Persistent Panniculitis in Dermatomyositis

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PRACTICE **POINTS**

- Clinical panniculitis is a rare subcutaneous manifestation of dermatomyositis (DM) that dermatologists must consider when evaluating patients with this condition.
- Panniculitis can precede, occur simultaneously with, or develop up to 5 years after onset of DM.
- Many patients suffer from treatment-resistant panniculitis in DM, suggesting that therapeutic management of this condition may require long-term and more aggressive treatment modalities.

To the Editor:

A 62-year-old woman with a history of dermatomyositis (DM) presented to dermatology clinic for evaluation of multiple subcutaneous nodules. Two years prior to the current presentation, the patient was diagnosed by her primary care physician with DM based on clinical presentation. She initially developed body aches, muscle pain, and weakness of the upper extremities, specifically around the shoulders, and later the lower extremities, specifically around the thighs. The initial physical examination revealed pain with movement, tenderness to palpation, and proximal extremity weakness. The patient also noted a 50-lb weight loss. Over the next year, she noted dysphagia and developed multiple subcutaneous nodules on the right arm, chest, and left axilla. Subsequently, she developed a violaceous, hyperpigmented, periorbital rash and erythema of the anterior chest. She did not experience hair loss, oral ulcers, photosensitivity, or joint pain.

Laboratory testing in the months following the initial presentation revealed a creatine phosphokinase level of 436 U/L (reference range, 20–200 U/L), an erythrocyte sedimentation rate of 60 mm/h (reference range, <31 mm/h), and an aldolase level of 10.4 U/L (reference range, 1.0–8.0 U/L). Lactate dehydrogenase and thyroid function tests were within normal limits. Antinuclear antibodies, anti–double-stranded DNA, anti-Smith antibodies, anti-ribonucleoprotein, anti–Jo-1 antibodies, and anti–smooth muscle antibodies all were negative. Total blood complement levels were elevated, but complement C3 and C4 were within normal limits. Imaging demonstrated normal chest radiographs, and a modified barium swallow confirmed swallowing dysfunction. A right quadricep muscle biopsy confirmed the diagnosis of DM. A malignancy work-up including mammography, colonoscopy, and computed tomography of the chest, abdomen, and pelvis was negative aside from nodular opacities in the chest. She was treated with prednisone (60 mg, 0.9 mg/kg) daily and methotrexate (15–20 mg) weekly for several months. While the treatment attenuated the rash and improved weakness, the nodules persisted, prompting a referral to dermatology.

Physical examination at the dermatology clinic demonstrated the persistent subcutaneous nodules were indurated and bilaterally located on the arms, axillae, chest, abdomen, buttocks, and thighs with no pain or erythema (Figure). Laboratory tests demonstrated a normal creatine phosphokinase level, elevated erythrocyte sedimentation rate (70 mm/h), and elevated aldolase level (9.3 U/L). Complement levels were elevated, though complement C3 and C4 remained within normal limits.

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The authors report no conflict of interest.

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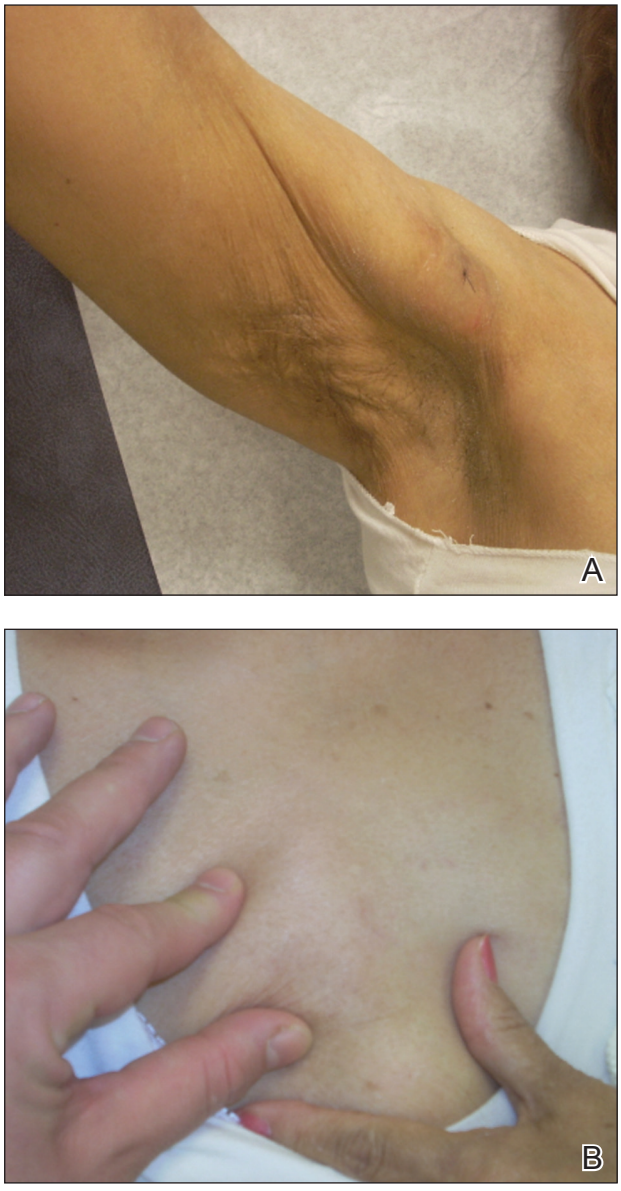

