A Brazilian registry of juvenile dermatomyositis: onset features and classification of 189 cases

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Abstract

Objective

To describe onset features, classification and treatment of juvenile dermatomyositis (JDM) and juvenile polymyositis (JPM) from a multicentre registry.

Methods

Inclusion criteria were onset age lower than 18 years and a diagnosis of any idiopathic inflammatory myopathy (IIM) by attending physician. Bohan & Peter (1975) criteria categorisation was established by a scoring algorithm to define JDM and JPM based on clinical protocol data.

Results

Of the 189 cases included, 178 were classified as JDM, 9 as JPM (19.8: 1) and 2 did not fit the criteria; 6.9% had features of chronic arthritis and connective tissue disease overlap. Diagnosis classification agreement occurred in 66.1%. Median onset age was 7 years, median follow-up duration was 3.6 years. Malignancy was described in 2 (1.1%) cases. Muscle weakness occurred in 95.8%; heliotrope rash 83.5%; Gottron plaques 83.1%; 92% had at least one abnormal muscle enzyme result. Muscle biopsy performed in 74.6% was abnormal in 91.5% and electromyogram performed in 39.2% resulted abnormal in 93.2%. Logistic regression analysis was done in 66 cases with all parameters assessed and only aldolase resulted significant, as independent variable for definite JDM (OR=5.4, 95%CI 1.2-24.4, p=0.03). Regarding treatment, 97.9% received steroids; 72% had in addition at least one: methotrexate (75.7%), hydroxychloroquine (64.7%), cyclosporine A (20.6%), IV immunoglobulin (20.6%), azathioprine (10.3%) or cyclophosphamide (9.6%). In this series 24.3% developed calcinosis and mortality rate was 4.2%.

Conclusion

Evaluation of predefined criteria set for a valid diagnosis indicated aldolase as the most important parameter associated with definite JDM category. In practice, prednisone-methotrexate combination was the most indicated treatment.

Key words
Idiopathic inflammatory myopathy, juvenile dermatomyositis, juvenile polymyositis, methotrexate, steroids.

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Introduction

Idiopathic inflammatory myopathies (IIM) are a group of rare diseases in children, presenting with progressive muscle weakness mediated by autoimmune mechanism. Juvenile dermatomyositis (JDM) and juvenile polymyositis (JPM) are the main diagnoses in this group (1). Two recent studies reported an incidence of JDM from 0.19 to 0.32/100 000 (2, 3). However, JPM is rare and less reported in the paediatric literature.

Overall, the prognosis of JDM has improved over the last 3 decades, when 30% mortality rates, calcinosis and complications due to gastrointestinal vasculopathy were frequently reported. The current treatment approach, with long term high dose steroid associated with steroid-sparing agents like methotrexate, has changed JDM outcome, but still a chronic disease course is observed in a high proportion of patients (4-6). It is now clear that JDM presentation and disease course are variable (4), and it is possible that ethnic-geographic differences may account for variable clinical features in a global context. Multicentric collaboration is needed in order to address newer treatment options and outcome, therefore a standardised approach for diagnosis and treatment is also needed.

Both, JDM and JPM, are usually diagnosed under the classification criteria of Bohan & Peter (1975) (7, 8). Despite its current use, these criteria were not validated in large scale in the paediatric population. Besides, they were not examined after recent developments in diagnostic tools like imaging and histopathology. An international survey among paediatric rheumatologists worldwide examined their usefulness in current practice, according to specialist opinion (9).

The aims of this study were: to review a paediatric case-series, identified within the spectrum of the IIM (1) for demographic and onset features, laboratory assessment, Bohan & Peter classification criteria (7, 8), outcome and standard of treatment, in order to establish a repository for future multicentric research collaboration.

Subjects and methods

Subjects

Data collection was carried out in 2007, in 9 paediatric rheumatology centres. Inclusion criteria were: the established diagnosis of any of the idiopathic inflammatory myopathies listed according to Rider & Miller (1997) (1) by the attending physician, age at disease onset less than 18 years and completeness of a clinical protocol for demographics, onset features, diagnosis, treatment over time and outcome, all fulfilled by a paediatric rheumatology specialist.

The catchment area was chosen for capturing JDM patients seen in academic centres run by paediatric rheumatology specialists in the state of São Paulo, which is located in the southern region of the country. The area population comprises 39.6 million inhabitants, being 10.9 million in the capital and 28.7 million in the province. Five of the participating centres are located in the capital and 4 in the province.

