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## Case report

### Improvement of nailfold capillary microangiopathy after immunosuppressant therapy in a child with clinically amyopathic juvenile dermatomyositis



### Melhoria na microangiopatia capilar periungueal após terapia imunossupressora em uma criança com dermatomiosite juvenil clinicamente amiopática

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#### Introduction

Juvenile dermatomyositis (JDM) is a rare disease that belongs to the group of idiopathic inflammatory myopathies.<sup>1</sup> Clinically amyopathic dermatomyositis (CADM) is an even rarer entity in pediatrics, with only 75 cases described in the literature.<sup>2</sup> CADM patients present mild or no muscle involvement and the cutaneous manifestations are indistinguishable from those seen in classical dermatomyositis (DM).<sup>3,4</sup>

Systemic inflammatory vasculopathy is an important characteristic of JDM affecting especially the microcirculation.<sup>5</sup> Nailfold capillaroscopy (NFC) is a non-invasive method that allows the direct visualization of nailfold capillaries.<sup>6</sup> Decreased number of capillary loops (devascularization) associated with enlarged capillaries and branching capillary loops

are the most characteristic findings observed in JDM.<sup>7</sup> In addition, several studies have described an association between NFC abnormalities and JDM severity and activity.<sup>8</sup> To the best of our knowledge, NFC abnormalities have not been systematically studied in CADM. We describe herein the case of a 4-year-old child diagnosed with juvenile CADM with important changes in NFC, whose response to treatment was followed by significant improvement in capillaroscopy abnormalities.

#### Case report

In June 2008, a 4-year-old girl was attended with a four months complaint of malar rash, photosensitivity, and erythematous lesions over the proximal interphalangeal joints, elbows and

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**Table 1 – Sequential capillaroscopic evaluation performed from June 2008 to October 2013 in a patient with Juvenile Amyopathic Dermatomyositis.**

	Capillaroscopy parameters (mean value for ten fingers)				
	Branched capillary loops	Dilated capillary loops <sup>a</sup>	Megacapillary loops <sup>b</sup>	Number of capillary loops/mm	Avascular score <sup>c</sup>
June/2008	0.2	3.6	0.1	5.2	2.0
February/2009	0.0	2.1	0.0	5.7	1.8
November/2009	0.1	1.6	0.0	5.7	1.7
December/2010	0.4	0.5	0.0	8.2	0.2
November/2011	0.0	0.2	0.0	8.7	0.1
November/2012	0.0	0.0	0.0	9.6	0.0
October/2013	0.0	0.0	0.0	9.7	0.0

<sup>a</sup> The three limbs of the capillary loop should be enlarged over 4 times.

<sup>b</sup> The three limbs of the capillary loop should be enlarged over 10 times.

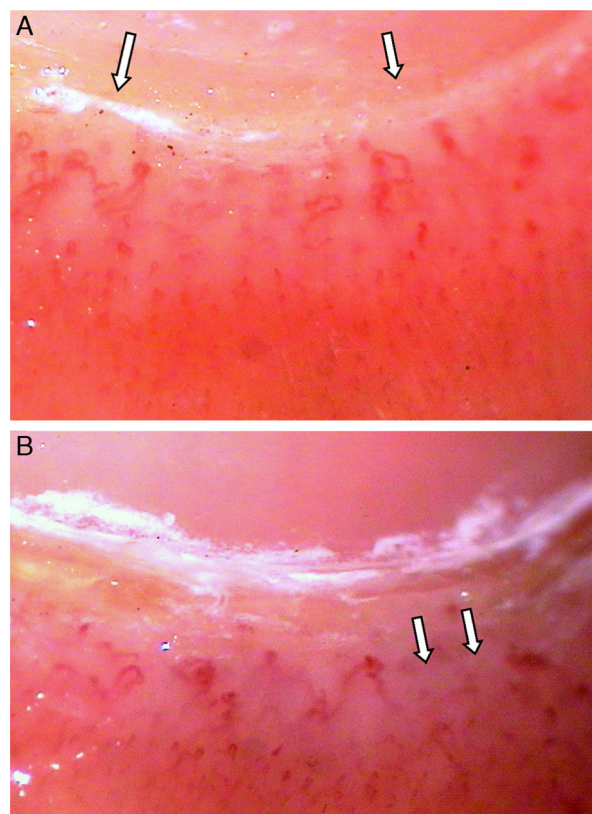
<sup>c</sup> Avascular area is defined as the lack of more than two successive capillary loops; grade 0 (no avascular area); grade 1 (one or two discrete avascular areas); grade 2 (more than two discrete avascular areas); grade 3 (extensive and coalescent avascular areas).