A and B, Indurated subcutaneous nodules on the right axilla and chest consistent with panniculitis.

Histopathology of nodules from the medial right upper arm and left thigh showed lobular panniculitis with fat necrosis, calcification, and interface changes. The patient was treated for several months with daily mycophenolate mofetil (1 g increased to 3 g) and daily hydroxychloroquine (200 mg) without any effect on the nodules.

The histologic features of panniculitis in lupus and DM are similar and include multifocal hyalinization of the subcuticular fat and diffuse lobular infiltrates of mature lymphocytes without nuclear atypia.[1] Though clinical panniculitis is a rare finding in DM, histologic panniculitis is a relatively common finding.[2] Despite the similar histopathology of lupus and DM, the presence of typical DM clinical and laboratory features in our patient (body aches, muscle pain, proximal weakness, cutaneous manifestations, elevated creatine phosphokinase, normal complement C3 and C4) made a diagnosis of DM more likely.

Clinical panniculitis is a rare subcutaneous manifestation of DM with around 50 cases reported in the literature (Table). A PubMed search of articles indexed for MEDLINE was conducted using the terms *dermatomyositis* and *panniculitis* through July 2019. Additionally, a full-text review and search of references within these articles was used to identify all cases of patients presenting with panniculitis in the setting of DM. Exclusion criteria were cases in which another etiology was considered likely (infectious panniculitis and lupus panniculitis) as well as those without an English translation. We identified 43 cases; the average age of the patients was 39.6 years, and 36 (83.7%) of the cases were women. Patients typically presented with persistent, indurated, painful, erythematous, nodular lesions localized to the arms, abdomen, buttocks, and thighs.

While panniculitis has been reported preceding and concurrent with a diagnosis of DM, a number of cases described presentation as late as 5 years following onset of classic DM symptoms.[12,13,31] In some cases (3/43 [7.0%]), panniculitis was the only cutaneous manifestation of DM.[15,33,36] However, it occurred more commonly with other characteristic skin findings, such as heliotrope rash or Gottron sign. Some investigators have recommended that panniculitis be included as a diagnostic feature of DM and that DM be considered in the differential diagnosis in isolated cases of panniculitis.[25,33]

Though it seems panniculitis in DM may correlate with a better prognosis, we identified underlying malignancies in 3 cases. Malignancies associated with panniculitis in DM included ovarian adenocarcinoma, nasopharyngeal carcinoma, and parotid carcinoma, indicating that appropriate cancer screening still is critical in the diagnostic workup.[2,11,22]

A majority of the reported panniculitis cases in DM have responded to treatment with prednisone; however, treatment with prednisone has been more recalcitrant in other cases. Reports of successful additional therapies include methotrexate, cyclosporine, azathioprine, hydroxychloroquine, intravenous immunoglobulin, mepacrine, or a combination of these entities.[19,22] In most cases, improvement of the panniculitis and other DM symptoms occurred simultaneously.[25] It is noteworthy that the muscular symptoms often resolved more rapidly than cutaneous manifestations.[33] Few reported cases (6 including the current case) found a persistent panniculitis despite improvement and remission of the myositis.[3,5,10,11,30]

Our patient was treated with both prednisone and methotrexate for several months, leading to remission of muscular symptoms (along with return to baseline of creatine phosphokinase), yet the panniculitis did not improve. The subcutaneous nodules also did not respond to treatment with mycophenolate mofetil and hydroxychloroquine.