Investigators in each of the centres compiled the clinical protocol during the last visit of the patient in the centre, to ensure the diagnosis based on clinical features and investigation results, after obtaining the informed consent. For the deceased, the last visit of the patient was reviewed from medical records. Ethics approval was obtained in each of the centres for all research procedures. The Brazilian national ethics board (CONEP) approved the study protocol.

Data collection

Patients were selected by the attending physician in each centre. The analysis was retrospective and carried out by means of completing a protocol that covered outcomes of practice consultation, hospitalisation, referrals, key test results and prescriptions. Patients were only enrolled if all of the data selected in the standard protocol were in their medical records. Patients diagnosed from 1986 to 2007 were identified and selected. In all the centres, full catchment was ensured by physicians who provided combined care with other specialists, such as neurologists or dermatologists.

Patient data in the database included the following variables at disease onset:

age, gender, diagnosis, follow-up duration, age at onset, personal and family history of autoimmune diseases, clinical features with specified signs and symptoms at disease onset and treatment with cumulative medication received until the date of the last visit. The clinical features recorded were: typical rash, muscle weakness, constitutional symptoms (fever, alopecia, weight loss, fatigue, headache, irritability), skin ulcerations, musculoskeletal symptoms (myalgia, arthralgia, morning stiffness, joint swelling), dyspnoea, dysphagia, dysphonia, chest pain, gastrointestinal symptoms (abdominal pain, diarrhoea, gastrointestinal bleeding), haematuria, facial and body swelling. Typical signs were recorded on physical exam: heliotrope eyelid rash, Gottron sign, edema, photosensitivity, calcinosis, skin ulceration, palate petechiae, periungual erythema, arthritis and muscle atrophy.

Investigation results included serum muscle enzymes, as creatine phosphokinase (CPK), lactic dehydrogenase (LDH), aspartate aminotransferase (AST), alanine aminotransferase (ALT) and aldolase, all performed according to the laboratory routine of each participant centre and converted from the local reference to a common standard reference range. Antinuclear antibody titres (ANA) were considered positive with titres ≥1:80 and the autoantibody titres (anti-DNA, anti-ENA, rheumatoid factor) were considered positive if the titres were above the upper range of reference values in each participating centre. Electromyogram (EMG), magnetic resonance imaging (MRI) scan, muscle or skin biopsy were reported as normal or abnormal according to each centre records.

The conversion to an equivalent standard value for serum muscle enzymes in international units (IU) was performed in order to establish normality range for reclassification of diagnosis according to Bohan & Peter (1975) (7, 8). The standardisation of the normality range (10) was calculated according to the formula: $x\ ref=[(range_{ref} * x_{rel})/100]+\min$ ref, where the x ref-value is in international units (IU), range ref - IU range , min ref-*IU* minimum value; and $x_{rel}=[(x_i-\min_i) / range_i]* 100$, where x_{rel} 0-100 scale range, $range_i$ - original measure variation (OMV), $\min_i$ - minimum value of the OMV.

For those under regular follow-up, a query about the time of calcinosis development was posed. Calcinosis was defined by the presence of calcium deposits, either palpable on physical examination or visible on x-rays, with deposition on soft tissues, fascia, muscle or tendons and involving face, trunk, abdomen, upper and/or lower limbs, as well as specific treatment, at any time throughout the disease course.

A family history of autoimmune diseases, as well as previous immunisation, was included in the data-collection protocol, as it is part of the standard medical history.

Statistical analysis

Descriptive analysis of demographic data, clinical features, investigations and treatment categorical variables were reported by correspondent absolute and percentual frequencies. Quantitative variables were described by median and range.

Diagnosis reclassification was performed with anonym data and independently from the physician's established diagnosis. The Bohan & Peter (1975) (7, 8) classification criteria algorithm was calculated from the record of signs, symptoms and investigation results and individualised for each of the alpha numeric codified cases in a MS Excel work sheet, in the following sequence: 1) patients were grouped according to the presence or absence of typical skin rash; 2) the four remaining criteria were codified as yes = 1 or no = 0; for the muscle enzymes it was codified to 1 if at least one of them had abnormal result; 3) the scoring sum up ranging from 0 to 4 and the reclassification of patients was according to the following: a) in the presence of typical rash and; if scoring sum = 3 or 4 definite JDM; if scoring sum = 2 probable JDM; if scoring sum = 1 possible JDM; if scoring sum = 0 JDM diagnosis was ruled out; b) in the absence of skin rash; if scoring sum = 4: definite JPM; if scoring sum = 3: probable JPM; if scoring sum = 2: possible JPM; d) if scoring sum ≤1: JPM diagnosis was ruled out.

