CASE REPORT

MULTICENTRIC RETICULOHISTIOCYTOSIS (MRH): A CASE REPORT ON A RARE DESTRUCTIVE ARTHRITIS

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Multicentric Reticulohistiocytosis is a rare disorder of unknown aetiology which affects skin and joints predominantly. There are no specific laboratory investigations for diagnosis. Diagnosis can be made clinically and on a histopathological basis. There is no consensus on treatment. We report a case from Pakistan with classical presentation who did well on methotrexate and low dose steroids. Prompt diagnosis and early treatment may save from significant disability.

Keywords: Multicentric Reticulohistiocytosis; MRH; Arthritis; Inflammatory arthritis; Citation

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INTRODUCTION

Multicentric Reticulohistiocytosis (MRH) is an extraordinarily rare multisystem disorder of undetermined aetiology. It usually affects Caucasian females in their 50s. Clinically it is recognized by a combination of symmetric erosive polyarthritis and characteristic papulo-nodular skin lesions.[1] Its prevalence is unknown. Only a few hundred cases have been reported in the literature, are mostly from Western countries. Arthritis described in the literature is mostly symmetrical, erosive, affecting the joints of hands, elbows, knees and shoulders. In hands the distal joints maybe predominantly involved, helping to differentiate it from rheumatoid arthritis. If left untreated it may become progressively destructive. Arthritis mutilans has been described in 45% of the cases.[2] The classical skin eruptions are red to brown in colour and in the form of papules and nodules. The lesions typically appear on the face, hands, dorsal aspects of small joints and elsewhere. The lesions may coalesce to give an appearance, which is described as coral beads or strings of pearls.[3] Malignancy has been reported in up to a quarter of cases.[4] We report a case of Multicentric Reticulohistiocytosis in a Pakistani man who presented with classical findings.

CASE REPORT

A 64-year-old Pakistani man with no previously known co-morbidities presented to our clinic with complaints of painful joints and extensive skin rash. His problems started two years ago when reddish bumps started appearing on his hands, elbows, scalps, back and thighs. These bumps were not painful or itchy. The rash would spontaneously resolve and recur. Months later, the patient developed pain in multiple joints, which was associated with swelling and early morning stiffness for more than one hour. Affected joints included small joints of hands, elbows, shoulders, knees and ankles. He also reported subjective fever and undocumented weight loss.

On examination, multiple red-brown macules and papules were observed in a symmetrical fashion over the dorsum of hands, elbows, around the ears, along the neck, the back and thighs. Musculoskeletal examination revealed swelling and tenderness in the proximal and distal interphalangeal joints, metacarpophalangeal joints, elbows, shoulders, knees and ankles. The rest of the systemic examination was unremarkable. Investigations revealed normal Complete blood count, liver and muscles enzymes and renal function tests. ESR was elevated (85 mm/hour). Rheumatoid arthritis (RA) factor, Anti-citrullinated peptide antibodies (anti-CCP), anti-nuclear antibodies (ANA), and extractable nuclear antibodies (ENA) were negative. Initial differentials included rheumatoid arthritis, dermatomyositis and carcinomatous arthritis.

Skin biopsy revealed dense infiltrate in the dermis laden by histiocytes and multinucleated giant cells. Mild to moderate amount of lymphocytic infiltrate was scattered around the giant cells. X-ray of the hand revealed erosive changes in the left carpus and right second proximal interphalangeal join (PIP). On clinical grounds and histopathology of the skin specimen, a diagnosis of MRH was made. Patient was started on low dose prednisolone (7.5 mg/ day) and low dose methotrexate (7.5 mg/ week). An extensive workup to rule out an underlying malignancy was done. As malignancy could not be detected patient was discharged and followed up. Arthritis resolved in three months and skin rashes improved on subsequent visits.

