Multicentric reticulohistiocytosis as a manifestation of reoccurrence of malignancy: a case report

Phurichaya Teyateeti MD,

Penvadee Pattanaprichakul MD.

ABSTRACT:

TEYATEETI P, PATTANAPRICHAKUL P. MULTICENTRIC RETICULOHISTIOCYTOSIS AS A MANIFESTATION OF REOCCURRENCE OF MALIGNANCY: A CASE REPORT. THAI J DERMATOL 2019; 35: 81-88.

DEPARTMENT OF DERMATOLOGY, FACULTY OF MEDICINE SIRIRAJ HOSPITAL, BANGKOK, THAILAND.

Multicentric reticulohistiocytosis (MRH) is a rare, unknown etiologic, non-Langerhans cell histiocytosis, which is characterized by papulonodular skin lesions with destructive polyarthritis and may affect other visceral organs as a systemic disease. The association of MRH with malignancies has been reported up to 15-31% in various types of both solid and hematologic malignancies. We report a case of 62-year-old Thai female with clinical remission after treatment of left breast cancer two years ago, who presented with polyarthralgia preceding the gradual eruption of multiple tender cutaneous papules and nodules on face and extremities. Lesional skin biopsy from the right elbow showed a well-circumscribed nodular infiltration composed of multinucleated giant cells with eosinophilic ground glass cytoplasm, leading to the diagnosis of MRH. Further thorough work-up evaluation revealed reoccurred breast cancer with left supraclavicular and axillary nodal metastasis.

Key words: multicentric reticulohistiocytosis, malignancy

From: Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Corresponding author: Phurichaya Teyateeti MD., email: eclair.changmin@gmail.com

Received: 22 October 2018 Revised: 28 December 2018 Accepted: 29 December 2018

Introduction

Multicentric reticulohistiocytosis (MRH) is a rare non-Langerhans cell histiocytosis disease with approximately 300 cases reported worldwide. Most cases reported were women in the 4th-5th decade of life with only a few reports in children and pregnant women.[1,2] MRH is characterized by papulonodular skin lesions with symmetrical destructive polyarthritis. Involvement of visceral organs as a systemic disease has been observed. The association of MRH with malignancies has been established in 15-31% of cases in which various types of both solid and hematologic malignancies are noted.[3] Most reported associated malignancies were found in bronchial, breast, gastric, uterine cervix, as well as hematologic malignancy.[4] Similar cutaneous and histopathologic findings are present in solitary and multiple reticulohistiocytoma, both of which lack of systemic involvement and polyarthritis as found in MRH.[5]

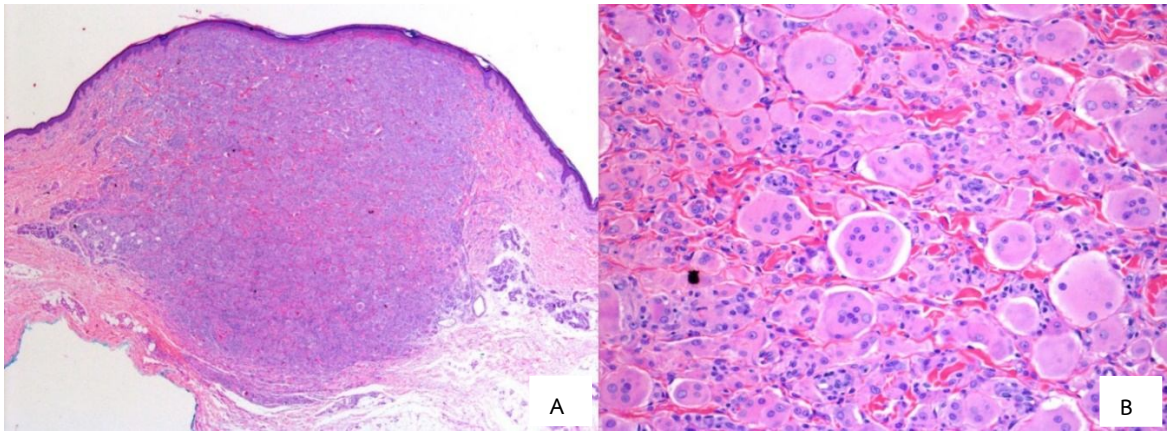

Figure 1 Histopathology reveals a nodular infiltrate in dermis (A) by numerous multinucleated giant cells with eosinophilic ground glass cytoplasm and scattered lymphocytes without eosinophils (B)

The histopathological evaluation from affected skin or synovium typically reveals nodular infiltrate of predominantly large mononuclear cell histiocytes in early lesion with eosinophilic non-foamy ground glass cytoplasm multinucleated giant cells in older lesions.[6] Mixed diffuse infiltrate of lymphoid cells, neutrophils or eosinophils may be seen in the section. The immunohistochemical study demonstrates the neoplastic cells highlighted by CD45 and CD68 in most cases.