The effect of following variables of the Bohan & Peter (7, 8) criteria: individual results of muscle enzymes, electromyogram and muscle biopsy, as predictors of "definite" category (outcome variable) were investigated using logistic regression analysis, aimed at identifying which among these variables were significantly associated to definite JDM diagnosis. Results are presented as odds ratio and 95% confidence interval.

A survival analysis was conducted with the time of calcinosis development in all IIM and presented with a Kaplan-Meier curve, where the censored observations were from those who had not developed calcinosis. Probability of developing calcinosis was calculated by the complementary values (1-p), where p is the probability of not having calcinosis.

All the analysis were performed using the statistics software SAS 9.0.1 for Windows considering 5% the level of significance and correspondent p-value ($p<0.05$) in all the tests.

Results

Patient description

Subjects were sampled in 9 centres and those with regular follow-up and complete notes were selected. Of 255 identified cases, 189 (74%) were included and 66 (26%) were not included. Among the 189 IIM coded subjects, the diagnostic algorithm classified 178 (94.2%) as having JDM, and 9 (4.8%) as having JPM according to the Bohan & Peter (7, 8) criteria. Two cases (1%) did not fit in any of the criteria and they were ruled out, one diagnosed with amyopathic dermatomyositis and the other was ruled out as JDM or JPM, having only muscle weakness and calcinosis. Median onset age was 7 (range 0.3–17.7) years, and median follow up duration was 3.6 (range 0–18.6) years. Demographic and clinical data with the distribution of the diagnoses are presented in Table I.

Of those 189 cases, there was a connective tissue disease overlap in 6.9% (n=13), being 8 with chronic arthritis, 2 with juvenile systemic lupus erythematosus (JSLE), 1 with scleroderma and 2 further diagnosed with mixed connective tissue disease (MCTD) as reported by the attending physician. Two of the

Table I. Demographic features, clinical characteristics and diagnosis classification of 189 patients with idiopathic inflammatory myopathies (IIM).

	Total
Female, n. (%)	117 (61.9)
Male, n. (%)	72 (38.1)
F: M	1.63: 1
Onset age in years, median (minimum, maximum)	7 (0.3–17.7)
Follow up duration in years, median (minimum - maximum)	3.6 (0–18.6)
Diagnoses n=187 (%)§	
Definite juvenile dermatomyositis	124 (66.3)
Probable juvenile dermatomyositis	46 (24.6)
Possible juvenile dermatomyositis	8 (4.3)
Definite juvenile polymyositis	4 (2.1)
Probable juvenile polymyositis	4 (2.1)
Possible juvenile polymyositis	1 (0.5)
Proportion JDM: JPM	19.8 : 1

JDM: juvenile dermatomyositis; JPM: juvenile polymyositis.
§Diagnoses established according to the Bohan & Peter criteria.

Table II. Clinical features at disease onset in 189 patients diagnosed with idiopathic inflammatory myopathies (IIM).

Clinical features	Number (%) with available information	Number (%) with the feature present
Muscle weakness	189 (100)	181 (95.8)
Rash	189 (100)	179 (94.7)
Musculoskeletal symptoms*	179 (94.7)	145 (81.0)
Systemic symptoms†	189 (100)	148 (78.3)
Facial edema	178 (94.2)	61 (34.3)
Dysphagia	179 (94.7)	39 (21.8)
Body edema	175 (92.6)	26 (14.9)
Gastrointestinal symptoms‡	178 (94.2)	26 (14.6)
Dysphonia	178 (94.2)	26 (14.6)
Dyspnoea	178 (94.2)	24 (13.5)
Chest pain	177 (93.7)	6 (3.4)
Haematuria	176 (93.1)	3 (1.7)
Heliotrope rash	188 (99.5)	157 (83.5)
Gottron plaques	189 (100)	157 (83.1)
Photosensitivity	176 (93.1)	89 (50.6)
Arthritis	186 (98.4)	84 (45.2)
Muscle atrophy	174 (93.5)	69 (39.7)
Periungual erythema	170 (89.9)	65 (38.2)
Calcinosis	188 (99.5)	10 (5.3)
Skin ulcers	186 (98.4)	26 (14.0)
Palate petechiae	164 (86.8)	4 (2.4)

