

## Anti-Mi-2 antibody–associated atypical dermatomyositis with extensive subcutaneous calcinosis

Dear Editor,

Calcinosis cutis is frequently found in juvenile dermatomyositis but is uncommon in adults.<sup>1</sup> Anti-Mi-2 antibody is typically not linked to calcinosis,<sup>2</sup> but rather to pathognomonic skin lesions of dermatomyositis such as Gottron's sign and Gottron's papules.<sup>3</sup> We report a case of 38-year-old woman, who tested positive for anti-Mi-2 antibodies and developed skin nodules with calcinosis. However, she did not exhibit most of the typical skin manifestations of dermatomyositis usually seen in such cases.

A 38-year-old woman was diagnosed with dermatomyositis twelve years ago based on clinical findings, histopathological findings of skin and muscles, and elevated muscle enzymes. Her autoantibody profile at the time was not recorded. She presented with multiple, firm nodules over the arms, lateral

hips and thighs of four years duration. The nodules started over the thighs, gradually enlarged in size, became painful and many exuded a calcium-like white chalky material. She denied any inciting trauma. She had been on low-dose oral prednisolone for twelve years before being started on mycophenolate mofetil 2 gm since the appearance of the skin nodules. She has also been on alendronate 70 mg weekly for one year and on diltiazem 60 mg daily for two months but this failed to prevent the progression of lesions.

Physical examination revealed confluent hyperpigmentation over the face and upper chest with induration of skin over forearms and legs, and multiple hard, hyperpigmented nodules over the arms, thighs, upper chest and iliac crest, some of which exuded chalky white material [Figures 1a and 1b].



**Figure 1:** (a) Confluent hyperpigmented macules over the face and sides of the neck, (b) Multiple hyperpigmented nodules over the thigh, with a few showing central openings.

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Laboratory studies revealed elevated levels of creatine phosphokinase (660 IU/L), serum aspartate aminotransferase (41 IU/L) and lactate dehydrogenase (691 IU/L). Serum calcium, inorganic phosphate, alkaline phosphatase, calcium-phosphate product (33.8 mg/dL), parathyroid hormone, vitamin D and renal function were all within normal limits. Antinuclear antibody profile was negative. Myositis-specific and associated antibody profile by immunoblot were strongly positive for anti-Mi-2 antibody (+++) and only borderline for anti-MDA5 (anti-melanoma differentiation-associated gene 5) and anti-PM-Scl 70 antibodies.

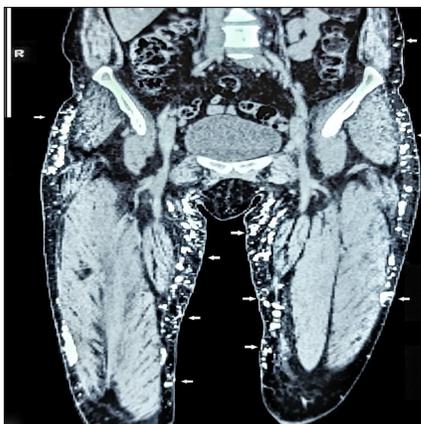
X-ray of indurated areas and computerized tomography (CT) scan identified symmetrical coarse calcification in the subcutaneous fat overlying the arms, upper chest, abdominal wall, and thighs, as well as diffuse atrophy of latissimus dorsi and gluteus maximus bilaterally with normal intra-abdominal viscera [Figures 2a, 2b and 3a–3c]. Histopathology of nodule showed homogenization of collagen in dermis without interface changes suggestive of scleroderma and calcification of the subcutis with foreign body cell reaction. Fourier transform infrared spectroscopy analysis (FTIR Analysis) of the extruded chalky material showed calcium hydroxyapatite.



**Figure 2a:** X-ray showing multiple calcifications (white arrows) over the right arm.



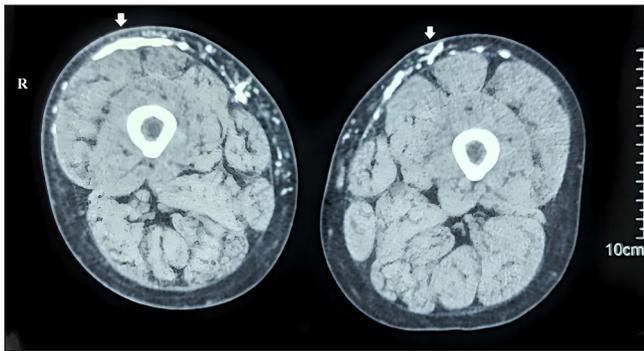
**Figure 2b:** X-ray showing multiple calcifications (white arrows) over both thighs.



