Panniculitis in Adult Onset Dermatomyositis
—Report of Two Cases and Review of the Literature

Jen-Hsin Lin¹ Chia-Yu Chu² Ruey-Yi Lin¹

Panniculitis is an exceedingly rarely reported clinical finding in dermatomyositis (DM) with a total of only 18 cases reported in the literature. Although panniculitis sometimes occurs during the course of connective tissue disease, it has most often been associated with lupus erythematosus rather than dermatomyositis. Because the reported cases are few, it is difficult to know the significance of this association. Here we report two additional cases of DM in whom clinically manifest panniculitis developed during the course of disease. Panniculitis can be a cutaneous features of DM and it may be prudent to include DM in the differential diagnosis of lobular panniculitis. (Dermatol Sinica 24: 194-200, 2006)

Key words: Panniculitis, Dermatomyositis

From the Department of Dermatology,¹ Taipei City Hospital, and National Taiwan University Hospital,² Taipei, Taiwan
Accepted for publication: December 29, 2005
Reprint requests: Chia-Yu Chu, M.D., Department of Dermatology, National Taiwan University Hospital, No. 7, Chung-Shan South Road, Taipei 100, Taiwan
TEL: 886-2-23562141 FAX: 886-2-23934177
INTRODUCTION

Polymyositis (PM) and dermatomyositis (DM) are idiopathic inflammatory myopathies. DM is distinguished from PM by the presence of skin rash. Diagnostic criteria for DM include proximal symmetric muscle weakness, elevated skeletal-derived enzymes, lack of neuropathy on electromyography, consistent muscle biopsy changes, and cutaneous findings. Clinically apparent panniculitis in DM patients is unusual with a total of only 18 cases reported in the literature, although microscopic focal changes of panniculitis may be more common. Here we report two additional cases of DM in whom clinically manifest panniculitis developed during the course of disease.

CASE REPORT

Patient 1

A 56-year-old woman was a case of lymphoepithelioma-like carcinoma of the left side parotid gland. She came to our clinic presenting as facial erythema and edema, heliotrope sign, Gottron’s sign, periungual erythema, and mild proximal muscle weakness. Abnormal laboratory results of blood test included antinuclear antibody (ANA) 1:640+ (speckled pattern), and C4 9.7 mg/dl (normal range: 27.45 ± 10.72). The serologic studies of anti-DNA, anti-RNP, and anti-ENA (Scl-70, Sm, SS-A, SS-B) antibodies were all negative. The serum creatine kinase (CK) level was 62 U/L (normal range <167 in female), serum alanine aminotransferase (ALT) was 24 U/L (normal range: 7-53), and serum aspartate aminotransferase (AST) was 22 U/L (normal range: 11-47). The electromyography (EMG) study demonstrated short and small polyphasic waves compatible with inflammatory myopathy. She was therefore diagnosed as having dermatomyositis according to the diagnostic criteria of Bohan. She was treated with prednisolone (30 mg/day) with gradual improvement of the muscular symptoms and skin lesions. However the skin lesions exacerbated with facial erythema, edema, and heliotrope sign (Fig. 1A), as well as poikiloderma of the upper chest in June 2003 when prednisolone was tapered to 15 mg per day. Besides,
several newly occurred erythematous to violaceous indurated plaques with mild depression were also noted on both upper arms (Fig. 1B). In February 2004, an incisional biopsy from the upper arm demonstrated lobular panniculitis with mainly lymphoplasma cell infiltration, and focal lipomembranous change (Fig. 2A). The alcian blue staining revealed mucinosis in the reticular dermis (Fig. 2B). The direct immunofluorescence (DIF) study of skin biopsy was negative. Now she was treated with azathioprine (100 mg/day) and prednisolone (20 mg/day).

