



Case Report

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Calcinosis cutis universalis in adult dermatomyositis

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Abstract

Introduction: Characteristic of juvenile dermatomyositis, calcinosis cutis remains rare on adults and the diffuse form (calcinosis cutis universalis) is exceptional. We report two observations of calcinosis cutis universalis in adult dermatomyositis. **Observations:** Two women aged 29 and 24 years respectively, diagnosed with primitive dermatomyositis according to the criteria of Tanimoto and al. and the European neuromuscular centre, developed after 2 years and 16 months of the beginning of the disease a calcinosis cutis universalis confirmed by radiological explorations and biopsy. They were treated by Cochlincine and Diltiazem with relative stabilization. **Conclusion:** As rare as it is, calcinosis cutis universalis is an entity which deserves to be well-known during adult dermatomyositis in order to ensure an adequate and fast treatment especially with the possible risk, recently proven, of malignancy arising from this dystrophic calcifications.

Keywords: Dermatomyositis, Calcinosis cutis universalis.

INTRODUCTION

Dermatomyositis (DM) is an inflammatory, chronic, nonsuppurant, immune disorder associating primitive inflammatory myopathy, myogenic syndrome, and characteristic cutaneous signs. It's a rare disease: incidence estimated at 2-8 cases/million inhabitants and is particularly common in women with two frequency peaks: the first during infancy (5-14 years) and the second between 45-65 years^[1]. Its diagnosis is based on the criteria of Tanimoto et al. established since 1995 and more recently the criteria of the European Neuromuscular Centre (ENMC) which offer a more rigorous approach to the diagnosis of these diseases^[2].

The occurrence of subcutaneous calcinosis (SCC) during dermatomyositis is a serious complication. Particularly frequent in DM of the child, it's rare in adults and diffuse forms called calcinosis cutis universalis are exceptional^[3-5].

Through two cases of diffuse SCC occurring during DM in adults, we expose the different aspects: clinical, pathogenic, therapeutic, and evolutive of this rare disease.

CASE REPORT 1

N.C. is a Tunisian female with known DM diagnosed at the age of 29 years. Diagnosis was based on the association of a bilateral and symmetrical proximal muscle weakness with typical cutaneous lesions of type: heliotrope rash, Shawl sign, Gottron's papules and Gottron's sign. The laboratory examinations showed an erythrocyte sedimentation rate at 100 mmH1 and a major elevation of muscle enzymes: Creatinine Phosphokinase (CPK) at 3618 IU/l and lactic dehydrogenase (LDH) at 1323 IU/l. Electromyogram (EMG) objectified proximal and distal myogenic changes in the four limbs. The antinuclear antibodies were positive anti-Jo-1 antibodies were positive at 1/800.

Systemic manifestations consisted of pharyngeal muscles' involvement and diffuse interstitial lung disease. The investigations for an underlying cancer were negative.

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The patient was treated with oral Prednisone at an initial dose of 1.5 mg/kg/day, followed by a gradual degression and Azathioprine at a dose of 2mg/kg/day with resuscitation in intensive care unit for the specific pharyngeal damage. The outcome was favorable with disappearance of skin lesions, recovery of muscle weakness, and complete normalization of her laboratory values.

She was hospitalized two years later for indurated and infiltrated cutaneous plaques involving the two thighs, two buttocks and left arm (**Figure 1**). These plaques were erythematous and painful with a feeling of stony armor on palpation. Both standard radiographs and CT-scans with the three-dimensional reconstruction showed images of thin, reticulate and superficial calcifications in the roots of limbs, hips and abdomen (**Figures 2, 3 and 4**).

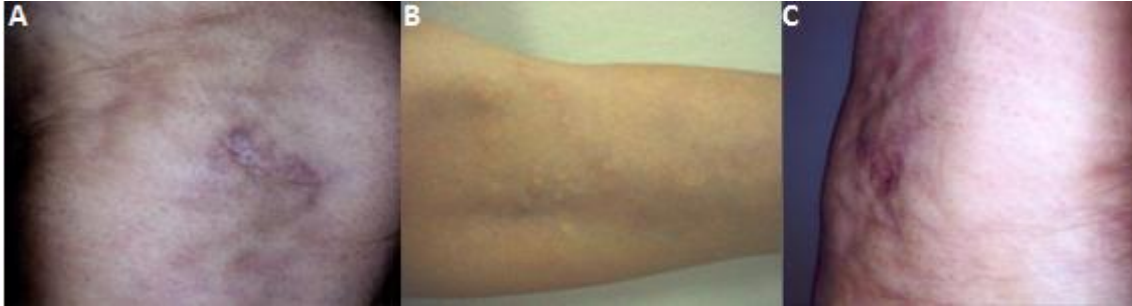


Figure 1: Clinical aspects of SCC in the left buttock (A), the left arm (B) and the root of the right lower limb (C)

