REVISTA BRASILEIRA DE REUMATOLOGIA

www.reumatologia.com.br

SOCIEDADE BRASILEIRA DE REUMATOLOGIA

Original article

Different aspects of magnetic resonance imaging of muscles between dermatomyositis and polymyositis

Sofia Silveira de Castro Miranda[a], *Daniel Alvarenga*[b], *João Carlos Rodrigues*[b], *Samuel Katsuyuki Shinjo*[a,c,*]

[a]*Rheumatology Service, Hospital das Clínicas, Medicine School, Universidade de São Paulo, São Paulo, SP, Brazil*
[b]*Department of Radiology, Orthopedia and Traumatology Institute, Hospital das Clínicas, Medicine School, Universidade de São Paulo, São Paulo, SP, Brazil*
[c]*Medicine School, Universidade de São Paulo, São Paulo, SP, Brazil*

ARTICLE INFO

Article history:
Received 28 January 2014
Accepted 7 April 2014

Keywords:
Dermatomyositis
Muscle diseases
Polymyositis
Magnetic resonance

ABSTRACT

Introduction: Although dermatomyositis (DM) and polymyositis (PM) share many clinical features in common, they have distinct pathophysiological and histological features. It is possible that these distinctions reflect also macroscopically, for example, in muscle alterations seen in magnetic resonance images (MRI).
Objectives: To compare simultaneously the MRI of various muscle compartments of the thighs of adult DM and PM.
Materials: The present study is a cross-sectional that included, between 2010 and 2013, 11 newly diagnosed DM and 11 PM patients (Bohan and Peter's criteria, 1975), with clinical and laboratory activity. They were valued at RM thighs, T1 and T2 with fat suppression, 1.5 T MRI scanner sequences.
Results: The mean age at the time of MRI, the time between onset of symptoms and the realization of the MRI distribution of sex and drug therapy were comparable between the two groups ($p>0.050$). Concerning the MRI, muscle edema was significantly found in DM, and mainly in the proximal region of the muscles. The area of fat replacement was found predominantly in PM. The partial fat replacement area occurred mainly in the medial and distal region, whereas the total fat replacement area occurred mainly in the distal muscles. There was no area of muscle fibrosis.
Conclusions: DM and PM have different characteristics on MRI muscles, alike pathophysiological and histological distinctions.

* *Corresponding author.*
E-mail: samuel.shinjo@gmail.com (S.K. Shinjo).

0482-5004/$ - see front matter.
http://dx.doi.org/10.1016/j.rbr.2014.04.004

Aspectos distintos de ressonância magnética de músculos entre dermatomiosite e polimiosite

Palavras-chave:
Dermatomiosite
Doença muscular
Polimiosite
Ressonância magnética

RESUMO

Introdução: Embora a dermatomiosite (DM) e a polimiosite (PM) compartilhem diversos aspectos clínicos em comum, cada uma delas apresenta características fisiopatológicas e histológicas próprias. É possível que estas diferenças também se reflitam macroscopicamente, como, por exemplo, em imagens musculares vistas em ressonância magnética (RM).
Objetivos: Comparar simultaneamente a RM de diversos compartimentos musculares das coxas de pacientes com DM e PM adultos.
Materiais: Estudo transversal, em que foram avaliadas, entre o período de 2010 a 2013, as imagens de RM das coxas realizadas em aparelho de 1,5 Tesla (T) com sequências ponderadas em T1 e T2 com supressão de gordura, para rastreamento, de 11 DM e 11 PM (Bohan e Peter, 1975) recém-diagnosticados, em atividade clínica e laboratorial.
Resultados: A média de idade na ocasião da RM, o tempo entre o início de sintomas e a realização das RM, a distribuição de sexos e a terapia medicamentosa foram comparáveis entre os dois grupos (p>0,050). Em termos de RM, edema muscular foi encontrado significantemente em DM, e principalmente na região proximal dos músculos. A área de lipossubstituição dos músculos foi encontrada predominantemente em PM. Essa lipossubstituição, quando de uma forma parcial, ocorreu principalmente nos terços médio e distal, enquanto que a forma total transcorreu apenas no terço distal dos músculos. Não houve nenhuma área de fibrose muscular.
Conclusões: A DM e a PM apresentam características distintas entre si em RM de músculos, a exemplo de distinções fisiopatológicas e histológicas.