**Patient 2**

A 35-year-old woman came to our clinic and complained of many erythematous to violaceous maculopapules on the forehead (Fig. 3A), several large, tender poikilodermatous, indurated plaques with ulcers and depressed scars on the posterior aspect of the right arm of 3 months’ duration (Fig. 3B). Bilateral proximal muscle weakness, soreness of both thighs, periungual erythema (Fig. 3C), and exertional dyspnea of several weeks’ duration were also noted. The CK level was 62 U/L at that time. Results of the biochemical, hematologic, and immunologic studies, as well as malignancy screening were all within normal limits.

Histopathologic examination of the arm lesion demonstrated mild interface vacuolar change, moderate perivascular and periappendageal lymphoplasma cell infiltration, dense lymphoplasma cell infiltration in the hypodermis and subcutis, and focal lipomembranous change with araboque pattern in the subcutis (H & E, x20). (B) Compact, acellular, homogenous collagen bundles on the lower dermis (H & E, x100). (C) Lymphocytic infiltration of the wall of venules (H & E, x100).

Eight months later, in July 1999, difficulty in climbing stairs, generalized myalgia, facial...
rash, and progressive exertional dyspnea were noted. Besides, fever, productive cough with yellowish sputum, and elevated plasma CK level to 612 U/L were noted. Pulmonary function test revealed moderate restrictive ventilatory defect and severe impairment of diffusion capacity. EMG showed polyphasic waves compatible with inflammatory myopathy. According to the diagnostic criteria of Bohan,\textsuperscript{1} she was diagnosed as having definite dermatomyositis with interstitial lung disease. The patient was treated with cyclophosphamide pulse therapy (600 mg/month) for 6 courses and prednisolone (50 mg/day) with marked improvement of the exertional dyspnea, the muscular weakness, and skin lesions. Thereafter, the dose of prednisolone was tapered without recurrence.

DISCUSSION

Panniculitis in dermatomyositis (DM) is most commonly found only incidentally on biopsy. Janis and Winkelmann\textsuperscript{3} found 5 of 55 cases of DM to have a focal, subclinical panniculitis. One was in the lesional skin biopsy specimen, and four were found in muscle biopsy specimen.\textsuperscript{3} Panniculitis is a rarely reported clinical finding seen in association with DM. In 1924, Weber and Gray\textsuperscript{4} first described a 22-year-old woman with painful inflammatory nodules of the arms and thighs that appeared concurrently with muscle weakness, facial edema, and a diffuse cutaneous eruption. A biopsy demonstrated a heavy lobular lymphocytic and plasma cell infiltrate in the hypodermis with occasional giant cells. Only 18 cases\textsuperscript{4-19} of clinical panniculitis associated with DM have been documented since 1924 (Table I), including one patient with PM.\textsuperscript{5} Of the documented patients, three had juvenile DM.\textsuperscript{6-15} Clinically, panniculitis in DM typically presents as painful and erythematous indurated nodules and plaques primarily located on the arms, thighs, buttocks, and abdomen.\textsuperscript{18} Three exceptional presentations must be highlighted here. First, two reported patients\textsuperscript{12,13} and one of our patients (patient 2) presenting as unhealed ulcers in addition to painful reddish indurated plaques. Second, one reported patient presenting as multifocal lipoatrophy without preceding inflammation.\textsuperscript{19} Third, a reported case presenting as vesiculobullous lesions and reddish indurated plaques.\textsuperscript{19} Localized lipoatrophy has also been described in a variety of conditions, including metabolic abnormalities, local injections, local trauma (reversible lipoatrophy), scleroderma, lupus panniculitis, juvenile rheumatoid arthritis, lichen sclerosus et atrophicus, and DM.\textsuperscript{10} It has been suggested that panniculitis may represent an early stage of lipoatrophy. In the previously reported patients, clinical panniculitis preceded the onset of DM/PM (polymyositis) in 6 cases,\textsuperscript{5,7,9,13,16} while those were concurrent with DM in another 6 cases,\textsuperscript{4,8,11,17,19} and those appeared after the onset of DM in the other 6 cases.\textsuperscript{10,12,14,15,18} In our patient 1, clinical panniculitis appeared two years after the onset of DM; in our patient 2, clinical panniculitis was concurrent with DM.

