CASE REPORT

Multicentric Reticulohistiocytosis with Dermatomyositis-like Eruptions

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Abstract

A 68-year-old man presented with polyarthritis, proximal muscle weakness, and erythema of the face, arms, neck, and anterior chest that resembled the V-neck sign. Initially, dermatomyositis (DM) was considered because of the erythema, polyarthritis, and muscle weakness. He also had mediastinal and hilar lymphadenopathy on contrast-enhanced computed tomography. Unexpectedly, a biopsy of the forehead skin revealed numerous multinucleated giant cells. A biopsy of a solitary nodule on the dorsum of his right middle finger revealed similar multinucleated giant cells with ground-glass cytoplasm, leading to the diagnosis of multicentric reticulohistiocytosis (MRH). Although MRH is rare, it should be remembered that MRH can mimic DM.

Key words: dermatomyositis, multicentric reticulohistiocytosis, rheumatoid arthritis, sarcoidosis

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Introduction

Multicentric reticulohistiocytosis (MRH) is a rare form of histiocytosis that is characterized by erosive polyarthritis and papulonodular skin lesions (1). The joint symptoms of MRH resemble those of rheumatoid arthritis (RA), and it is sometimes confused with RA or other inflammatory arthritides, especially when arthritis develops without skin manifestations (2). Unlike RA, the distal interphalangeal joints are commonly affected in MRH (1, 3). Skin lesions consist of multiple dark reddish-brown to flesh-colored papules and nodules that typically occur on the face and hands (1). These lesions are sometimes confused with gouty tophi or rheumatoid nodules (4).

The skin manifestations of MRH occasionally resemble those of dermatomyositis (DM), including Gottron’s papule, heliotrope rash, V-neck sign, and shawl sign (5, 6). Furthermore, MRH occasionally presents with systemic symptoms, such as fever, weakness, myalgia, dysphagia, and even Raynaud’s phenomenon (7). In such patients, MRH might be misdiagnosed as DM if a skin biopsy is not performed. We herein report a patient with MRH who had polyarthritis and DM-like skin lesions, as well as mediastinal and hilar lymphadenopathy on computed tomography (CT). A biopsy of a small solitary nodule on the dorsum of a finger led to the diagnosis of MRH.

Case Report

A 68-year-old man was referred to our hospital with polyarthritis. Sixth months before admission, erythema appeared on the forehead and chest after playing golf. Five months before admission, he developed polyarthritis of the fingers and proximal muscle weakness. RA was diagnosed by an orthopedic surgeon, and he was prescribed bucillamine, with little effect.

A physical examination revealed diffuse erythema on the forehead, neck, shoulders, upper arms, and anterior chest (Fig. 1). Erythema on the anterior chest resembled the “V-neck sign”. The lungs were clear on auscultation. The superficial lymph nodes were not palpable. He had polyarthritis with involvement of the proximal interphalangeal joints, metacarpophalangeal joints, and knee joints, as well as pain in the wrists and left shoulder joint. Manual muscle testing revealed mild proximal muscle weakness (grade 4/5).

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The present patient with polyarthritis was initially thought to have DM due to the characteristics of his skin rash and muscle weakness. However, a biopsy of the forehead skin and a solitary nodule on the dorsum of the right middle finger revealed the infiltration of multinucleated giant cells with ground-glass cytoplasm, leading to the diagnosis of MRH. If a biopsy had not been performed, the correct diagnosis might not have been made. He also had mediastinal and hilar lymphadenopathy on contrast-enhanced CT, which was considered to be another manifestation of MRH.

Skin manifestations of MRH occasionally resemble those of DM. The distribution of skin lesions is similar in both diseases, including the face, chest, neck, and dorsal skin of the hands. So far, more than 10 cases of MRH featuring a DM-like rash have been reported (5, 6, 8-15). However, papulonodular eruptions, which are pathognomonic of MRH, are usually mixed with the erythematous rash in such patients (13, 14, 16), while our patient had no papulonodular lesions in the erythematous areas. Furthermore, his rash developed after sun exposure. This suggested that he might have had photosensitivity, which is a feature of connective tissue diseases, although a photosensitive rash is also a skin manifestation of MRH (7, 17). There has been a case report of MRH in which skin lesions developed after repeated ultraviolet B irradiation (18).

The diagnosis of MRH is based on the detection of characteristic multinucleated giant cells with pale ground-glass cytoplasm (3). Multinucleated giant cells are also found in sarcoidosis. These cells are classified as Langhans- or foreign-body-type based on the distribution of their nuclei, which is arcuate and peripheral in Langhans-type giant cells but is random in foreign-body-type giant cells (5). Multinucleated giant cells are of the foreign-body-type in MRH, while these cells are mainly of the Langhans-type in sarcoidosis. Although the nuclear arrangement is not decisive, distinguishing between MRH and sarcoidosis is not difficult (4, 15), because epithelioid granulomas with few lymphocytes are only found in sarcoidosis and not in MRH. In our patient, no giant cells were detected on a biopsy of the anterior chest skin, but this was consistent with a previous report that found that early MRH lesions can feature lymphocyte infiltration with few giant cells (4).

