# Multicentric Reticulohistiocytosis: A Case Report and Review of the Literature

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*We report a case of multicentric reticulohistiocytosis (MRH) demonstrating classic clinical and histologic findings. This rare idiopathic disease is manifested by severe destructive polyarthritis and papulonodular mucocutaneous lesions. The characteristic clinical and histologic findings are discussed as well as the workup and treatment of the disease.*

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## Case Report

A 74-year-old woman presented with a 3-year history of progressive, painful, arthritis mutilans of both hands. In the year prior to presentation she began to develop multiple, firm, asymptomatic, reddish brown papules scattered over the dorsal aspects of the fingers and hands. The arthritis had been treated with prednisone and hydroxychloroquine sulfate without benefit. On physical examination, numerous firm papules and nodules ranging in size from 4 mm to 1 cm were scattered over the dorsal aspect of the fingers and hands, particularly over the joint spaces and proximal nail folds (Figure 1). In addition, marked deformities of her distal interphalangeal joints and severe subluxation of the thumbs were noted (Figure 2).

Skin biopsies obtained from the dorsal aspect of the right thumb and index finger revealed a diffuse dermal infiltrate composed of histiocytes and foreign body giant cells with irregular size and shape admixed with lymphocytes (Figure 3). The cytoplasm was eosinophilic with a ground glass appearance (Figure 4) and stained positive for periodic acid–Schiff after diastase digestion. The histiocytic cells were $CD68^+$ by immunohistochemistry. Laboratory testing revealed a hemoglobin level of 11.3 g/dL (reference range, 14.0–17.5 g/dL); erythrocyte sedimentation rate of 32 mm/h (reference range, 0–20 mm/h); and otherwise normal serum chemistry, kidney function, and liver function. The antinuclear antibody titer was negative and rheumatoid factor was not present. Radiography of the hands and wrists revealed edematous soft tissue, juxta-articular erosions, and no loss of articular cartilage. Age-appropriate malignancy screens and computed tomography of the chest, abdomen, and pelvis were unremarkable. Given the typical clinical and histologic findings, multicentric reticulohistiocytosis (MRH) was diagnosed.

## Comment

Multicentric reticulohistiocytosis falls under the general rubric of reticulohistiocytosis, which consists of idiopathic granulomatous disorders characterized by a reactive proliferation of histiocytes.[1] It is a rare systemic disease manifested by severe destructive polyarthritis and papulonodular mucocutaneous lesions.[2] It predominantly affects women in the fifth to sixth decades of life, presenting insidiously with joint symptoms preceding cutaneous disease in 45% of cases. Skin lesions are the presenting symptoms in 25% of cases, while joint and skin symptoms simultaneously occur in the remaining 30%.[3]

Typical skin lesions are asymptomatic, firm, flesh-colored to reddish brown papules and nodules. They vary in size from 1 mm to 2 cm in diameter and may coalesce to form plaques. The dorsal aspect of the hands, forearms, pinna of the ear, and face commonly are involved, with sparing of the lower trunk and extremities.[4] The nodules also can occur in the periungual regions, giving a characteristic coral bead appearance.[2]

Histopathologic findings reveal polymorphous dermal infiltrates consisting of large histiocytes and multinucleate giant cells with eosinophilic ground glass cytoplasm. The cytoplasm is resistant to diastase and is positive with periodic acid–Schiff stain.[5] The immunophenotypic profile is positive for vimentin,

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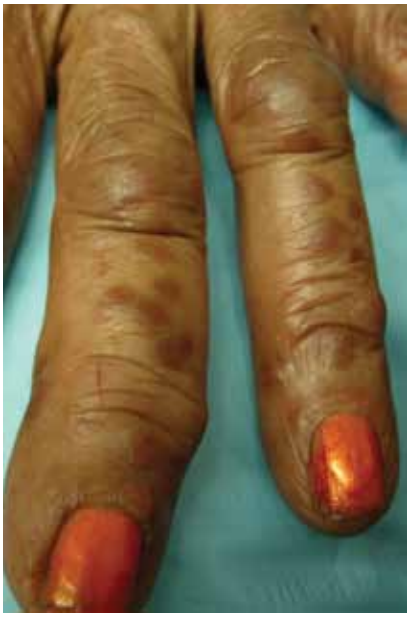

**Figure 1.** Numerous firm, reddish brown papules and nodules ranging in size from 4 mm to 1 cm on the dorsal aspect of the fingers, especially over the joint spaces and proximal nail folds.

