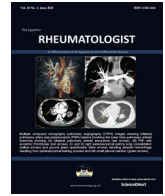




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Juvenile clinically amyopathic dermatomyositis (CADM): Case-based review

Wahinuddin Sulaiman^{a,b,*}, Farisya Mohd Lepatoni^a, Jyi Jong Tang^c, Nurul Bahiyah Baharudin^d^a Faculty of Medicine, Universiti Kuala Lumpur Royal College of Medicine, Perak, Malaysia^b KPJ Ipoh Specialist Hospital, Jalan Raja DiHilir, Ipoh, Perak, Malaysia^c Dermatology Clinic, Hospital Raja Permaisuri Bainun, Perak, Malaysia^d Pathology Department, Hospital Raja Permaisuri Bainun, Perak, Malaysia

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ABSTRACT

Background: Clinically amyopathic dermatomyositis (CADM) is rare as the classical cutaneous features are present with absence of myopathy and the serum creatinine kinase, electromyographic examination and muscle biopsy are usually normal.

Aim of the work: To report a young girl with juvenile CADM who responded to corticosteroid and mycophenolate mofetil, without progressing to myopathy and other systemic complications over a 3-year period.

Case presentation: An 11-year-old Malay girl was afebrile and presented with debilitating polyarthritides and classical cutaneous manifestations of dermatomyositis which was confirmed by histological findings, but without myopathy and systemic involvement. The anti-nuclear antibody (ANA) was positive 1:160, with speckled pattern and anti-p155/140 antibodies (anti-transcriptional intermediary factor 1, anti-TIF1 γ antibody) were positive. Skin biopsy revealed typical histological findings consistent with dermatomyositis including vacuolar changes of the basal layer, increased lymphocytic infiltrate and increased mucin deposition in the dermis. She received pulse methylprednisolone (250 mg/day/3 days) followed by oral prednisolone 1 mg/kg/day tapered until her cutaneous lesions showed marked improvement. Hydroxychloroquine (HCQ) (200 mg/day) and oral methotrexate (10 mg/week) were added. Six months after initial treatment, mycophenolate mofetil (MMF) 1 g/day was added in view of the slow improvement of her cutaneous lesions and was discontinued a year later as she demonstrated favourable outcome. Besides the skin lesions, her arthritis also responded well to treatment.

Conclusion: Juvenile CADM is rare but with early recognition and treatment, the prognosis is good especially in children as this may reduce the risk of systemic complications and progression to myopathy.

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1. Introduction

Dermatomyositis (DM) is a rare condition of idiopathic inflammatory myositis (IIM). Patient with DM may present with classical cutaneous lesions (Götrtron's papules, heliotrope rash, shawl and V signs of violaceous plaques) and may or may not be associated with myositis (clinically amyopathic dermatomyositis, CADM). Juvenile dermatomyositis (JDM) is the most common IIM in children accounting for 85% of cases [1–3] with an annual inci-

dence of 2–4 cases /1 million children [4–6]. Cutaneous manifestations in JDM are similar to adults [7].

Juvenile CADM or dermatomyositis sine myositis is uncommon and affects 22% of patients with JDM [1,8,9]. Juvenile CADM is suspected when patient presents with classical cutaneous features of DM for at least 6 months without clinical and laboratory evidence of myositis [9,10]. It usually has a favourable outcome. A systematic review on 68 cases reported that only three cases developed calcinosis cutis but none developed severe vasculopathy (ulceration), interstitial lung disease (ILD) or malignancy [11]. We report a young girl who presented with typical manifestations of juvenile CADM.

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* Corresponding author at: Professor of Medicine, Faculty of Medicine, Universiti Kuala Lumpur Royal College of Medicine Perak, No. 3, Jalan Greentown, 30450 Ipoh, Perak, Malaysia.

E-mail address: wahinuddin@unikl.edu.my (W. Sulaiman).

