Internal Medicine: Open Access

Attar et al., Intern Med 2016, 6:5
DOI: 10.4172/2165-8048.1000224

Research Article Open Access

Inflammatory Muscle Disease, 15-Year Experience at Tertiary Centers

Suzan M Attar[1], Esraa A Babaeer*, Maria A Bagais, Wed A Alrehaily, Mashail F Mozahim, Basem Aldeek[1],Fahdah Alokaily, Seham Alrashidi, Maysoon Albalawi[2] Matouga A Baamer[3], Sultana A Abdulaziz[4], Basant M Elnady[5]

[1]Department of Internal Medicine, King Abdulaziz University, Jeddah, Saudi Arabia

[2]Department of Medicine, Prince Sultan Military City, Riyadh, Saudi Arabia

[3]Department of Medicine, King Abdulaziz Hospital, Jeddah, Saudi Arabia

[4]Department of Medicine, King Fahad General Hospital, Jeddah, Saudi Arabia

[5]Al Hada Armed Forces Hospital, Taif, Saudi Arabia

[6]Benha University Hospital, Egypt.

***Corresponding author:** Babaeer EA, Department of Internal Medicine, King Abdulaziz University Hospital, Jeddah, Saudi Arabia, Tel: 0561162262; Fax: 2631088; E-mail: dr.israa.ali@gmail.com

Received date: September 12, 2016, **Accepted date:** October 13, 2016, **Publication date:** October 26, 2016

Abstract

Objectives: Idiopathic inflammatory myopathies (IIM) are a group of inflammatory muscle diseases with a paucity of data and literature from Saudi Arabia. The aim was to describe the demographics, evaluate clinical features, organ involvement, investigations, treatment strategies, and to assess factors affecting remission in IIM patients.

Methods: We conducted this retrospective study at 5 medical tertiary centers in Saudi Arabia to analyze the records of patients with IIM from 1999 to 2014.

Results: A total of 28 patients with IIM were identified with a female to male ratio of 3:1. Pure polymyositis accounted for (32.1%), pure dermatomyositis (21.4%), juvenile dermatomyositis (10.7%), and IIM mixed with connective tissue diseases (35.7%) of the patients. The most common presentation was proximal myopathy (93.9%). The musculoskeletal system was the most commonly involved (78.6%), followed by the gastrointestinal system (39.3%). Investigations revealed an elevated CK of 2995.12 ± 3431.51 (mean ± SD), EMG was positive in (92.9%) of patient, and muscle biopsy in (42.9%). Treatment data showed a good response to Prednisolone (96.4%).

Conclusion: The results of this multiregional retrospective study from Saudi Arabia on IIM patients showed similar clinical features to other reviews; however, malignancy percentages were lower. We found a strong relation between comorbid illnesses and relapse. Normalization of muscle power is a reliable prognostic factor that may help assess the efficacy of treatment.

Keywords: Dermatomyositis; Polymyositis; Inflammatory myopathy

Introduction

The idiopathic inflammatory myopathies (IIM) are systemic connective tissue diseases characterized by symmetrical, proximal muscle weakness and chronic inflammation in muscle tissue. They can be subclassified into dermatomyositis (DM), polymyositis (PM), and inclusion body myositis (IBM) according to differences in clinical as well as histopathological features, and they frequently involve other systems with interstitial lung disease, esophageal dis-motility, and heart failure being the most common [1-4].

The study of many reports suggests that the average age of diagnosis for adults is between 40 to 50 years, with a female to male ratio of 2:1. The most common presentation is proximal muscle weakness in almost all the patients [5-7]. The diagnostic criteria are based on the Bohnas and Peter criteria of 1975 [8,9].

Currently IIM is treated with corticosteroids, methotrexate, rituximab, and other immunosuppressants. Many reports proved the effectiveness of corticosteroids in most of the cases, with some patients requiring a combined therapy of corticosteroid with methotrexate or azathioprine [10,11].

Little is known about the pattern of IIM in Arabic countries. A limited number of studies have been conducted in Riyadh, Kingdom of Saudi Arabia, on juvenile dermatomyositis [12,13]. Al-Ballaa [14] studied the pattern of IIM and its association with malignancy, but there is still a lack of solid basic data on the clinical features, laboratory investigations, and effective management of patients with IIM.

Therefore, we conducted this study to explore the demographic characteristics, clinical features, and effective management of patients with IIM at 5 tertiary centers in Saudi Arabia.

