Dermatomyositis associated with hyponatremia and anasarca

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INTRODUCTION

Dermatomyositis (DM) is a rare inflammatory disorder commonly manifesting with proximal muscle weakness and characteristic skin findings. Classic findings include erythematous papules or macules over the small joints of the hand, periungual changes, pruritic/erythematous skin on areas including the scalp, chest, upper back, and other surfaces, as well as interstitial lung disease. Anasarca[1] and chronic hyponatremia[2] have rarely been reported in cases of DM, and have only been reported separately. Here, we present a case of dermatomyositis associated with both anasarca and hyponatremia.

CASE REPORT

A 60-year-old woman presented to the dermatology clinic with a history of gastroesophageal reflux disease, hypertension, migraines, seizure disorder, Sjogren disease, swelling of the lower portion of the leg, and chronic hyponatremia. At presentation, the patient was found to have dusky red-to-bluish discoloration and swelling of the hands worsened by cold exposure and associated with red papules and macules on fingers, periungual erythema and edema, nail dystrophy, and fissuring of the fingertips (Fig 1). She was initially started on hydroxychloroquine but developed an eczematous total body rash, and it was discontinued. Trialing quinacrine resulted in a similar skin eruption.

Abbreviations used:

DM: dermatomyositis
NXP-2: nuclear matrix protein 2

Erythema and scale developed on the forehead, malar area, and bilateral elbows of the patient several months later. She also complained of scalp pruritus. She was started on methotrexate and worked up to a dose of 25 mg weekly, which improved all symptoms. However, shortly after starting methotrexate, she had an increase in seizure episodes, stomach upset, and diarrhea.

She was switched to mycophenolate mofetil with a maximum dose of 3000 mg/d. However, she soon developed worsening of her hand swelling and erythema as well as swelling of her feet, legs, and abdomen. She was switched back to methotrexate with careful monitoring, and pentoxifylline 400 mg 3 times daily was added for antiinflammatory effect. The patient achieved some improvement in her skin symptoms as well as swelling of her hand and lower portion of the leg while on 20 mg/wk of methotrexate, which she has now been stable on for several years. Due to the patient's cutaneous and systemic response to methotrexate, additional medications for DM were not trialed.

The patient had been followed for chronic hyponatremia (baseline serum sodium of 129 mmol/L) for approximately a decade associated

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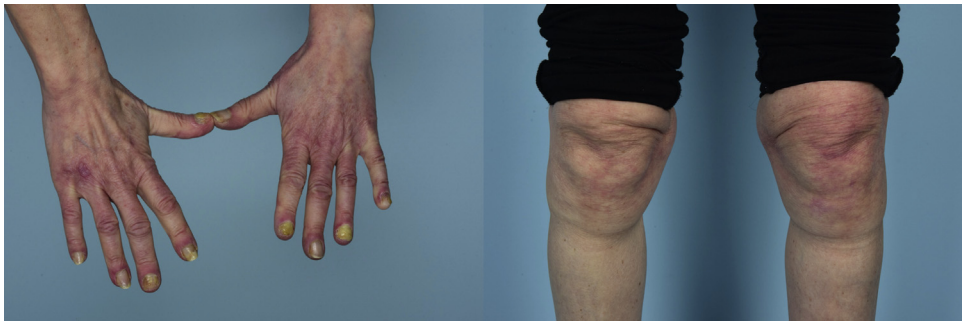

Fig 1. Erythema overlying joints of hand, periungual area, and knees.

with lightheadedness and mild intermittent leg swelling, unresolved with salt tablets. However, after being treated with methotrexate for several years, the patient developed bilateral erythematous leg swelling and was found to be hyponatremic with a serum sodium of 122 mmol/L, down from her baseline hyponatremia of approximately 129 mmol/L. Diffuse anasarca in the patient's superficial subcutaneous fat was also found on abdominal and pelvic computed tomography, which was ordered to evaluate the bilateral lower extremity edema and weight loss (Fig 2). Previously, findings of computed tomography and x-ray of the chest were within normal limits, as was a pelvic ultrasound, colonoscopy, and mammogram.

Values for antidiuretic hormone, serum cortisol, salivary cortisol, serum thyroid-stimulating hormone, urine osmolality, aldosterone, albumin, and renin were within the normal range. Urine osmolality ranged between 119 to 495 mOsm/kg (reference range, 50-1200 mOsm/kg) during this time of more pronounced swelling and hyponatremia below her baseline. Therefore, the typical differential diagnoses for other causes of hyponatremia were largely ruled out, leaving no clear explanation for her clinical findings and serum sodium.