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2. Case report

An 11-year-old Malay girl presented in January 2020 with worsening generalised pruritic, scaly erythematous rashes for 2 years and was diagnosed with psoriasis or possible cutaneous lupus prior to admission. However, neither skin biopsy nor serological evidence was available. She was on hydroxychloroquine 200 mg daily and the patient's parents also sought traditional therapy. Despite treatment, cutaneous lesions deteriorated, and she developed severe debilitating arthritis with flexion deformity of knees and elbow joints. She had mild fever, hair loss, photosensitive facial erythema with recurrent oral ulcers but no proximal myopathy. She also had loss of appetite and weight (unable to quantify). Complete written informed consent was obtained from the parent for publication and accompanying images.

Physical examination revealed a small built and thin young girl, fretful and agitated, afebrile with generalised erythematous scaly rashes and on the face spared the nasolabial folds. Gottron's papules on the knuckles and proximal interphalangeal (PIP) joints both hands, periungual telangiectasia, ragged cuticles and bilateral heliotrope rash were present. Poikilodermic rashes were observed on the trunk and neck, both anteriorly and posteriorly (V and shawl signs). Palmar erythema and alopecia were also seen (Fig. 1). However, there was no cutaneous ulceration. The PIP, metacarpophalangeal (MCP) and wrist joints of both hands were warm and tender with reduced range of movement. Other systems including the heart, lungs and abdomen were unremarkable.

Laboratory investigations revealed positive anti-nuclear antibody (ANA) 1:160, with speckled pattern, and strongly positive anti-p155/140 (anti-transcriptional intermediary factor 1, anti-TIF1 γ) autoantibodies. The anti-dsDNA, anti-extractable nuclear antigens antibodies (anti Jo-1, anti PM-Scl 75, anti-PM-Scl 100, anti-Ku, anti-Ro-52, anti-SSA, anti-SSB, anti-Sm) and myositis specific antibodies (anti-Mi, -OJ, -EJ, -PL-2, -PL-7, -SAE 1, -MDA5/CADM 140) were all negative. The complement levels were normal (C3, 1.21 g/L; C4, 0.28 g/L). The creatinine kinase (CK), lactate dehydrogenase (LDH), serum ferritin, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) (186 U/L, 437 U/L, 70.6 ng/mL, 20 mm/hr, 0.08 mg/L, respectively), and aspartate and alanine transaminases (AST, ALT) were within normal limit. Full blood count showed normal haemoglobin, white blood cell and platelet counts (13.9 g/dL, $6.2 \times 10^3/\mu\text{L}$, $333 \times 10^3/\mu\text{L}$, respectively). Urinalysis was unremarkable. Venereal Disease Research Laboratory (VDRL), human immunodeficiency virus (HIV), hepatitis B and C screening were also negative.

Skin biopsy revealed typical histological findings consistent with dermatomyositis i.e., vacuolar changes of the basal layer (deepest layer of epidermis or stratum basale), increased lymphocytic infiltrate, and increased mucin deposition in the dermis (Fig. 2). Magnetic resonance imaging (MRI) of the thigh muscles, electromyography with nerve conduction studies and muscle biopsy were not performed.

She was given intravenous methylprednisolone 250 mg daily for 3 days followed by oral prednisolone 1 mg/kg/day with tapering dose over a period of 3 to 4 weeks and was maintained at 5–7.5 mg daily for 12 weeks until her cutaneous lesions showed marked improvement. Hydroxychloroquine (HCQ) 200 mg daily, oral methotrexate 7.5 mg weekly (increased to 10 mg weekly a month later and was stopped approximately a year later) and folate 5 mg weekly were added without documented untoward effects. Six months after initial treatment regimen, mycophenolate mofetil (MMF) 500 mg daily was added and subsequently increased to 1 gm daily a month later in view of slow improvement of her cutaneous lesions. MMF was discontinued a year later as she demonstrated favourable outcome. Besides the skin lesions, her

arthritis also responded well to treatment. To date, she shows no evidence of systemic complications such as interstitial lung disease (ILD) and ulcer or myositis, both clinically and in laboratory testing. Her cutaneous lesions continue to improve albeit gradual. She is currently on hydroxychloroquine, antihistamines, and topical moisturizing cream.