Histological findings were similar in all reports, consisting of lobular panniculitis with dense lymphocyte and plasma cell infiltration, focal vacuolar changes at the dermoepidermal junction, superficial and/or deep lymphohistiocytic infiltration, and occasionally membranocystic change.\textsuperscript{11,14,18} Calcium deposits may occur in the skin and soft tissue in the late stages of DM. The reported cases displayed a calcified area in only three cases, and all of them were adult.\textsuperscript{11,14,18} Only 3 of 18 reported cases had vasculitis.\textsuperscript{5,7,17} In our patient 2, we could see almost all the above findings except calcification. However, sclerosis with compact, acellular, homogenous collagen bundles in the lower dermis was found. DM can be a component of an overlap connective tissue disorder, in which systemic sclerosis is the most commonly associated disorder: Raynaud’s phenomenon, sclerodactyly, sclerosis of the skin, and characteristic hyperpigmentation are all present, and the term “sclerodermatomyositis” has been used to describe it.\textsuperscript{20} During the follow-up period, our patient 2 was not exactly a case of overlap connective tissue disorder. There was no enough evidence to confirm that patient 2 fit this entity nicely, and we will follow this
<table>
<thead>
<tr>
<th>Age/Sex</th>
<th>Time sequence between diagnosing panniculitis and DM/PM</th>
<th>Location of panniculitis</th>
<th>Malignancy</th>
<th>Treatment</th>
<th>Treatment response</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>22F</td>
<td>Concurrent with DM</td>
<td>Arms, thighs</td>
<td>No</td>
<td>PDN 60 mg/d</td>
<td>il</td>
<td>4</td>
</tr>
<tr>
<td>58F</td>
<td>2 wk before PM</td>
<td>Buttocks, thighs, abdomen</td>
<td>No</td>
<td>PDN 50 mg/d</td>
<td>transient</td>
<td>5</td>
</tr>
</tbody>
</table>
| 51M     | 14 mo before DM                                         | Buttocks                | Rhabdomyosarcoma | PDN 60 mg/d, MTX 7.5 mg/wk | yes | 6
| 24F     | 4 mo before DM                                          | Arms                    | No         | PDN 1 mg/kg/d, MTX | yes | 7   |
| 3F      | Concurrent with DM                                      | Arms                    | No         | PDN 1 mg/kg/d | yes | 8   |
| 42F     | 10 mo before DM                                         | Buttocks, thighs, abdomen, arms, breast | No         | PDN 1 mg/kg/d | yes | 9   |
| 10M*    | 1 y after DM                                           | Buttocks, thighs         | No         | PDN 2 mg/kg/d | yes | 10  |
| 65F†    | Concurrent with DM                                      | Buttocks, left thigh, lower leg | No         | PDN 60 mg/d | yes | 11  |
| 42F     | 5 y after DM                                           | Buttocks                | No         | IVIG 2 mg/kg monthly for 5 months, CVC A: 5 mg/kg/d, PDN | yes | 12  |
| 78F     | 5 mo before DM                                          | Arms, thighs             | No         | PDN 1 mg/kg/d | yes | 13|
| 42F     | 17 mo after DM                                          | Arms, thighs, abdomen    | No         | PDN 1 mg/kg/d, MTX, CYC A | yes | 14  |
| 80F     | 10 mo after DM                                          | Arms, thighs             | No         | PDN 1 mg/kg/d, AZT 2 mg/kg/d | yes | 15  |
| 14M     | 4 y after DM                                            | Forearms, thighs, flanks | No         | PDN 0.3 mg/kg/d | yes | 16  |
| 44F     | 2.5 mo before DM                                        | Shoulders, back, forearm, abdomen, buttocks, thighs | No         | PDN 120 mg/d, MTX 7.5 mg/wk, AZT 250 mg/wk, IVIG 5% 500 mL x 5 months | yes | 17  |
| 54F     | Concurrent with DM                                      | Arms                     | No         | PDN 1 mg/kg/d, AZT 2 mg/kg/d | yes | 17  |
| 57F     | Concurrent with DM                                      | Buttock, thighs, sacral area | No         | CYC A 3 mg/kg/d | yes | 17  |
| 42M†    | 5 y after DM                                            | Left buttock, inguinal area | No         | PDN 30 mg/d, Hydroxychloroquine 60 mg/d, Colchicine 1.8 mg/d, Pentoxifylline 1200 mg/d x 3 days (pulse therapy), PDN 60 mg/d | yes | 18  |
| 60F     | Concurrent with DM                                      | Arms                     | No         | Methylprednisolone 1000 mg/d x 3 days (pulse therapy), PDN 60 mg/d | yes | 19  |
| 56F†    | 2 y after DM                                            | Arms                     | Lymphoepithelioma-like carcinoma | PDN 30 mg/d, AZT 100 mg/d | yes | p.r. |
| 35F†    | Concurrent with DM                                      | Right arm                | No         | Cyclophosphamide 600 mg/mo, PDN 50 mg/d | yes | p.r. |