Laboratory studies revealed a high titer of antinuclear antibodies (1:2560), positive findings for SS-A/SS-B; mildly low C4 (16; lower limits of normal, 19), negative myositis antibodies, and a creatine phosphokinase level of 308 U/L (upper limit of normal, 234). Laboratory workup for international normalized ratio, anti−double stranded DNA, anti-C3, and antiribonucleoprotein antibodies, and aldolase levels were normal. Electromyography and muscle magnetic resonance imaging did not show changes of myositis, though the patient did report myalgia. Skin biopsies of the leg (Fig 3) and neck revealed interface dermatitis, spongiosis with a mixed perivascular inflammatory infiltrate, and the neck biopsy also demonstrated an additional follicular infiltrate consisting of neutrophils, lymphocytes, histiocytes, and eosinophils. MxA staining (Fig 3) of both biopsies was diffusely positive, as was expression of interleukin 4 and interleukin 31 (Fig 4). All findings were consistent with a diagnosis of DM in the context of the patient's clinical findings. Spongiotic dermatitis can be seen in DM, and increased MxA distinguishes DM from the spongiosis seen in eczema.[3]

DISCUSSION

Both adult- and juvenile-onset DM with anasarca as well as peripheral limb edema have been reported in the literature,[1] although rarely so, and only included in a handful of case reports. DM is also reported to be associated with hyponatremia in rare cases.[2] DM-associated hyponatremia is a difficult diagnosis, as it can be confused with hyponatremia associated with rhabdomyolysis, especially in the setting of elevated creatine phosphokinase levels.[2] The diagnosis of DM-associated anasarca also often proves difficult for clinicians to make and is frequently only made when other causes of edema have been ruled out. Although the mechanism of edema associated with DM is not well understood, it is thought to be related to increased permeability as a result of immune complex deposition or vascular change.[4] Recognizing generalized or isolated limb edema in the setting of DM is important, as it can be a sign of more severe autoimmune disease requiring prompt treatment with aggressive immunosuppression, which may also be indicated if patients have cutaneous or systemic involvement.[1] Patients in a case series did not show improvement of edema with steroids but did improve with immunosuppressive therapies used to treat DM.[1] Patients with DM-associated hyponatremia are treated for their DM with immunosuppression, while sequelae of hyponatremia are frequently managed with water restriction or other interventions as determined by endocrinology. Hyponatremia should be corrected slowly to avoid central pontine myelinolysis.

In cases of DM presenting with peripheral edema, it may be worthwhile to order a nuclear matrix

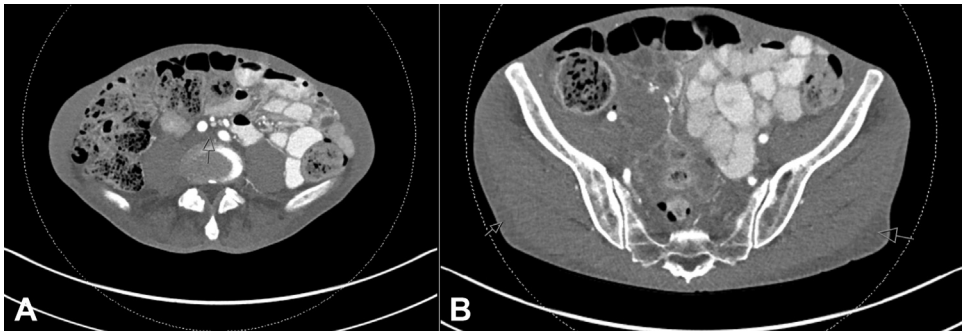

Fig 2. Computed tomography scans of abdomen/pelvis showing (**A**) diffuse subcutaneous anasarca with (**B**) notable mesenteric/retroperitoneal edema.

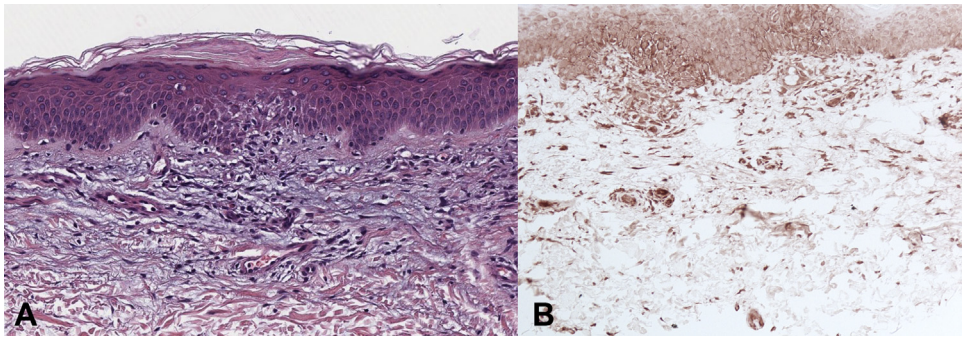

Fig 3. **A**, A skin biopsy of the upper portion of the left thigh demonstrating spongiosis with a mixed perivascular inflammatory infiltrate, focal interface dermatitis, and (**B**) diffusely positive MxA staining. (**A**, Hematoxylin-eosin stain; **B**, MxA stain; original magnifications: **A**, ×150; **B**, ×20.)

