Anti-MDA5–Positive Dermatomyositis: A Description of the Cutaneous and Systemic Manifestations in 2 Cases☆

Dermatomiositis anti-MDA-5 positivas. Descripción de clínica cutánea y sistémica a propósito de dos casos

To the Editor:

Since the initial description of antibodies against melanoma differentiation-associated protein 5 (anti-MDA-5–CADM-140 antibodies) in 2004,[1] their presence has been linked to amyopathic dermatomyositis (DM)[2] associated with rapidly progressive interstitial lung disease.[3,4] Single case reports and case series have provided evidence that, in addition to the presence of these antibodies, these diagnoses share clinical features as well as laboratory and radiologic findings that distinguish them from classical forms of DM.

Our first patient was a 49-year-old man diagnosed with DM by cutaneous biopsy from the dorsal surface of the hand and the trunk (Fig. 1) in the context of edema, eyelid erythema, and arthritis. Laboratory findings included an erythrocyte sedimentation rate of 64 mm/h, a ferritin level of 609 ng/mL, and aspartate transaminase and alanine transaminase levels both of 107 U/L. On diagnosis of amyopathic DM, we started treatment with oral prednisone (1 mg/kg/d) plus weekly doses of methotrexate (10 mg). When painful ulcers developed on the palmar surfaces of the fingers (Fig. 2), plantar surfaces of the feet, and the trunk, bosentan (62.5 mg/12 h) and cyclophosphamide (1000 mg/cycle) were started. After the second cycle the patient was admitted for sudden dyspnea and suspicion of interstitial pneumonia related to immunosuppression. A chest computed tomography scan showed dense subpleural reticulation in both lung fields. The patient's condition worsened in spite of antibiotic treatment and admission to the intensive care unit under mechanical ventilation. A rash developed and was biopsied. Histology showed extensive epidermal necrosis, leading to suspicion of toxic epidermal necrolysis. The patient was transferred to the burns unit of Hospital Universitario de la Paz. The skin condition resolved with administration of immunoglobulins, but the respiratory symptoms continued to worsen. Interstitial lung disease due to amyopathic DM was suspected. We started treatment with rituximab and plasmapheresis. A broader immunologic study (immunoblotting) confirmed the presence of anti-MDA-5 antibodies and the absence of transcriptional intermediary factor 1 autoantibodies (anti-TIF-1γ). The patient died from respiratory failure in spite of all measures.

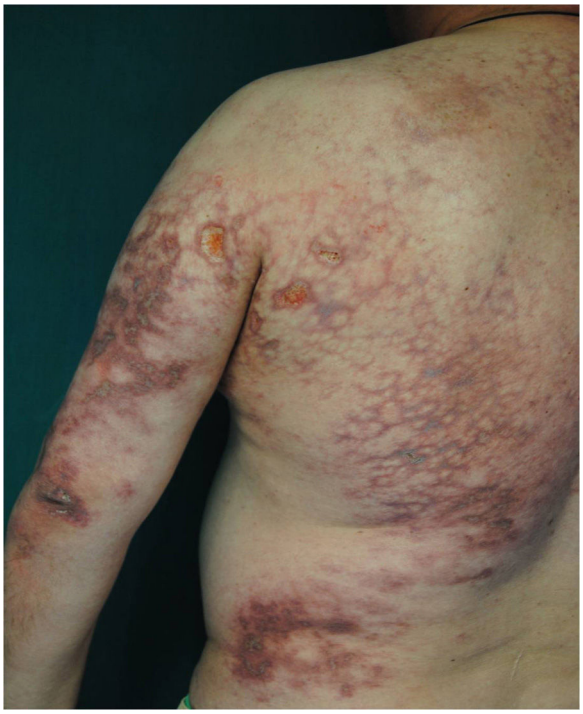

Figure 1 Ulcers, crusts, and multiple chylous lesions in the first patient.

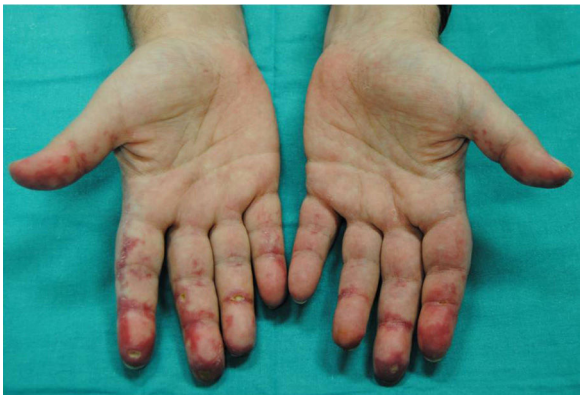

Figure 2 Ulcers on the palms and palmar surfaces of fingers in the first patient.