*Musculoskeletal symptoms: myalgia, arthralgia, stiffness, arthritis. †Systemic symptoms: fever, alopecia, weight loss, fatigue, headaches, irritability. ‡Gastrointestinal (GI) symptoms: abdominal pain, diarrhoea or GI bleeding.

cases had associated malignancy, 1 diagnosed with Hodgkin lymphoma at the time of JDM presentation, when a mediastinal mass was identified on chest x-ray and CT scan, also confirmed by lymph node histology. The other developed lymphoblastic leukaemia 5 years after JDM diagnosis. By that time, this patient was in remission of JDM, out of medication for 29 months. Both cases had JDM typical features.

Other associated morbid conditions were reported, one case with cystic fibrosis and another with pulmonary haemosiderosis. Fourteen patients (7.4%) had a family history of first and second degree relatives with autoimmune diseases or chronic inflammatory diseases namely rheumatoid arthritis (6), systemic lupus erythematosus (2), rheumatic fever (2), diabetes (2), Behçet's disease (1), glomerulonephritis (1). One patient had 3 cases of systemic lupus erythematosus in the family history.

Six reported cases had received immunisations during the previous 6 months of disease onset: B-hepatitis (2), not identified (2), adult-type diphtheria-tetanus toxoid (1) and diphteria-tetanus-pertussis vaccine (1), the last was given 24 hours before the onset symptoms.

Nutritional status at disease onset was evaluated by measures of weight, height and body mass index (BMI) compared to reference values for age and gender (11), with 52.9% within the normal range for the Brazilian population, 6.3% underweighted, 12.7% over weighted and 5.8% in the obesity range. BMI was not calculated in 5.3%, for those who had disease onset before two years of age, and in 16.9% due to missing data.

Clinical presentation

The signs and symptoms at presentation or at diagnosis are described in Table II. Muscle weakness was present in 95.8% and typical skin rash in 94.7%, being the eyelid heliotrope rash and Gottron plaques recorded in 83.5% and 83.1%, respectively. The majority presented with musculoskeletal (81%) and systemic (78.3%) signs and symptoms, with the following distribution: myalgia (62.4%), arthralgia (55.9%), arthritis (45.2%), joint stiffness (25.4%), fatigue (53.4%), fever (53.2%), weight loss (43.8%), headaches (19%), alopecia (18.6%) and irritability (12.3%). Facial edema occurred in 34.3% and body edema in 14.9%. Dysphagia occurred in 21.8%, dysphonia in 14.6% and dyspnoea in 13.5%. There was periungual erythema in 38.2%. Skin ulcerations signs occurred in 14%, indicating severe vasculopathy. Less than 15% of the patients had gastrointestinal, respiratory or urinary symptoms and signs indicating multisystem organ involvement. Two patients (1%) had gastrointestinal bleeding, but only one of those had findings of intestinal vasculitis, presenting with abdominal pain, diarrhoea along with severe skin ulceration. Subcutaneous atrophy was reported in 7 (3.7%) cases but lipodystrophy-associated metabolic derangements were not reported.

Investigations

The main abnormal investigation results are presented in Table III. Of all IIM, 92% had at least one abnormal muscle enzymes result. There were no abnormal muscle enzymes in 14 patients (8%). Twenty-five (13.2%) patients had abnormal results of all tested

Table III. Investigations performed in 189 cases diagnosed with idiopathic inflammatory myopathies (IIM).

Investigation	n. (%) with investigation documented	n. (%) with abnormal results
Muscle enzymes	175 (92.6)	161 (92)
CPK	173 (91.5)	93 (53.8)
LDH	159 (84.1)	128 (80.5)
Aldolase	75 (39.7)	63 (84)
AST	141 (74.6)	98 (84)
ALT	136 (72)	65 (47.8)
EMG	74 (39.2)	69 (93.2)
Muscle biopsy	141 (74.6)	129 (91.5)
ANA antibodies	169 (89.4)	70 (41.4)
Anti-ENA antibodies	108 (57.1)	6 (5.6)
Anti-DNA antibodies	114 (60.3)	6 (5.3)
Rheumatoid factor	92 (48.7)	5 (5.4)
MRI	25 (13.2)	18 (72)
Skin biopsy	22 (11.6)	17 (77.3)

AST: aspartate aminotransferase; LDH: lactic dehydrogenase; CPK: creatine phosphokinase; ALT: alanine aminotransferase; EMG: electromyogram; ANA: antinuclear antibodies; Anti-ENA: anti-extracted nuclear antibodies; Anti-DNA: anti-desoxyribonucleic antibodies; MRI: magnetic resonance imaging.