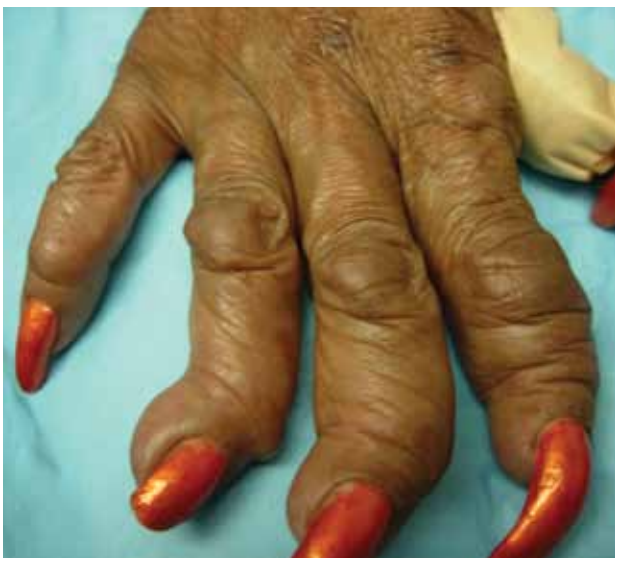

**Figure 2.** Marked deformities of the distal interphalangeal joints and severe subluxation of the thumbs.

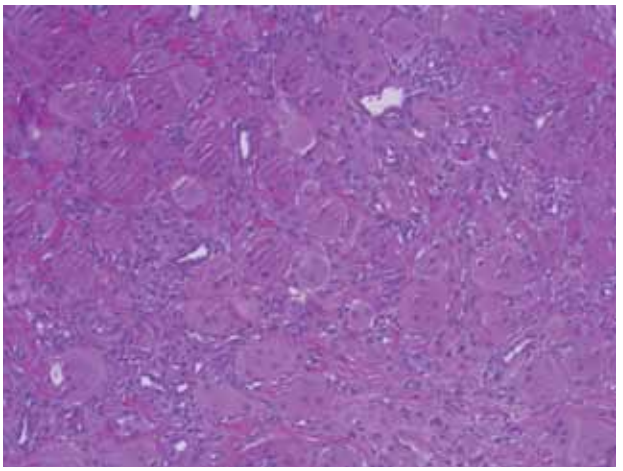

**Figure 3.** Diffuse dermal infiltrate composed of histiocytes and foreign body giant cells with irregular size and shape admixed with lymphocytes (H&E, original magnification ×40).

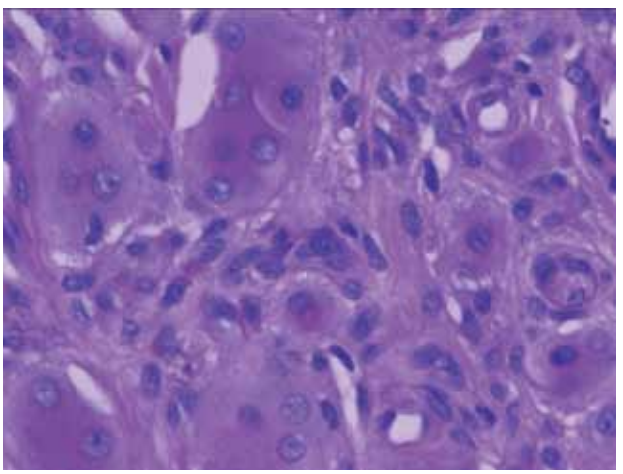

**Figure 4.** Characteristic multinucleate giant cells with abundant eosinophilic cytoplasm with a ground glass appearance (H&E, original magnification ×200).

CD68, and CD45, and negative for S-100 protein, CD34, and factor XIIIa.[6]

The diffuse, bilateral, symmetric, destructive arthritis of MRH can be distinguished from rheumatoid arthritis because of a negative serology for rheumatoid factor and a more aggressive course. In descending order, MRH affects the hands (81%), knees (71%), wrists (66%), and hips (50%). Distal interphalangeal destruction is one of the clinically distinguishing features of MRH.[7]

Radiologic investigations typically demonstrate findings consistent with destructive secondary osteoarthritis, including erosions of articular surfaces, widening of joint spaces, and resorption of subchondral bone.[8]

Because MRH principally presents as a disfiguring disease of the joints and skin, its systemic manifestations can be easily overlooked. Other affected sites include the heart, kidneys, skeletal system, larynx, pharynx, gastrointestinal tract, liver, and lungs.[4,5] Coexistence of autoimmune disease has been identified in 6% to 17% of cases, hyperlipidemia in 30% to 58%, and positive purified protein derivative (tuberculin) in 12% to 50%.[8]

Most importantly, MRH has been associated with malignancies in 25% of cases and has been known to precede the diagnosis of cancer in most cases. Associated malignancies include but are not limited to breast, cervix, colon, ovary, lung, and stomach cancer, with no particular malignancy known to be overrepresented.[5]

Successful treatment of MRH has proven to be a challenge, and evaluation of the efficacy of various treatments has been difficult because of the rarity of the disease and the fluctuating course of both the joint and cutaneous symptoms. Nonsteroidal anti-inflammatory drugs have been recommended for patients with mild symptoms, and for patients with aggressive symptoms, combination therapy with prednisone, cyclophosphamide, and/or methotrexate has been suggested.[9] Drugs associated with partial or complete remission include the aforementioned drugs as well as chlorambucil, azathioprine, hydroxychloroquine sulfate, and alendronate sodium.[9-11] Moreover, the incidence of cutaneous sensitivity to tuberculin skin tests is increased in patients with MRH; however, cultures typically are negative for acid-fast organisms.[12] Patients with MRH with positive tuberculin skin tests may benefit from antituberculous therapy, as demonstrated in a case report of complete resolution of MRH in a patient following therapy with ethambutol hydrochloride and rifampin.[13] Another promising medication in the treatment of MRH is etanercept, which has been reported to lead to resolution of arthralgia and cutaneous lesions of MRH in combination therapy with methotrexate and prednisone.[14]

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