Methods

Study design

We conducted this retrospective study in 5 tertiary medical centers in Saudi Arabia; King Abdulaziz University Hospital, King Abdulaziz Hospital, King Fahad Hospital in Jeddah, Prince Sultan Medical

Military City, Riyadh, and Al-Hada Armed Hospital, Taif to analyze the records of patients with IIM from 1999 to 2014. Patients with the diagnosis of pure PM, pure DM, juvenile dermatomyositis (JDM), and PM/DM/JDM mixed with other connective tissue diseases; namely, rheumatoid arthritis (RA), scleroderma, and seronegative arthritis were included. The IIM diagnostic criteria were based on the Bohans and Peter criteria [8,9]. Selection at King Abdulaziz University hospital was based on ICD9 and ICD10 codes (710.3, 710.4, 729.1, M33.0, M33.2, and M60.90).

All patients fulfilling the above criteria were included from the other 4 centers attending the Rheumatology clinic. In total, the medical records of 28 patients (6 DM, 9 PM, 3 pure JDM, and 10 with overlap or mixed connective tissue disorder [MCTD]) were reviewed. The study excluded IBM, infectious myositis, unspecified myositis, myositis ossificans, myositis due to diabetes mellitus, drug induced myositis, myositis due to radiation, and myositis due to trauma or any myopathy related to general medical illness.

Data collection

Data were collected from the medical records using a questionnaire including: demographic data, family history of IIM, type of myositis, age of diagnosis, duration of the disease and association with malignancy or connective tissue diseases, clinical features recorded at the time of the diagnosis and during follow up, and other systemic involvement.

Laboratory tests comprised biochemical tests: creatinine kinase enzyme (CK) level, aspartate aminotransferase (AST)/alanine aminotransferase (ALT)/lactate dehydrogenase (LDH) levels, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and rheumatoid factor (RF); serology: anti-neutrophilic antibody (ANA), anti-transfer ribonucleic acid (anti-tRNA), anti-double strand deoxyribonucleic acid (anti-dsDNA), anticardiolipin G and anticardiolipin M (anti-CCP), anti-jo-1 and anti-ribonuclear protein (anti-RNP).

Electromyography (EMG) and muscle biopsy results were recorded at the time of diagnosis for each patient. Muscle biopsy was considere positive if showed necrosis of myofibers, phagocytosis, regeneration with basophils, large vesicular sarcolernmal nuclei, and prominent nucleoli, atrophy in a perifascicular distribution, variation in fiber size and an inflammatory exudate, often perivascular according to Bohan's and Peter criteria [8,9].

Modalities of treatment used for IIM: steroids, methotrexate, azathioprine, cyclophosphamide, chlorambucil, intravenous immunoglobulin (IVIG), and rituximab as the approved treatment for IIM [10,11]. The course and outcome of the disease: the outcome of patients was classified into respondent and resistant.

Assessment of response was based on normalization of CK, muscle power, or improvement of clinical features. The number of relapses was reviewed and recorded. Relapse was defined as a return of the signs and symptoms after remission due to dose reduction or cessation of medication. The comorbidities were assessed as follows: systemic arterial hypertension (HTN), diabetes mellitus, and ischemic heart diseases (IHD).

The diagnosis of HTN was based on the eighth HTN report [15], and diabetes mellitus on the American Diabetes Association guidelines [16]. Finally, IHD was defined according to the American College of Cardiology [17]. Causes of mortality were recorded (respiratory failure from respiratory muscle weakness, IHD, malignancy, sepsis). Patients who died from other causes were categorized as others.

Statistical analysis

The Statistical Package for Social Sciences, version 20 (IBM SPSS Statistics for Windows, IBM Corp, Armonk, NY, USA) was used for data analysis any p-value below 0.05 was considered significant. Numerical results were expressed as mean and attribute results were expressed as frequencies and percentage.

Results

Demographic and general background

A total of 28 patients with IIM were identified, 9 patients had PM, 6 had DM, 3 had JDM, and 10 patients had IIM mixed with connective tissue diseases (6 scleroderma, 3 ankylosing spondylitis, and one with RA). There were 21 females and 7 males patients giving a female to male ratio of 3:1.Twenty-four patients were Saudis (85.7%) and 4 were non-Saudi (14.3%). Their ages ranged from 14-83 years, with a mean age of 37.7 years with mean disease duration of 7.09 years. The most common clinical presentation was muscular weakness with predominance of proximal myopathy in (93.9%) of patients, followed by arthralgia/arthritis (82.1%), generalized rash (64.3%), facial/heliotrope rash (60.7%), fever (50%), Gottorn sign (46.4%), and dysphagia (35.7%). Table 1 shows that the most commonly involved system was the musculoskeletal system (78.6%), manifesting as muscle pain and tenderness. Eleven patients (39.3%) exhibited gastrointestinal involvement with gastritis being the commonest cause. The respiratory system accounted for 28.6% of organ involvement, mostly with interstitial lung disease and aspiration pneumonia as clinical presentations.