Recent immunohistochemical studies have suggested that panniculitic lesions show better outcomes with immunosuppressive therapy when compared with other DM-related skin lesions.[40] However, this was not the case for our patient, who after months of immunosuppressive therapy showed complete resolution of the periorbital and chest rashes with persistence of multiple indurated subcutaneous nodules.

Our case adds to a number of reports of DM presenting with panniculitis. Our patient fit the classic demographic of previously reported cases, as she was an adult woman without evidence of underlying malignancy; however, our case remains an example of the therapeutic challenge that exists when encountering a persistent, treatment-resistant panniculitis despite resolution of all other features of DM.

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Reported Cases of Dermatomyositis With Panniculitis[a]

Patient	Age, y/ sex	Time of panniculitis onset relative to diagnosis of DM	Location of panniculitis lesions	Other cutaneous manifestations	Treatment	Treatment response	Interval between therapy initiation to final treatment response	Malignancy
1	20/F[3]	19 mo later	Supraclavicular, axillary, inguinal regions; arms	Periorbital erythema, heliotrope rash	Methylprednisolone 1000 mg daily for 3 d, prednisolone 40 mg daily, MTX 10 mg weekly	Panniculitis persisted after 5 mo	-	-
2	10/F[4]	Concurrent	Palm, heel	Reddish scaly rashes on elbows	Prednisolone 2 mg/kg daily, AZA 75 mg daily	Resolved, recurred with steroid taper	3 wk	-
3	49/F[5]	1 y later	Upper limbs, thighs, back, breasts, gluteal region, abdomen	Erythematous papules on the MCP joints; violaceous erythema on the face, cervical region, upper back, and upper limbs	Before panniculitis: pulse methylprednisolone; then prednisone 0.5 mg/kg daily; then pulse cyclophosphamide with corticosteroids; then HCQ; then AZA; after panniculitis: prednisone and chlorambucil, then pulse methylprednisolone and prednisone, then MTX for 5 mo, then prednisone 1 mg/kg daily and chlorambucil	Panniculitis persisted after 1 y	-	-
4	46/F[6]	Concurrent	Thighs, dorsal feet	Reticulated erythema overlying the acral surfaces; thin violaceous plaques on the MCP joints, eyelids, and patellar surface; reticulated ulcerations on the palmar surfaces, extensor surface of the forearms, and distal toes	IV rituximab 1 g every 15 d, IV prednisolone 60 mg daily, IVIG 1 g/kg for 2 consecutive days every 15 d for 24 mo	Resolved	4 mo	-
5	51/F[7]	3.5 mo prior	Right mandible, neck	Gottron papules on the elbows and dorsolateral aspects of the proximal and distal interphalangeal joints, papules overlying both palms	Methylprednisolone 1000 mg daily for 3 d, oral prednisolone 1 mg/kg daily, oral tacrolimus 4 mg daily; then IV cyclophosphamide and IVIG	Dysarthria/muscle weakness persisted and creatine kinase/ ferritin/myoglobin increased, so IV cyclophosphamide and IVIG were given, which led to resolution	-	-
6	66/F[8]	2 mo prior	Limbs, buttock	Nonscarring diffuse alopecia on the scalp	Methylprednisolone 1 g daily for 3 d; then oral prednisolone 1 mg/kg once daily, IV cyclophosphamide15 mg/kg once daily	Improved	-	-
7	15/F[9]	Concurrent	Thighs	Periorbital violaceous erythema and edema, purplish papules over the MCP joints	Prednisolone 1 mg/kg daily, MTX 7.5 mg weekly; then corticosteroid pulse therapy, MTX 25 mg weekly, and cyclosporine 100 mg daily	Cutaneous lesions improved with prednisolone, MTX added for muscle weakness	2 wk	-