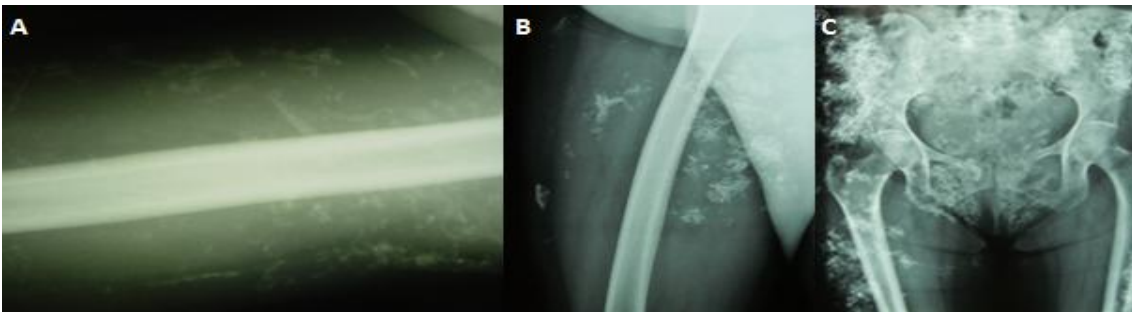


Figure 2: Standard x-rays showing thin and diffuse SCC in the left arm (A), right thigh (B) and abdominal wall (C)



Figure 3: CT-scan of the left arm in coronal sections (A and B) and in sagittal reconstruction (C) showing extended SCC



Figure 4: CT-scan with three-dimensional reconstruction showing diffuse subcutaneous calcifications in the left arm (A) and right thigh (B and C)

The biopsy confirmed the diagnosis of subcutaneous calcinosis by demonstrating the presence of dense fibrosis with multiple calcifications reaching the hypoderm.

The patient was treated with Colchicine (1mg/day) and Diltiazem (120 mg/day) in addition to her maintenance treatment of DM.

The evolution was marked by the relative regression of the SCC (disappearance of clinical signs, radiological stabilization, and absence of complications). After eight years of this episode, the evolution is still stationary.

CASE REPORT 2

B.H, a Tunisian female aged 24, was initially admitted for fever, arthralgia, and diffuse myalgia progressively evolving towards a functional impotence of the four limbs. Physical examination noted a fever at 38.5 °C, myalgia caused by palpation of muscle, bilateral and symmetrical distal polyarthritis involving peripheral joints, bilateral symmetrical and predominantly proximal muscle deficit of the four limbs, periorbital erythroedema and Gottron's papules in both hands.

Laboratory tests showed a high erythrocyte sedimentation rate at 84 mmH1, elevated muscle enzymes with CPK at 1342 IU/l and LDH at 1622 IU/l, positive antinuclear antibodies, and positive anti-JO-1 antibodies at 1/1200.

The EMG objectified pure myogenic impairment. Investigations for an underlying malignancy were negative and no systemic visceral involvement was noted. The diagnosis of dysimmune primitive DM was retained and the patient was treated with oral Prednisone at a dose of

1 mg/kg/day, followed by a gradual degression until a maintenance dose of 10 mg/day, the outcome was favorable with disappearance of cutaneous lesions, normalization of muscle enzymes and slow and gradual recovery of muscle strength. She was admitted, 16 months later, for infiltrated and erythematous cutaneous plaques, ecchymotic in places, in both arms and left buttock.

The standard radiographs found heterogeneous, linear, and disseminated opacities in the pelvis and the arms in favor of the diagnosis of diffuse SCC.

The patient was treated with Diltiazem (180mg/day) and Colchicine (1mg/day) in addition to her corticosteroid treatment. The evolution was marked by the incomplete regression of clinically palpated indurations with asymmetric retraction of the left brachial and gluteal muscles (**Figure 5**) and compensatory hypertrophy of the right triceps. A few months later, other asymptomatic localizations of calcinosis have been revealed by systematic radiographic exams (forearms, thighs and abdomen).



Figure 5: Sequelae of SCC: cutaneo-muscular retractions at the left buttock (A), abdominal wall (B) and root of the right lower limb (C)

DISCUSSION

SCC is a rare complication in DM of the adult; it is mainly observed in children where it can complicate up to 70% of juvenile dermatomyositis [3] thus making DM the leading cause of diffuse calcinosis of the child.

In adults, the incidence of SCC in DM does not exceed 15% [3] and the diffuse forms (calcinosis cutis universalis) are exceptional [4,5].