Introduction

Dermatomyositis (DM) and polymyositis (PM) are part of a group of systemic autoimmune diseases characterized by symmetric and progressive proximal muscle weakness of limbs. Moreover, extramuscular manifestations (i.e. articular, heart, lung and gastrointestinal tract involvement) may occur.[1,2] In the case of DM, typical skin changes still occur, such as heliotrope and/or Gottron's papules.

Although DM and PM share many similar clinical and laboratory features, each of these conditions also exhibit distinct epidemiological, pathophysiological and histological characteristics. Thus, from the histological and physiopathological standpoint, in PM there is a focal infiltrate of CD8 (+) lymphocytes and macrophages in the muscle fibers, which, in turn, express high levels of MHC class I antigens and release perforin granules,[3] resulting in lysis and necrosis of the muscle fibers themselves,[4] as well as fat in replacement areas and tissue fibrosis. In the case of DM, there are several features that suggest an important role of B cells in the pathogenesis of the disease, such as the presence of autoantibodies, immune complex deposition in the dermo-epidermal junction in skin lesions, the presence of B cells in sore muscles,[5,6] and in perivascular areas.[7,8] In addition to this, the deposition of complement and immunoglobulin in the perifascicular endothelium can lead to muscle ischemia and atrophy, showing the importance of humoral immunity.[9]

It is plausible that these differences observed between DM and PM are also macroscopically reflected, such as in muscle images obtained from studies of magnetic resonance imaging (MRI), although to date there are no studies in the literature demonstrating these possible differences.

MRI has been used in idiopathic inflammatory myopathies as an additional instrument to assess disease activity, therapeutic monitoring, and prognosis of disease, as well as a guide to the most likely location to find positive areas of inflammatory infiltrate in a muscle biopsy.[10-23] However, most of these studies are based on juvenile DM.[10,11,13,14,17,18,22] On the other hand, there is paucity of MRI studies on adult DM patients, as well as on PM ones,[12,16,23] and this served as motivation for us to conduct this study.

Patients and methods

This was a cross-sectional study that, during the period from 2010 to 2013, assessed 11 DM patients and 11 PM patients defined by Bohan and Peter criteria and recently diagnosed as with clinical and laboratory activity.[24,25] Patients with a diagnosis of amyopathic DM, myopathies associated with malignancy or other types of collagenosis were not included, as well as patients under the age of 18 years.

The present work is a sequel of a study previously approved by the local Ethics Committee [HC 0039/10].

Originally, all patients had been hospitalized in our department for a clinical research of progressive proximal muscle weakness in their limbs, and also because of an increase in serum levels of muscle enzymes without an apparent cause. According to our service protocol, possible

differential diagnoses were dismissed; and, prior to muscle biopsy for diagnostic purposes, the patients underwent a MRI of the muscles of the thighs. Searching a database of previously standardized electronic data (electronic medical record), the following data were collected: current age; ethnicity; gender; time between onset of symptoms and MRI; limb muscle strength (grade 0: absence of muscle contraction; grade I: signs of slight contractility; grade II: normal range of motion, but without overcome the action of gravity; grade III: normal range of motion against gravity; grade IV: full mobility against gravity, with a certain degree of resistance; and grade V: complete mobility against strong resistance and against gravity);[26] serum levels of muscle enzymes [creatine phosphokinase (normal range: 24-173 U/L) and aldolase (normal range: 1.0-7.5 U/L) determined by an automated kinetic method]; autoantibodies against cellular components, determined by indirect immunofluorescence, using Hep-2 cells as substrate; pre-MRI medicamentous history (corticosteroids and/or immunosuppressants).

