Case Report

Multicentric reticulohistiocytosis

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DOI: 10.4103/0378-6323.66598

ABSTRACT

A 50-year-old male presented with fever, joint pain and skin lesions since eight months. Examination showed multiple papules and nodules with periarticular predisposition. Swelling of knees and elbows with flexion deformity of distal interphalangeal joints was present. Investigations revealed anemia and raised ESR. Histopathology was pathognomonic of multicentric reticulohistiocytosis. Patient was treated with bisphosphonates along with systemic steroids and methotrexate to which he responded well.

Key words: Multicentric reticulohistiocytosis, skin lesions, arthritis, bisphosphonates

INTRODUCTION

Multicentric reticulohistiocytosis is a rare histiocytic proliferative disease which manifests as skin nodules and rapidly destructive polyarthritis. Caro and Senear first described this disorder in 1952 as reticulohistiocytic granuloma.[1] Goltz and Laymon originally coined the term multicentric reticulohistiocytosis in 1954 because of the multifocal origin and systemic nature of the process.[2] The etiology has not been fully elucidated, and no consistently effective treatment has been identified. We report this case for its rarity. The presentation with aggressive skin lesions and excruciating joint pain with minimal bone erosion in the absence of systemic involvement was striking. The beneficial effect of bisphosphonates on both skin and joint lesions is also noteworthy.

CASE REPORT

A previously healthy 50-year-old male presented with severe debilitating joint pains involving both shoulders, elbows, hips, knees and hands since eight months and multiple cutaneous lesions since four months. This was associated with swelling and deformity of joints, recurrent episodes of high grade fever, loss of appetite, significant weight loss and painless oral lesions. There was no history of morning stiffness of joints or past major medical or surgical illness. On examination, patient was febrile and pale with restricted mobility of metacarpophalangeal, proximal and distal interphalangeal, knee, elbow and shoulder joints with flexion deformity of bilateral distal interphalangeal joints [Figure 1]. Patient weighed 48 kilograms. Rest of the systemic examination was within normal limits.

Dermatological examination revealed discrete but grouped, firm, reddish brown, non scaly, non tender papules and nodules ranging from 2 mm to 2 cm over arms, lower abdomen, back, buttocks and bilateral knees and feet [Figures 2-4]. Single ill defined erosion was noted over right buccal mucosa.

Hemogram revealed anemia (6 gm %) and raised Erythrocyte Sedimentation Rate (38 mm/hr). Routine haematological investigations, lipid profile, thyroid profile, rheumatoid factor and C reactive protein were normal. ELISA for Human immunodeficiency virus (HIV) was non reactive. Electrocardiogram, chest X-ray, ultrasound abdomen/pelvis was unremarkable. X-ray hands showed mild osteopenia with flexion deformity of distal interphalangeal joints.

Histopathological examination of skin nodule revealed diffuse infiltration of dermis by mononucleated and multinucleated histiocytes with an eosinophilic ground glass cytoplasm [Figures 5 and 6].

After consultation with a rheumatologist patient was started on Tab. Prednisolone 1 mg/kg (50 mg/day) for a period of two months and gradually tapered by 5 mg

How to cite this article: Kaul A, Tolat SN, Belgaumkar V, Mhaske CB. Multicentric reticulohistiocytosis. Indian J Dermatol Venereol Leprol 2010;76:404-7.

Received: December 2009. **Accepted:** March, 2010. **Source of Support:** Nil. **Conflict of Interest:** None declared.

