

Failure to over express MHC-CLASS-1 on muscle biopsy in a case of amyopathic juvenile dermatomyositis

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ABSTRACT

The concept of amyopathic dermatomyositis or dermatomyositis sine myositis, is contentious, particularly within paediatrics. We report an 8-year-old girl presenting with dermatological dermatomyositis without muscle weakness. Muscle biopsy changes are described, in particular, the absence of MHC class 1 over expression. This supports the concept of amyopathic dermatomyositis as a subgroup of juvenile dermatomyositis (JDM) and suggests that immunohistological analysis may be a valuable in excluding a myositic element in such cases.

Introduction

MHC class 1 over expression on muscle has been identified in JDM in the context of muscle inflammation and damage (1). This case report highlights that in the absence of myopathy, MHC expression may be normal.

Case report

An 8-year-old girl presented with a 4-month history of rash. Examination revealed Gottron's papules, over metacarpophalangeal and interphalangeal joints (Fig. 1), elbows and knees. Perioral erythema, livedo reticularis, eyelid oedema and heliotrope rash were evident. Detailed examination of nail beds revealed capillary loop dilatation consistent with JDM. Skin features were sufficiently pathognomonic for a skin biopsy not to be taken.

Despite fatigue, a history of proximal muscle weakness was lacking. This was confirmed by normal CMAS (2) score (53/53), and Manual Muscle Testing (3) (5/5) in all muscle groups. There was no joint restriction and systemic examination was unremarkable.

Symptoms included nocturnal cough (known asthma), and occasional mouth ulcers. Systemic features were absent. There was longstanding Raynaud's, but extensive questioning and investigations did not reveal any features of overlap syndrome. CHAQ (4) score was 0/3 (no functional impairment) and patient Visual Analogue Scale (5) was 0/100 (indicating 'very well'). Physician's Global Assessment (5) was 8/100. Past medical and family histories were unremarkable.

CK at symptom onset was 66 IU / Litre (24-174), LDH tested one month later was 603 U/L (420-750), aldolase not routinely available. ESR was elevated at 20 mm / hour (0-12). Full blood count, coagulation screen, renal, liver, bone and thyroid function were normal. ANA, Jo-1, RF and anti-cardiolipin antibody (IgG and IgM) were negative. C3 (1.02G/L) and C4 (0.33G/L) were within normal range (0.75 - 1.65 and 0.14 - 0.54 respectively). Chest X ray, pulmonary function tests, and video fluoroscopy were entirely normal.

Magnetic Resonance Imaging (MRI) of thighs (axial turbo STIR, T1 and T2 spin echo) showed normal muscle bulk, no fatty replacement and no signal abnormality within muscle or subcutaneous tissue.

Muscle biopsy showed mild increase in number of small fibres, which were scattered and not at fascicular borders, thus not suggestive of peri-fascicular atrophy. There was no significant inflammation seen morphologically, with absence of necrotic or regenerating fibres, no excess of internal nuclei and no infiltrating inflammatory cells. Capillary numbers were normal with no capillary drop out. Stains for muscle fibre architecture (NADH) and connective tissue (picosirius and Gomori's trichrome stain), were normal, with no ragged red fibres or rods. Histochemical stains for glycogen (PAS) and lipid (oil-red-O) were normal for age. Acid phosphatase staining showed mild increase in perimysial connective tissue macrophage activity. ATPase staining at pH 4.6 and 9.4 showed mild excess of type 1 (slow) fibres. Expression of MHC Class I protein, by monoclonal antibody immunostaining (1), was not up-regulated on this biopsy.



Fig.1. Image of hand showing Gottron's patches over MCP and PIP joints.