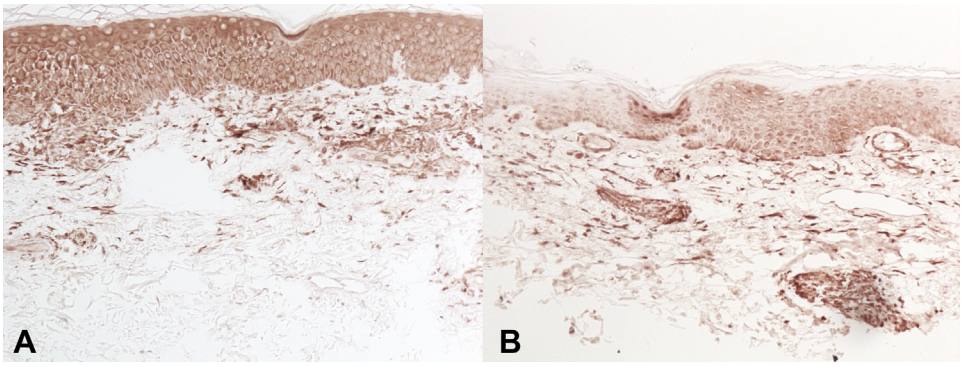

Fig 4. Diffusely positive interleukin 4 (**A**) and interleukin 31 (**B**) staining in the biopsy of the upper portion of the left thigh. (Original magnifications: **A**, ×20; **B**, ×20.)

protein 2 (NXP-2) antibody test, which is often not included in routine myositis panels and may be associated with DM-related anasarca.[5] In fact, patients with DM and a positive anti—NXP-2 antibody test can have a severe disease phenotype characterized by peripheral edema, myopathy, dysphagia,[6] and mild skin involvement, often including erythematous macules and papules over the joints and an erythematous rash over the eyelids. NXP-2's function is related to response to oncogenic signals associated with p53 stimulation.[6] NXP-2 was not included in our patient's initial myositis panel but was negative on a recent panel. However, many patients with DM do not test positive for antibodies on commercial myositis panels.[7]

In conclusion, anasarca and hyponatremia can be rare complications of DM. This phenotype may require immunosuppression with second-line agents and coordination of care with multidisciplinary teams. For some patients, it appears that treating their dermatomyositis with immunosuppressive therapy improves symptoms of edema.[1] It is unclear

whether hyponatremia improves with such therapy. Our patient is chronically hyponatremic with some improvement of her lower extremity swelling, which we believe is associated with DM, on immunosuppressive therapy.

Conflicts of interest

None disclosed.

REFERENCES

1. Chai Y, Bertorini TE, Li YD, Mitchell C, Guan H. Limb edema and anasarca associated with severe dermatomyositis: report of four cases. *Neuromuscul Disord*. 2011;21(6):439-442.
2. Kumar AH, Vikranth V. A rare case of dermatomyositis with hyponatremia. *J Med Sci*. 2015;1(3):58-59.
3. Zeidi M, Chen KL, Patel B, Ravishankar A, Lim R, Werth VP. Increased MxA protein expression and dendritic cells in spongiotic dermatitis differentiates dermatomyositis from eczema in a single-center case-control study. *J Cutan Pathol*. 2021;48(3):364-373.
4. Jung KD, Kim PS, Park HY, et al. Dermatomyositis associated with generalized subcutaneous edema and Evans syndrome. *J Am Acad Dermatol*. 2012;66(1):144-147.
5. Butt Z, Patel L, Das MK, Mecoli CA, Ramji A. NXP-2 positive dermatomyositis: a unique clinical presentation. *Case Rep Rheumatol*. 2017;2017:4817275.
6. Rogers A, Chung L, Li S, Casciola-Rosen L, Fiorentino DF. Cutaneous and systemic findings associated with nuclear matrix protein-2 antibodies in adult dermatomyositis patients. *Arthritis Care Res (Hobobken)*. 2017;69(12):1909-1914.
7. Ravishankar A, Concha JS, Yan D, et al. Accuracy of commercial panels to evaluate myositis autoantibodies: a single-institution perspective. *J Am Acad Dermatol*. 2021;84(2):572-574.