Dermatomyositis and Granulomatous Myopathy Associated with Sarcoidosis

Jeffrey H. Lipton, B. Daniel McLeod and A. Keith W. Brownell

ABSTRACT: A previously healthy, 21-year-old female presented with acute dermatomyositis. Chest X-ray revealed bilateral hilar adenopathy, and mediastinal lymph node biopsy demonstrated noncaseating granulomata compatible with sarcoidosis. The patient improved spontaneously. The significance of bilateral hilar adenopathy in association with dermatomyositis and implications for management are discussed.

RÉSUMÉ: Dermatomyosite et myopathie granulomateuse associées à la sarcoïdose Une femme âgée de 21 ans, antérieurement en bonne santé, s'est présentée avec une dermatomyosite aiguë. La radiographie pulmonaire a montré une adénopathie hilaire bilatérale et la biopsie d'un ganglion lymphatique médiastinal a montré une granulomatose non caséeuse compatible avec une sarcoïdose. L'état de la patiente s'est amélioré spontanément. Nous discutons de la signification de l'adénopathie hilaire bilatérale associée à la dermatomyosite et de la conduite à suivre dans de tels cas.

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A diagnosis of dermatomyositis (DM) can be made with certainty when the following five criteria are present: 1. weakness, 2. an electromyogram (EMG) which shows myopathic features plus fibrillations, 3. an elevated creatine kinase (CK), 4. a muscle biopsy which shows an inflammatory myopathy, and 5. the typical skin rash.[1] An association between DM and malignancy is recognized.[1-3] Sarcoidosis is a systemic disease of unknown etiology characterized by non-caseating granulomata involving multiple organs and almost invariably the lung.[4] In this report, we describe a patient with DM and hilar adenopathy. The co-occurrence of bilateral hilar adenopathy and DM suggested malignancy, however mediastinal lymph node biopsy showed noncaseating granulomata. The possibility of an association between DM and sarcoidosis is discussed.

Case Report

The patient, a twenty-one-year-old, single, female, physical education student, was first seen in consultation in February 1986. She had been entirely well until December 1985, when she developed myalgias, dysphonia, dysphagia, malar erythema and erythematous, non-puritic plaques over the dorsa of her hands and the extensor surfaces of her elbows and knees. A skin biopsy showed flattening of the papillae with an inflammatory cell infiltrate, most marked in the region of the small blood vessels. There was no evidence of other changes known to be associated with DM.[5] CK was elevated at 760 U/L (N 160 U/L). Rheumatoid factor (RF) and antinuclear antibodies (ANA) were negative. Shortly thereafter, she developed diffuse muscle weakness, fatigability, exertional dyspnea and diffuse swelling of her forearms. Treatment with non-steroidal anti-inflammatory drugs coincided with improvement in the swelling of the forearms but there was no improvement in the other symptoms. In February of 1986, while not taking any specific therapy, her muscle strength began to improve. There was no history suggestive of Raynaud's phenomenon, Sjogren's syndrome, erythema nodosum, pleurisy, pericarditis, arthritis, or any renal, hematological or neurological disorder. She was taking the birth control pill. Reiter's syndrome was diagnosed in an older brother when he was 27 years old.

Physical examination showed malar erythema, heliotrope discoloration of her eyelids and an erythematous, scaly rash with Gottron's papules over her knuckles. A similar rash was noted over the extensor surfaces of her elbows, knees and ankles. Muscle strength testing revealed 4/5 power in her deltoids, biceps, triceps, wrist extensors, wrist flexors, neck flexors and hip extensors, other muscle groups were normal. Speech was normal.

The following laboratory tests were normal: hemoglobin, white blood cell count, serum electrolytes, calcium, creatinine, urea nitrogen, glucose, magnesium, CK (had been 4.75X normal 1 month earlier), serum protein electrophoresis, and thyroid function tests. Serum lactate dehydrogenase (LDH) was elevated at 297 U/L (N 70-185 U/L). Erythrocyte sedimentation rate (Westergreen) was 27 mm/hr (N 25 mm/hr). ANA and RF were, again, negative.