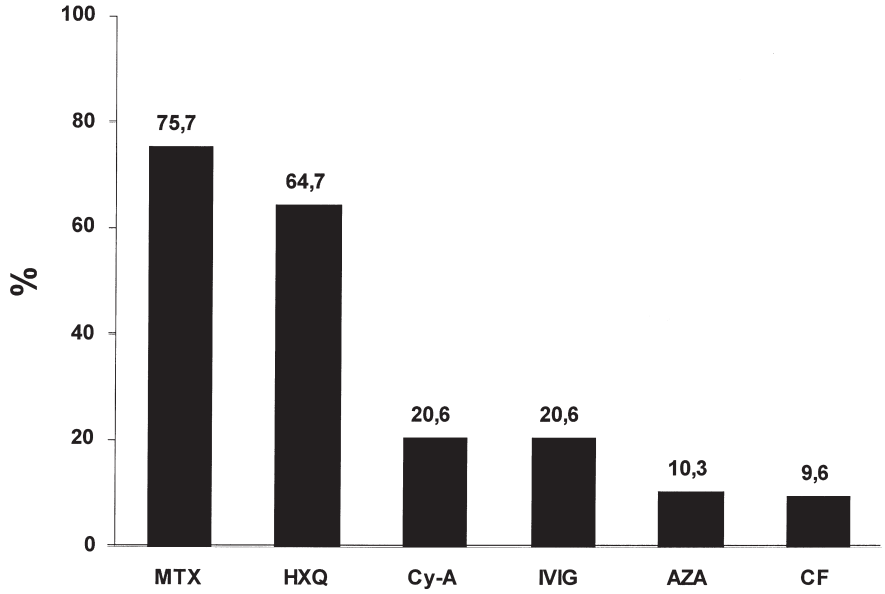

Fig. 1. Percentual distribution of prednisone-associated drugs (n=136) received by patients diagnosed with idiopathic inflammatory myopathies during their disease course.
MTX: methotrexate; HXQ: hydroxychloroquine; Cy-A: cyclosporine-A; IVIG: intravenous immunoglobulin; AZA: azathioprine; CF: cyclophosphamide.

muscle enzymes. In 29 (15.3%) there was only 1 abnormal muscle enzyme result. When such occurred, the most frequently elevated was the LDH, reported in 15 cases.

ANA positive was recorded in 41.4% (n=70), with following titres: 1:80 (2), 1:160 (7), 1:320 (23), 1:640 (7) and 1:1280 (6). ANA titres were missing in 25. Anti-ENA antibodies and rheumatoid factor were recorded in 6 and 5 cases, respectively. Myositis-specific antibodies were not determined in any of the centres and results of complement factors were reported in only 1 centre, with all the values within normal range.

Treatment

Over time, 186 (97.9%) patients received steroids, 108 received prednisone or prednisolone and 76 had it combined with bolus methylprednisolone (pulses). One patient received only pulses and 4 had no steroid treatment. Only oral steroid treatment was reported in 52 patients (27.5%). One of the reported patients had no treatment at all, evolving into remission with no complications. In 136 patients (72%), treatment included additionally one or more of the following: hydroxychloroquine (HXQ), methotrexate (MTX), cyclosporine A (CyA), intravenous immunoglobulin (IVIG), azathioprine (AZA) or cyclophosphamide (CF). Methotrexate was the most common treatment, in 103 (75.7%). In 49 (25.9%), at least 1 association of drugs was used, in these cases also MTX was the most frequent combination. Seventeen other cases had HXQ as the only therapy in addition to steroids. When 2 or more drugs were used in addition to steroids, the most frequent association was MTX and HXQ. Eighty-seven cases (46%) were treated with 2 or more drugs in addition to steroids. Two of the patients received thalidomide as attempt to control refractory skin rash. Specific treatments for calcinosis were reported in 22 (11.6%); of those the most frequently prescribed, were diltiazem in 10 (5.3%), bisphosphonates in 9 (4.8%), colchicine in 6 (3.2%) and surgical excision in 1 case. The frequency of main drug prescription during the whole disease course, identified in the last visit, is presented in Figure 1.