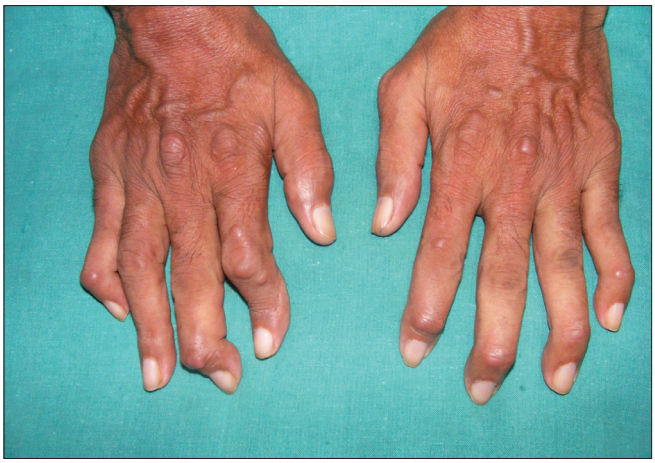

Figure 1: Flexion deformity of distal interphalangeal joints of both hands

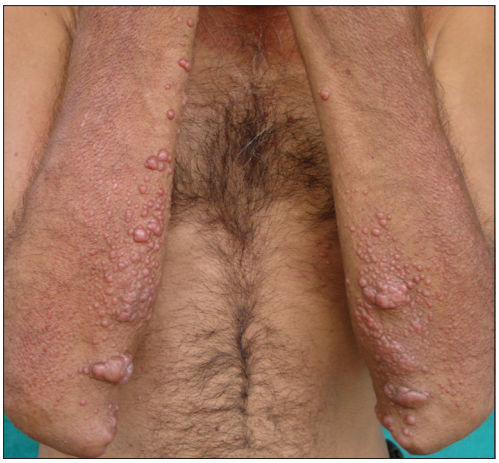

Figure 2: Papulonodular lesions along the extensor aspect of forearms and the elbow (periarticular location)

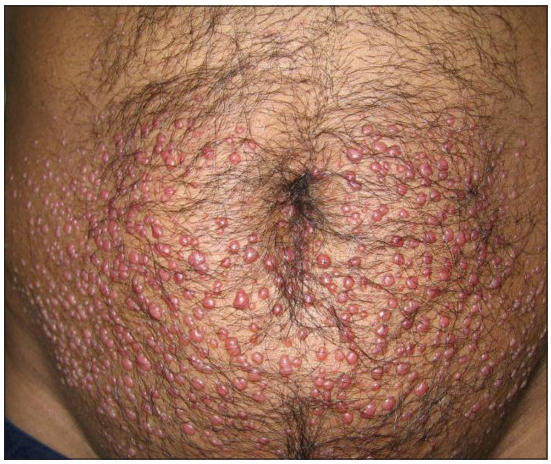

Figure 3: Multiple discrete erythematous papules over abdomen

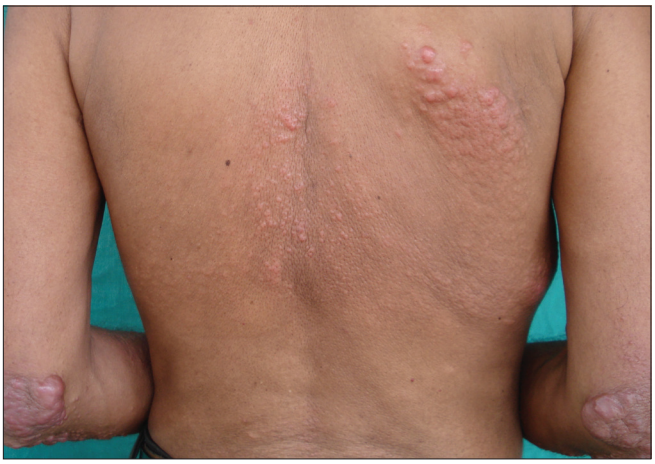

Figure 4: Papular lesions present on upper back, coalescing to form a plaque

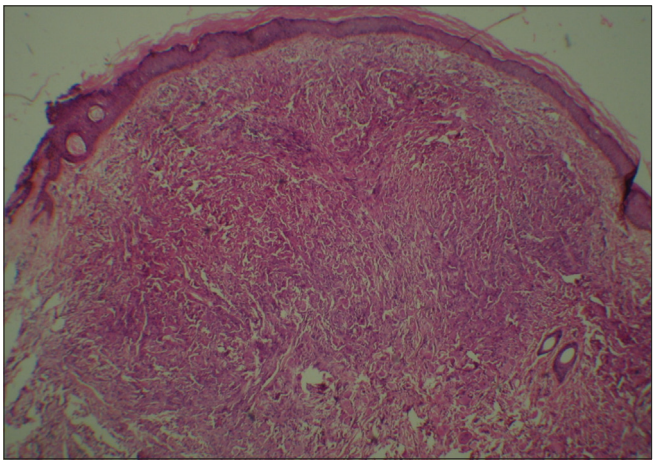

Figure 5: Biopsy sample from a papule over abdomen. Histopathology shows diffuse infiltration of the dermis by histiocytes (H&E, ×40)