The second patient was a 31-year-old woman admitted with fever, dyspnea, and arthritic joint pain in her hands as well as lesions on her palms (Fig. 3) and elbows. An extensive test battery revealed vacuolar dermatitis at the dermal–epidermal junction, an aspartate transaminase level of 172 U/L, an alanine transaminase level of 109 U/L, elevated ferritin level of 1185 ng/mL, an erythrocyte sedimentation rate of 64 mm/h, an anti-Sjögren's-syndrome-related antigen A antibody level of 103.80 U/mL), and anti-MDA-5 positivity (by immunoblotting). Lung function tests showed restriction with a

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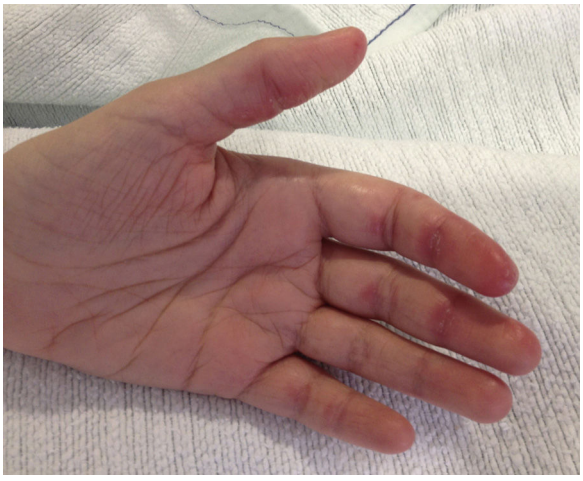

Figure 3 Papules on the palmar surface of the hand of the second patient.

bilateral interstitial pattern in the lower lobes. Treatment with prednisone (1 mg/kg/d), cyclophosphamide in bolus form, and hydroxychloroquine (200 mg/d) was ordered. The patient did not improve on that regimen, so mycophenolate mofetil (2 g/d) was substituted for cyclophosphamide. Slow improvement was noted, and the patient remained stable when the prednisone dosage was reduced to 10 mg/d.

Anti-MDA-5 antibodies have been reported in up to 80% of amyopathic DM cases, and in 60% to 100% of cases of progressive interstitial lung disease in different series.[3–5] The possible presence of skin signs has been noted in this clinical variant in recent years. Radiologic findings different from those usually described for DM have also been noted. Fiorentino et al[3] found that 10 in a series of 77 patients with DM showed anti-MDA-5 positivity and that this finding was significantly associated with hand edema, arthritis, skin ulcers, palmar macules and papules, mechanic's hands, alopecia, panniculitis, elbow erythema, and oral ulcers. However, Labrador-Horrillo et al[6] were unable to confirm those findings in a Mediterranean series, possibly because both studies were retrospective and done in different populations. The discrepancies might also be due to small sample size, since this condition is uncommon and conclusions are difficult to draw. In our series of Caucasian patients, we saw several of the signs Fiorentino et al reported (eg, arthritis, joint pain, hand edema, ulcers, and palmar papules). The lesions in our first patient (Fig. 1) were severe, and the maculopapular lesions both patients had between their fingers were very similar (Figs. 2 and 3). Our second patient's skin signs were milder, but we note that lesions as subtle as palmar macules were key to this diagnosis. The skin signs described by Fiorentino et al have been reported in other cases along with skin ulcers, especially around the nail.[3,7] Narang et al[8] concluded that skin ulcers in DM might be related to anti-MDA-5 antibodies, predict lung involvement, and tend to be caused by vascular compromise. Finding these signs in the context of DM, therefore, can suggest a clinical strategy and call for anti-MDA-5 testing, which is not routinely ordered in most centers.

A noteworthy laboratory result is that the creatine kinase level tends to be normal whereas the components of liver function tests and ferritin tend to be very high,[9] as we observed in our patients. High ferritin levels in DM suggest the likelihood of anti-MDA5 positivity and rapid progression of lung disease.

