# Erosive polyarthritis in multicentric reticulohistiocytosis mimics rheumatoid arthritis

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Multicentric reticulohistiocytosis (MRH) is a very rare multisystemic syndrome.[1,2] The first case of MRH was described by Goltz and Layman in 1954 and so far only less than 200 cases have been reported.[3-5] It is characterized by the insidious onset of polyarthritis that often evolves into a severe erosive deforming arthritis and characteristic skin lesions composed of nodules and plaques containing lipid-laden (periodic acid-Schiff-positive) histiocytes and multinucleated giant cells.[6] It most commonly affects the hands and cervical spine.[7] MRH is also known as lipoid dermatoarthritis, lipoid rheumatism, and giant cell reticulohistiocytosis.[4] MRH is occured due to infiltration of multinucleated giant cells and histiocytes into various tissues. The typical pictures include skin nodules and destructive polyarthritis.[3] This entity is frequently mistaken for rheumatoid arthritis (RA).[3] MRH is often associated with systemic complication and various types of malignancy. Therefore, sometimes it is considered a paraneoplastic syndrome.[8]

## CASE REPORT

A 26 year-old Javanese women was admitted due to abdominal pain since three days before admission. The pain was described as sharp like being stabbed and continuous. She sufferred from cough with whitish sputum and sometimes accompanied with shortness of breath in the last two months. She also had decreased body weight for the last two years. The patient was diagnosed with RA since two years ago due to pain, swelling and stiffness on her hand joints, arms, and shoulder joints symmetrically. She was treated with weekly oral dose of methotrexate and low dose methylprednisolone. Patient had been married for seven years and had a three year old child. Recently she had three painless lumps on her back which was not enlarged and sometimes would become reddish.

Physical examination showed she was underweight (body mass index 13,3 kg/m$^2$), tachypnea (respiratory rate 24 x/min), had pale conjungtiva and thin hair. She also had soft mobile painless nodules on her back (figure 1). Abdominal examination revealed hepatomegaly with liver span 18 cm, blunt margin, smooth surface, pain on palpation, and splenomegaly with Schuffner 2. Joint examination showed swollen and tender joint on proximal interphalangeal (PIP) joint I-V and metacarpophalangeal (MCP) joint I-V bilaterally (figure 2). There was tenderness on elbows, knees, shoulders, and hips.

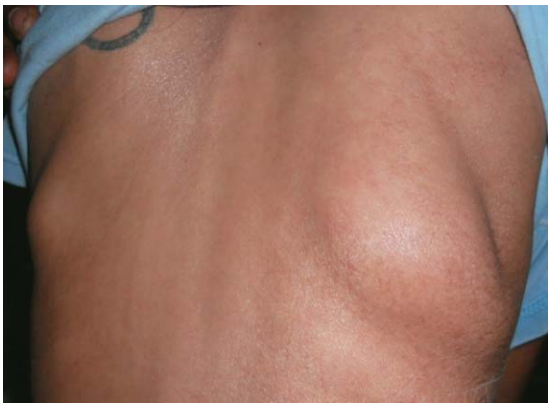

**Figure 1** Lumps on the patient's back

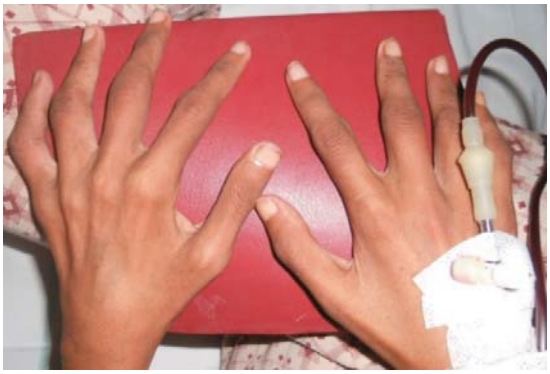

**Figure 2** Symmetric polyarthritis on both hands.

Laboratory results showed leukocyte count 11.800/µl, hemoglobin level 5.6 g/dl, MCV 81 fl, MCH 27.0 pg, hematocrite 16.8%, thrombocyte count 104,000/µl, random blood glucose 137 mg/dl, urea 46.0 mg/dl, creatinine 0.80 mg/dl, SGOT 46 mU/ml, SGPT 15 mU/ml, serum sodium 133 mmol/l, serum potassium 3.72 mmol/l, serum chloride 112 mmol/l. Urinalysis showed leukocyturia 2+, positive nitrite, proteinuria 2+, erythrocyturia 4+, and granule sedimentation in urine 3-5. Rheumatoid factor was negative, CRP 6.06 mg/dl, and erythrocyte sedimentation rate 70 mm/hour.