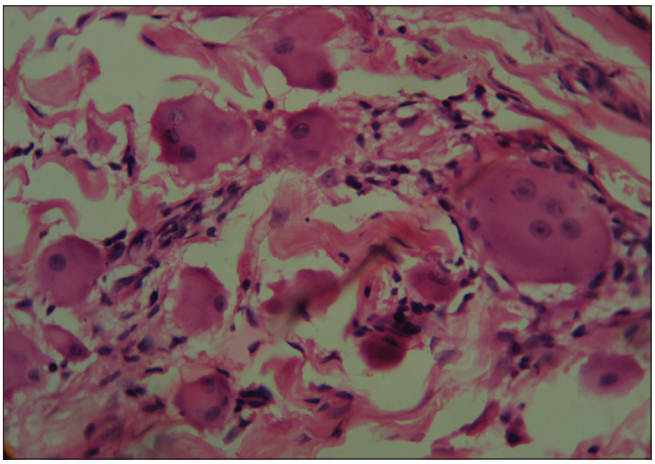

Figure 6: Higher magnification shows dermal infiltration with multinucleated giant cells with an amorphous, eosinophilic, "ground-glass" cytoplasm (H&E, ×400)

every two weeks for another four months till a dose of 10 mg was reached which was kept as a maintainence for another six months. Simultaneously Methotrexate was started at a dose of 15 mg/week for eight months then reduced to 7.5 per week and kept on that dose for another four months. Along with these, monthly intravenous injections of 4 mg Zolidronic acid were given for a period of four months. Within first month of starting treatment there was striking improvement in joint pain, fever and decreased appetite without any effect on deformities. Subsequent treatment for six months resulted in significant reduction in the size and number of skin lesions with marked improvement in joint pain and mobility [Figures 7-9]. However, the deformities persisted.

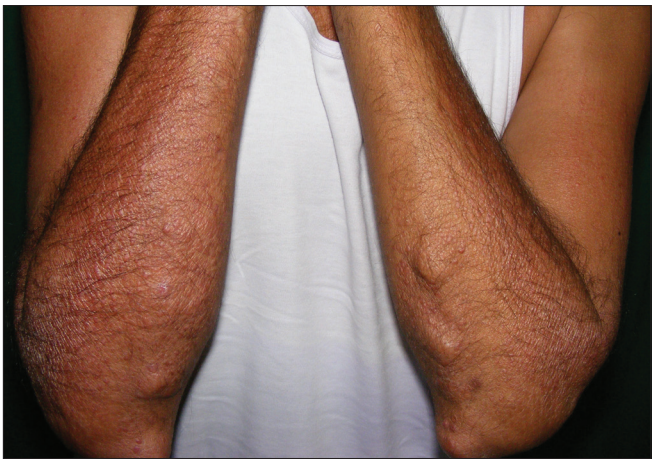

Figure 7: Post treatment photograph with significant redution in size and number of papulonodular lesions

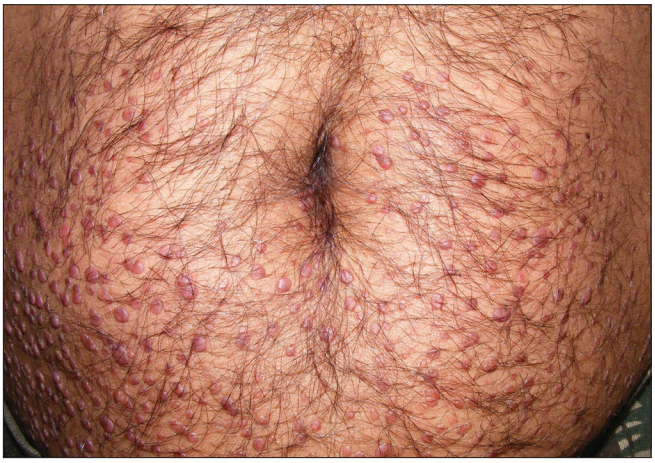

Figure 8: Post treatment photograph of lower abdomen with striking reduction in the number, size and erythema of lesions