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Patient	Age, y/sex	Time of panniculitis onset relative to diagnosis of DM	Location of panniculitis lesions	Other cutaneous manifestations	Treatment	Treatment response	Interval between therapy initiation to final treatment response	Malignancy
8	60/F[10]	2 y later	Thighs, buttocks	DM with typical skin changes	Before panniculitis: prednisone 10 mg twice daily, IVIG 2 g/kg monthly, cyclophosphamide 50 mg daily; after panniculitis: prednisone 25 mg twice daily, cyclophosphamide 50 mg daily, IVIG 2 g/kg monthly	Panniculitis persisted	-	-
9	26/F[11]	26 mo later	Arms, legs, abdomen	Gottron papules, heliotropes	Before panniculitis: chloroquine 250 mg daily, azathioprine 100 mg daily, and prednisolone 30 mg daily); after panniculitis: then colchicine 0.6 mg daily	Panniculitis persisted	-	Nasopharyngeal cancer
10	15/F[12]	5 y later	Proximal upper and lower extremities, back	Cutaneous lesions in the malar region and on dorsal hands	Before panniculitis: IV methylprednisolone 30 mg/kg monthly, MTX 10 mg weekly, folic acid, HCQ 200 mg daily); after panniculitis: 3 boli of IV methylprednisolone 0.5 mg/kg, prednisone 60 mg daily, cyclosporine 150 mg twice daily	Resolved	4 wk	-
11	40/F[13]	5 y later	Axillae, abdomen	Erythema on the eyelids; keratotic erythematous plaques on the elbows, knees and dorsal aspects of the fingers; erythematous lesions on the neck and chest	Before panniculitis: prednisolone 60 mg daily, MTX 4 mg weekly; after panniculitis: cyclosporine 150 mg daily	Improved	-	-
12	55/M[14]	Concurrent	Feet	Livedoid erythematoviolaceous macules on the palmar aspects of some interphalangeal joints with small ulcerated papules; fissured erythematous and edematous plaques on the fingertips, splinter hemorrhages, necrotic plaques and painful ulcerations on the hands and feet	Prednisone and AZA; then cyclophosphamide and IVIG	Patient died due to atrioventricular block	-	-
13	65/F[15]	11 mo prior	Arms, legs	None	Prednisolone with recurrence; then MTX and prednisolone	Improved	-	-
14	63/F[2]	25 mo later	Arms, thighs, buttocks	Periorbital violaceous erythema, lichenoid violaceous papules overlying the knuckles and dorsal hands	Prednisone 20 mg daily, MTX 15 mg weekly, and folic acid (AZA discontinued due to leukopenia, and mycophenolate mofetil discontinued due to generalized morbilliform eruption	Improved	1 mo	Ovarian adenocarcinoma

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Patient	Age, y/sex	Time of panniculitis onset relative to diagnosis of DM	Location of panniculitis lesions	Other cutaneous manifestations	Treatment	Treatment response	Interval between therapy initiation to final treatment response	Malignancy
15	30/F[16]	2 mo later	Upper and lower limbs	Edematous purplish eyelids, patches of alopecia with desquamation on the scalp	Meprednisone 60 mg daily	Resolved	1 wk	-
16	64/F[17]	2 mo later	Elbows, wrists, toes	Erythematous rashes on the arms, trunk, legs, and face	Prednisolone 40 mg daily	Resolved	3 mo	-
17	23/F[18]	Concurrent	Legs	Erythema the over eyebrows and cheeks	Stopped minocycline; then prednisone 40 mg daily and MTX 15 mg weekly	Resolved	9 mo	-
18	73/F[19]	4 mo later	Thighs, upper arms	Erythematous eruption over the central chest, jawline, eyelids, and scalp	Prednisolone 40 mg daily, cyclosporine 100 mg twice daily; then HCQ 200 mg twice daily; then MTX 22.5 mg weekly; then prednisolone, mepacrine 100 mg twice daily	Improved	-	-
19	50/F[19]	2 y later	Arms and legs	Erythematous facial rash, Gottron papules, vasculitic lesions	Before panniculitis: prednisolone 20 mg daily, AZA 100 mg daily, IVIG, MTX, cyclosporine); after panniculitis: mepacrine, HCQ, prednisolone, IVIG weekly for 6 wk	Improved	-	-
20	23/F[20]	Later	Upper limbs	Erythematous violaceous rash on the face, neck, chest and limbs; heliotrope rash; red to violaceous plaques on sun-exposed areas on the dorsum of the fingers and hands; periungual erythema and telangiectasia; diffuse alopecia	-	-	-	-
21	29/F[20]	Concurrent	Fingers, thighs	Erythematous violaceous rash of the face, neck, chest and lower extremities; periungual erythema; digital petechiae	-	-	-	-
22	19/M[21]	15 mo later	Thigh	Violaceous rash on the upper eyelids, sternum, and knuckles	Before panniculitis: prednisone 1 mg/kg daily, AZA 2.5 mg/kg daily, then taper; after panniculitis: prednisone 1 mg/kg daily, AZA 3 mg/kg daily	Resolved	4 wk	
23	35/F[22]	Concurrent	Right arm	Erythematous to violaceous maculopapules on the forehead, periungual erythema	Cyclophosphamide 600 mg monthly for 6 mo, prednisolone 50 mg daily	Improved	-	-

