LDL-c were measured enzymatically via a colorimetric method. Risk lipoprotein levels were determined according to the National Cholesterol Education Program-Adult Treatment Panel III (NCEP/ATPIII) [17].

Statistical analysis

Results are presented as the mean standard deviation, median (25th- 75th interquartile) or percentage (%).

Results

Sixty-nine patients were analyzed (53 DM and 16 PM). There was a high frequency of women and Caucasians in both groups. Moreover, the mean age of the patients with DM and PM was 35.4±9.4 and 33.7±7.9 years, respectively (Table I).

Patients with DM and PM had a body mass index of 26.7kg/m^2 and 28.3kg/m^2, respectively, and systemic arterial hypertension in 22.6% and 31.3% of the cases, respectively. Concerning drugs, 66.0% of DM patients were using prednisolone with a median dose of 10 mg/day, whereas 43.8% of PM patients were using this drug with a median dose of 2.5 mg/day. The different parameters regarding the current status (analogic visual scale, MMT8, HAQ, muscle enzymes) of DM and PM are shown in (Table I). Moderate and elevated risk levels for lipoproteins, according to the NCEP/ATPIII were found along with high total cholesterol in patients with DM (37.7%) and PM (37.5%), and low HDL-c was found in 22.6% of patients with DM and 25% of patients with PM. Moreover, high LDL-c was observed in 28.3% of patients with DM and 25% in patients with PM, where as the serum levels of triglycerides were elevated in 41.5% of DM and 37.5% of PM patients. Furthermore, 69.8% and 68.6% of patients with DM and PM, respectively, showed alterations in at least one of the previous NCEP/ATPIII parameter (Table 2). No anti-LPL antibodies measured by ELISA were detected in patients with DM and PM.

Discussion

Our results showed that patients with DM and PM did not have anti-LPL autoantibodies, although 69.8% of DM and 68.8% of PM patients had at least one lipid risk level for cardiovascular disease. The advantage of the present study was that we excluded patients with conditions that may have interfered with the lipid profile or the characterization of the antibody anti-LPL. Furthermore, we analyzed patients with a defined diagnosis of DM or PM according to Bohan and Peter's criteria [11]. We also excluded patients with neoplasia, overlapping autoimmune systemic diseases and other myopathies.

Despite of using these rigorous criteria of rare diseases (DM and PM), the present study analyzed the presence of anti-LPL in a reasonable sample. The present data reinforce previously published findings [2,3]. Our patients showed low serum levels of HDL-c and high serum levels of total cholesterol, LDL-c and triglycerides. This profile is similar that found insystemic lupus erythematosus [8].

The presence of the anti-LPL antibody has been perceived as a possible mechanism of dyslipidemia. Thus, in patients with systemic lupus erythematosus, this antibody is considered the cause of the dyslipidemia reaction with lipoprotein lipase, which is responsible for normal lipid metabolism, causing increase on levels of total cholesterol and LDL-c, and decreased levels of HDL-c. Therefore, the presence of the anti-LPL antibody is considered responsible for dyslipidemia in some autoimmune diseases [6]. According to Reichlin et al. [9], the anti-LPL antibody frequency was 46.7% in systemic lupus erythematosus patients, 40% in polymyositis, 41.9% in systemic sclerosis, 12.5% in rheumatoid arthritis and 10% in Sjögren syndrome. However, the authors did not provide details for the therapeutic, clinical, laboratory and demographic features of their patients with PM. Second, positive results were defined as those with a value exceeding the mean ± 2 standard deviations of the optical density units from the four control individuals not matched with patients for age, ethnicity and gender. Third, 28% of the healthy individuals had a positive antibody against LPL.

The presence of the anti-LPL antibody has been studied in other rheumatism diseases, such as Takayasu's arteritis [18]. However, in this disease, there no association between anti-LPL antibody and the physiopathological mechanism of the disease [18]. Similar to that study [18], we did not observe the presence of the anti-LPL antibody in DM. Moreover, in contrast to a previously published study [9], we did not find the anti-LPL antibody in patients with PM. Thus, ours result suggest that the mechanism of dyslipidemia in our patients is distinct from anti-LPL antibody activity. There are some limitations in the present study. First, we did not exclude individuals with a high body mass index (> 30 kg/m^2), which could modify the lipid profile [19]. Second, we did not analyze a higher carbohydrate diet, which is also associated with dyslipidemia. Third, our study included the characteristics of a study population that was from a tertiary care center and most likely represented a more severe disease spectrum; therefore, the frequency of dyslipidemia might have been overestimated.

Conclusion

Our results show that anti-LPL antibodies are not implicated in the pathophysiology of dyslipidemia in patients with DM or PM.

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