The cardiovascular system was considered the least involved system as pericarditis was recorded in only 2 patients (17.9%). Three patients developed malignancies (10.7%). The first patient, a female diagnosed with DM at the age of 78 years, had breast cancer, and there were 2 male patients, one with nasopharyngeal carcinoma at the age of 49, and the other with non-hodgkin lymphoma at the age of 43 years.

Laboratory results showed the mean value of CK was 2995.12 Ug/l (22 Ug/l to 11998 Ug/l), ALT was 151.50 U/L (27 U/L to 373 U/L), AST was 152.33 U/L (26 U/L to 649 U/L), and LDH was high at 547.87 U/L (00.0 U/L to 1983 U/L) at the time of diagnosis. Inflammatory markers were documented; ESR results showed a mean of 67.84 mm/h (1 mm/h to 529 mm/h), and CRP was positively elevated in 15 patients at the time of diagnosis. For autoimmune markers, ANA was positive in 53.6%, anti-double strand DNA was positive in 10.7%, anti-cardiolipin was positive in 10.7%, RF was positive in 10.7%, and anti-jo-1 was positive in 7.1% of patients. The EMG findings were consistent with PM in 13 patients, 8 were positive for DM, and 5 patients for JDM. The EMG was positive in 26 (92.9%) patients, and muscle biopsy was positive in 12 patients (42.9%) which showed consistent features of inflammatory myopathies.

Demographic and clinical characteristics		
	Number	**%**
Age at onset mean ± SD (range) years	37.70 ± 17.17 (14.00-83.00)	
Disease duration mean ± SD (range) years	7.09 ± 3.82 (3.00-15.00)	
Classification		
Polymyositis	9	(32.14%)
Dermatomyositis	6	(21.43%)
Juvenile dermatomyositis	3	(10.72%)
IMD associated with connective tissue diseases	10	(35.71%)
IMD associated with malignancy	3	(10.70%)
Clinical features		
Proximal muscle weakness	26	(93.90%)
Fever	14	(50.00%)
Dysphagia	10	(35.70%)
Arthralgia/arthritis	23	(82.10%)
Facial rash/heliotrope rash	17	(60.70%)
Gottron's sign	13	(46.40%)
Generalized rash	18	(64.30%)
Organ involvement		
Muscle pain and tenderness	22	(78.60%)
Cardiovascular diseases	5	(17.90%)
Gastrointestinal diseases	11	(39.30%)
Respiratory diseases	8	(28.60%)
LAB results		
CPK mean ± SD (range)	2995.12 ± 3431.51 (22.00-11998.00)	
ESR mean ± SD (range)	67.84 ± 101.35 (1.00-529.00)	
LDH mean ± SD (range)	547.87 ± 407.78 (00.00-1983.00)	
AST mean ± SD (range)	152.33 ± 157.00 (26.00-649.00)	
ALT mean ± SD (range)	151.50 ± 116.06 (27.00-373.00)	
C-reactive protein mean ± SD (range)		
Positive	15	(53.60%)
ANA		
Positive	15	(53.60%)
Antids DNA		
Positive	3	(10.70%)
Anti- RNP		

Positive	0	(0%)
Anti-jo-1		
Positive	2	(7.10%)
Muscle biopsy results		
Positive	12	(42.90%)
EMG		
Positive	26	(92.90%)
Drug therapy		
Prednisone	27	(96.40%)
Methotrexate	16	(57.10%)
Hydroxychloriquine	16	(57.10%)
Cyclophosphamide	2	(7.10%)
IVIG	12	(42.90%)
Rituximab	8	(28.60%)
Response to treatment		
Remission	17	(60.70%)
Relapse	11	(39.30%)

Table 1: Demographic and clinical characteristics in patients with IIM.

