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Case Report .

Multicentric Reticulohistiocytosis: A Rare Case Report

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ABSTRACT

Multicentric reticulohistiocytosis (MRH) is a rare multisystem disorder of unknown etiology, characterized by erosive polyarthritis and papulonodular lesions on the skin, mucous membranes, and internal organs. There is no published data on incidence and prevalence of MRH. As MRH is a rare entity so modem of information is available only in the form of case reports. Although clinically it mimicks rheumatoid arthritis and psoriatric arthritis, its spectrum is aggressive and poses a diagnostic challenge for rheumatologists and dermatologists. Diagnosis is made clinically by the characteristics cutaneous and joint manifestations and is confirmed by typical histopathological appearance of non-Langerhans cell histiocytosis on skin biopsies. Prompt diagnosis and early treatment of this rare entity is vital as untreated cases can progress to severe destructive arthritis and disability.

Keywords: Multicentric Reticulohistiocytosis, Erosive Arthritis, Papulonodular Lesions.

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INTRODUCTION

MRH is a rare form of symmetric erosive polyarthritis with worldwide prevalence. Originally it was described as lipoid dermatoarthritis, giant cell reticulohistiocytosis, giant cell histiocytoma, lipid rheumatism and granulomatous reticulohistiocytosis.[1] Although it is sporadic in nature and can involve various ethnicities, but many literatures have reported an increased incidence in caucasians.

MRH is most common in the 4th decade of life, more common in women compared to men in a ratio of 3:1.[2] It usually begins with either isolated polyarthritis (50%) or cutaneous lesions (25%) or at times both occurring concurrently (25%). The exact pathogenesis is unclear but probably has immunological basis. Elevated levels of cytokines, TNF alpha, and IL 1B, IL 6, IL -8 are detected during early phase of MRH.[3] In one case report overexpression of MCP-1 ,stimulated by TNF alpha is believed to play a role in the pathogenesis. The authors hypothesized that MCP-1 may play a role in attracting histiocytes and giant cells in patients with MRH.[4] Here in we describe the case of the patient found to have MRH along with overlap of Rheumatoid arthritis.

CASE PRESENTATION

A 40 year female was admitted with chief complaints of multiple reddish brown papules over face, ear, back of the neck, back of the arms, hands & oral mucosa since 2 months and pain in small joints of hand, b/l wrist joint, elbow, knee joints since 2 months **Fig.1[a.b.c.d].** She developed multiple translucent reddish brown papulonodules of varying size over ears followed by face, above eyebrows, and nasolabial fold followed by back of the neck and oral mucosa which was insidious in onset and gradually progressive in nature. The papulonodules are isolated from one another as well as clustered. Discrete papulonodules present over DIP of both hands. Patient developed pain in b/l small joints of hand (DIP PIP MCP), wrist, elbow, knee joints which was also gradually progressive. EMS->2hrs. No history of low backache, uveitis, diarrhoea, bloody motion, Raynauds phenomenon, proximal muscle weakness, and exertional dyspnoea. Patient was under treatment of the Dermatologists and was receiving NSAIDs. On examination there was moderate degree pallor, no icterus, cyanosis, clubbing, lymphadenopathy and pedal edema and no thyromegaly. Vitals were within normal limits. Hb was 7g% and ESR was 50mm at end of 1 hour, ANA HEP2: Negative, RF FACTOR: Q 110 (+ve), Anti CCP: 38.59 (7-17), Serum calcium: 2.1 (2.1-2.7), Serum ACE: 18U/l. Lipid and thyroid profiles were within normal limits.Examination of musculoskeletal system shows normal gait, arm shows tender b/l MCP, PIP, DIP elbow, wrist joints with flexion deformity of b/l elbow joints, with ROM , leg was tender swollen b/l knee joints and spine was normal. The rest of the systemic examination was within normal limits. Xray of joints **[Fig 2]** and chest Xray were also normal.

Histopathology is the gold standard for diagnosis. Diagnosis in our case is opined on basis of distinct histopathological findings on skin biopsy that demonstrates thinned out epidermis with hyperkeratosis, diffuse dermal giant cell infiltrate with sparse inflammation and, and presence of numerous multinucleated giant

cells and oncocytic macrophages showing abundant eosinophilic, finely granular cytoplasm,often with a “ground glass appearance” replacing the upper dermis. Giant cells are large and irregular containing haphazardly arranged nuclei Fig [3 a,b,c]. So final histopathological diagnosis of Multicentric reticulohistiocytosis was rendered.