Forty-one percent (41%) of the patients received calcium and vitamin D and 16.9% received a non-steroid anti-inflammatory drug (NSAID), 41% used gastro-protective medication, with either ranitidine or omeprazol. Physical therapy was recorded in 37.6% of the patients.

Outcome

Calcinosis development was documented in 46 (24.3%) patients; of those, in 10 (21.7%) it was present at diagnosis, in 30 (65.3%) it occurred during disease course and 6 (13%) had no available information about calcinosis onset. It was localised in 29, disseminated in 13, superficial in 23 and deep in 8. There was no data available for the calcinosis distribution in only 1 case. Survival rates using the Kaplan-Meier method,

expressed as percentage of cases developing calcinosis are presented in Figure 2. The probability of calcinosis was 33.5%, 39.4% and 51.9% at 1, 2 and 5 years, respectively. Mean follow-up time for calcinosis development was 4.7±0.5 years. Mean follow-up time for those with calcinosis was 5.6±4.9 years, and for those without calcinosis was 4.5±4.1 years.

Death was reported in 8 cases (4.2%), but no established causality relationship by autopsy was reported. The precedent events were clinically defined as respiratory failure and sepsis in 5, all occurring during active disease phase. One had myocarditis, 1 had sclerosing colangitis, but the cause of death could not be identified, and 1 developed sepsis due to neutropenia as a complication of lymphoblastic leukaemia, when JDM was considered in remission for more than 2 years. Of those with fatal outcome, 5 had definite JDM and 3 had probable JDM. Four (50%) died within the first year of follow-up, 1 after 36 months and 1 after 14 years. Follow-up duration was not reported in 2 cases. Steroid treatment was used for all, prednisone or prednisolone in 8, pulses of methylprednisolone in 2, HXQ in 2, MTX in 1.

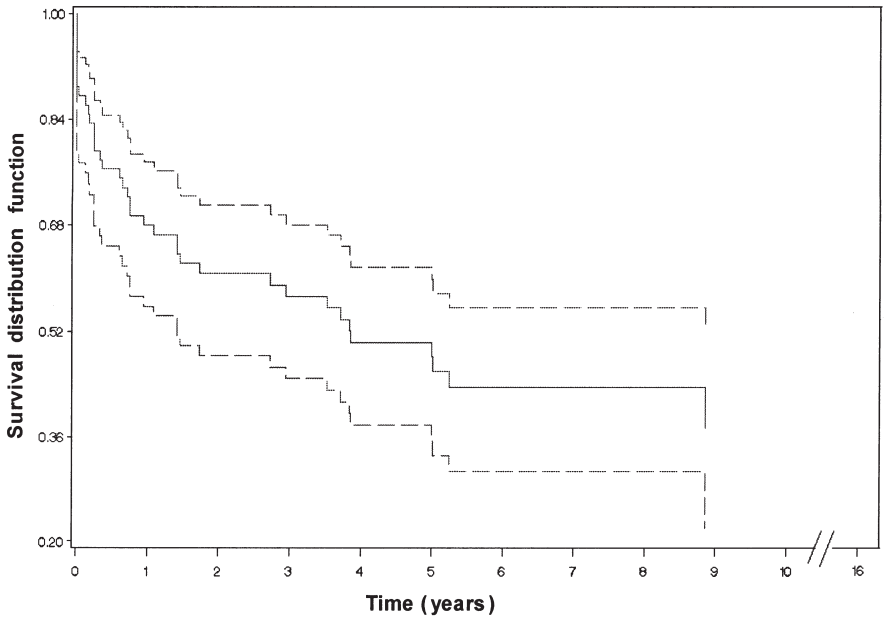

Fig. 2. Calcinosis survival rates with 95% confidence interval (– – –). The y-axis shows the proportion of patients who have not developed calcinosis. The x-axis shows the follow-up time in years after diagnosis. Mean follow-up time for calcinosis development was 4.7±0.5 years. The probability of calcinosis was 33.5%, 39.4% and 51.9% at 1, 2 and 5 years, respectively.