3. Discussion

Juvenile CADM is a rare variant of JDM characterized by classical cutaneous manifestations without clinical and investigational evidence of myositis (i.e., normal muscle enzymes, EMG, MRI) [9,12,13]. Nevertheless, they share similar histological findings on skin biopsy [14]. The incidence of juvenile CADM is unknown [11,15] while the mean age reported is 11 years with a female predominance [11]. In a review by Mamyrova *et al*, juvenile CADM occurred at a younger age compared to JDM (median 4.1 and 7.3 years respectively) [16]. Shenavandeh *et al* in their 10-years review showed almost similar range of age i.e., 4 to 17 years for JDM [17].

Juvenile CADM has a low risk of association with vasculopathy (severe ulceration), ILD and calcinosis in contrast with JDM [11,18]. Juvenile CADM may evolve into classical JDM over a period of time, and some may actually present with subclinical JDM [19]. In the systematic review by Gerami *et al*, 59% of juvenile CADM remained amyopathy even after 18 years of follow-up and in 26% of children, presence of cutaneous DM without myositis for 6 months evolved to classical JDM [11]. Mildly deranged muscle enzymes should not be ignored but should instead be considered a herald of JDM.

Muscle enzymes including creatine kinase (CK), aldolase, AST, ALT and lactate dehydrogenase (LDH) supported by ancillary diagnostic means including MRI and EMG could delineate JDM and juvenile CADM. MRI is useful especially in early DM cases in which patients may have subclinical myositis with presence of classical cutaneous manifestations (*dermatomyositis sine myositis*) [20]. Mamyrova *et al* demonstrated that serum muscle enzymes were raised in patients with hypomyopathy and almost half of the cases had abnormal MRI or EMG. Muscle enzymes are of lower value and are less frequently raised in juvenile CADM compared to JDM [16].

Qualitative tests of myositis specific antibody (MSA) and myositis associated antibody (MAA) had been made available in Malaysia for the past 10 years. Both have an important clinical implication as a diagnostic tool in distinguishing the different phenotypes of autoimmune myositis [21]. Anti-Jo1 antibody (anti-histidyl-tRNA synthetase) has been used as a marker for IIM and is more commonly present in polymyositis (PM) than in DM [20].

Myositis may rarely occur in juvenile CADM at a very low frequency with a more favourable outcome than JDM. 75% of juvenile CADM cases remained free from myositis after years of follow-up, and 25% evolved to having classic JDM. However, there was no definite clinical, laboratory or ancillary parameters to predict this transition [11,16,22]. Anti-P155/140 (TIF1 γ) antibody is associated with severe cutaneous lesions i.e., photosensitivity, lipodystrophy and a chronic clinical course [23,24]. Nevertheless, this autoantibody is commonly found in juvenile CADM with a milder clinical phenotype with favourable prognosis [20].

Anti-TIF1 γ antibody is present in 18–30% of children with JDM and is usually associated with a more prolonged disease course and severe cutaneous manifestations (lipodystrophy, skin ulceration and oedema) [25,26]. The current case had juvenile CADM and presented with unexplained severe clinical phenotype (cutaneous, lipodystrophy and arthritis) and demonstrated positive anti-TIF1 γ antibody. Another DM-specific marker is anti-melanoma differentiation-associated gene 5 (anti-MDA5) antibody which



Fig. 1. A and B: Erythematous scaly rashes with sparing of nasolabial fold, and poikilodermic rash upper trunk and neck (V sign). C: Gottron's papules on knuckles. D: Periungual telangiectasis with ragged cuticle. E: Erythematous macular rash on the palms F: alopecia. G: Erythematous scaly rashes at the upper back and neck (shawl signs).