Chest X-ray showed cardiomegaly, batwing infiltrate in both lungs with prominent fissures, blunting on right sinus phrenicocostalis representing lung edema and pleural effusion dextra (figure 3). Hand X-ray showed periarticular osteoporosis at os carpalis, metacarpophalangeal and interphalangeal

joints digiti I – V manus dextra and sinistra. This similar appearance was also shown at distal radius and ulna, with joint narrowing at proximal interphalangeal proximal and digiti II – V distal. There was joint erosion at PIP digiti II – V manus dextra and sinistra and DIP digiti II – IV manus dextra (figure 4). Pedis X-ray showed porotic periarticular metatarsophalangeal and interphalangeal.

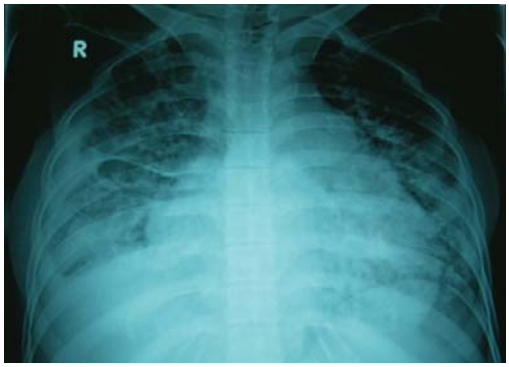


**Figure 3** Chest x-ray showing cardiomegaly with pulmonary edema and right pleural effusion.

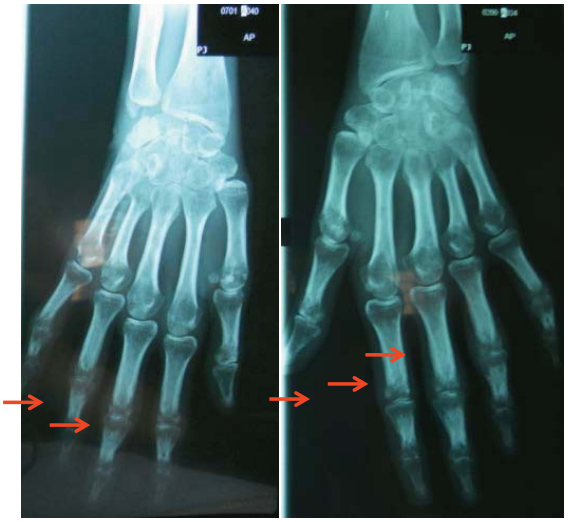

**Figure 4** Hand X-ray showing juxta-articular osteoporosis with erosions (red arrow) on PIP joints.

Fine needle aspiration biopsy of the lumps on her back showed necrotic tissue with many polimorphonuclear inflammatory cells and histyocytes with vacuolated cytoplasm (Figure 5).

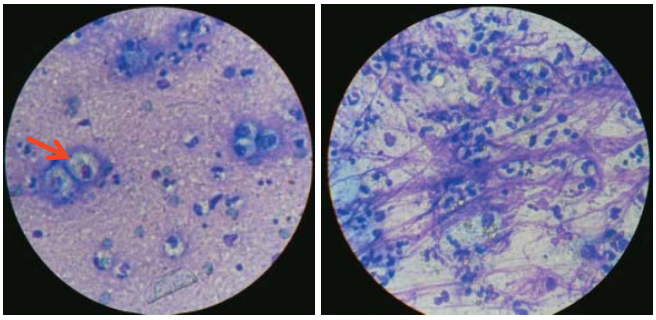

**Figure 5** Microscopic finding from the lumps showing histiocytes (red arrow) with vacuolated cytoplasm

Pleural fluid cytology analysis showed malignant cell adenocarcinoma which supported the diagnosis of adenocarcinoma of lung. Finally, patient was diagnosed with multicentric reticulohistiocytosis (MRH) associate with lung malignancy, and she was planned for chemotherapy. Patient passed away due to respiratory failure one month after the diagnosis of MRH was confirmed. She did not have chemotherapy.

## DISCUSSION

Multicentric reticulohistiocytosis is a chronic, symmetric inflammatory polyarthritis, most commonly affecting the hands and cervical spine. It may resemble RA,[9,10] but has prominent distal interphalangeal joint synovitis and can cause a severely deforming arthritis mutilans in 50% cases.[7,9] Systemic proliferation of multinucleated lipid-laden histiocytes causes swelling in the small joints of the hands and a characteristic erosive pattern on radiographs.[1] A typical 'string of pearls' may be seen around the cuticle in some patients.[1] Compared with RA, MRH has the potential to be much more rapidly destructive. Characteristic skin lesions and a negative rheumatoid factor also distinguish MRH from RA.[11] Clinical manifestations of MRH and RA are summarized on table 1. The etiology of MRH remains unclear.[8] The pathophysiology of MRH is not known. A relationship has been made between MRH and infection, malignancy, and autoimmune disease. Such associations suggest that MRH is a reactive inflammatory response with uncontrolled proliferation of the reticulohistiocytes. The strong link with visceral malignancy is consistent with a paraneoplastic process. Most reports support monocytes/ macrophages origin for MRH based on histologic features.[9]