Chest X-ray (Figure 1) revealed bilateral hilar and paratracheal adenopathy. A computerized tomogram (CT) of her thorax showed extensive mediastinal and hilar adenopathy and several small nodules in the lung parenchyma. A 5 Tuberculin Unit Mantoux skin test was negative.

EMG showed myopathic units plus fibrillations. A muscle biopsy was taken from her right deltoid and was processed for frozen and paraffin sections and for electron microscopy using routine methodology. The presence of many muscle fibers with prominent "punched out" areas of myofibrillar loss, located mainly in the perifascicular area, was

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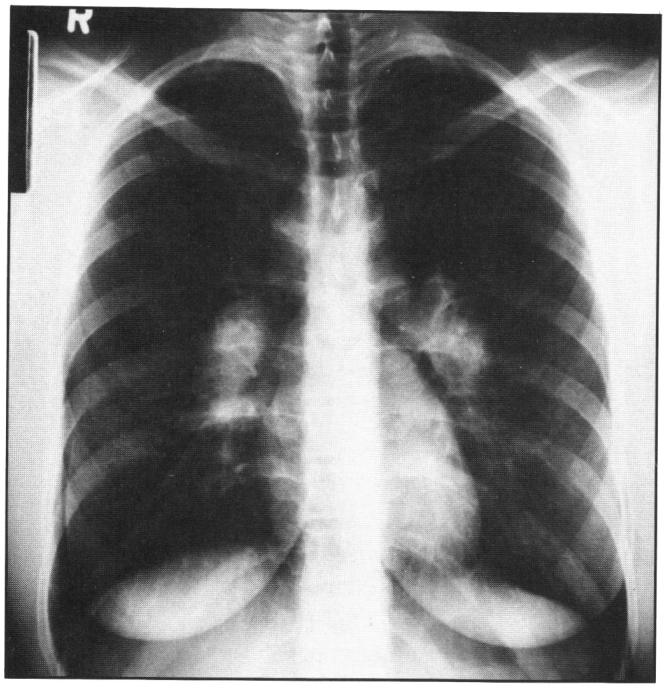

Figure 1. — Chest x-ray showing hilar and paratracheal lymphadenopathy.

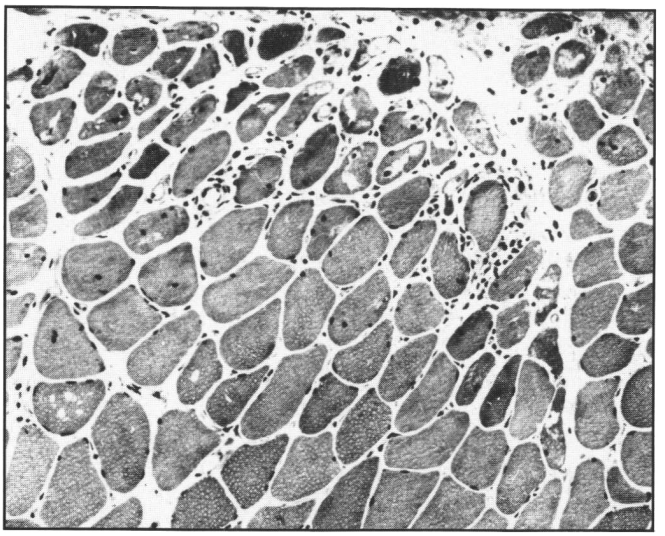

Figure 2 — Hematoxylin and eosin stained frozen section of skeletal muscle showing the perifascicular pattern of muscle fiber involvement. Many of the fibers show punched out areas of myofibrillar loss. Inflammatory cells, mainly lymphocytes, are seen in the interstitum (Original magnification X100).

the most prominent abnormality demonstrated by light microscopy (Figure 2). There was also pathological variation in muscle fiber diameters, an increase in the number of internal nuclei, and regeneration. Inflammatory cells, mainly lymphocytes, were noted around vessels as well as in the interstitium of fascicles.