Treatment

Twenty-seven patients (96%) received oral corticosteroid (prednisolone), with normalization of CK enzymes in 57.1%, and muscle power in 71.4%. Other treatments included 16 (57.1%) patients that received methotrexate and hydroxychloroquine, 12 (42.9%) patients received IVIG in the emergency room setting, eight (28.6%) patients were on rituximab, and 2 (7.1%) patients received cyclophosphamide. There was no resistance detected in all patients. Seventeen (60.7%) patients showed total remission, and 11 (39.3%) patients relapsed.

The characteristics of patients who relapsed and those in remission are summarized in Table 2. Patients in remission showed lower percentages of DM (23.1%), JDM (15.4%), and both groups showed equal percentages of PM (53.85%), and malignancy association (7.7%).

There were no significant differences in medical complaints recorded at the time of diagnosis for remissions and relapsing patients; however, patients in remission had lower presentation of proximal muscle myopathy (23.1%), fever (11.5%), dysphagia (7.7%), arthralgia/arthritis (19.2%), and skin manifestations (38.5%).

As this study recorded the organ involvement of all IIM patients, there were slight differences between remission and relapsed patients as shown in Table 2.

For patients in remission, their lab results showed positive CRP (58.8%), anti dsDNA (11.7%), RF (11.7%), anti-jo-1 (5.9%), and ANA (64.7%).

Among all 35.2% of the patients with positive muscle biopsy, and 100% with positive EMG results showed complete remission, 70.6% of patients who received methotrexate, hydroxychloroquine, and rituximab, 100% receiving prednisone, 5.9% receiving cyclophosphamide, and 35.3% receiving IVIG exhibited good clinical regression of the disease.

Involvement of the respiratory system (OR=3.89, 95% CI: 0.53-31.4, p=0.180), and positivity of ANA (OR=3.21, 95% CI: 0.52-10.53, p=0.092) was statistically significant.

Demographic and clinical characteristics	**Remmission**		**Odds ratio (confident interval)**	**P-value**
	Yes	**No**		
	N=17	N=11		
Age at onset mean ± SD (range) years	29.53 ± 15.4	36 ± 21.37		P=0.86

Disease duration mean ± SD (range) years	6.5 ± 3.93	6.83 ± 4.3		P=0.86
Classifications				
Polymyositis	7 (41.1%)	7 (63.6%)	2.5 (41-16.21)	0.445
Dermatomyositis	6 (35.2%)	3 (27.2%)	0.69 (0.10-4.7)	0.483
Juvenile dermatomyocitis	3 (17.7%)	2 (8%)	1.4 (0.09-10.3)	0.887
IMD associated with connective tissue diseases	5 (29.4%)	5 (45.5%)	2 (0.32-13.21)	0.44
IMD associated with malignancy	2 (11.7%)	1 (9%)	0.79 (0.02-13.21)	0.724
Clinical Features				
Proximal muscle weakness	14 (82.3%)	10 (83.3%)	2.14 (0.15-62.26)	0.446
Fever	8 (47.1%)	6 (54.5%)	1.35 (0.23-8.13)	1
Dysphagia	6 (35.2%)	4 (36.2%)	1.05 (0.16-6.69)	0.82
Artheralgia/arthritis	13 (76.4%)	10 (90.9%)	3.08 (0.24-84.6)	0.887
Facial rash/heliotrope rash	10 (58.8%)	7 (63.6%)	1.23 (0.20-7.7)	0.823
Gottorn's sign	8 (47.1)	5 (45.5%)	0.94 (0.16-5.58)	0.662
Generalized rash	10 (58.8%)	8 (72.7%)	1.87 (0.28-13.2)	0.82
Organ Involvement				
Muscle pain and tenderness	12 (70.5%)	10 (90.9%)	4.17 (0.28-13.2)	0.595
Cardiovascular diseases	2 (11.7%)	3 (27.2%)	2.81 (0.28-111.13)	0.393
Gastrointestinal diseases	8 (47.1%)	3 (27.2%)	0.42 (0.42-2.76)	0.18
Respiratory diseases	3 (17.6%)	5 (45.5%)	3.89 (0.53-31.4)	0.184
Lab results				
C-reactive protein mean ± SD (range) Positive				
Positive	10 (58.8%)	5 (45.4%)	1.71 (0.29-10.53)	0.558
ANA Positive	11 (64.7%)	4 (36.3%)	3.21 (0.52-10.53)	0.092
Antids DNA				
Positive	2 (11.7%)	1 (9.09%)	1.33 (0.08-43)	0.927
Anti-RNP Positive				
Positive	1 (5.88%)	0 (0%)	-	0.392
RF Positive				
Positive	2 (11.7%)	1 (9.09%)	3.56 (0.28-116)	0.662
Anti-jo-1				
Positive	1 (5.88%)	1 (9.09%)	1.6 (0.4-67.6)	0.662
Muscle biopsy results				
Positive	6 (35.2%)	6 (54.5%)	2.2 (0.36-13.98)	0.288
EMG				
Positive	11 (100%)	5 (45.4%)	-	0.001**