While CD1a, S100, and factor XIIIa are frequently negative,—which supports monocyte-macrophage origin and excludes Langerhans-cell and dermal dendrocytic origin.[7]

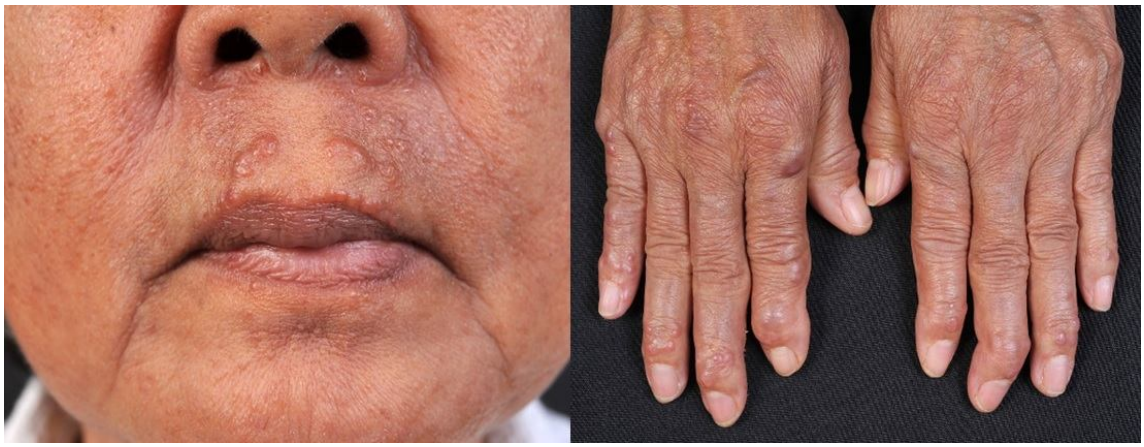

Figure 2 Multiple discrete firm erythematous papules and plaques at perioral area and some small erythematous papules arranged in coral-bead pattern

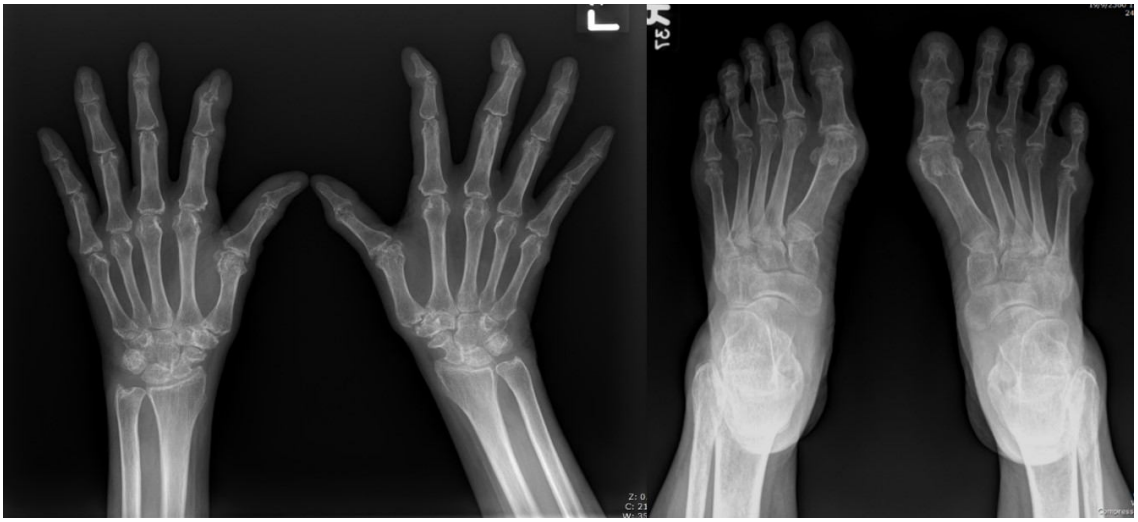

Figure 3 X-ray of both hands and feet showed diffused narrowing joint spaces and bony erosion of almost all DIP and PIP joints

Report of a case

A 62-year-old Thai female patient presented with symmetrical polyarthralgia of both hands, wrists, knees, ankles and toes for one and a half year. There was a concurrent morning stiffness of hand joints for 1-2 hours. The joint pain could be partially relieved by over-the-counter pain-controlled medications. A few months later, multiple erythematous and some skin-colored papules and nodules were occurred on the face, dorsum of hands, proximal and distal phalanges of all fingers. The lesions were slowly increased in numbers with progressive deformities of hands and feet for over a year. She denied systemic symptoms such as fever, weight loss, dysphagia, dyspnea, chest pain, or any palpable mass over the body.