DM=Dermatomyositis; PM=Polymyositis; PDN=Prednisolone; MTX=Methotrexate; CYC A=Cyclosporin A; AZT=Azathioprine; IVIG=Intravenous immunoglobulin; p.r.: present report;  il: unknown; d: day(s); mo: month(s); wk: week(s); y: year(s).

* Patient presented with lesions of lipoatrophy that were not indurated or tender.
† Pathology showed membranocystic change or lipomembranous change.
‡ Only review the abstracts and other articles (Ref. 14).
patient. The second most common associated connective tissue disorder is systemic lupus erythematosus (SLE), followed by rheumatoid arthritis and Sjögren’s syndrome.20 Yoo et al.21 presented a case of lobular panniculitis with combined features of lupus erythematosus and dermatomyositis. They also stated that generalized forms of lupus panniculitis have been associated with hereditary complement deficiencies, particularly of C2 and C4.20 Our patient 1 had a high titer of ANA (1:640+) and persistent low level of C4. The cause of low level of C4 can not be confirmed to be a genetic deficiency or consumption with immune reaction. It is necessary to confirm it, and we will follow this patient.

Nearly all the cases of DM with panniculitis responded well to prednisolone or methotrexate treatment, except for two patients who needed intravenous immunoglobulins.12, 16 Our patient 2 has been treated with cyclophosphamide pulse therapy without obvious side effects.

Including our cases, an internal malignancy was detected in two cases (2/20, 10%); therefore the incidence of malignancy was similar to that of usual DM (6-50%).2

A number of factors suggest that panniculitis should be included in the cutaneous features of DM: (1) the parallel course and treatment response of panniculitis and the underlying DM in all the reported cases; (2) histological examination revealed focal vacuolar change of the epidermal basal layer in nine reported cases, including one of our cases (patient 2).7, 15, 17, 18, 19 Thus, there is histologic evidence that subcutaneous involvement and the epidermal features of DM can occur together. We believed that panniculitis may be an important and underreported finding in DM. Further study in a large series is needed to clarify the significance of panniculitis in DM.

In conclusion, as Winkelmann et al.7 and Fusade et al.2 had mentioned, panniculitis may be an inherent part of DM. We proposed that DM- or PM-related panniculitis should be included in the differential diagnosis of lobular panniculitis. It may be prudent to consider the possibility of dermatomyositis with panniculitis while a patient complains of proximal muscle weakness with normal level of muscle enzyme, and painful erythematous indurated nodules or plaques were also noted on the arms, thighs, buttocks, or abdomen.

REFERENCES