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RESEARCH ARTICLE

FATTY DEGENERATION AND ATROPHY IN SKELETAL MUSCLES IN CHILDREN WITH DERMATOMYOSITIS AND/OR POLYMYOSITIS

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ABSTRACT

Background: Idiopathic inflammatory myopathies (IIMs) are chronic autoimmune connective tissue disorder which involve dermatomyositis (DM) and polymyositis (PM). **Objectives**: To study abnormal changes in affected muscles in dermatomyositis and polymyositis patients. **Methods**: The study sample comprised 27 patients (9 males, 18 females) ages 8–16 years who were diagnosed with PM or DM according to of Bohan and Peter criteria. In each case, age, sex, duration of the disease, clinical symptoms, cutaneous manifestations, clinical morphology, laboratory investigations, electromyographic findings, musculoskeletal ultrasound, histopathologic features in the skeletal muscle biopsy, treatment and response were recorded. Results: Musculoskeletal ultrasound and Doppler showed that 21 patients (77.8%) had hyperechoic muscle, fatty tissue infiltration, decrease of muscle thickness and hypervascular changes on power Doppler in active early disease and six patients (22.2%) showed decrease of muscle thickness only. **Conclusion**: Fat substitution and fibrosis can be developed in affected muscles, that is transformed into hyperechoic due to increased amount of muscle reflective surfaces. Alterations in muscle thickness throughout the affected muscles might also take place.

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INTRODUCTION

Idiopathic inflammatory myopathies (IIMs) are chronic autoimmune connective tissue disorder which occur in children and adults and involve dermatomyositis (DM) and polymyositis (PM). It mostly affects weak muscles, however the systemic inflammatory feature of such disorders may lead to other disorders, which involve the skin, joints, lung or heart (Dalakas, 2015). Regarding to EULAR/ACR classification criteria, the IIMs may categorize into: polymyositis (PM), inclusion body myositis (IBM), dermatomyositis (DM), amyopathic DM, juvenile dermatomyositis (JDM), and juvenile myositis other than JDM (Selva-O'Callaghan, 2018). Immune Mediated Necrotizing Myopathy (IMNM) has been recently identified as a separate, unique diagnostic criterion described in the subtype of PM mainly by muscle necrosis on biopsy with low inflammatory infiltration (Leeuwenberg, 2019). DM and PM both are curable types of IIMs with proximal weaknesses in the limb with different cutaneous presentations in DM (Dimachkie, 2014).

Management involved Immunosuppressive therapy, including glucocorticoids, disease modifiers (e.g. methotrexate and mycophenolate), and frequently intensive/targeted therapy (e.g. cyclophosphamide and rituximab). HYPERLINK "https://onlinelibrary.wiley.com/doi/full/10.1111/1756-185X.13929", 5 We aimed to study abnormal changes in affected muscles in dermatomyositis and polymyositis patients.

PATIENTS AND METHODS

The study sample comprised 27 patients (9 males, 18 females) ages 8–16 years who were diagnosed with PM or DM according to Bohan and Peter criteria (Bohan, 1975).These patients were enrolled from Rheumatology and Rehabilitation Department, Faculty of Medicine, Zagazig University Hospitals. All participants enrolled in this study had an informed consent before joining our study and all had the rights to take away from the study without any interruption of their treatment plan and rights. All personal data of our enrolled patients were preserved and kept away from data retrieving personnel.

METHODS

In each case, age, sex, duration of the disease, clinical symptoms, cutaneous manifestations, clinical morphology, laboratory investigation, electromyographic findings, musculoskeletal ultrasound, histopathologic features in the skeletal muscle biopsy, treatment and response were recorded. Medical records with these diagnoses have been reviewed separately and the following information have been gained: 1- age at initial diagnosis 2- date of illness (first symptom) ; 3- PM, DM, neoplasms and other connective tissue diseases relevant information containing medical historical data and general/neurological clinical assessment analysing characteristic skin rash, proximal and distal muscular strength, tonus and reflexes in upper and lower limbs; 4- laboratory data: leucocyte count, erythrocyte sedimentation rate (ESR), creatine kinase (CK), lactate dehydrogenase (LDH), AST and ALT and urea, 5- Electromyographic needle (EMG) abnormalities 6- ultrasonography of affected muscles; and 7- histopathological results on fresh-frozen muscle biopsies, which were carried out using the following staining and histochemical reactions: hematoxilin-eosin, modified Gomori trichrome, oil red O, PAS, cresyl violet, sirius red, NADH-tetrazolium reductase, ATPases pH 4.3, 4.6, 9.4, myophosphorylase, non-specific esterase, alkaline phosphatase, acid phosphatase, succinic dehidrogenase and cytochrome c-oxidase (Werneck, 1981; Werneck, 1991).

Statistical analysis: Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. The data collected were tabulated and analyzed by SPSS (statistical package for social science) version 25 (IBM, Armonk, NY, USA) on IBM compatible computer. According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean ± SD.

RESULTS

The mean ±SD of age of the Twenty seven patients was 11.44 ± 3.32 years and mean ±SD duration of DM or PM was 2.56 ± 1.5 years.