Drug therapy				
Prednisone	17 (100 %)	9 (81.81%)	-	0.172
Methotrexate	12 (70.59%)	4 (36.36%)	0.24 (0.03-1.43)	0.172
Hydroxychloriquine	12 (70.59%)	4 (36.36%)	0.24 (0.03-1.53)	0.172
Cyclophosphamide	1 (5.90%)	1 (9.10%)	1.6 (0.002-67.7)	0.662
IVIG	6 (35.29%)	6 (54.54%)	2.2 (0.36-13.93)	0.172
Rituximab	6 (35.29%)	2 (18.18%)	0.41 (0.04-3.24)	0.454

Table 2: Factors affecting remission in patients with inflammatory muscle.

Discussion

Earlier studies describing the manifestations and clinical presentations of IIM published from the Western countries and East Asia include only vague characteristics of such diseases in Arab and Mediterranean populations.

In this study, we present the largest series of Arab IIM patients in the Eastern Mediterranean region reporting clinical and laboratory features as well as any association with malignancy, and also determining the patient and treatment related prognostic factors.

Our study comprised 28 consecutive patients without prior selection based on clinical presentation, which tends to be representative of IIM patients.

Determining a true age at onset of the disease is difficult to establish as many inflammatory myopathies have an insidious onset and early course.

In this study, we found a mean age at diagnosis of 37.70 ± 17.17 years, and the female:male ratio was 3:1. This is in accordance with Arabian Studis in Riyadh and Jordan where the mean age of onset was 37.3 ± 16.3, and the female:male ratio was 2.7:1 and 34.3 ± 9.2 years, and female:male ratio was 1.7:1 [14,18] and differing from data reported by Chinese,[19] and Tunisian [20] studies showing higher ratio and mean age.

Our analysis showed a PM predominance of (32.14%), consistent with the American and European reports [21-24], and in contrast to a Chinese study [19], which showed a DM predominance.

Generally, our results as compared to previous reported studies show clinical feature similarities. The most common clinical presentation was muscular weakness with predominance of proximal myopathy in (93.9%) followed by arthralgia/arthritis (82.1%), both with a higher prevalence than other studies [14,19]. Several non-muscular manifestations have been wildly described, and dysphagia is the most common among all [6,7,23,25,26], it is noted that we have lower prevalence of dysphagia (35.70%) than other studies [14,27] which could be contributed to early diagnosis and intervention.

The involvement of other organs with IIM has been well established, and we report consistent results [28]. Reinforcing the ideal comprehensive approach to patients with IIM, not only focusing on musculoskeletal involvement.

An association between IIM and malignancy has been widely reported in the literature [26,29-31] with a variety of types in different populations. It is suggested that malignancies usually associated with IIM in order are: ovarian cancer, lung cancer, and pancreatic cancer. The predominance of Nasopharengeal carcinoma (NPC) in the Asian population [32-35] could be because (NPC) is endemic to southeastern Asia, and is related to the chronic active infection of Epstein-Barr virus [36-39].

Our data showed 3 patients had malignancies (10.7%), a female with breast cancer and 2 male patients, one with nasopharyngeal carcinoma and one with non-hodgkin lymphoma. This low malignancy prevalence could be due to the lower mean age at presentation compared with other reports. Genetics or environmental differences may also have played a role.

Importantly, most of our patients had PM, and many studies have shown a strong association between DM and malignancy compared with lower malignancy prevalence in patients with PM [33-47].

Muscle enzyme, ESR, and EMG results were comparable with previous reports. The muscle biopsy results showed no significant difference, and were positive in (42.9%) and negative in (57.1%) in contract to other studies reporting a positive result in approximately (80%) of patients [6,48]. The ANA positivity varies from (40% to 60%) in the previous literature [6,49,50], and in our group ANA was positive in (53.6%) of patients. The anti-jo-1 antibody was positive in (7.1%) of patients, and this low percentage is not consistent with other reports of (16.1% to 23%) positivity [51,52], in our retrospective study (64.7%) with ANA went into remission can be explained with early diagnosis and initiation of treatment ,needs larger study to prove this observation.