The patient had history of left breast cancer in the past 2 years and was treated by surgery and chemotherapy with complete clinical remission without evidence of recurrence of the disease upon the follow up at her primary hospital.

At her primary hospital, skin biopsy from a nodule on the right elbow was performed and the section showed aggregation of numerous, non-foamy, multinucleated giant cells with ground glass eosinophilic cytoplasm and sparse lymphocytic infiltrate; compatible with multicentric reticulohistiocytoma (Figure 1). Immunohistochemical study was not further performed due to typical morphologic findings in hematoxylin-and-eosin staining section. Combined with clinical findings of symmetric arthritis mutilans, the patient was finally diagnosed of multicentric reticulohistiocytosis (MRH). The patient was then referred to our hospital, a tertiary medical center, for further management. The physical examination revealed bilateral, multiple discrete, firm erythematous papules, nodules and plaques on the forehead, perioral area, dorsal surface of proximal and distal phalanges of both hands, right elbow, and tip of toes. The lesions were varying in size, ranging from 0.4-1 cm. Some lesions on dorsum of distal phalanges were arranged in coral-bead pattern. A solitary mass on the hard palate was seen without any other mucosal lesion elsewhere. There were signs of arthritis of second and third metacarpophalangeal (MCP) together with first and second distal interphalangeal (DIP) joints of both hands, both knees, and left ankle joint. Moreover, flexion deformities of second to fourth DIP joints of both hands were observed (Figure 2). Non-tender, firm-consistency, movable lymph nodes, size 1 cm at left supraclavicular and 2 cm at left axilla were

found without any palpable breast mass. Other physical examinations were within normal limits.

Laboratory investigation revealed normal complete blood count (CBC), renal and liver function tests, C-reactive protein (CRP), and urinalysis. Mild elevation of erythrocyte sedimentation rate (ESR) of 30 mm/hour and serum cholesterol level at 208 mg/dl were found. X-ray findings of both hands and feet revealed diffused narrowing joint spaces and erosions of almost all joints, as shown in Figure 3. For autoimmune panel; antinuclear antibody (ANA) was borderline-positive (fine-speckled pattern titer 1:100), while rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) were negative. Due to suspicion of malignancy, fine needle aspiration from left supraclavicular lymph node was performed, and the result showed nodal involvement by metastatic carcinoma. Further investigation including bone scan and ultrasonography (US) of upper abdomen were unremarkable except a detection of enlarged left axillary lymph nodes from mammography and US of the breasts. Evaluation for hematologic and gynecologic malignancies and other age-related malignant screening revealed negative result. Thus, the final diagnosis was MRH with reoccurred breast cancer and nodal metastasis.

During malignancy work up, the patient was treated with naproxen 500 mg/day, chloroquine 125 mg/day, methotrexate 15 mg/week, prednisolone 5 mg/day, and salazopyrin 2,000 mg/day. After continuous treatment for 3 months, the cutaneous lesions and joint pain were much improved. The patient was referred back for further staging and treatment of reoccurred breast cancer at her primary hospital.

Discussion

The term “multicentric reticulohistiocytosis”, the disease with multifocal systemic involvement by macrophage in origin, was firstly established by Goltz and Laymon in 1954.[8] While the first case was described in 1937 by F. Parkes Weber and W. Freudenthal, in a 35-year-old man presented with multiple joints pain and stiffness accompanied by cutaneous nodules mostly located near joint area.[9]

The clinical presentation of MRH usually begins with polyarthralgia, in approximately 60-70% of cases. The clinical findings may mimic rheumatoid arthritis, consisted of periarticular soft tissue swelling, stiffness, and tenderness on motion of several joints, but commonly affects DIPs joint. The radiologic findings show severe destruction of articular structures in several areas of the body

including hands, knees, shoulders, elbows, hips, ankles, and feet, respectively. The course of articular involvement can be either progressive to arthritis mutilans or self-limited, or even presents in relapsing-remitting fashion in less aggressive cases.[10]

Cutaneous papulonodular lesions are ranging from 1 mm to 2 cm in skin-colored to brown-reddish or yellowish nodules, which can be confluent to a larger plaque or cobblestone appearance. These lesions are predilected on head, neck and acral areas, especially over the joints of hands and feet.[10,11] Moreover, half of the patients can have mucosal involvement, particularly in an oropharyngeal and nasal mucosa.[11] The cutaneous lesions tend to have relapsing-remitting in nature, resembling the articular involvement.