Although the majority of capillaries examined ultrastructurally were normal (no quantitation was done), in most sections it was possible to see abnormal capillaries (Figure 3). The changes observed consisted of one or more of the following: duplication of basement membrane, a decrease in the number of pinocytic vescicles, degenerative changes within the endothelial cell cytoplasm, and narrowing of the capillary lumen. In spite of an extensive search, no tubuloreticular structures were found in any endothelial cells.

The combination of these light and electron microscopic features are considered dignostic of DM.[6,7,7a] In addition, several granulomata were present (Figure 4), although this feature of the muscle pathology was much less prominent than the features which were diagnostic of DM.

The patient underwent mediastinoscopy and excision of a mediastinal lymph node which contained multiple non-caseating granulomata (Figure 5). Serum angiotensin converting enzyme (ACE) level was 1105 nmol/L/sec. (N 670 nmol/L/sec).

Spontaneous clinical improvement continued with complete clearing of the skin rash and improvement of her muscle strength to the point where she had resumed her normal activities, including athletic endeavors, by June of 1986. CK remained normal. Chest X-ray in May, 1986 showed considerable regression of her lymphadenopathy.

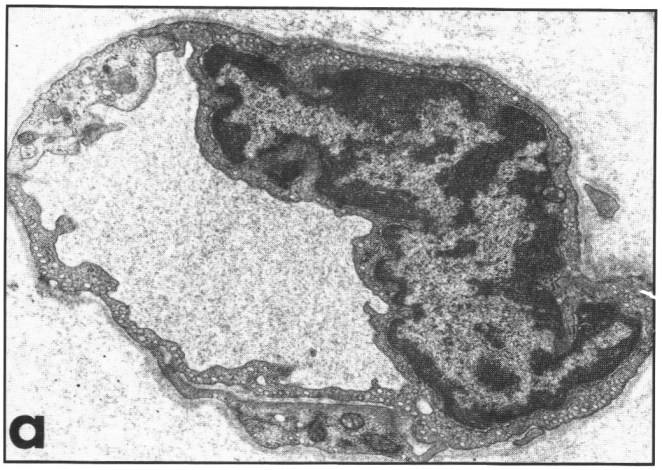

Figure 3 — Electron photomicrographs taken from three capillaries showing the spectrum of change that was observed at the ultrastructural level.

Figure 3(a) — This capillary is normal. Note the sparse cytoplasm, numerous pinocytic vesicles and a single layer of basement membrane (Original magnification X8000).

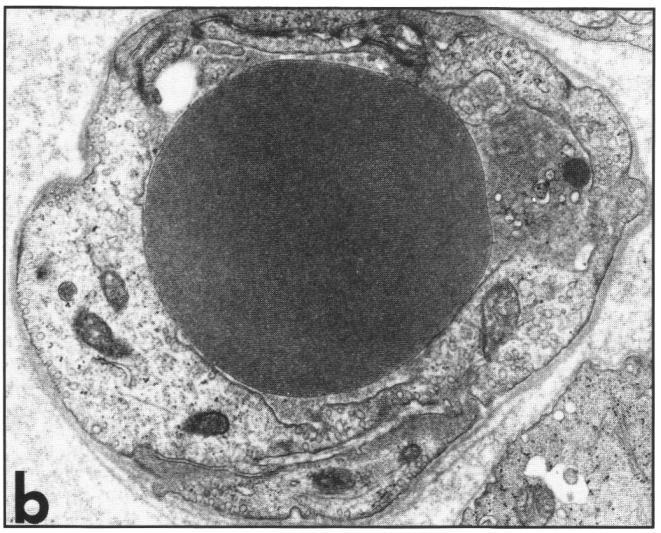

Figure 3(b) — A degenerating capillary containing a red blood cell in its lumen. Note the increase in thickness of the endothelial cells, a decrease in the number of pinocytic vesicles and duplication of portions of the basement membrane (Original magnification X12,000).