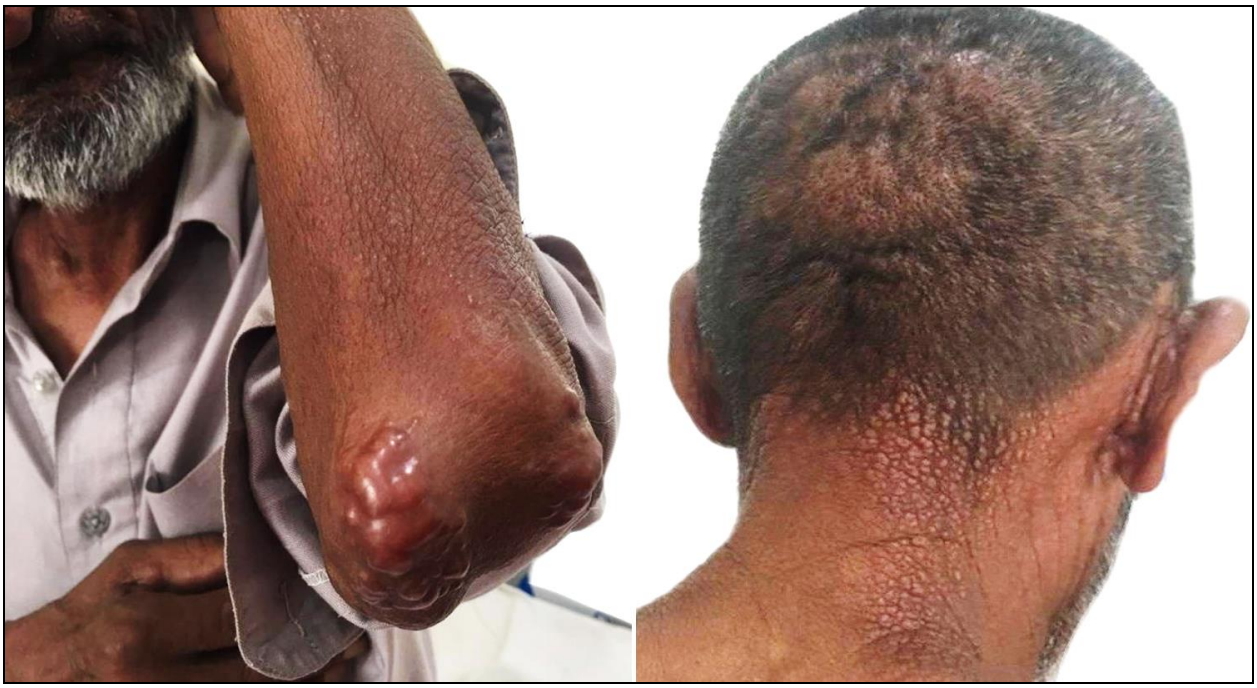

Figure-1: (A) and (B). Typical papulo-nodular eruption over elbow and at the back of neck giving coral bead appearance.

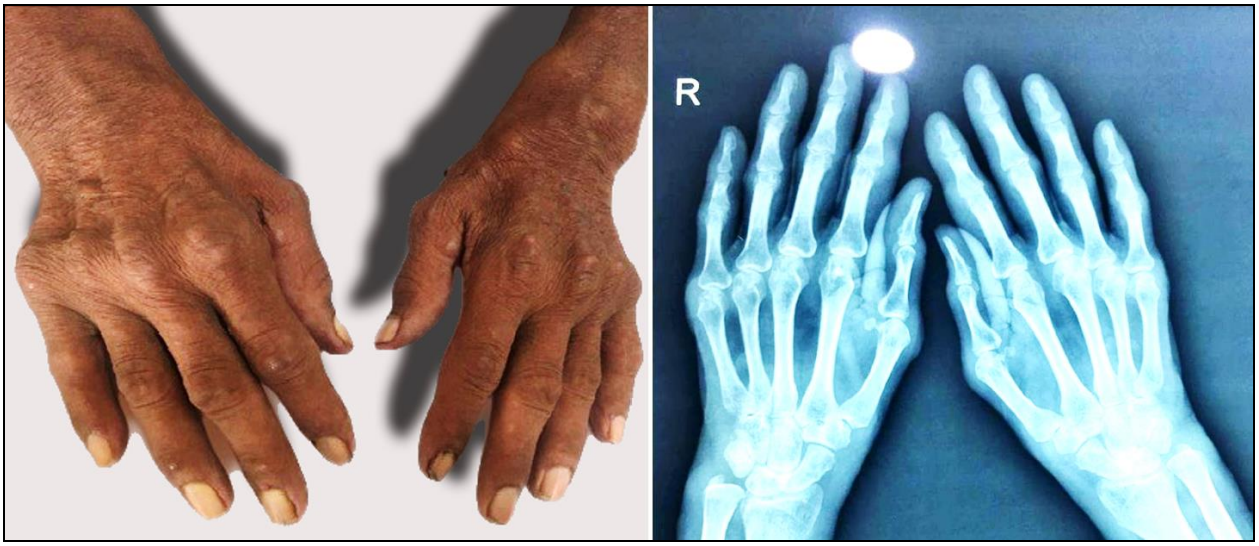

Figure-2: Rheumatoid arthritis like deformities affecting the hand. Figure-3: Radiographs of the hand showing erosions in the carpal and carpometacarpal joints.