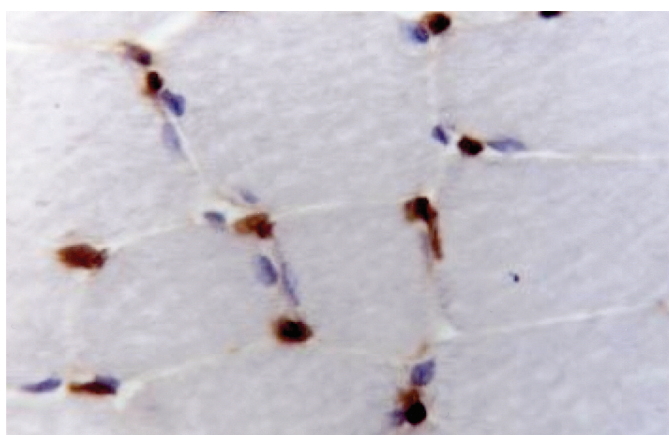
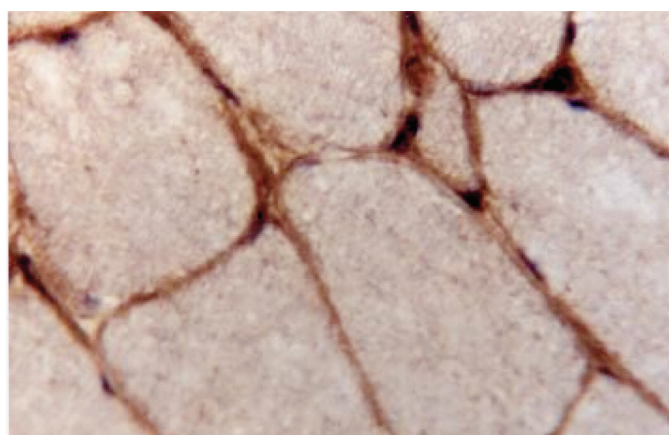
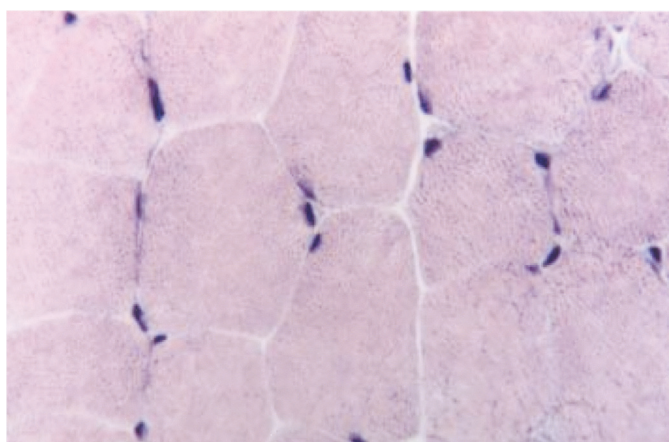


Fig. 2. Muscle biopsy demonstrating lack of MHC over expression in this case.

a. MHC class 1 staining of a muscle biopsy of this 8 year old girl showing staining of blood vessels but not muscle fibres.



b. MHC class 1 staining in a positive control muscle biopsy showing over-expression of MHC class 1 within the muscle fibres.



c. H&E staining of muscle biopsy of this 8-year old girl. There is no inflammatory infiltrate, and no fibre necrosis.

MHC staining was identified on the endothelium, but noticeably absent from muscle fibres (Fig. 2a). Slides were prepared and stained simultaneously with identical reagents, on another JDM patient, demonstrating positive staining for MHC Class I on muscle fibres (Fig. 2b).

Following investigations, low dose prednisolone (5mg, 0.2mg/kg/day, weaned over 6 weeks) and methotrexate (15mg orally per week) were given, with improvement in skin signs. Prospective follow up over 18 months showed no

evidence of weakness or muscle inflammation.

Discussion

There has been assorted opinion whether amyopathic dermatomyositis is a separate entity (6, 7), or if, in time, all patients develop muscle weakness (8, 9). The only validated criteria for JDM diagnosis by Bohan and Peter depend on evidence of proximal muscle weakness or muscle inflammation (abnormal muscle enzymes, biopsy necrosis or electromyogram abnormalities) (10).

Expanding this classification to include amyopathic dermatomyositis has been suggested (7).

Euwer and Sonteiher published diagnostic criteria in 1993 suggesting a combination of pathognomonic cutaneous changes, compatible skin biopsy findings, with no clinical evidence of proximal muscle weakness and normal skeletal muscle enzymes for 2 years after appearance of skin lesions (7). There has been a proposal to separate amyopathic dermatomyositis into 3 types; pure amyopathic dermatomyositis with skin disease only, skin disease with subjective myalgia and weakness but no laboratory evidence of muscle disease, and no clinical muscle weakness but evidence of abnormal laboratory tests during the disease course (11). Difficulties arise from reluctance to biopsy in the absence of clinical weakness, highlighted in a survey of paediatric rheumatologists and dermatologists (6). Even with investigations, there is debate regarding use of systemic therapy (6, 7). Some view amyopathic dermatomyositis as a benign disease, not requiring systemic corticosteroids (12) although early treatment may prevent development of muscle disease, or avoid long-term steroid treatment. In children, systemic therapy may be justified to prevent long-term complications such as calcinosis that is at least three times more common than in adults, or to avoid chronic joint morbidity (9, 13). The presence of sub-clinical myositis may prompt a more aggressive management in those presenting with an amyopathic picture.

Muscle biopsy abnormalities in JDM include inflammatory cell infiltration, muscle fibre necrosis, perifascicular atrophy, and increased perimysial connective tissue space (1, 14). MHC class 1 glycoprotein is expressed universally on nucleated cell surfaces, but level of expression on skeletal muscle is very low. The phenomenon of over-expression has been described in polymyositis and dermatomyositis of all ages (1, 15). MHC up-regulation is seen in children with weakness at time of biopsy, even in the absence of inflammatory cell infiltrate (1), and may be useful as a sensitive marker of muscle dysfunction.

tion. Lack of muscle MHC class I over expression in this case suggests a subgroup of JDM patients with inflammation only in the skin. Only one biopsy was taken, so sample bias is possible. Further testing is needed on more children with amyopathic dermatomyositis, and longer follow up. However, this report highlights that MHC up-regulation on muscle fibres is not a universal occurrence in JDM and may be absent in cases where clinical weakness is not apparent.

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