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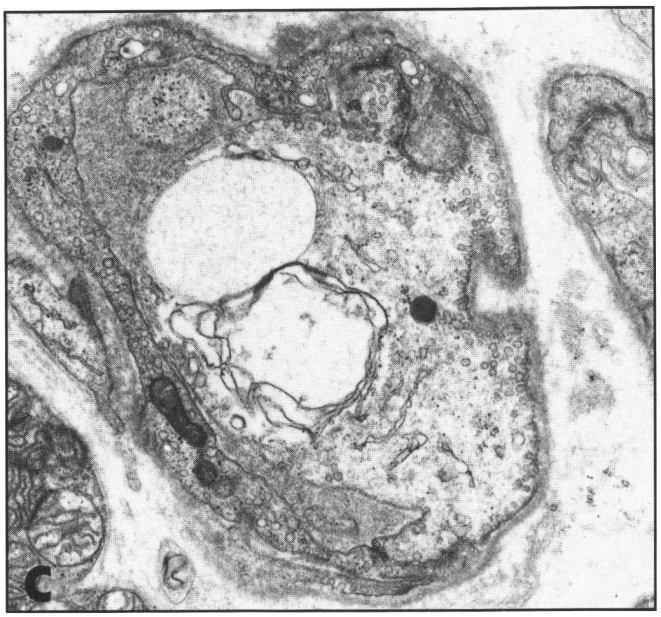

Figure 3(c) — A capillary showing more advanced degenerative change. The lumen of the capillary is almost totally occluded (Original magnification X12,000).

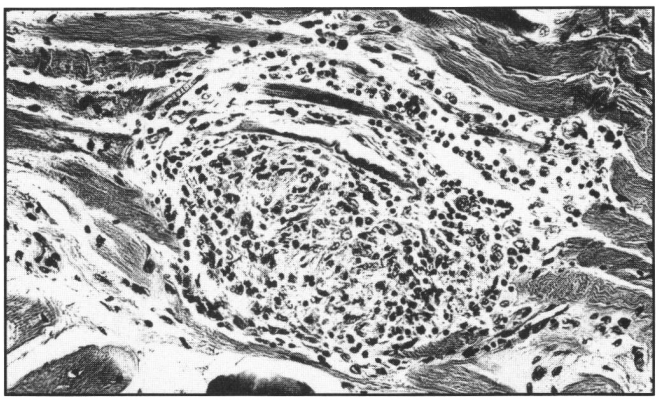

Figure 4 — Hematoxylin and eosin stained, paraffin embedded section of skeletal muscle demonstrating granuloma formation (Original magnification X250).

Comments

The patient's illness is of interest for several reasons. First, this is the only case report in the literature, unequivocally, documenting the association of DM and sarcoidosis. Second, because of the association of DM with malignancy,[1-3] including lymphomas,[8] we would have expected lymphoma to account for her chest findings and were surprised by the finding of sarcoidosis. Third, the patient's DM and sarcoidosis recovered spontaneously.

Although there is a single case report of sarcoidosis and DM occurring in the same patient,[9] when this report is carefully scrutinized, the patient did not fulfill the five diagnostic criteria which we believe must exist for DM to be diagnosed[1] with certainty, and therefore we cannot accept this case report as an example demonstrating the relationship. Also, we believe the evidence for making the diagnosis of sarcoidosis is poor, since