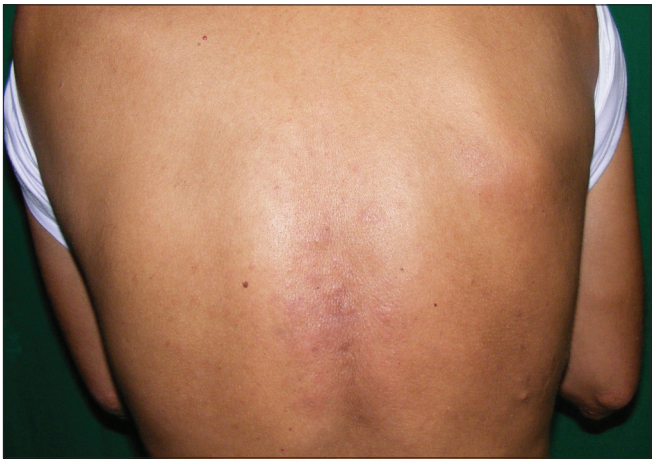

Figure 9: Plaque over the upper back has almost disappeared

DISCUSSION

Multicentric reticulohistiocytosis also known as lipoid dermatoarthritis has a worldwide distribution with a female preponderance (60-75%). It usually begins during fourth decade of life with isolated polyarthritis (50%), cutaneous lesions (25%) or both concurrently (25%).[2] The polyarthritis is usually diffuse, symmetric, progressive, and destructive with a predilection for distal interphalangeal joints.[3] Radiography shows disproportionate bone destruction as compared to articular cartilage loss; resorption of subchondral bone can develop over a fairly short period of time leading to striking sharply circumscribed erosions spreading from the margins to the joint surfaces. It has been proposed that liberation of urokinase by activated histiocytes play a role in erosion of cartilage and bone.[2] There are a variety of associated conditions reported including diabetes (6%), sjogrens syndrome, hypothyroidism (6%), primary biliary cirrhosis, tuberculosis (6%) and pregnancy.[2,4] Underlying malignancies like breast, cervix, colon, stomach, lung and melanoma have been reported in 25% of cases.[5] Multicentric reticulohistiocytosis precedes the diagnosis of malignancy in 75% of patients, sometimes by up to ten months.[4] Although joints and skin are commonly involved, mucosa, muscles, tendon sheaths, lymph node, bone marrow, eyes, salivary glands, larynx and thyroid may also be involved.[2] Except for skin and joints no other systemic involvement was detected in our patient. Small tumefactions around nail folds termed coral beads are characteristic. The skin lesions tend to wax and wane independent of arthritis.[2] The disease may slowly remit after 5 to 8 years leaving the patient with severe articular impairment.

Diagnosis is based on histological and immunological features of the proliferating histiocytes. On

histopathology, dermal infiltration of multinucleated giant cells with eosinophilic ground glass cytoplasm is characteristic. Immunohistologically they are positive for TRAP (tartrate resistant acid phosphatase),[6] CD68, lysozyme and Human alveolar macrophage-56 (HAM-56) whereas negative for S100 protein, CD1a, factor XIIIa.[5] Due to financial constraints, immunohistochemistry could not be done in our patient.

The main radiologic feature is bilateral, symmetric joint involvement with predilection for metacarpophalangeal and interphalangeal joints. Osteopenia is mild to moderate. Radiography shows disproportionate bony destruction compared to articular cartilage loss. Resorption of subchondral bone can lead to formation of erosions spreading from margin to joint surface.[5] The joint involvement in our patient was consistent with reported literature.

There is no effective treatment for MRH. Several treatment regimens have been tried with variable success. Systemic steroids, cytotoxic drugs like cyclophosphamide,[3] chlorambucil,[5] methotrexate,[3] etanercept[7] and infliximab[8] have been reported to be effective. Bisphosphonates like alendronate and zolidronate have been reported to improve both arthritis and skin lesions.[6,9] Bisphosphonates accumulate in the reticuloendothelial system and act on monocyte/macrophages to inhibit their infiltration into the skin or directly impair those cells once they have infiltrated into the skin by inducing their necrosis and apoptosis. The mechanism proposed for their direct action is the inhibition of farnesyl pyrophosphate synthase in the mevalonate pathway, thereby impairing isoprenylation of proteins and promoting apoptosis.[6]

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