DISCUSSION

This case report was written to create awareness about the clinical spectrum of MRH as knowledge about the disease and its outcomes are limited. It is rare and the number of cases described in the literature, do not exceed a few hundred. Furthermore, our review of the literature suggests most cases being reported from Western countries and amongst the white population. Worldwide, most cases report a Caucasian predominance.[5] The reason could be increased awareness and increased access to health care amongst these populations. The most common presentation is that of a female with an erosive arthritis and papulo-nodular rash. A retrospective medical record review conducted at the Mayo clinic revealed skin and joint involvement in all patients. Majority of patients had skin or mucosal papulo-nodular lesions followed by joint involvement, fatigue and unintentional weight loss. All patients had skin and joint involvement. The most commonly

affected areas of skin included hands, arms and back. The majority of the patients reported joint pains and most had clinically detectable joint effusion or synovitis. The hand joints including the DIPs, PIPs, MCPs and wrist were most commonly affected followed by the knees.[6] These findings are consistent with other cases reported worldwide.[7–10] Occasionally, patients may have popular xanthomas, which have distinct histopathological findings.[9,10]

Multicentric Reticulohistiocytosis can present with visceral involvement and overlap with other autoimmune conditions. Most commonly affected systems include the heart and lungs. When the pulmonary system is involved, the patient may present with pleural effusion, hilar lymphadenopathy and pulmonary fibrosis. Cardiac involvement may manifest as myocarditis and pericardial effusion.[11] Muscular involvement in the form of proximal muscle weakness and myalgia has also been documented.[12] In up to a third of patients, MRH may co-exist with other autoimmune conditions such as rheumatoid arthritis (RA), Systemic Lupus Erythematosus (SLE), Sjogren's syndrome, scleroderma or hypothyroidism.[13–15]Rheumatoid Factor, ANA and anti-CCP are usually negative but in case of overlapping autoimmune diseases antibodies may be positive.[9] Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP) maybe elevated. Workup should also include age and gender relevant malignancy screen. Reported associated malignancies affect various systems and organs including, sarcoma, lung, larynx, breast, cervix, colon, mesothelioma, haematological malignancies and others.[16]

Multicentric Reticulohistiocytosis may be easily confused with other inflammatory arthritis such as rheumatoid or psoriatic arthritis. Other important differentials that need to be ruled out include dermatomyositis, fibroblastic rheumatism, gouty arthritis etc. A good knowledge of its clinical features in addition to radiographic and histopathological investigation may aid in early diagnosis and differentiation from other diseases with similar presentations. Imaging may aid in diagnosis by identifying erosions, soft tissue swellings, contractures and deformities. Skin biopsy is the most useful and specific test to diagnose MRH. There is no biomarker that may be used specifically to diagnose this condition. Biopsy of the skin shows a histiocytes predominant infiltrate with “ground glass” or “foamy” Eosinophilic cytoplasm, multinucleated giant cells. These cells are positive for Cd-68, CD-163 and Ki-M1P. The giant cells stain positive for periodic acid-Schiff. Similar findings may be demonstrated in the synovial biopsy.[17,18]

To this day, no treatment consensus or guidelines exist for the treatment of Multicentric Reticulohistiocytosis. Case reports have suggested the use of various drugs including, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), glucocorticoids, bisphosphonates, and conventional synthetic and biological Disease Modifying Anti-Rheumatic drugs (DMARDs). NSAIDs may be beneficial in early and mild diseases. However, in case of aggressive and deforming disease DMARDs may be initiated as soon as the diagnosis is made and low dose corticosteroids should be given as a bridging therapy. The most effective initial treatment is methotrexate, which may benefit both skin and joint disease. Other conventional synthetic DMARDs that maybe tries include leflunomide, azathioprine and cyclophosphamide. Biological DMARDs mainly Tumour Necrosis Factor (TNF) inhibitors have been tried with variable success.[5,7,9–11] Bisphosphonates may be added in case of poor disease control, in the presence of osteoporosis or steroid use.[6,11,19] Majority of the cases respond well to the treatment and remit spontaneously. Thus, the disease carries a good prognosis in terms of survival. In case of concomitant malignancy, treatment of malignancy may lead to resolution of MRH.[12,19]

CONCLUSION

MRH is a rare disease of unknown aetiology. We presented a case of a Pakistani man with MRH who presented with typical maculopapular rash and inflammatory arthritis. Initiation of timely treatment with DMARDs in the patient resulted in remission of disease. Early and prompt diagnosis is the key to preventing disability. We could not find evidence of malignancy in our patient but it should be screened for in all cases of MRH.

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