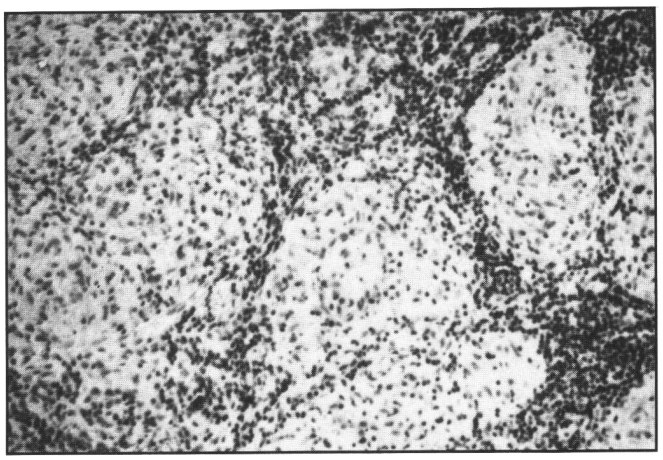

Figure 5 — Hematoxylin and eosin stained, paraffin embedded section of lymph node showing replacement of normal architecture with non-caseating granulomata with occasional giant cells (Original magnification X200).

the patient's chest x-ray was normal, the authors did not comment on any organ involvement other than skeletal muscle, and the patient's ACE level was normal. Our case, not only fulfills all five diagnostic criteria for the diagnosis of DM, but also shows a perifascicular pattern of involvement in the muscle biopsy, a pattern that is described as being morphologically diagnostic of dermatomyositis.[6]

Sarcoid myopathy is associated with the presence of granulomata in skeletal muscle.[10-14] These occur frequently with no evidence of muscle disease.[13] A clinically evident myopathy is unusual in sarcoidosis, being found in 3 out of 800 patients in one series[11] and in 2 out of 500 patients in another series.[15] In these reports, as well as several others,[12,14,16-18] the primary muscle pathology has always been reported to be a granulomatous myositis, in all but two of the cases[18].

We believe that the presence of a small number of granulomata within our patient's muscle does not preclude us from making a pathological diagnosis of an inflammatory myopathy diagnostic of DM, since the major pathological abnormalities in the biopsy were the changes that are typical for DM. It should not be surprising that a small number of granulomata might coexist in the biopsy, since asymptomatic granulomata have been reported to occur in from 50[13] to 55[10] per cent of all patients with sarcoidosis. The presence of sarcoid granulomata in muscle does not preclude making a second diagnosis, when the features of the second diagnosis are diagnostic, as demonstrated in the recent case report documenting the occurrence of inclusion body myositis in a patient with sarcoidosis.[19]

In an otherwise asymptomatic patient, the finding of hilar adenopathy on chest X-ray would suggest the diagnosis of sarcoidosis and a case has been made against biopsy confirmation.[20] Although the association of DM and malignancy is more likely in the older patient,[2] the finding of hilar adenopathy in our patient with DM had to be considered suggestive of malignancy, particularly lymphoma, making node biopsy mandatory. Although the finding of granulomata does not absolutely rule out the possibility of lymphoma,[21-23] her subsequent clinical course, characterized by spontaneous improvement, makes the diagnosis of lymphoma unlikely.

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An association between sarcoidosis and other autoimmune diseases such as systemic lupus erythematosus, scleroderma and Sjogren's syndrome has been postulated.[24-28] In reporting this case we are suggesting that DM may share a similar relationship and that what we have observed in this patient is more than simple coincidence.

The usual patient with DM requires treatment with prednisone and often immunosuppressives over extended periods[1,-3,21] and it is standard medical practice to begin all patients with DM on treatment. In spite of this pattern of practice, prior to the time steroid treatment came into widespread use for DM, Bitnum et al[29] had reported that spontaneous remission occurred in up to a third of patients with DM. Thus, the spontaneous improvement which our patient demonstrated, does not rule out the diagnosis of DM. If the DM in our patient is secondary to her sarcoidosis, as we have speculated, it should not be surprising that the DM would remit as the sarcoidosis resolved. An analogous situation is the response of DM in some patients with successfully treated malignancies.[1,2] Finally, although our patient fulfills all five diagnostic criteria for DM, she may in fact suffer from some other disorder which as yet remains to be further characterized.

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