Its pathogenesis is still poorly understood. These are dystrophic calcifications caused by a calciphylactic tissue alteration involving several hypothetical mechanisms: alkalization of the local pH due to inflammation, local release of mucopolysaccharides, minimal and repetitive infarcts as well as micro thrombosis consequent of the underlying vasculitis [6].

All these factors are promoted by the diagnostic and therapeutic delay of DM or the use of low doses of steroids.

Recently, it has been shown that subjects having DM with anti-p140 autoantibodies are significantly more likely to develop secondary SCC than those without these autoantibodies: $p < 0.005$ and odds ratio at 7 [7]. Similarly, the association with an HLA DRB1*08 allele is a predictive factor of SCC during DM [7].

In the majority of cases, SCC is diagnosed in patients already known to have DM; the delay varies from 6 months to 7 years but in a few cases the two conditions are diagnosed concomitantly [4]. The onset is classically insidious and the calcinosis often remains asymptomatic and would be discovered fortuitously during radiological examination.

Otherwise, it may be pain of a limb segment or soft tissue indurations [4]. Clinical examination notes the presence of superficial or deep subcutaneous nodules or plaques of varying sizes, irregular, painful,

and whitish or yellowish-white in color. The calcium deposits extend gradually causing a stony subcutaneous shielding of the affected limbs and more rarely of the abdominal or thoracic wall. The local inflammation accompanying these calcium deposits confers to the SCC its painful character at the moment of flare-ups, and explains the fever and the local inflammatory signs. More rarely cutaneous necrosis and/or hemorrhagic phlyctenules may be associated indicating an underlying cutaneous vasculitis.

The fistulization of these calcium concretions leads to the exteriorization of a whitish and chalky liquid and may give way to secondary cutaneous ulcerations that slowly heal. These lesions may be complicated by superinfections and sometimes even by true cellulitis [8]. The voluminous concretions are accompanied by an important muscular and cutaneous damage explaining the sequellar musculo-tendinous retractions [4,9].

The diagnosis is easy and based on medical imaging, in particular standard x-rays, computed tomography and magnetic resonance imaging. The 99m Technetium-pyrophosphate scintigraphy is less used but allows the early detection of these SCCs [4].

The use of biopsy is exceptional in this context; the histological examination shows a granular deposition of crystals of apatite or hydroxyapatite surrounded by a chronic inflammatory reaction of the type "foreign body reaction" and fibrosis [4,8]. The phosphocalcic balance is still normal during calcinosis of DM.

The differential diagnosis of these SCC includes diffuse calcinosis of scleroderma, systemic lupus or hyperparathyroidism [10,11] as well as Inlan tumoral calcinosis, myositis ossificans progressiva, and metastatic calcifications especially for localized forms of SCC. In DM, subcutaneous calcinosis doesn't affect the viscera and is independent of the skeleton, which distinguishes it from myositis ossificans and metastatic calcifications [4]. The treatment of SCC remains disappointing

in the absence of effective etiological treatment. The proposed molecules are Steroids, Colchicine, Diltiazem, Warfarin and Probenecide [2,12-14]. More interesting results are obtained with bisphosphonates and cortisone assaults particularly in juvenile DM with the possibility of complete regression of SCC [15]. Intra-lesional corticosteroids were also successfully used in localized forms of SCC [16] as well as Thalidomide in highly inflammatory forms [17].

Physiotherapy [4] and radiofrequency may be prescribed in addition to medical treatment. Recently, extracorporeal lithotripsy was very effective especially in radiopaque, ulcerated and small SCC forms [18]. It has in addition a demonstrated analgesic effect.

Surgery is indicated for pseudo-tumoral forms of SCC or if functional impairment is important. However, very exceptional spontaneous remissions have been reported [4].

The most classic complications of these calcifications are fistulization and superinfection. In the long term, musculo-tendinous retractions are very disabling [4,9]. Although very rare, malignant degeneration remains possible: indeed some observations of osteosarcomatous degeneration have been reported since 1981 [19] as well as two cases of lymphomatous B transformation [20].

CONCLUSION

In adult dermatomyositis, diffuse calcinosis cutis universalis remains an exceptional complication. It is characterized by an unexplained pathogenesis and an unfavorable evolution in the absence of an effective etiological treatment. Its functional impact is sometimes very disabling, which explains the importance of the early diagnosis and the rapid systemic corticosteroid therapy. Close monitoring is also justified in view of the potential risk, currently well documented, of malignant transformation of these calcifications.

Conflicts of Interest: No conflicts.

Authors contributions: Drafting the article: Salem Bouomrani, revising it: Maher Beji, all authors had participated in the management of this case. All authors read and approved the final version of the manuscript.

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