Frequency of the 1975 Bohan & Peter criteria for juvenile dermatomyositis

Of the 189 coded cases diagnosed by the attending physician as IIM, 187 met any of the defined categories of Bohan and Peter (1975) (7, 8) criteria by the calculated algorithm, with reported data on muscle weakness, typical skin rash, abnormal results of muscle biopsy, electromyogram and muscle enzymes and independently from attending physician diagnosis. Agreement between reclassification and physician diagnosis occurred in 66.1%.

Of those 187 cases, 124 (66.3%) met the criteria for definite JDM, 46 (24.6%) for probable JDM, 8 (4.3%) for possible JDM, 4 (2.1%) for definite JPM, 4 (2.1%) for probable JPM and 1 (0.5) for possible JPM (Table I). Of those without muscle weakness (8), 1 had definite JDM, 2 had probable JDM, 4 had possible JDM, none had JPM and one was ruled out, having amyopathic dermatomyositis as physician diagnosis. Of those with normal values for muscle enzymes (17), 3 had definite JDM, 8 had probable JDM, 5 had possible JDM, none had JPM and one was ruled out. The frequency of abnormal muscle enzymes is reported in Table III. For those under the IIM diagnosis, aldolase (84%) and AST (84%) were the most affected compared to abnormal CPK (53.8%). For those who reached the criteria for definite JDM, aldolase was also the most affected (89.5%) followed by LDH (85%), AST (77.5%) and CPK (56.4%).

Evaluation of diagnostic criteria by logistic regression analysis

The univariate analysis using CPK, LDH, aldolase, AST, ALT, electromyogram and muscle biopsy showed that only AST and aldolase were significantly associated with definite JDM diagnosis. Those variables entered into logistic regression procedures. Only patients with no missing data, either in the determinant or in the outcome variable (definite JDM) entered into the model (n=66). In the final analysis, only aldolase remained significant (OR=5.4; 95% CI 1.2-24.6; p=0.03) meaning that a patient with abnormal aldolase has 5 times more chance of being classified as definite JDM, in relation to the other parameters.

Discussion

This is the first multicentre registry of inflammatory muscle diseases in our country, and the largest data collection so far. The current approach was chosen to assess the proportion of patients with a predefined set of medical criteria in order to reach a valid diagnosis, independently from the attending physician opinion. International registries for IIM have been published recently (12-14). Previous reports with clinical and demographic characterisation of patients from a single Brazilian centre have also been published (5, 6). A comparison with these data indicates a similar profile of onset age, signs and symptoms, calcinosis, skin ulceration and ANA.

The diagnosis and classification criteria have been recently discussed, due to some concerns among paediatric rheumatologists about the value of invasive investigations such as EMG and muscle biopsy (9). Although JDM is the most common of the IIM, epidemiologic studies can be difficult because some studies estimate the incidence of JDM and JPM together, while others consider

them separately. Also, the age limits for 'juvenile' are not yet clearly defined as being 16, 17 or 18 years (15). More is now learned in adults about the IIM as a group encompassing different disease expressions, where marked differences were found in the dermatomyositis and polymyositis histopathology (16), but in paediatric patients it is still not well established. Evidence is missing, but to reach the appropriate number of patients, multicentre data collection is needed.

In a recent prospective single-centre study examining outcome predictors (4), definite and probable JDM were included, according to the Bohan & Peter criteria (7, 8) definitions. The diagnostic approach reported in the present study was intended firstly to address the current practice for the broad categories of IIM. The IIM classification includes also amyopathic dermatomyositis, focal myositis and overlap syndromes (1). Second, it was aimed at refining the diagnoses by fitting into strict criteria, independently of previous diagnosis by attending physician, and eventually assessing associations and the best predictor of definite JDM diagnosis. It was considered that sensitivity and specificity of each of the criteria were evaluated by Bohan & Peter in the validation (7, 8) of the classification criteria. Although assessing each of the Bohan & Peter (7, 8) categories independently might have resulted in redundancy, and ideally the best approach would include patients with and without myositis, this study was conducted in the standard routine care by retrospective approach.

Therefore, as a practical starting point, recognising the profile of patients with a valid diagnosis could be of interest. The age range was arbitrarily chosen, including patients under 18 years, where the frequency of polymyositis (4.8%), was lower than that referred for adults (9%) (16) , but it was higher than the previously described in the UK-Ireland registry (13) (2.6%) which included cases in the paediatric age range. However, in comparison with the same registry, connective tissue disease overlap rates were lower in the present series, 6.9% versus 13.9% in the previous series.