Fig 1 (A,B,C,D): Clinical photograph showing papulonodular lesions in eyebrow, back of neck, ear lobules and knuckles.

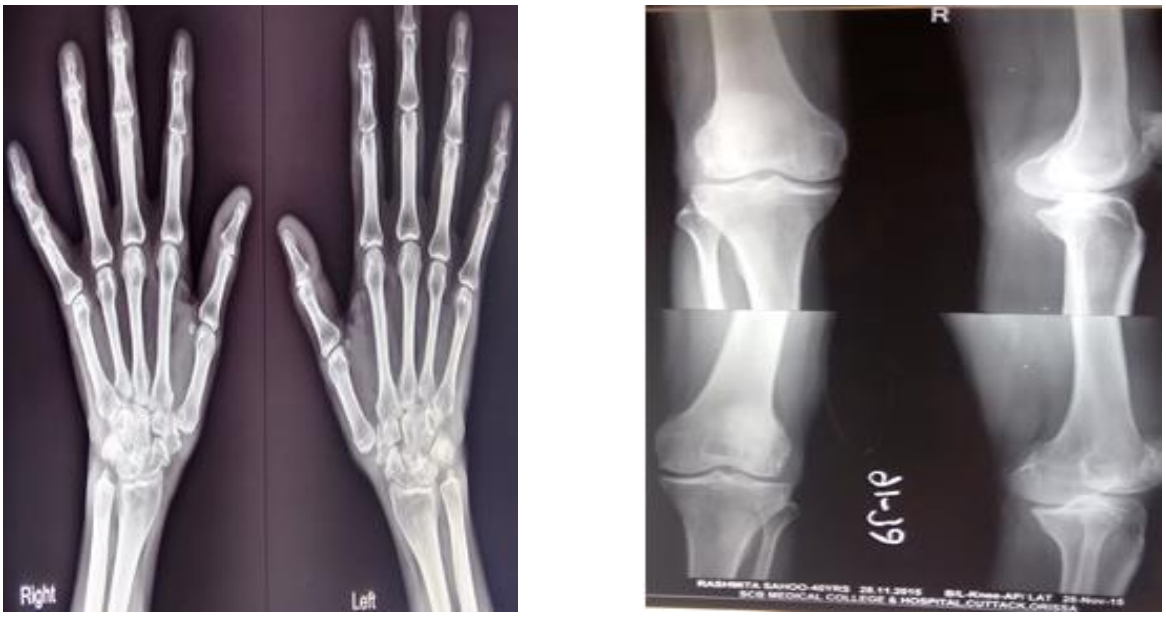

Fig 2: Normal X ray; No bone involvement.

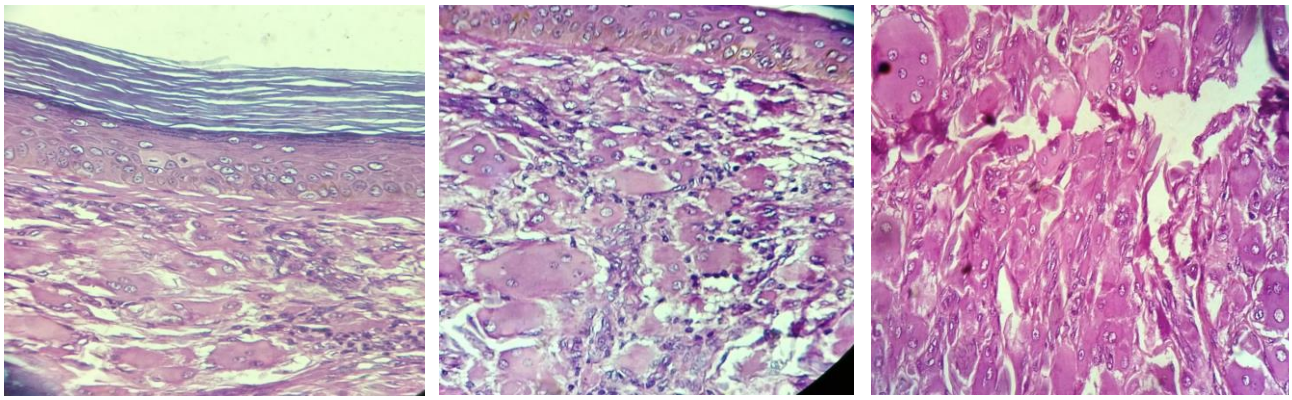

Fig 3: (400X) Thinned out epidermis with hyperkeratosis and presence of numerous multinucleated giant cells and oncocytic macrophages showing abundant eosinophilic, finely granular cytoplasm, often with a "ground glass appearance"