MRI was performed by fast spin echo technique, obtaining T1- and T2-weighted sequences with fat suppression, in multiplanar acquisitions, using a Philips 1.5 T unit from the Department of Radiology at our institution. Fifteen muscles were evaluated: sartorius, vastus lateralis, vastus intermedius, vastus medialis, rectus femoris, tensor fasciae latae, adductor longus, adductor brevis, adductor magnus, pectineus, gracilis, gluteus maximus, semitendinosus, semimembranosus and biceps femoris. The following parameters were evaluated for each muscle in its proximal, middle and distal thirds: presence or absence of an edema area, fibrosis, and fat replacement (partial or total). Furthermore, we evaluated the overall appearance of muscles, as being normal or hypo/atrophic. The images were evaluated by two radiologists with proven experience in muscle MRI analysis. These professionals worked independently and were unaware of the clinical cases.

Table 1 – Demographic, clinical, laboratory and drug therapy characteristics of patients with dermatomyositis and polymyositis

Characteristics	DM (n=11)	PM (n=11)	*p*
Age (years)	50.9±11.4	49.9±16.2	0.868
Female gender	9 (81.8)	10 (90.9)	1.000
Caucasian	9 (81.8)	8 (72.7)	1.000
Time: MRI – symptoms (months)	16.7±22.2	29.0±20.3	0.191
Muscle strength			
Upper limbs			
Grade V	1 (9.1)	5 (45.5)	0.155
Grade IV	5 (45.5)	4 (36.4)	1.000
Grade III	4 (36.4)	2 (18.2)	0.635
Grade II	1 (9.1)	0	1.000
Lower limbs			
Grade V	0	1 (9.1)	1.000
Grade IV	5 (45.5)	7 (63.6)	0.670
Grade III	5 (45.5)	2 (18.2)	0.361
Grade II	1 (9.1)	1 (9.1)	1.000
Muscle enzymes			
Creatine phosphokinase (U/L)	1340 (158-3489)	870 (207-2519)	0.768
Aldolase (U/L)	11.2 (7.4-29.0)	9.7 (6.6-20.6)	0.577
Antinuclear factor	7 (63.6)	5 (45.5)	0.670
Methylprednisolone (pulse therapy)	3 (27.3)	2 (18.2)	1.000
Prednisone	11 (100.0)	9 (81.8)	0.476
Cumulative dosage (mg), <1 m	1200 (180-2100)	300 (300-1500)	0.290
Cumulative dosage (g), <3 m	3.0±3.2	1.4±1.1	0.190
Immunosuppressants	3 (27.3)	6 (54.5)	0.387

Data are expressed as mean ± standard deviation, median (interquartils), or percentage (%).
DM, dermatomyositis; PM, polymyositis; MRI, magnetic resonance imaging.
Immunosuppressants, azathioprine (2-3 mg/kg/day), methotrexate (15-25 mg/week)

Statistical analysis

Our data were expressed as mean ± standard deviation (SD), median (interquartils) or percentage (%), being assessed for normal distribution by Kolmogorov-Smirnov analysis. The Student *t* test and Mann-Whitney test were used for the analysis of continuous data. The Fisher exact test was used to analyze categorical data. These calculations were performed with the computer program STATA version 7.0 (STATA, College Station, TX, USA). P-values <0.050 were considered statistically significant.