Joint manifestations usually precede nodular skin involvement and many patients have been first misdiagnosed with rheumatoid arthritis.[9] Two-thirds of patients present with arthritis and skin lesions appear at an average of three years later. About 15-50% progress to mutilating osteoarthropathy and disabling deformities. Some patients have self-limited disease with non-deforming arthritis.[2] In this case, patient already diagnosed with RA for two years then she developed skin nodule. Arthritis in this patient was also disabling, deforming, without mutilating osteoarthropathy.

In 66% of patients, skin lesion and nodules follow the onset of arthritis by months to years. The skin lesions have a diagnostic histology.[7] This patient was developed skin lesion after two years of fluctuated arthritis. In 20%, the skin nodules which are firm, flesh-colored to red, brown, or yellow papules are the presenting feature. Pathognomonic lesions are "coral bead" periungual papules, papules on the pinna and vermicular lesions bordering the nostrils.[2] Skin lesion wax and wane occur around the nailbeds and on the face, extensor surface of the hands and forearms, ears, at mucous membrane and other areas predominantly above the waist.[7,10] Pink to skin-colored papules that are firm, 2-5 mm in diameter, and often in a linear arrangement are seen in patient with papular mucinosis.[10] On histologic examination, the papules have characteristic giant cells that are not seen in biopsies of rheumatoid nodules.[10]

**Table 1**. Comparison of clinical manifestation between multicentric reticulohistiocytosis (MRH) and rheumatoid arthritis (RA).

| Clinical manifestation | MRH | RA |
|---|---|---|
| Joint stiffness | Yes* | Yes, typically morning stiffness |
| Tender and swollen joint | Polyarthritis* | Polyartrhtis* |
| Joint involvement | Hands*, cervical spine. Prominent on DIP* joints | Hands*, wrists, elbows*, shoulders*, knee*, ankle, feet. Rare on spine and DIP joints. |
| Symmetric joint involvement | Symmetric* | Symmetric* |
| Nodular skin lesion | Yes, with histiocytes cells on biopsy* | Rheumatoid nodule |
| Inflammation markers (ESR and CRP) | Increased* | Increased* |
| Anemia | Mild anemia* | Mild anemia* |
| Rheumatoid factor | Negative* | Commonly positive |
| Erosive joint | Yes, prominent on DIP* joints, more progressive erosions | Yes, prominent on carpal bones, MCP and PIP* joints |
| Juxtaarticular porotic | Yes* | Yes |
| Association with malignancy | 25% Associate with malignancy (breast, stomach, cervix, ovary, colon and lung* | None |

*was present on this patient

MRH can spontaneously resolve in 5-10 years, but it can progress to severe arthritis mutilans if not treated.[3] There is no effective treatment for MRH. There are several treatment regimens with variable result. The efficacy of these different drug therapies are difficult to assess due to the disease fluctuations and spontaneous remissions.[11]

All patients diagnosed with MRH should undergo a thorough workup for associated diseases, especially malignancy, because MRH most commonly precede the diagnosis of malignancy. When associated with malignancy, cytotoxic chemotherapy is recommended to control the symptoms of MRH. Non–paraneoplastic cases have been treated with a variety of agents. Nonsteroidal anti-inflammatory agents are not helpful in treating MRH-associated arthropathy. Systemic steroids are palliative, but do not induce remission. Another treatment of MRH consist of variety of medications, including prednisone, methotrexate, cyclosporine, alendronate, zolendronate, and etanercept, and also chlorambucil, and cyclophosphamide.[9]

## SUMMARY

A 26 year-old female was diagnosed with multicentric reticulohistiocytosis (MRH) based on symmetric polyarthritis involving PIP, DIP, elbow, shoulder, hip, and knee joints. Joint erosions were identified on PIP and DIP joints, with porotic juxta-articular. Laboratory results showed anemia, increased ESR and CRP levels, and negative rheumatoid factor. Biopsy from skin nodule showed hystiocytes suggestive of MRH. MRH in this patient was associated with lung malignancy and her pleural fluid cytology showed malignant adenocarcinoma cells. She had been misdiagnosed with RA for two years, suggesting that the clinical manifestation of MRH mimics rheumatoid arthritis. MRH should be considered as an important differential diagnosis in patient with erosive symmetric polyarthritis.

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