Clinical findings

Presenting symptoms: All patients presented with proximal muscle weakness in both lower limbs more in quadriceps which it's grade from fair to good while three cases have both upper and lower limbs weakness, also, six cases (22.2%) have weakness of neck flexors. Twenty one patients (77.8%) complain of arthralgia. (Table1 &5) (Fig. 1)

Skin and subcutaneous lesions: All the way through the disease, Eighteen patients (66.7%) presented with rash, subcutaneous swelling was in nine patients (33.3%) and three patients (11.1%) have Gottron's papules. (Table 1) (Fig. 1)

Systemic manifestations: Fever was the most prevalent constitutional symptom presented in Eighteen patients (66.7%) (persistent in six patients and irregular in Twelve patients), weight loss gained in nine (33.3%) patients. Six patients (22.2%) have interstitial lung disease (Table 1).

Table 1. Distribution of clinical symptoms

		Frequency	Percent
muscle weakness	Positive	27	100.0
Arthralgia	Negative	6	22.2
	Positive	21	77.8
Gottron's papules	Negative	24	88.9
	Positive	3	11.1
Heliotrope rash	Negative	9	33.3
	Positive	18	66.7
Fever	Negative	9	33.3
	Positive	18	66.7
Weight loss	Negative	18	66.7
	Positive	9	33.3
Other clinical features	ILD	3	11.1
	Negative	24	88.9

Table 2. Distribution of studied patients regarding Musculoskeletal ultrasound

		Frequency	Percent
Hyperechoic muscle	Negative	9	33.3
	Positive	18	66.7
Hypoechoic muscle	Negative	24	88.9
	Positive	3	11.1
Fatty tissue infiltration	Negative	6	22.2
	Positive	21	77.8
Hypervascular changes	Negative	6	22.2
	Positive	21	77.8
Decrease of muscle thickness	Negative	21	77.8
	Positive	6	22.2

Laboratory test results: Twenty six patients (96.3%) had elevated 1st hour ESR and three patients (11.1%) had leukocytosis. Abnormal biochemistry results were observed in all patients, which included elevated level of Creatine kinase (CPK) in nine patients (33.3%), Twenty one patients (77.8%) had elevated urea, Twenty six patients (96.3%) have elevated lactate dehydrogenase (LDH), six patients (22.2%) had high AST and nine patients (33.3%) had high ALT (Table 3).

Table 3. Laboratory results of studied patients

		Frequency	Percent
Leucocyte	Elevated	3	11.1
	Normal	24	88.9
1st hour ESR (mm/hr)	Elevated	26	96.3
	Normal	1	3.7
CPK (U/L)	Elevated	9	33.3
	Normal	18	66.7
Urea (mgldl)	Elevated	21	77.8
	Normal	6	22.2
Creatinine (mgldl)	Elevated	3	11.1
	Normal	24	88.9
LDH (U/L)	Elevated	26	96.3
	Normal	1	3.7
AST (U/L)	Elevated	6	22.2
	Normal	21	77.8
ALT (U/L)	Elevated	9	33.3
	Normal	18	66.7

Table 4. Distribution of studied patients regarding Electromyography (EMG) and biopsy results

		Frequency	Percent
Electromyography (EMG)	Normal	2	7.4
	Myopathic pattern	19	70.4
	Mixed potentials	3	11.1
	Chronic denervation	3	11.1
	Total	27	100.0
Biopsy	DM	18	66.7
	PM	9	33.3
	Total	27	100.0

DM: Dermatomyositis, PM: polymyositis

Table 5. Association between Muscle weakness and Musculoskeletal ultrasound

		Muscle weakness
Hyperechoic muscle	Count	18
	%	66.7%
Hypoechoic muscle	Count	3
	%	11.1%
Fatty tissue infiltration	Count	21
	%	77.8%
Hypervascular changes	Count	21
	%	77.8%
Decrease of muscle thickness	Count	6
	%	22.2%

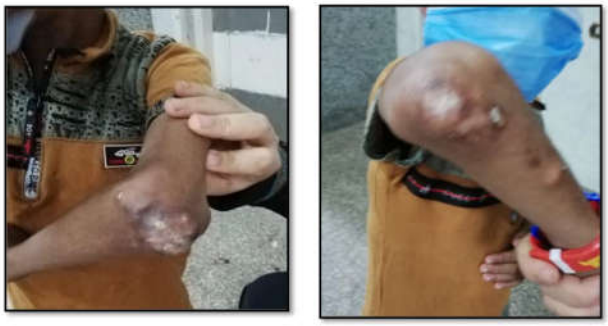

Figure 1. Nine years old child with cutaneous manifestations; heliotropic rash, subcutaneous swellings and muscle weakness proximal in both upper limbs and lower limbs more in quadriceps it's grade from fair to good