Results

The means of age at the time of MRI, gender distribution, and ethnicity, as well as the time interval between the onset of symptoms and MRI examination of thighs, were comparable between DM and PM patients ($p>0.050$), as shown in Table 1. The intensities of muscle weakness and levels of muscle enzymes were also similar in both groups ($p>0.050$). In terms of drug therapy, 100.0% of DM patients and 81.8% of PM patients were already on corticosteroids and/or immunosuppressants – eight patients with azathioprine (2-3 mg/kg/day), four with methotrexate (15-25 mg/week), one with cyclosporine (3 mg/kg/day), one with leflunomide (20 mg/day) and/or three with intravenous human immunoglobulin (2 g/kg/day), at the time of the clinical picture investigation and of MRI. Nevertheless, the cumulative dose of prednisone and the previous use of immunosuppressive drugs and of pulse therapy with methylprednisolone were similar in both groups ($p>0.050$).

In MRI, a significant muscle edema was found in DM patients (41.7 to 91.7% of muscle compartments) compared with PM patients (from 8.3% to 33.3% of the muscle compartments) ($p<0.050$). Moreover, in 50% of the examined muscles in DM patients, the edema decreases in the proximal-distal direction, as shown in Fig. 1.

The area of fat replacement of muscles was predominantly observed in different muscle compartments in PM patients, when compared to DM patients. When partial, this fat replacement affected mainly the middle and distal thirds of the muscles of PM patients (0% to 41.7% of the muscles; Fig. 2), while a total fat replacement was observed only in the distal third of muscles of PM patients (0% to 16.7% of the muscles; Fig. 3).

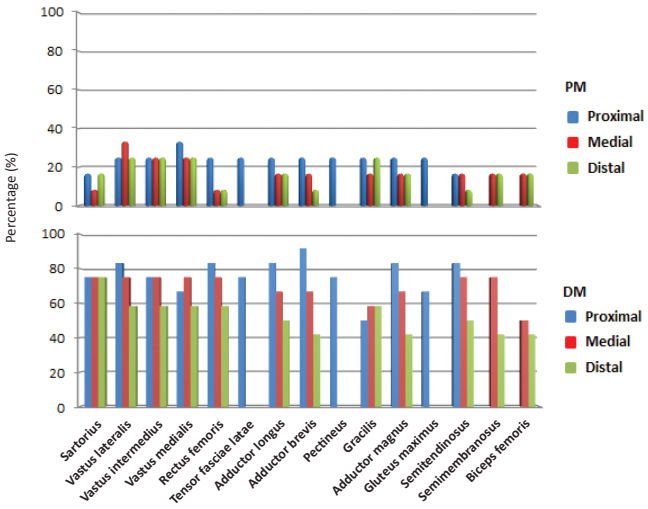

Fig. 1 – Distribution of edema area in different muscle compartments of the thigh by MRI in patients with dermatomyositis and polymyositis

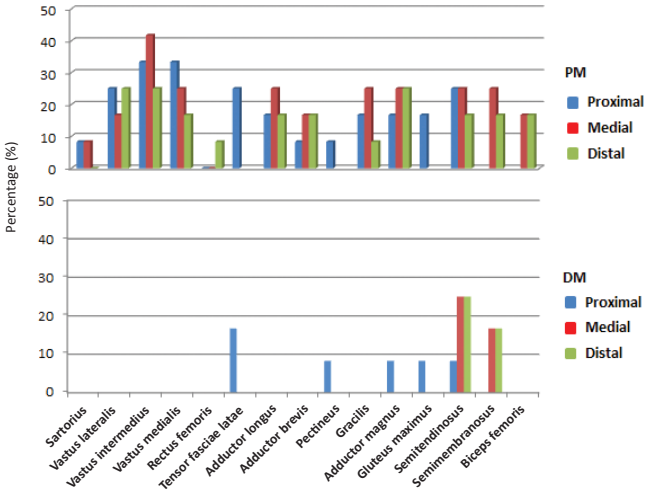

Fig. 2 – Distribution of partial fat replacement area of different muscle compartments of the thigh by MRI in patients with dermatomyositis and polymyositis

In the present study, no area of muscle fibrosis was identified.

Discussion

The present study showed that DM and PM, although sharing many clinical and laboratory aspects in common, have different characteristics from the point of view of muscle MRI.