Rheumatoid factor was positive in (10.7%) of patients and this percentage was closed to previous study [53]. Though anti ds DNA and anticardiolipin antibodies were not evaluated in previous studies, it was positive in (10.7%) of our patients may be due to high number of overlap syndrome we had in this study.

Regarding treatment, the number of patients treated with oral corticosteroids, hydroxychloroquine, and cyclophosphamide were comparable to a previous analysis of 109 patients with DM [54]. We identified that patients who received steroids exhibited an impressive improvement in their symptoms (71.4%; p=0.023) reinforcing the most favorable outcome achieved with steroid treatment [10,11]. The percentage of patients treated with methotrexate was higher than previous study (57% of our patients compared with 34% in other study [54]). A Brazilian study [54] reported clinical relapse in (53%) of patients, which differs to the (39.3%) found in our study.

On the basis of our results, patients who relapsed had other comorbid diseases such as hypertension (OR: 0.059; 95% CI: 0.006-0.628).

Previous studies did not explore improvement of muscle power as a prognostic factor for the disease, and our study revealed normalization of muscle power in (71.4%; p=0.023). This reliable prognostic factor may help physicians to assess the efficacy of their treatment and monitor progression of the disease.

Limitations and Recommendations

Our study has several limitations due to its retrospective design and small sample size. A longer follow up would intensify the outcome. A low prevalence of IIM was an issue, which may have led to overstatement of the results. Mortality was not assessed. Different subgroup of IIM outcome is lacking primary IIM or IIM related to malignancy/associate with other connective tissue diseases.

We recommend conducting large multiregional prospective cohort studies with long follow up duration.

In conclusion, our results showed similar clinical features to previous reviews. We found lower malignancy prevalence compared with studies from America, Europe, and East Asia, and a strong relation between comorbid illnesses and remission. Normalization of muscle power is a reliable prognostic factor that may help to assess the efficacy of patient treatment and to monitor disease progression.