DISCUSSION:

MRH is classified as non-Langerhans cell histiocytosis-class II b, as per the Histiocyte Society recommendations by Zelger et al in the year 1996.[5] It was first identified as a separate disease entity by Weber and Freudenthal (1937)[6] and the term was coined by Goltz and Laymon (1549) because of the multifocal origin and systemic nature of the disease.[7] The first working definition of MRH was Provided by Barrow et al. (1969).8

The polyarthritis is most common manifestation with a predilection for the distal interphalangeal joint. It is usually inflammatory in nature, diffuse, symmetric, progressive, and destructive.9 MRH differs from other types of erosive arthritis, like rheumatoid arthritis, in that typically involves PIP joint.[10] If not treated early can lead to the disabling "accordion" or "opera glass" hand.[8]

Second most common manifestation is the skin involvement that manifests as multiple flesh-colored to reddish-brown nonpruritic firm papules and nodules, ranging in size from a few millimeters to 2 cm in size. They are located over the dorsal aspects of the hands, the elbows, and on the head. Papules often occur in a periungual distribution, producing a characteristic, 'coral beads' appearance.

Internal organs such as the lungs (resulting in pleural effusion) and heart (case reports of pericardial effusion and congestive heart failure) are rarely affected, in addition to rare cases of mesenteric lymphadenopathy and urogenital lesions.[11] Systemic features like weight loss, fatigue, fever, myalgia are also seen in some cases. Mucosal involvement, which includes the tongue and buccal or nasal mucosa, are seen in roughly one-third of the cases.[12]

There are certain conditions that are known to be associated with MRH like hyperlipidemia, positive skin tuberculin test,and many autoimmune diseases like RA ,Sjogren's syndrome[13],primary biliary cirrhosis[14], and systemic vasculitis.[15] A higher incidence of underlying internal malignancy are seen in 25% of MRH patients with breast, hematological and stomach carcinomas being very common.[16] A thorough investigation should be done to exclude malignancy in a newly diagnosed case of MRH. However controversy still exist that whether MRH is a true paraneoplastic disorder? As there is no consistent type of cancer associated with MRH and a correlation between removal of cancer and disappearance or improvement of arthritis and skin symptoms of MRH has not been established.

There are a panel of Laboratory investigations to diagnose MRH but it lacks specificity and diagnostic relevance .The investigations may reveal microcytic anemia, elevated ESR , elevated CRP and hyperlipedemia. Rheumatoid factor (RF), Antinuclear antibody (ANA), anti-cyclic citrullinated peptide (anti-CCP), anti-double-stranded antibody (anti-ds-DNA), anti-SSA, anti-SSB, and perinuclear anti-neutrophils cytoplasmic antibody (P-ANCA) can also be positive. TNF-alpha levels, proinflammatory cytokines, such as IL-1, IL-6, and IL-8, are also elevated.

Differential diagnosis includes solitary giant cell rich reticulohistiocytoma and Juvenile xanthogranuloma (JXG) which are a part of spectrum and some degree of overlap is seen. Solitary reticulohistiocytoma affects younger age and solitary lesions are seen not on digits or face. JXG usually affects children have scattered Touton type of histiocytic giant cells and numerous eosinophils, but large epitheloid histiocytes are not prominent. Gout ,RA,sarcoidosis, dermatomyositis and even lepromatous leprosy may be considered as other differentials.

MRH is regarded as a systemic osteoplastic disease.[17] This finding is based on the fact that MRH showing good response to treatment with biphosphonates and its staining pattern which is PAS positive and osteoclast markers tartrate-resistant acid phosphatase and cathepsin k. They are also positive for CD 68, lysozyme, human alveolar macrophage-56 (HAM-56), whereas negative for S100 protein, CD 1a, and factor XIIIa. IHC was not done in our case due to financial constraints of the patient.

Several drugs have been used in various combinations like NSAID, hydroxychloroquine and corticosteroids[18] but successful response to azathioprine and anti TNF alpha like infliximab has been noted. Recent data showed that the use of biphosphonates is more promising in treatment of MRH.[17]

CONCLUSION

Clinicians should always keep MRH as one of the differential diagnosis when dealing with a patient with erosive polyarthritis and papulonodular skin lesion. Early diagnosis is crucial to halt the progression to debilitating arthritis mutilans which is seen in 45% of cases. Joint involvement and internal malignancy may result in significant morbidity and mortality. We reported this case because of its rarity, its atypical presentation of mimicking with RA and its typical histopathological findings.

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