Of the few studies that addressed the use of MRI in idiopathic inflammatory myopathies,[10-23] most are restricted to juvenile DM.[10,11,13,14,17,18,22] In the case of PM and DM in adults,[12,16,23] the studies available in the literature are scarce.

Kaufman et al.[23] globally analyzed five PM patients and eight DM patients with a broad age range (12-77 years). The authors made no mention of the disease duration or type of

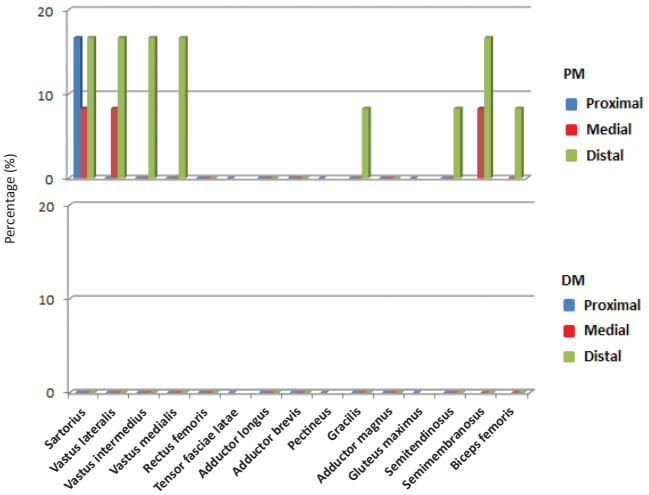

Fig. 3 – Distribution of total fat replacement area of different muscle compartments of the thigh by MRI in patients with dermatomyositis and polymyositis

drug therapy received by their patients prior to MRI,[23] and compared the MRI findings according to disease activity. We chose to evaluate and compare concomitantly adult DM and PM patients in various muscle compartments of their thighs at an early stage of the disease. Furthermore, our patients had similar demographic, clinical, laboratory, and therapeutic characteristics to each other, allowing a meaningful comparison of MRI findings.

Tomasová et al.[16] evaluated nine PM patients and 20 DM patients, with a mean duration of disease of 2.3 years. All patients exhibited clinically and biochemically active disease, and 63.2% of these cases had never received drug therapy. These authors showed a correlation between the intensity of muscle edema observed by MRI with the degree of disease activity and the positivity for an inflammatory infiltrate found in muscle biopsies guided by MRI.[16] However, these authors did not make comparisons regarding possible changes on MRI in PM and DM.

Reimers et al.[12] evaluated MRI studies of various muscle compartments of lower limbs of 58 patients aged 21-83 years-old. However, in addition to the 14 DM patients and 25 PM patients, eight patients with granulomatous myositis and 11 patients with inclusion body myositis were included. Moreover, Reimers et al. did not mention the type of drug treatment received by the participants in the study, who were arbitrarily classified as acute (less than one year disease), or chronic (when there is significant evidence of fat replacement and of muscle fibrosis in muscle MRI) patients. Despite these limitations, the authors observed that the presence of areas of muscle edema and of fat replacement were respectively more and less frequent in patients with acute DM, when compared to the other diseases included in the analysis.

Our results showed that the area of muscle edema was present mainly in DM patients, when compared with PM patients. This may be a result of the previous use of corticosteroids, which may influence the intensity and presence of muscle edema.[16] However, we observed that both the use of corticosteroids (cumulative dose) and immunosuppressants

were similar in both DM and PM groups of patients. Moreover, other parameters – such as the time of drug treatment, and the time between the MRI and the onset of muscle weakness symptoms were similar in both groups, which shows that the presence of muscle edema was an inherent characteristic of patients with active and newly diagnosed DM.

In addition, the fact that the swelling is mainly located on the proximal thigh, compared to the distal region, is compatible with the clinical findings, in those there is objective evidence of increased muscle weakness in so far as we get closer to the waists.