Radiologic findings also vary. The most common pattern in anti-MDA-5–positive cases is a subpleural ground-glass opacity in lower lung fields.[10]

In summary, we have described 2 cases of anti-MDA-5 positivity in 2 patients with amyopathic DM and characteristic skin signs such as ulcerations around the nails and palmar papules. We have attempted to describe this rare condition, which has certain clinical features that differ from classical DM. Understanding this phenotype will contribute to improved diagnosis and better follow-up of patients with a condition that requires us to watch for possible lung involvement.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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A 65-Year-Old Woman With Multiple Papules in a Unilateral Segmental Distribution☆

Pápulas múltiples con distribución unilateral y segmentaria en mujer de 65 años

To the Editor:

Basaloid follicular hamartoma (BFH) is an uncommon benign neoplasm that may be familial or acquired, generalized or localized. Because the malignant transformation of this tumor to basal cell carcinoma has been reported, it is considered a premalignant lesion.[1]

The characteristic histologic features of BFH are the proliferation of strands of basaloid epithelial cells that originate in the infundibular portion of hair follicles, branch outward, and are surrounded by a loose fibrous stroma. There is usually a clear transition between tumor cells and the adjacent stroma. The tumor cells do not usually display pleomorphism, nuclear atypia, or mitotic activity.[2]

BFH treatments include surgical excision, cryotherapy, laser therapy, topical imiquimod or retinoids, and photodynamic therapy.[3,4] In case of malignant transformation to basal cell carcinoma, surgical removal is the treatment of choice because it has the lowest recurrence and complication rates.

We report the case of a 60-year-old woman who complained of a pruritic lesion on her chest that had grown in recent months. She also reported having had many small lesions on the right side of her chest, pubic area and groin since the age of 30 years, although she never sought care because they were stable and asymptomatic. She did not report hair loss, ptosis, difficulty swallowing, or any other systemic symptoms, and she could not recall similar complaints in relatives. A physical examination revealed multiple skin-colored erythematous papules on the right side of her chest, right breast, pubic area, and groin. The lesions followed Blaschko lines, and some were comedones measuring less than 1 cm in diameter (Fig. 1). Above the right breast was an erythematous plaque measuring 1 cm. The surface was pearly and dermoscopy revealed telangiectases and blue-gray globules.

A biopsy of the supramammary plaque showed nests of basaloid cells that originated in the epidermal basement membrane; they were separated by fragments of healthy epidermis. The periphery was pale, and mitotic figures and apoptotic bodies were numerous. The lesion also contained areas where basaloid cells proliferated, arranged in strands with pilar differentiation, low mitotic activity, and a loose fibroblastic stroma (Fig. 2).

A diagnosis of basal cell carcinoma arising in a BFH was based on the clinical history, physical examination, and biopsy.

This type of acquired, segmental, unilateral BFH can appear at birth or develop in adolescence. Unlike generalized familial forms, this phenotype is not associated with hypotrichosis, cystic fibrosis, or other autoimmune diseases such as myasthenia gravis or systemic lupus erythematosus.[5]

A diagnosis of BFH does not require laboratory tests or imaging. However, a complete medical history and physical examination is essential even though associations between localized BFH and systemic diseases have not been reported. If there is clinical suspicion of autoimmune disease, antinuclear antibody and antiacetylcholine receptor tests should be ordered in addition to any other tests the patient's symptoms suggest.

The main differential diagnoses are infundibulocystic basal cell carcinoma (IBCC)[2] and trichoepithelioma,[5] which are also hair follicle tumors. BFH tends to center around the follicle and involve the interfollicular dermis less than IBCC. Deep infiltration, epidermal ulceration, and rapid growth would suggest IBCC. Some authors nevertheless consider BFH and IBCC to be the same diagnosis because their morphology is so similar and both express cytokeratin 20.[6]

Trichoepithelioma can be distinguished from BFH by the greater stromal cellularity of the former. In addition, a trichoepithelioma shows fissures caused by retraction as the tumor stroma separates from the adjacent dermis.

Because of the coincidence of unilateral BFH and basal cell carcinoma lesions distributed along Blaschko lines in this case, segmental Gorlin syndrome had to be considered in the differential diagnosis.[7] However, such a diagnosis was unlikely because of the absence of a family history of this syndrome or characteristic signs such as the presence of basal cell carcinoma from an early age, keratocystic

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