Other particular features observed in the present series, it is the greater proportion of musculoskeletal and systemic symptoms, 81% and 78.3%, respectively. It may be due to the fact that these symptoms were grouped in the description, where more than half had myalgia, arthralgia, fever and fatigue. In comparison, the rates of dysphagia, dysphonia and dyspnoea were close to the previous series (13, 14).

Interestingly, the value of muscle enzymes for the diagnosis was documented with a high proportion of cases with at least one abnormal muscle enzyme result, for all IIM and this proportion increased to 97.5% for those eventually classified as definite JDM. Examining the results for each of the enzymes, for all IIM cases, aldolase and AST were the most frequently elevated. When considering only cases of definite JDM, aldolase was the most frequently elevated followed by LDH. Only 53.8% of the patients had elevated CPK. By comparison, Sallum *et al*. (5) reported in a single-centre Brazilian series, abnormal CPK in 68.5% of JDM patients. Abnormal aldolase resulted the only predictor of definite JDM, although it was tested in only 39.7% of the cases, suggesting its availability should be reconsidered in the centres.

Muscle biopsy was performed in 141 (74.6%) cases in the present series, being abnormal in 91.5%. Only 74 (39.1%) patients underwent EMG, with abnormal results in 93.2%. The proportion of performed EMG and muscle biopsy was higher in our case-series compared with previously published series (13, 14). However, MRI was performed in only 25 (13.2%), either at disease-onset or follow up and this may reflect cost-effective restrictions, as reported previously in an international survey (9).

Rare disease features have been described. Amyopathic dermatomyositis was reported in 1 case. Associated malignancy has been rarely reported in association of any of the paediatric IIM (17, 18); it occurred in 2 of our cases, but its relationship with the disease itself is still unclear, as all had typical features of dermatomyositis, but one had a long time gap between JDM symptoms and malignancy presentation. The strength of this association still remains elusive and more data is needed to better evaluate the risks.

Standard adult classification criteria (7, 8) for JDM and JPM were applied to our patients presenting with IIM, as umbrella term encompassing many diseases with possibly different pathogenic mechanisms (16). Although no classification system for inflammatory muscle diseases of children has proved satisfactory, specially concerning the overlap features, Bohan & Peter (7, 8) defined categories calculated by individualised algorithms for definite, probable and possible JDM and JPM have shown to be useful to distinguish classic JDM and JPM.

Other point to consider is the standard of treatment for all myositis (19, 20) as the main outcome determinants. Systematic high-dose regimen of prednisone has been recommended, but no standard regimen has yet been established, as the doses and time for steroid tapering, as well as additional disease modifying drugs for steroid-sparing regimen, are under the physician's discretion and also dependent on patients individual response. In this survey, it was observed that the frequency of prednisone use was comparable to previous retrospective studies (13), indicating that in spite of the absence of controlled trials, it is standard of care. The same is true for other disease-modifying drugs with steroid-sparing effect. It has been shown over the years that early association of these drugs may result in shorter time for symptoms resolution, for both rash and muscle weakness. This concept was reflected in our practice by the frequency of MTX use during disease course.

All limitations of a retrospective data collection must be acknowledged. Data was obtained from a convenience sample, selected by completeness of relevant clinical data and retrieved from prevalent cases in paediatric rheumatology referral centres. Quantitative measures for muscle strength, functional status and quality of life could not be assessed due to retrospective approach . Also, it was not possible to obtain accurate records of disease-modifying drug regimen and combination of drugs; all

treatment regimens were under physician's discretion in each of the centres, thus becoming difficult to compare. With regards to calcinosis, there are limited conclusions about intervention. But, interestingly, results about its time length have shown that, overall, it occurred late in disease course, although early calcinosis was reported.

It is important to stress those recent changes on the JDM treatment, as long term high dose steroid treatment and early use of disease-modifying drug are the main determinants for better outcome (4, 19-21). JDM and, moreover, JPM, are relatively uncommon paediatric rheumatic diseases, and a representative population with homogeneous criteria is needed for conducting clinical studies. Collaborative multicentre inclusion is often required for testing new drugs and also for outcome assessments, therefore a valid diagnosis in current practice data may provide the basis for future studies.

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