The prevalence of presence of fat replacement areas was low in our study, probably because we evaluated only cases of newly diagnosed DM and PM. Partially impaired muscle areas (partial fat replacement) were present in most muscle compartments, especially in PM. On the other hand, significantly compromised areas (total fat replacement) were only present in the muscles of PM patients, mainly in the long muscles, in the distal area, and in the posterior muscle group of thighs. These findings can be explained by the fact that these muscles are subjected to less traction and mechanical stimulation during the ambulation.

Previous studies have shown the benefit of physical exercise in patients with idiopathic inflammatory myopathies. Resistance exercises, for example, can reduce the expression of genes involved in the inflammatory process and fibrosis in the muscle tissue.[27]

In the present study, no areas of muscle fibrosis were observed, both in DM as in PM patients. In general, the presence of areas of muscle fibrosis, as well as those of fat replacement, are commonly observed in patients with a diagnosis of chronic myositis unresponsive to medical therapy.[28]

Our study has its limitations: it has a cross-sectional design, and therefore the correlation between muscle MRI findings and clinical and laboratory manifestations of patients were not evaluated. Second, ours was a small sample. Third, we evaluated only the muscle groups of the thighs and therefore did not have enough substrate to generalize this difference in muscle MRI findings to other muscle compartments of DM and PM patients. Fourth, no correlation between the muscle MRI data with possible findings of muscle biopsy was performed. And last but not least, not all patients were naïf as to drug therapy at the time of MRI, which may under or overestimate the muscle MRI findings of the patients analyzed.

In summary, our results showed that DM and PM patients have different characteristics from the point of view of muscle MRI, just like physiopathological and histological findings.

Conflicts of interest

The authors declare no conflicts of interest.