References

1. Longo DL, Fauci A, Kasper D, Hauser S, Jameson J, et al. (2011) Harrison internal medicine book (18th edition). New York: McGraw-Hill, USA.
2. Connors GR, Christopher-Stine L, Oddis CV, Danoff SK (2010) Interstitial lung disease associated with the idiopathic inflammatory myopathies: what progress has been made in the past 35 years? Chest 138: 1464-1674.
3. Tomimitsu H, Ohta A, Nagai M, Nishina M, Ishihara S, et al. (2015) Epidemiologic analysis of the clinical features of Japanese patients with polymyositis and dermatomyositiss. Mod Rheumatol 26: 398-402.
4. Denbow CE, Lie JT, Tancredi RG, Bunch TW (1979) Cardiac involvement in polymyositis: a clinicopathologic study of 20 autopsied patients. Arthritis Rheum 22: 1088-1092.
5. Souza FH, Levy-Neto M, Shinjo SK (2011) Prevalence of clinical and laboratory manifestations and comorbidities in polymyositis according to gender. Rev Bras Reumatol 51: 428-483.
6. Mustafa KN, Dahbour SS (2010) Clinical characteristics and outcomes of patients with idiopathic inflammatory myopathies from Jordan 1996-2009. Clin Rheumatol 29: 1381-1385.
7. Hoffman GS, Franck WA, Raddatz DA, Stallones L (1983) Presentation, treatment, and prognosis of idiopathic inflammatory muscle disease in a rural hospital. Am J Med 75: 433-438.
8. Bohan A, Peter JB (1975) Polymyositis and dermatomyositis (second of two parts). N Engl J Med 292: 403-407.
9. Bohan A, Peter JB (1975) Polymyositis and dermatomyositis (first of two parts). N Engl J Med 292: 344-347.
10. Dalakas MC (1994) Current treatment of the inflammatory myopathies. Curr Opin Rheumatol 6: 595-601.
11. Mastaglia FL, Phillips BA, Zilko P (1997) Treatment of inflammatory myopathies. Muscle Nerve 20: 651-664.
12. Shehata R, Al-Mayouf S, Al-Dalaan A, Al-Mazaid A, Al-Balaa S, et al. (1999) Juvenile dermatomyositis: clinical profile and disease course in 25 patients. Clin Exp Rheumatol 17: 115-118.
13. Al-Mayouf S, Al-Mazyed A, Bahabri S (2000) Efficacy of early treatment of severe juvenile dermatomyositis with intravenous methylprednisolone andmethotrexate. Clin Rheumatol 19: 138-141.
14. Al-Ballaa ST, Al-Dalaan AN, El-Ramahi KM, Al-Janadi MA, Al-Shaikh A, et al. (1993) Pattern of adult onset of polymyositis and dermatomyositis and association with malignancy. Ann Saudi Med 13: 525-529.
15. James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, et al. (2014) Evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA 311: 507-520.
16. American Diabetes Association (2008) Diagnosis and classification of diabetes mellitus. Diabetes Care 31: S55-S60.
17. Go AS, Bauman MA, Coleman King SM, Fonarow GC, Lawrence W, et al. (2014) An effective approach to high blood pressure control: A science advisory from the American Heart Association, the American College of Cardiology, and the Centers for Disease Control and Prevention. J Am Coll Cardiol 63: 1230-1238.
18. Ungprasert P, Leeaphorn N, Hosiriluck N, Chaiwatcharayut W, Ammannagari N, et al. (2013) Clinical features of inflammatory myopathies and their association with malignancy: a systematic review in asian population. ISRN Rheumatol 2013: 509354.
19. Shu XM, Lu X, Xie Y, Wang GC (2011) Clinical characteristics and favorable long term outcomes for patients with idiopathic inflammatory myopathies: a retrospective single center study in China. BMC Neurol 11: 143.
20. Toumi S, Ghnaya H, Braham A, Harrabi I, Laouani-Kechrid C (2009) Polymyositis and dermatomyositis in adults. Tunisian multicentre study. Rev Med Interne 30: 747-753.
21. Chow WH, Gridley G, Mellemkjaer L, McLaughlin JK, Olsen JH, et al. (1995) Cancer risk following polymyositis and dermatomyositis: a nationwide cohort study in Denmark. Cancer Causes Control 6: 9-13.
22. Zhang W, Jiang SP, Huang L (2009) Dermatomyositis and malignancy: a retrospective study of 115 cases. Eur Rev Med Pharmacol Sci 13: 77-80.
23. Stockton D, Doherty VR, Brewster DH (2001) Risk of cancer in patients with dermatomyositis or polymyositis, and follow-up implications: a Scottish population-based cohort study. Br J Cancer 85: 41-45.
24. Sigurgeirsson B, Lindelöf B, Edhag O, Allander E (1992) Risk of cancer in patients with dermatomyositis or polymyositis. A population-based study. N Engl J Med 326: 363-367.
25. DeVere R, Bradley WG (1975) Polymyositis: its presentation, morbidity and mortality. Brain 98: 637-666.
26. Marie I, Hachulla E, Hatron PY, Hellot MF, Levesque H, et al. (2001) Polymyositis and dermatomyositis: short term and longterm outcome, and predictive factors of prognosis. J Rheumatol 28: 2230-2237.
27. Klein RQ, Teal V, Taylor L, Troxel AB, Werth VP (2007) Number, characteristics, and classification of patients with dermatomyositis seen by dermatology and rheumatology departments at a large tertiary medical center. J Am Acad Dermatol 57: 937-943.
28. Sigurgeirsson B, Lindelöf B, Edhag O, Allander E (1992) Risk of cancer in patients with dermatomyositis or polymyositis. A population-based study. N Engl J Med 326: 363-367.
29. Maugars YM, Berthelot JM, Abbas AA, Mussini JM, Nguyen JM, et al. (1996) Long-term prognosis of 69 patients with dermatomyositis or polymyositis. Clin Exp Rheumatol 14: 263-274.
30. Medsger TA, Robinson H, Masi AT (1971) Factors affecting survivorship in polymyositis. A life-table study of 124 patients. Arthritis Rheum 14: 249-258.
31. Dankó K, Ponyi A, Constantin T, Borgulya G, Szegedi G (2004) Long-term survival of patients with idiopathic inflammatory myopathies according to clinical features: a longitudinal study of 162 cases. Medicine 83: 35-42.
32. Leow YH, Goh CL (1997) Malignancy in adult dermatomyositis. Int J Dermatol 36: 904-907.