**Figure 3a:** CT scan: Coronal section showing coarse subcutaneous calcifications in flanks and thighs (white arrows).



**Figure 3b:** CT scan: Axial section showing calcification (white arrows) in subcutis of upper thighs.



**Figure 3c:** CT Scan: Axial section showing calcification (white arrows) in subcutis of lower thighs.

Dermatomyositis (DM) is an idiopathic inflammatory myopathy characterized by heliotrope rash, Gottron’s papules, photo-distributed erythema, poikiloderma, periungual telangiectasia, and alopecia.<sup>1</sup> Calcinosis is a frequent complication of dermatomyositis that affects up to 40% of patients with juvenile dermatomyositis (JDM).<sup>1,4</sup> However, with a prevalence of 20%, it is only about half as prevalent as in adults and usually develops later in the course of the disease.<sup>2,5</sup>

Calcinosis in dermatomyositis can present as small superficial plaques or nodules on the skin and around joints (superficial calcaneal), deeper nodules in the dermis, subcutis or muscles (deep calcaneal), and as deposits along myofascial planes (calcinosis universalis), or as a generalised form covering all surfaces with joint contractures and immobility (exoskeleton).<sup>4,6</sup>

Calcinosis in adults often presents as firm, yellow or flesh-coloured dermal or subcutaneous papules or nodules over elbows, knees, buttocks and hands (areas of repeated microtrauma). Calcinosis associated with dermatomyositis

is most commonly found in the extremities and trunk, but it can occur anywhere on the body.<sup>4,5</sup> The distribution of dermatomyositis-associated calcinosis differs from that of systemic sclerosis in that it prominently affects both the trunk and the extremities. Extrusion of these nodules through the skin can occur and may cause secondary infection.<sup>5</sup> Muscle calcification is generally asymptomatic and can only be detected radiologically.<sup>1</sup>

Each myositis-specific antibody is linked to a distinct clinical phenotype, with anti-NXP2, anti-Ro-52 and anti-MDA-5 autoantibodies most closely linked to calcinosis in both adult dermatomyositis and juvenile dermatomyositis.<sup>2,4</sup> Anti-Mi-2 antibodies are highly specific for dermatomyositis, with no data correlating antibody titre with disease activity (sensitivity: 4.8–28.1%, specificity: 98.7–99.6%).<sup>3,7</sup> Anti-Mi-2 is significantly associated with typical dermatomyositis skin lesions such as heliotrope rash, Gottron’s papules, V-sign and shawl-sign rashes, and cuticular overgrowth,<sup>3</sup> but not with calcinosis in adult or juvenile dermatomyositis.<sup>2</sup>

This patient lacked most of the typical skin lesions despite having anti-Mi-2 antibodies, which differentiates this case from previous reports. The present case and previous reports of adult dermatomyositis with extensive calcinosis successfully treated with various treatment modalities have been summarized in Table 1. No known association has been reported so far between calcinosis and anti-Mi2-associated dermatomyositis in children or adults.<sup>2,3</sup> The present case shows that patients with anti-Mi-2 antibodies may rarely present with skin findings other than those classically described.

**Table 1: Comparison of present case with previous cases of adult DM with extensive calcinosis successfully treated with various treatment modalities**

Cases	Age and gender	Site of calcinosis	Skin findings	Myositis-specific antibody (MSA)	Treatment given
Present case	38, Female	Arms, upper chest, abdominal wall and thighs	Hyperpigmentation over face and chest	Anti Mi-2	None started on any specific treatment
Vinen <i>et al.</i> , <sup>8</sup> 2000	20, Male	Proximal limbs and trunk	Not mentioned	Not mentioned	Diltiazem
Sultan-Bichat <i>et al.</i> , <sup>9</sup> 2012	46, Male	Left thumb, right knee	Not mentioned	Not mentioned	Extracorporeal shock-wave lithotripsy
Garel <i>et al.</i> , <sup>10</sup> 2015	49, Female	Arm, abdomen	Heliotrope rash, Gottron’s papules	Anti-NXP-2	Intravenous immunoglobulin
Del Barrio-Díaz <i>et al.</i> , <sup>11</sup> 2016	65, Female	Trunk, elbows, knees	Not mentioned	Not mentioned	Topical sodium metabisulfite
Fodil <i>et al.</i> , <sup>12</sup> 2016	48, Male	Proximal limbs, abdomen	Heliotrope rash, v-sign, shawl sign, gottron papules	Anti-NXP2	Zolendronate
Goossens <i>et al.</i> , <sup>13</sup> 2017	44, Female	Forearms, elbow, hips, back	Not mentioned	Anti-NXP2	Intralesional sodium thiosulfate
Xie <i>et al.</i> , <sup>14</sup> 2020	24, Female	Upper arms and legs	Heliotrope rash, v-sign, shawl sign, gottron papules	Anti-SAE	Adalimumab
Shneyderman <i>et al.</i> , <sup>15</sup> 2021	50, Female	Neck, arm, lower back, abdomen	Heliotrope rash, Gottron’s papules	Anti-TIF-1γ	Tofacitinib

Anti-NXP-2: Anti-nuclear matrix protein 2, Anti-SAE: Small ubiquitin-like modifier-activating enzyme, Anti-TIF-1γ: Transcription intermediary factor 1-gamma

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent.

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There are no conflicts of interest.

**Use of artificial intelligence (AI)-assisted technology for manuscript preparation**

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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