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Patient	Age, y/ sex	Time of panniculitis onset relative to diagnosis of DM	Location of panniculitis lesions	Other cutaneous manifestations	Treatment	Treatment response	Interval between therapy initiation to final treatment response	Malignancy
24	56/F[22]	2 y later	Arms	Facial erythema and edema, heliotrope sign, Gottron sign, periungual erythema	Before panniculitis: prednisolone 30 mg daily; after panniculitis: prednisolone 20 mg daily, AZT 100 mg daily	Improved	-	Parotid carcinoma
25	21/F[23]	6 wk prior	Right lower abdomen, labia majora, inner thigh	Malar rash, violaceous infiltrated plaques on the ears, periungual telangiectasia, heliotrope rash, Gottron papules	Oral prednisolone 25 mg daily, HCQ 200 mg daily; then IV methylprednisolone 60 mg daily for 1 mo; then methylprednisolone 1 g for 3 d, then taper	Patient died 9 mo after disease onset, probably due to complications from gastrointestinal ischemia/perforation	-	-
26	60/F[24]	Concurrent	Arms	Heliotrope periorbital edema; periungual nailfold telangiectasia; Gottron papules; erythema on the face, trunk, and extremities	Methylprednisolone 1000 mg daily for 3 d, prednisolone 60 mg daily, then taper	Resolved	-	-
27	42/F[25]	17 mo later	Arms, thighs, abdomen	Eyelid erythema	Prednisone 1 mg/kg daily, AZA 100 mg daily, HCQ 100 mg twice daily; then prednisone 20 mg daily, MTX 7.5 mg weekly; then prednisone 0.5 mg/kg daily, cyclosporine 100 mg twice daily	Improved, recurred, resolved	-	-
28	80/F[25]	10 mo later	Arms, thighs	Eyelid erythema, erythematous cutaneous lesions on the elbows and knees	Prednisone 1 mg/kg daily, AZA 100 mg daily; then diclofenac 50 mg twice daily; then prednisone 0.5 mg/kg daily; then prednisone 7.5 mg daily	Improved, recurred, resolved	-	-
29	44/F[26]	2.5 mo prior	Shoulders, back, chest, abdomen, buttock, thighs	Diffuse erythematous to violaceous swelling of the face, neck, and shoulder	Prednisolone 120 mg once daily, MTX 7.5 mg weekly, AZT 250 mg weekly, IVIG 25 g 5 times monthly	Resolved	6 mo	-
30	42 /M[27]	1 y prior	Left buttock, left inguinal area	Periorbital erythema and edema; telangiectatic erythema on the cheeks, neck, and forearms; erythematous papules on the hands over the joints	Prednisolone and MTX; then prednisolone 30 mg daily, HCQ 600 mg daily, colchicine 1.8 mg daily, pentoxifylline 1200 mg daily	Improved	-	-
31	14 /M[28]	4 y later	Forearm, thigh, flank	Heliotrope rash, Gottron papules, poikiloderma, dilated nailfold capillaries, photosensitive eruption localized to the face and extensor aspects of the upper extremities	Before panniculitis: HCQ 400 mg daily, prednisone 2.5 mg daily; after panniculitis: prednisone 0.3 mg/kg daily, then taper	Resolved	2 wk	-