33. Ang P, Sugeng MW, Chua SH (2000) Classical and amyopathic dermatomyositis seen at the National Skin Centre of Singapore: a 3-year retrospective review of their clinical characteristics and association with malignancy. Ann Acad Med Singapore 29: 219-223.
34. Lynn SJ, Sawyers SM, Moller PW, O'Donnell JL, Chapman PT (2005) Adult-onset inflammatory myopathy: North Canterbury experience 1989-2001. Intern Med J 35: 170-173.
35. Holden DJ, Brownell AK, Fritzler MJ (1985) Clinical and serologic features of patients with polymyositis or dermatomyositis. Can Med Assoc J 132: 649-653.
36. Buchbinder R, Forbes A, Hall S, Dennett X, Giles G (2001) Incidence of malignant disease in biopsy-proven inflammatory myopathy. A population-based cohort study. Ann Intern Med 134: 1087-1095.
37. Shotelersuk K, Khorprasert C, Sakdikul S, Pornthanakasem W, Voravud N, et al. (2000) Epstein-Barr virus DNA in serum/plasma as a tumor marker for nasopharyngeal cancer. Clin Cancer Res 6: 1046-1051.
38. Lin JC, Wang WY, Chen KY, Wei YH, Liang WM, et al. (2004) Quantification of plasma Epstein-Barr virus DNA in patients with advanced nasopharyngeal carcinoma. N Engl J Med 350: 2461-2470.
39. Uchiyama T, Arai K, Yamamoto-Tabata T, Hirai K, Kishimoto K, et al. (2005) Generalized myositis mimicking polymyositis associated with chronic active Epstein-Barr virus infection. J Neurol 252: 519-525.
40. András C, Ponyi A, Constantin T, Csiki Z, Szekanecz E, et al. (2008) Dermatomyositis and polymyositis associated with malignancy: a 21-year retrospective study. J Rheumatol 35: 438-444.
41. Lee SW, Jung SY, Park MC, Park YB, Lee SK (2006) Malignancies in Korean patients with inflammatory myopathy. Yonsei Med J 47: 519-523.
42. Maoz CR, Langevitz P, Livneh A, Blumstein Z, Sadeh M, et al. (1998) High incidence of malignancies in patients with dermatomyositis and polymyositis: an 11-year analysis. Semin Arthritis Rheum 27: 319-324.
43. Hill CL, Zhang Y, Sigurgeirsson B, Pukkala E, Mellemkjaer L, et al. (2001) Frequency of specific cancer types in dermatomyositis and polymyositis: a population-based study. Lancet 357: 96-100.
44. Airio A, Pukkala E, Isomäki H (1995) Elevated cancer incidence in patients with dermatomyositis: a population based study. J Rheumatol 22: 1300-1303.
45. Antiochos BB, Brown LA, Li Z, Tosteson TD, Wortmann RL, et al. (2009) Malignancy is associated with dermatomyositis but not polymyositis in Northern New England, USA. J Rheumatol 36: 2704-2710.
46. Goh CL, Rajan VS (1983) Dermatomyositis in a skin clinic. Ann Acad Med Singapore 12: 6-12
47. Chen YJ, Wu CY, Shen JL (2001) Predicting factors of malignancy in dermatomyositis and polymyositis: a case-control study. Br J Dermatol 144: 825-831.
48. Koh TE (1993) Adult onset polymyositis/ dermatomyositis: clinical and laboratory features and treatment response in 75 patients. Ann Rheum Dis 52: 857-861.
49. Marie I, Guillevin L, Menard JF, Hatron PY, Cherin P, et al. (2012) Hematological malignancy associated with polymyositis and dermatomyositis. Autoimmun Rev 11: 615-620.
50. Fernandez C, Bardin N, De Paula AM, Salort-Campana E, Benyamine A, et al. (2013) Correlation of clinicoserologic and pathologic classifications of inflammatory myopathies: study of 178 cases and guidelines for diagnosis. Medicine (Baltimore) 92: 15-24.
51. Hochberg MC, Feldman D, Stevens MB, Arnett FC, Reichlin M (1984) Antibody to Jo-1 in polymyositis/dermatomyositis: association with interstitial pulmonary disease. J Rheumatol 11: 663-665.
52. Leu CC, Lan JL (1992) Anti-Jo-1 antibody in patients with polymyositis/ dermatomyositis. Zhonghua Min Guo Wei Sheng Wu Ji Mian Yi Xue Za Zhi 25: 41-47.
53. Ortigosa LC, Reis VM (2014) Dermatomyositis: analysis of 109 patients surveyed at the Hospital das Clínicas (HCFMUSP), São Paulo, Brazil. An Bras Dermatol 89: 719-727.
54. Souza FH, Barros TB, Levy-Neto M, Shinjo SK (2012) Adult dermatomyositis: experience of a Brazilian tertiary care center. Rev Bras Reumatol 52: 897-902.