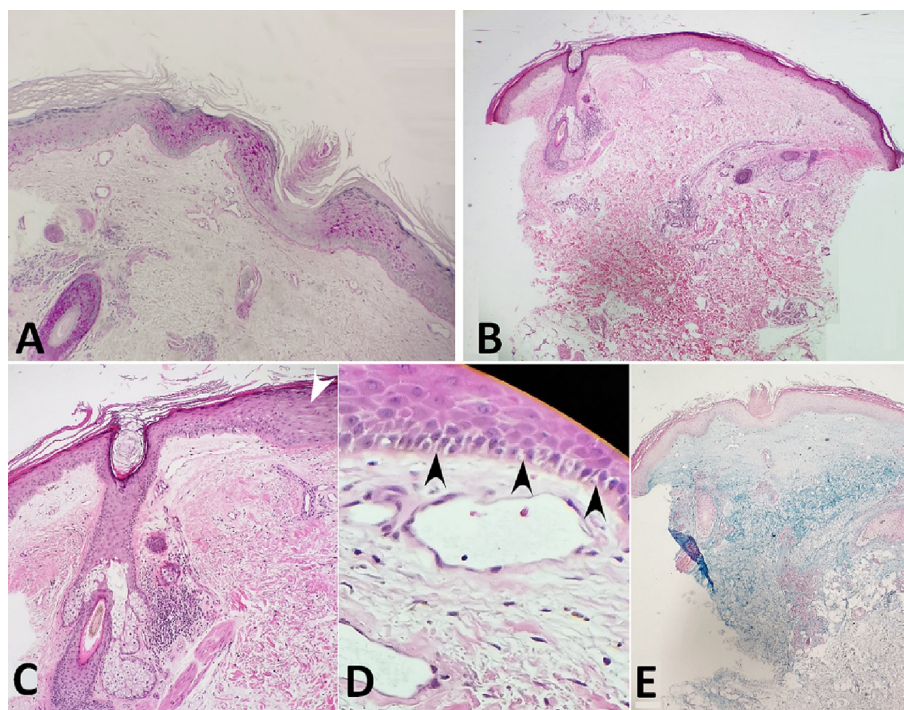


Fig. 2. Histopathological examination from skin biopsy showing (A) thickened basement membrane (PAS staining) (B) Vacuolar change in the basal layer with edema in upper dermis (low magnification) (C) Edematous upper dermis with thickened basement membrane (arrowhead) (D) Dilated superficial vessel, perivascular infiltrate with vacuolar change (arrowheads) (E) Alcian b.

has been identified in CADM and is commonly associated with rapidly progressive ILD (RP-ILD). The prevalence of anti-MDA5 antibody is 10–40% in children with JDM [27]. RP-ILD has been reported in juvenile CADM with positive anti-MDA5 antibody [28,29]. Positive ANA (commonly speckled pattern) is present in 50% of juvenile amyopathic DM [2,11].

There are no randomized controlled studies and specific management guidelines for juvenile CADM. Treatment usually targets the systems involved and comprises of non-pharmacological and pharmacological approaches. HCQ has been shown to be effective for cutaneous DM in juveniles [30]. Although few cases of juvenile CADM using HCQ were reported, Bradley *et al* indicated that HCQ was commonly used in its initial therapy [19]. Systemic corticosteroid in combination with methotrexate had been shown to result in a satisfactory treatment outcome especially in cases which there was inadequate response to the former [31]. In other instances, methotrexate, a steroid-sparing immunosuppressant, had been used to minimize long term unfavourable effect of steroid [32]. Other immunosuppressants as IV immunoglobulin, azathioprine, MMF, cyclophosphamide, and cyclosporine are commonly prescribed in DM and JDM while they have only been considered in very few juvenile CADM cases which were refractory to corticosteroids [22]. Shahin *et al* had reported that cyclophosphamide (myopathy, ulcer) and rituximab (cardiac and bulbar involvement) resulted in sustained improvement in both DM and JDM [33].

In conclusion, we report a rare case of juvenile CADM in a young girl which did not evolve into JDM after 3 years of follow-up. Prolonged follow up is needed to effectively manage any possible complications.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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