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Multicentric Reticulohistiocytosis:  
A Case Report of Twenty Years Follow Up

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Kosaku Mizuno³

We describe a 42-year old women with over a twenty-year history of arthritis mutilans-like destructive joint changes and with two year history of nodules on the fingers, ears, face and eyelid. She was suspected as having rheumatoid arthritis, however, biopsies from the nodules and synovial membrane of the knee joint revealed multicentric reticulohistiocytosis. Histology of the both lesions disclosed an infiltrate composed primarily of histiocytic cells. The radiographic features of the case were most marked in the interphalangeal joints of the hands. Very little osteoporosis was evident despite the marked destruction. The whole process resembles an arthritis mutilans. She had been treated by using gold sodium thiomalate over 20-years. To our knowledge it has not been used previously to multicentric reticulohistiocytosis. She has been long term remission with gold treatment. We are continuing the treatment and follow up the patient.

Key Words
Multicentric reticulohistiocytosis, Arthritis mutilans, Histocytocyte, Radiographic features, Gold treatment.

Introduction

Multicentric reticulocytosis (lipoid dermatooarthritis) is a rare disease of unknown etiology that affects the joints and skin by virtue of the accumulation of lipid-laden histiocytes and multinucleated giant cells¹-⁴. Other names for this disorder have included lipoid dermatooarthritis and normocholesterol xanthomatosis⁵.

Women are affected more often than men, and the disease usually begins insidiously as a symmetric arthritis which is sometimes confused with rheumatoid arthritis⁶. The natural course of this disease is variable. Polyarthritis is the presenting sign in about two third of cases and in the other one third of cases, the skin nodules may accompany the arthritis. Skin nodules usually follow months to years later, but they can precede or occur simultaneous with the arthritis², ⁴.

Striking resorption of subchondral bone can develop over a fairly short period of time and lead to arthritis mutilans (opera-glass hand), ie, marked shortning of the fingers, flail digits. A symmetric inflammatory polyarthritis involves most commonly the diatal interphalangeal joints, but also other joints such as the proximal interphalangeal joints, knees, hips, shoulders, and elbows. In the present study we describe a typical case of this
disease and review the clinical and radiological course of 20 years long.

**Case Report**

The patient, a 42-year-old woman, presented in September 1977 with a week history of dysphagia, hoarseness, laryngeal pain with slight fever. Both the arthritis and skin lesions began when the patient had the symptoms described above. The arthritis involved her knees, wrists, distal and proximal interphalangeal joints, and metacarpophalangeal joints in a symmetric pattern. Morning stiffness also occurred.

The nodular skin eruption over her hands and face were also noted. The brown-yellow nodules varied in size and covered fingers, nailbeds, forarms, nasal septum and eyelids (Figure 1). The nodules were firm, non-tender and mobile in nature. Similar lesions on the oral mucosa became painful ulcerations. She had also paresthesias on both hands.

Laboratory results included a sedimentation rate of 33 mm/hr; leukocyte count of 5,400/mm³, with 51% mature neutrophils, 4% bands, 39% lymphocytes, 5% eosinophils and 4% monocytes; and positive rheumatoid factor; but antinuclear antibody was negative. C-reactive protein was also positive.

The radiologic appearances were slightly erosive bone destruction with small marginal erosions similar to those of rheumatoid arthritis at 1978 (Figure 2). There was juxtaarticular osteoporosis of the hip joints (Figure 3).

Diagnosis was established by skin biopsy. The nodules of fingers were excised under local anesthesia and fixed in formaldehyde for light microscopy and in osmium tetroxide for electron microscopy. At the same time synovial biopsy of right knee was also done. Light microscopy of the skin lesions disclosed an infiltrate composed primarily of histiocytic cells. Consistent with multicentric reticulohistiocytosis, these cells had glassy

![Figure 1. Multiple nodules are present on the eyelids and facial skin (A) and hands (B).](image-url)
Figure 2. X-ray of both hands taken in 1978 showing osseous destruction of metacarpophalangeal and interphalangeal joints.

Figure 3. Early erosions of hip joints (1978).

eosinophilic cytoplasm and round or oval vesicular nuclei with prominent nucleoli. The cells were moderately large, oval, polygonal or slightly elongated and predominantly mononuclear cells. Synovial tissue of the right knee showed a histiocytic (Figure 4) and giant-cell proliferation in an edematous and highly vascular stroma. An electron microscopic study showed some large histiocytic cells that contained profuse endoplasmic reticulum, mitochondria (Figure 5).