knees, with no complaints regarding muscle strength loss or pain. The Manual Muscle Testing (MMT)<sup>9</sup> score was 80/80, Childhood Myositis Assessment Scale (CMAS)<sup>9</sup> was 48/52, muscular Disease Activity Score (DAS) was 2/11 and cutaneous DAS was 6/9.<sup>10</sup> Laboratory tests showed hemoglobin 13.6 g/L, hematocrit 38.5%, leukocytes 21,000/mm<sup>3</sup> (76% neutrophils, 16% lymphocytes), platelets 289,000/mm<sup>3</sup>, erythrocyte sedimentation rate (ESR) 23 mm/1st hour, C-reactive protein (CRP) undetectable, aldolase 20.8 IU/L (normal < 7.6), creatine kinase (CK) 130 IU/L (normal < 204), lactate dehydrogenase (LDH) 575 IU/L (normal < 480), aspartate aminotransferase (AST) 29 IU/L (normal < 34), alanine aminotransferase (ALT) 14 IU/L (normal < 44), and positive antinuclear antibody (1/640, homogeneous fine speckled pattern). Capillaroscopy was performed in all fingers of both hands using a stereomicroscope (Olympus SZ40) at 10× to 16× magnification under epi-illumination at 45°, analyzing number of capillary/mm, enlarged, giant and branched capillaries, and avascular score.<sup>11</sup> Capillaroscopy showed a scleroderma (SD) pattern, with severe microangiopathy, characterized by decreased number of the capillary loops with intense avascular areas, few branching and frequent dilated capillary loops (Table 1; Fig. 1). Clinically amyopathic dermatomyositis (CADM) diagnosis was established,<sup>3</sup> since Bohan and Peter criteria were not fulfilled.<sup>12</sup> Treatment with prednisolone (0.5 mg/kg/day), hydroxychloroquine (5 mg/kg/day), and photoprotection was then introduced.

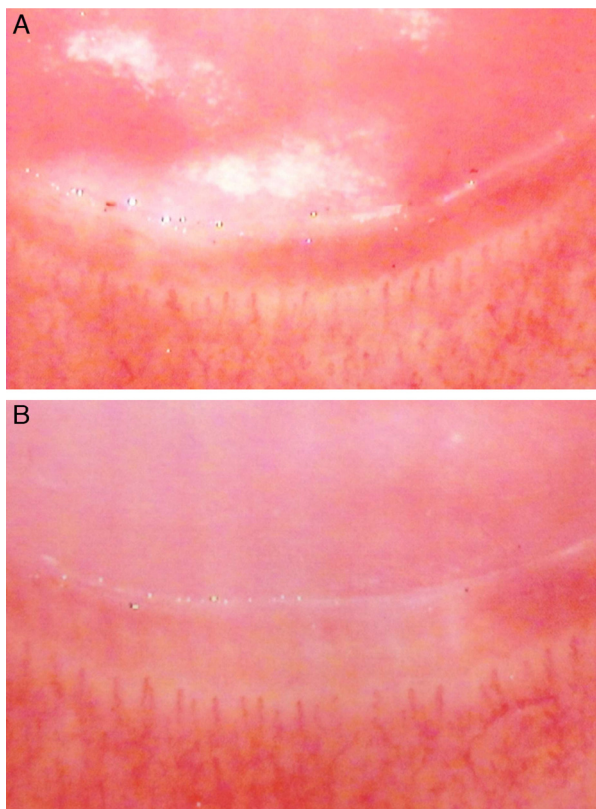
After four months, the patient persisted with disease activity. Muscle magnetic resonance imaging (MRI) and muscle biopsy were normal. Electromyography was not performed. Hydroxychloroquine dose was increased, and methotrexate (0.5 mg/kg/week), folic acid and topical tacrolimus were associated, with partial improvement of symptoms, which allowed gradual reduction of prednisolone dose. In July 2009, the patient started complaining of fatigue and new Gottron's papules and elevation of LDH serum levels (666 IU/L) were observed. Prednisolone and methotrexate doses were increased and thalidomide (50 mg/day) was introduced with satisfactory response. In October 2009, the patient was considered in clinical remission, with MMT 80/80, CMAS 48/52, muscular DAS 1/11, cutaneous DAS 0/9, normal ESR and CRP, aldolase 8.7 IU/L, CK 64 IU/L, LDH 524 IU/L, AST 22 IU/L, and ALT 18 IU/L. Capillaroscopy presented slight improvement. At this

moment, hydroxychloroquine was discontinued, followed by withdrawal of topical tacrolimus (February 2010), prednisolone (April 2010), methotrexate (December 2010), and thalidomide (July 2011).