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Patient	Age, y/ sex	Time of panniculitis onset relative to diagnosis of DM	Location of panniculitis lesions	Other cutaneous manifestations	Treatment	Treatment response	Interval between therapy initiation to final treatment response	Malignancy
32	54/F[29]	Concurrent	Arms	Periorbital edema; erythema on the arms, face, eyelids, fingers, knees, and thorax; erythematous papules over the MCP joints	Prednisolone 1 mg/kg daily, AZT 2 mg/kg daily	Resolved	-	-
33	57/F[29]	Concurrent	Buttocks, left thigh, sacral region	Facial rash	Methylprednisolone 1 mg/kg daily for 2 wk, then cyclosporine 3 mg/kg daily	Resolved	-	-
34	65/F[30]	Concurrent	Buttocks, thighs, lower right leg	Brownish erythematous lesions with telangiectasia on the neck, back, buttocks, and extensor surfaces of the forearms and lower legs; slightly keratotic erythematous lesions on the elbows, poikilodermatous changes on the neck, upper chest, and back	Prednisolone 60 mg daily, then taper; then methylprednisolone 1000 mg one time, prednisolone 60 mg daily	Panniculitis persisted	-	-
35	42/M[31]	5 y later	Buttocks	Erythematous swollen skin over the extensor surfaces of the hand joints, elbows, and knees and over the medial and lateral ankle malleoli, buttocks, ear tragi, right upper eyelid; nail fold infarcts, ragged cuticles, periungual telangiectasia	IV/IM/oral steroids, IV/oral cyclophosphamide, cyclosporine, AZA, MTX, HCQ, mepacrine, chlorambucil, plasma exchange, antithymocyte globulin, IVIG 2 mg/kg monthly for 5 mo	Resolved	-	-
36	3/F[32]	Concurrent	Right inner arm	Faint erythema and edema of the eyelids, fingers, knees, and abdomen; erythematous papules over the MCP joints; dilated proximal nailfold capillaries	Oral prednisone 1 mg/kg daily; then MTX and increased systemic steroids	Panniculitis resolved, other cutaneous manifestations did not; weakness recurred	-	-
37	42/F[33]	10 mo prior	Buttocks, thighs, arms, abdomen, breasts	None	Prednisone 1 mg/kg daily, then taper	Resolved, recurred with steroid taper, then improved	29 mo	-
38	24/F[34]	3 mo prior	Left arm	Infraorbital erythema and edema, periorbital discoloration, Gottron papules	HCQ 200 mg twice weekly increased to daily doses; then prednisone 60 mg daily, MTX 7.5 weekly, then taper	Improved	-	-
39	7/M[35]	1 y later	Buttocks, thighs	Erythematosquamous eruption on the backs of fingers, hands, elbows, and plantar surfaces; facial erythema	Prednisone 2 mg/kg daily, then taper, then increase	Improved	-	-

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Patient	Age, y/ sex	Time of panniculitis onset relative to diagnosis of DM	Location of panniculitis lesions	Other cutaneous manifestations	Treatment	Treatment response	Interval between therapy initiation to final treatment response	Malignancy
40	58/F[36]	4.5 mo prior	Left thigh, abdomen, buttocks	None	Prednisone 60 mg daily, then taper	Resolved, recurred with steroid taper, then resolved	-	
41	40/F[37]	1 y later	Legs	Scaly erythematous rash on shoulders, neck, knees	Prednisone 80 mg daily	Resolved	-	-
42	2/M[38]	7 mo later	Extremities, chest, gluteal region	Facial erythema, heliotrope rash, edema around eyelids	Prednisolone 25 mg daily for 3 weeks, then taper	Resolved	6 wk	-
43	22/F[39]	Concurrent	Arms, thighs	Blotchy erythematous eruption with pruritus over the backs of hands (especially the dorsal surfaces of the MCP joints), face (butterflylike distribution), and upper sternum	-	-	-	
Current case	62/F	Following year	Arms, axillae, chest, abdomen, buttocks, thighs	Violaceous, hyperpigmented, periorbital rash and erythema of the anterior chest	Prednisone 0.9 mg/kg daily, MTX 15–20 mg weekly; then mycophenolate mofetil 1–3 g daily, HCQ 200 mg daily	Panniculitis persisted	-	-

Abbreviations: DM, dermatomyositis; F, female; MTX, methotrexate; NA, not available; AZA, azathioprine; MCP, metacarpophalangeal; HCQ, hydroxychloroquine; IV, intravenous; IVIG, intravenous immunoglobulin; M, male; IM, intramuscular.

[a]Literature review included cases through July 2019.