Weakness is common in patients with MRH (19). Therefore, if patients have a DM-like rash and weakness, MRH becomes clinically indistinguishable from DM. CK levels are usually normal, but there are exceptional cases with elevated CK levels (8, 15, 20). The present patient not only had weakness but also had a slightly abnormal electromyogram. Several MRH patients with muscle involvement and electromyographic abnormalities have been reported, with some showing histiocytic infiltration of the muscles (8, 21). Muscle biopsy was not performed in our patient. Gallium scintigraphy or fluorodeoxyglucose-positron...
emission tomography may reveal subtle muscle involvement in MRH (22).

Lymphadenopathy is also a manifestation of MRH, and this disease has induced bilateral hilar lymphadenopathy in a few cases (23-25). A histological examination of the mediastinal lymph nodes was not performed in the present patient. Sarcoidosis and malignancy should also be considered if lymphadenopathy is detected, and up to 25% of MRH patients have concomitant malignant neoplasms (26). In one patient with MRH, enlargement of the mediastinal lymph nodes was found to be due to metastatic large cell carcinoma (27). Because the mediastinal lymph nodes were unchanged after 4 months in our patient, malignancy is unlikely, but careful follow-up will be necessary.

| Variable                                | value | reference ranges |
|-----------------------------------------|-------|------------------|
| Hemoglobin (g/dL)                       | 13.5  | 13.5-17.6        |
| White blood cell count (μL)             | 7.4×10³ | 3.9-9.8×10³     |
| Neutrophils (%)                         | 65.2  | 42.0-72.2        |
| Lymphocytes (%)                         | 16.8  | 9.9-46.1         |
| Platelet count (μL)                     | 22.3×10⁴ | 13.0-36.9×10⁴   |
| Erythrocyte sedimentation rate (mm/hr)  | 21    | 0-10             |
| Albumin (g/dL)                          | 4.0   | 3.9-5.1          |
| Aspartate aminotransferase (IU/L)       | 27    | 11-30            |
| Alanine aminotransferase (IU/L)         | 40    | 4-30             |
| Alkaline phosphatase (IU/L)             | 216   | 107-330          |
| Lactate dehydrogenase (IU/L)            | 215   | 109-216          |
| Urea nitrogen (mg/dL)                   | 17    | 8-20             |
| Creatinine (mg/dL)                      | 0.98  | 0.63-1.03        |
| Creatine kinase (IU/L)                  | 112   | 59-248           |
| Aldolase (U/L)                          | 5.7   | 2.1-6.1          |
| Angiotensin-converting enzyme (IU/L)    | <8.3  | 8.3-21.4         |
| IgG (mg/dL)                             | 1,007 | 870-1,700        |
| Complement components                   |       |                  |
| C3 (mg/dL)                              | 94    | 86-160           |
| C4 (mg/dL)                              | 21    | 17-45            |
| C-reactive protein (mg/dL)              | 0.17  | <0.14            |
| Rheumatoid factor (IU/mL)               | 18    | <15              |
| Antinuclear antibody                    | 40    | <40              |
| Anti-cyclic citrullinated peptide antibody | (-)     | (-)             |
| Anti-aminocyl-tRNA synthetase antibodies | (-)   | (-)             |
| Anti-SS-A antibody                      | (-)   | (-)             |
| Urinalysis                              |       |                  |
| protein                                 | 1+    | (-)             |
| occult blood                            | -     | (-)             |

**Figure 2.** A small red to flesh-colored nodule on the dorsum of the right middle finger (arrowhead).

**Figure 3.** Numerous multinucleated giant cells and slight lymphocyte infiltration. The nuclei are arranged haphazardly or clustered at the center. The cells have prominent nucleoli and pale cytoplasm (periodic acid-Schiff staining, ×400).
The optimum treatment of MRH has not yet been defined, and management remains largely empirical. Glucocorticoids are often used both locally and systemically but only provide symptomatic relief without inducing remission (1). It has been reported that methotrexate, cyclophosphamide, and other cytotoxic drugs are effective when combined with glucocorticoids. Tumor necrosis factor (TNF)-α inhibitors are promising as a treatment for MRH, since elevated TNF-α levels have been demonstrated in the tissues and serum of MRH patients (26). Bisphosphonates may be another option for preventing bone destruction by inhibiting osteoclast formation and the resorptive ability. However, while MRH lacks an established treatment regimen, high-dose glucocorticoid therapy is the mainstay treatment for DM. Because the treatment of these two diseases differs considerably, correctly diagnosing MRH is very important.

In conclusion, we herein reported a patient with MRH who presented with cutaneous manifestations that resembled DM. Although MRH is rare, physicians should remember that it can cause DM-like skin manifestations as well as polyarthritis. A skin biopsy may therefore be required to exclude other diseases, rather than to diagnose DM.

Author’s disclosure of potential Conflicts of Interest (COI).
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