REFERENCES

1. Callen JP. Dermatomyositis. In: Callen JP. 2 ed. Dermatological signs of internal disease. Saunders. 1995.
2. Fathi M, Lundberg IE. Interstitial lung disease in polymyositis and dermatomyositis. Curr Opin Rheumatol. 2005;17:701-6.
3. Nyberg P, Wikman AL, Nennesmo I, Lundberg I. Increased expression of interleukin 1 alpha and MHC Class I in muscle tissue of patients with chronic, inactive polymyositis and dermatomyositis. J Rheumatol. 2000;27:940-8.
4. Goebels N, Michaelis D, Engelhardt M, Huber S, Bender A, Pongratz D et al. Differential expression of perforin in muscle-infiltrating T cells in polymyositis and dermatomyositis. J Clin Invest. 1996;97:2905-10.
5. Emslie-Smith AM, Engel AG. Microvascular changes in early and advanced dermatomyositis: a quantitative study. Ann Neurol. 1990;27:343-56.
6. Engel AG, Arahata K. Mononuclear cells in myopathies: quantitation of functionally distinct subsets, recognition of antigen specific cell-mediated cytotoxicity in some diseases, and implications for the pathogenesis of the different inflammatory myopathies. Hum Pathol. 1986;17:704-21.
7. Botet JC, Grau JM, Casademont J, Urbano-Marquez A, Rozman C. Characterization of mononuclear exudates in idiopathic inflammatory myopathies. Virchows Arch Pathol Anat Histopathol. 1988;412:371-4.
8. Dalakas MC. The future prospects in the classification, diagnosis and therapies of inflammatory myopathies: a view to the future from the "bench-to-bedside". J Neurol. 2004;251:651-7.
9. Noss EH, Hausner-Sypek DL, Weinblatt M. Rituximab as therapy for refractory polymyositis and dermatomyositis. J Rheumatol. 2006;33:1021-6.
10. Keim DR, Hernandez RJ, Sullivan DB. Serial magnetic resonance imaging in juvenile dermatomyositis. Arthritis Rheum. 1991;34:1580-4.
11. Hernandez RJ, Sullivan DB, Chenevert TL, Keim DR. MR imaging in children with dermatomyositis: musculoskeletal findings and correlation with clinical and laboratory findings. AJR Am J Roentgenol. 1993;161:359-66.
12. Reimers CD, Schedel H, Fleckenstein JL, Nägele M, Witt TN, Pongratz DE et al. Magnetic resonance imaging of skeletal in idiopathic inflammatory myopathies of adults. J Neurol. 1994;241:306-14.
13. Kimball AB, Summers RM, Turner M, Dugan EM, Hicks J, Miller FW et al. Magnetic resonance imaging detection of occult skin and subcutaneous abnormalities in juvenile dermatomyositis. Implications for diagnosis and therapy. Arthritis Rheum. 2000;43:1866-73.
14. Maillard SM, Jones R, Owen C, Pilkington C, Woo P, Wedderburn LR et al. Quantitative assessment of MRI T2 relaxation time of thigh muscles in juvenile dermatomyositis. Rheumatology. 2004;43:603-8.
15. Gendek-Kubiak H. Idiopathic inflammatory myopathies. Pol Merkur Lekarski. 2005;18:590-4.
16. Studynková JT, Charvát F, Jarosová K, Vencovsky J. The role of MRI in the assessment of polymyositis and dermatomyositis. Rheumatology. 2007;46:1174-9.
17. Peters SA, Köhler C, Schara U, Hohendahl J, Vorgerd M, Nicolas V et al. Muscular magnetic resonance imaging for evaluation to myopathies in children. Klin Padiatr. 2008;220:37-46.
18. Davis WR, Halls JE, Offiah AC, Pilkington C, Owens CM, Rosendahl K. Assessment of active inflammation in juvenile dermatomyositis: a novel magnetic resonance imaging-based scoring system. Rheumatology. 2011;50:2237-44.
19. Del Grande F, Carrino JA, Del Grande M, Mammen AL, Stine LC. Magnetic resonance imaging of inflammatory myopathies. Top Magn Reson Imaging. 2011;22:39-43.
20. Carstens PO, Schmidt J. Diagnosis, pathogenesis and treatment of myositis: recent advances. Clin Exp Immunol, 2013. Available at http://onlinelibrary.wiley.com/doi/10.1111/cei.12195/pdf [Access in27 August2013]

21. Ernste FC, Reed AM. Idiopathic inflammatory myopathies: current trends in pathogenesis, clinical features, and up-to-date treatment recommendations. Mayo Clin Proc. 2013;88:83-105.
22. Malattia C, Damsio MB, Madeo A, Psitorio A, Providenti A, Pederzoli S et al. Whole-body MRI in the assessment of disease activity in juvenile dermatomyositis. Ann Rheum Dis, 2013. Available at http://ard.bmj.com/cgi/pmidlookup?view=long&pmid=23636654 [Access in 1 May 2013]
23. Kaufman LD, Gruber BL, Gerstman DP, Kaell AT. Preliminary observations on the role of magnetic resonance imaging for polymyositis and dermatomyositis. Ann Rheum Dis. 1987;46:469-572.
24. Bohan A, Peter JB. Polymyositis and dermatomyositis. Pt I. N Engl J Med. 1975;292:344-403.
25. Bohan A, Peter JB. Polymyositis and dermatomyositis. Pt II. N Engl J Med. 1975;292:403-7.
26. Medical Research Council. Aids to the investigation of peripheral nerve injuries. War Memorandum n. 7, 2 ed. Londres: Her Majesty's Stationery Office, 1943.
27. Lundberg IE, Nader GA. Molecular effects of exercise in patients with inflammatory rheumatic disease. Nat Clin Pract Rheumatol. 2008;4:597-604.
28. Adams E, Chow CK, Premkumar A, Plotz PH. The idiopathic inflammatory myopathies: spectrum of MR imaging findings. RadioGraphics. 1995;15:563-74.