Imaging and Pathologic features

The patients had undergone musculoskeletal ultrasound and Doppler, eighteen patients (66.7%) showed hyperechoic muscle, three (11.1%) were hypoechoic, twenty-one (77.8%) showed both fatty tissue infiltration and hypervascular changes on power Doppler in active early disease, also, six patients (22.2%) showed decrease of muscle thickness only (Table 2 &Table 5). The electromyography presented a myopathic pattern in Nineteen (70.4%) patients, mixed potentials in three patients (11.1%), chronic denervation in three patients (11.1%) and normal pattern in two patients (7.4%) (Table 4). Muscle biopsy revealed that eighteen patients (66.7%) had perivascular and perimysial inflammatory infiltrate and perifascicular atrophy, so diagnosed as DM while the other nine patients (33.3%) showed that tissue infiltration is almost endomysial with Inflammatory cells, which invade individual muscle fibers, and myofiber injuries seem to be mediated with CD8+ cytotoxic T lymphocytes, macrophages and major histocompatibility I (MHC-I) that invade myofibers, so diagnosed as PM (Table 4).

Treatment: The initial treatment used for all patients was a combination of high-dose oral prednisone (2 mg/kg/day bid, maximum 80 mg/day), methotrexate (15 mg/m2, maximum 25 mg/dose once weekly, administered as a subcutaneous injection) and folic acid at 1 mg per day to limit methotrexate toxicity. Eighteen patients showed normalization of elevated serum muscle enzymes, increased muscle strength both by history & Childhood Myositis Assessment Scale (CMAS) and resolution of skin rash while there were nine patients experienced persistent and increasing symptoms so needed additional therapy in the form of cyclosporine (Sandimmune @) 3 mg/kg given once daily and intravenous immune globulin (IVIG) 2 g/kg (maximum dose 70 g), administered as a single dose. IVIG is given every two weeks, initially for five doses, and is then monthly.

DISCUSSION

Because there were no strongly outlined diagnostic criteria, many reports on DM and PM were usually conflicting and contradicting (Bohan, 1975). In the current work, myalgia was the main complaint after proximal muscle weakening same as other reports (Lundberg, 2017). We discovered that PM and DM were more found in females with F:M ratio of 2:1. The prevalence of idiopathic inflammatory myopathies is usually thought to be higher in females than in males (Lundberg, 2018). The most prominent symptom detected in all patients was proximal muscle weakness. Although all cases had proximal muscle weakness in certain trials, PM cases having significantly greater symptoms of muscular weakness than DM cases (Femia, 2013).

The concentrations of muscle enzymes, particularly CK and ALT, were elevated in the majority of cases, as evidenced by prior research that found CK values to be up to 50 times higher than normal in polymyositis cases (Lundberg, 2018). In the majority of cases, electromyography (EMG) revealed myopathic potentials. Nevertheless, several cases revealed a mixture of myopathic and neurogenic potentials in EMG. The neurogenic potentials are frequently the result of muscle fiber regeneration and the disease's chronicity (Kalita, 2012). The myopathic sequence in EMG is characterised by short-term, low-bulb polyphasic units on voluntary action and enhanced spontaneous activity fibrillation, complex repeating discharges and positive high waves. EMG of both DM and PM are identical. EMG usually used to diagnose neurogenic conditions that diminish the number of axons that generate polyphasic units with a higher amplitude and extended length (Goyal, 2014). Normal EMG usually reported in patients with DM and is probably associated in early stage of the disease as reported in Dalakas diagnostic criteria (Lundberg, 2018). In the majority of cases, electromyography (EMG) revealed myopathic potentials. Nevertheless, several cases revealed a mixture of myopathic and neurogenic potentials in EMG. The neurogenic potentials are frequently the result of muscle fiber regeneration and the disease's chronicity (Kalita, 2012).

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concomitant atrophy. A remarkable variation in muscle echo intensity was an important observation with variations in the angulation of transducer in the acute DM. The authors thought that this was associated with perifasicular atrophy, but this effect was also observed in healthy muscles (Reimers, 1997). The majority of patients in our study showed hyperechoic muscle, fatty tissue infiltration, decrease of muscle thickness and hypervascular changes on power Doppler in active early disease and six patients showed decrease of muscle thickness only. Maurits, et al. (2003) and Bhansing, et al. (2015) reported a reduction of muscle thickness in DM and PM in comparing with controls. Chi-Fishman, et al. (2015) study included 9 cases with DM and PM, revealed that the muscles with myositis are smaller than healthy muscles due to contraction alterations in rectus femoris' muscle diameter. A recent report with mostly PM/DM cases has shown that US results are well linked with disease severity (Sousa Neves, 2018). Stonecipher, et al. revealed a rising in echo intensity of biceps, triceps and deltoid muscles in DM cases even with normal muscle enzymes (Stonecipher, 1994).

Conclusion

Many alterations are structurally apparent in affected muscles in DM and PM. Fat replacement and fibrosis may occur for affected muscles, which turns hyperechoic due to rising in the number of reflecting surfaces through the muscle. In addition, in the affected muscles also alterations in muscle thickness might develop.

Conflict of interest: The authors of this manuscript declare no relevant conflicts of interest, and no relationships with any companies, whose products or services may be related to the subject matter of the article

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