The disease was treated with nonsteroidal antiinflammatory drugs without any effect on both of the skin and joint disease. She was consulted by Dr. Morris Ziff, Professor of the internal medicine, The University of Texas, Southwestern Medical School. Gold sodium thiomalate (GST) 10 mg/month and nonsteroidal anti-inflammatory drugs (NSAIDs) were commenced with 5 mg prednisone/day. This resulted extremely reduction of skin and joint involvements. She did not visit us for three years because of her condition of symptom free. However, when she visited us in November 1981, she was confined to a wheelchair because of severe arthritis of both knees. Multiple nodules were present on the patient’s face and hands. Markedly deformed by mutilating arthritis, the patient’s hands showed the classic telescoping finger deformities of this disorder. The patient had been treated again by GST and NSAIDs and 5 mg prednisone. After six months, prednisone was then discontinued and GST 10 mg/month was maintained for 16 years. The patient had no relapse of arthritis or skin nodules when she was last seen in March 1998, 20 years after she had the disease. Radiographic deterioration were not remarkable on both hands and hips (Figure 6).

Discussion

Multicentric reticulohistiocytosis (MRH)

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is an uncommon disease first described by Weber and Freudenthal in 1937\textsuperscript{7}, which has an important association with disabling, destructive polyarthritis. The disorder is characterized by the gradual development of nodules in the skin, mucosa, subcutaneous tissues, synovia, periosteum, and bone, resulting in destructive arthritis and facial disfigurement\textsuperscript{6, 8, 10}. As described in our case, women are affected three times more often than men\textsuperscript{2}. Systemic signs and symptoms, including fever and paresthesias occurred in our patient as reported previously\textsuperscript{9}.

Although there are no specific laboratory abnormalities in MRH\textsuperscript{4, 11}, the case presented here has had a positive rheumatoid factor during past 20 years. Therefore our patient was at first considered as having rheumatoid arthritis, with
Multicentric Reticulohistiocytosis

Figure 6. Radiographs taken 20 years after onset did not show progressive deterioration on both hands (A) and hips (B).

typical destructive polyarthritis and with radiographic findings showing erosive changes very similar to those of rheumatoid arthritis.

Diagnosis was established by skin and synovial biopsies. The synovial lesions consisted of an infiltration of histiocytic multinucleated giant cells. Lymphocytes and plasma cells were evident, and vessels showed intimal thickening. Although we have not studied the immunohistochemical analysis, immunophenotypic studies have shown that histiocytic cells are of monocyte/macrophage origin. These histiocytes might have undergone down regulation of their monocytic differentiation antigen due to their activation and acquired T cell markers from their intimate interaction with T-lymphocytes. Goette and associates classified reticulohistiocytic disorders into three categories based on clinical patterns: (1) solitary cutaneous reticulohistiocytoma, (2) multiple cutaneous reticulohistiocytoma, and (3) multicentric reticulohistiocytosis. Identical histopathologic findings are found in all three categories and form the basis for the classification. This classification is based solely on histopathologic similarities and may be artificial. Clinically and histopathologically, there is little doubt that the patient in the present study has multicentric reticulohistiocytosis. Clinically, the most remarkable features of this patient's disease are the extensive involvement of her facial skin by nodules and crippling arthritis that has destroyed her hands.

Widening of joint space, relatively mild osteoporosis despite severe erosive destruction, circumscribed erosions over the articular surface spreading centrally, common involvement of distal interphalangeal joints as observed in our case, are radiographic characteristics of MRH. The radiographic features of MRH are obvious enough to differentiate them from the radiologic features in rheumatoid arthritis, psoriatic arthritis. In half of the cases the arthritis progress to an arthritis mutilans over a 7 to 8-year period. These radiographic features may become severe, although associated clinical symptoms may be mild as reported case here.

Recently it was suggested that the arthropathic effects of MRH may be mediated through cytokines such as tumor necrosis factor, which can be elaborated by activated macrophage. Several drugs have been tried in treatment. However, no therapy has been shown to consistently improve the arthritis or skin lesions of MRH. On the
other hand, there are reports indicating partial or long-term remission with some trials. Some case reports noted improvement with cyclophosphamide\(^{17}\), methotrexate\(^{18}\). Gold therapy which we have used to our patient over 20 years period, as far as we know, have not been used previously. Treatment with GST appears to be indicated in patients with aggressive MRH. We are continuing the treatment and follow up of the patient.

References