At her last appointment (October 2013), the patient remained on remission, MMT 80/80, CMAS 51/52, muscular DAS 0/11, cutaneous DAS 0/9, normal ESR and CRP, aldolase 5.1 IU/L, CK 115 IU/L, LDH 400 IU/L, AST 20 IU/L, and



**Fig. 1 – Capillaroscopy (June, 2008). Nailfold capillaroscopy showing presence of dilated and branched capillaries (arrows) (Fig. 1A), and avascular areas (Fig. 1B) (arrows) in the second and fourth digit from the left hand respectively (15× magnification).**



**Fig. 2 – Capillaroscopy (October, 2013). Nailfold capillaroscopy showing a normal pattern, with a normal number of capillaries/mm, no dilated or megacapillaries and revascularization of avascular areas in the second and fourth digit from the left hand respectively (15× magnification) (Fig. 2A and B).**

ALT 14 IU/L. Capillaroscopy was normal, showing significant improvement in the microangiopathy, normal number of capillaries/mm, no avascular areas and no branching or dilated capillary loops (Table 1; Fig. 2).

## Discussion

This is the first report on the presence of exuberant peripheral microangiopathy evaluated by NFC in a child with CADM, followed by a progressive and significant improvement of NFC changes after successful immunosuppressive treatment.

Although there are not studies reporting the dynamic nature of NFC microangiopathic abnormalities (dilated capillary loops, megacapillaries and avascular areas) and its correlation with disease activity in CADM patients, as described in the case presented herein, this aspect has been observed in several studies including classical JDM.<sup>7,8</sup> Capillaroscopy was evaluated in 61 JDM children over 36 months. The improvement in the number of loops/mm was associated with less intense cutaneous activity and monocyclic disease course. On the other hand, polycyclic disease was associated with maintenance of cutaneous activity and persistent capillaroscopy changes. There was no correlation between NFC and muscle disease activity, suggesting that there are different

mechanisms underlying the pathogenesis of skin and muscle in JDM vasculopathy.<sup>13</sup> Although NFC abnormalities are not included in JDM classification criteria,<sup>12</sup> they seem to reflect systemic vasculopathy, and some authors suggest its inclusion among classification criteria for JDM.<sup>14</sup> Since CADM could be considered part of the spectrum of JDM, it could be assumed that both situations share the same NFC behavior.

In the present case, the patient was diagnosed as CADM, most specifically the subphenotype denominated juvenile hypomyopathic dermatomyositis (HDM), which designation is applied for patients with cutaneous DM and no clinical evidence of muscle disease (*i.e.* weakness), whose sub-clinical evidence of myositis upon laboratory (*e.g.* muscle enzymes), electrophysiological, and/or radiological evaluation is found during investigation.<sup>3,4</sup> In fact, she presented major skin disease manifestations associated with slight increased muscle enzymes (aldolase and LDH), but without muscle complaints or weakness. Muscular activity scores were considered as within the normal ranges.<sup>15</sup> The small decrease in CMAS observed in this patient at disease presentation may be attributed to her early age and lack of cooperation in carrying out some of the exercises required. The normal results of MRI and muscle biopsy could be partially affected by the low-dose corticosteroid use, since this therapy had been initiated four months before these tests were performed.

In a review describing 68 cases of juvenile CADM, 56% was classified as amyopathic DM (ADM), 18% as HDM and 26% progressed to classical JDM after a median follow up of 1.9 years. However, it was not possible to determine the parameters that could predict the outcome of patients with CADM to the classic form of JDM. Calcinosis was present in less than 5% of the cases and no children had cutaneous or gastro-intestinal vasculitis, pulmonary infarction, interstitial pneumonitis or malignancy, which suggests a good prognosis for this variant of JDM.<sup>2</sup>

The best therapeutic option in CADM is still controversial, since there are no randomized studies in this field. Some authors argue that early use of corticosteroids and immunosuppressive drugs could prevent progression to JDM. Alternatively, in a review of juvenile CADM treatment, the authors concluded that only photoprotection, topical medications and oral hydroxychloroquine should be initially used and corticosteroids and immunosuppressant therapy should be reserved for refractory cases.<sup>2,16</sup> Our patient presented severe skin manifestations and the use of concomitant photoprotection, topical therapy, hydroxychloroquine and immunosuppressant drugs was necessary. However, resolution of the skin and capillaroscopic abnormalities was more clearly attained after the introduction of thalidomide. Indeed, the efficacy of thalidomide in the treatment of refractory forms of JDM, as well in CADM, has been previously described.<sup>17</sup>

Due to the dynamic characteristics of NFC changes in JDM compared to other autoimmune rheumatic diseases, NFC seems to be a useful tool for the follow-up and in monitoring treatment response in this group of patients. Although NFC has not been systematically studied in CADM, the present report suggests that NFC can also be used as a convenient prognostic and monitoring parameter for the skin involvement in these patients.

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## Conflicts of interest

The authors declare no conflicts of interest.

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