Because of insidious nature of the disease, the articular and cutaneous involvement may not emerge at the same onset. Therefore, lists of clinical differential diagnosis in case of erosive arthritis predominantly are rheumatoid arthritis (RA), psoriatic arthritis (PsA), gout, and Reiter's syndrome. While cutaneous xanthomatosis, multiple juvenile xanthogranuloma, generalized eruptive histiocytosis, neurofibromatosis, sarcoidosis, cutaneous Rosai-Dorfman disease, multibacillary leprosy, and reticulohistiocytoma should be considered if cutaneous lesions are prominent.[11-13]

The tissue biopsy from a cutaneous lesion or synovium for definite diagnosis should be interpreted with caution, especially in an early phase that the characteristic feature of multinucleated giant cells with eosinophilic ground glass cytoplasm may not be completely demonstrated.[14] However, additional immunohistochemical analysis may be beneficial for making the diagnosis.[15]

Although MRH is a disease of unknown etiology, it has been described in association with malignancies, autoimmune diseases including systemic lupus erythematosus, dermatomyositis, Sjogren's syndrome, celiac disease, primary biliary cirrhosis, non-autoimmune diseases such as diabetes mellitus, dyslipidemia, thyroid disease, colitis, and tuberculosis.[10] The diagnosis of MRH mostly precedes the onset of malignancy and may present in concurrent with the recurrence of the malignancy.[5] However, the documentation of MRH as a paraneoplastic disease is still controversy.[9,16]

There is no consensus guideline for the treatment of MRH due to its rarity and lack of sufficient cohort for clinical trials. Nonsteroidal anti-inflammatory drugs (NSAIDs) and

corticosteroids are generally prescribed as first-line of treatment. Combination of disease-modifying antirheumatic drugs (DMARD) including leflunomide, hydroxychloroquine, and immunosuppressive drugs such as methotrexate, azathioprine, cyclosporine A, cyclophosphamide, and chlorambucil has been reported as effective in single cases. Emerging data on efficacy of biologics have been reported for TNF-alpha inhibitors such as etanercept, infliximab and adalimumab.[10] In the absence of associated malignancy, MRH typically regresses in an average of 7-8 years, but may leave permanent articular damage.

To be described, MRH in our case is the manifestation of the reoccurrence of previous malignancy without history of previous episode of MRH. This valuable case report adds on the reassurance of MRH as the manifestation of the reoccurrence of pre-existing malignancy. Therefore, physicians taking care of the patient with newly diagnosis of MRH, should be highly aware and are encouraged to perform thorough investigation for occult malignancy or recurrent malignancy in the patient with malignancy-indicated history.

References

1. Matiz C, Ferguson PJ, Zaenglein A, Groh B, Bingham CA. Papular xanthomas and erosive arthritis in a 3-year-old girl, is this a new MRH variant? Pediatr Rheumatol Online J 2009; 7: 15.
2. Brackenridge A, Bashir T, Wheatley T. Multicentric reticulohistiocytosis and pregnancy. BJOG 2005; 112: 672-3.
3. Luz FB, Gaspar NK, Gaspar AP, Carneiro S, Ramos-e-Silva M. Multicentric reticulohistiocytosis: a proliferation of macrophages with tropism for skin and joints, part I. Skinmed 2007; 6: 172-8.
4. Gelmetti C. Non-Langerhans Cell Histiocytosis. In: Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, Wolff K, editors. Fitzpatrick's Dermatology in General Medicine. 8th ed. New York: McGraw-Hill; 2012. p. 1795-808.
5. Tran TH, Pope E, Weitzman S. Cutaneous Histiocytosis. In: Christopher EM Griffiths, Barker J, Bleiker T, Chalmers R, Creamer D, editors. Rook's Textbook of Dermatology. 9th ed. United States: John Wiley & Sons; 2016. p. 136.1-29.
6. Rapini RP. Practical dermatopathology. Edinburgh: Elsevier Health Sciences; 2012. p. 112-4.
7. Gorman JD, Danning C, Schumacher HR, Klippel JH, Davis Jr JC. Multicentric reticulohistiocytosis: case report with immunohistochemical analysis and literature review. Arthritis Rheum 2000; 43: 930-8.
8. Goltz RW, Laymon CW. Multicentric reticulohistiocytosis of the skin and synovia: reticulohistiocytoma or ganglioneuroma. AMA Arch Derm Syphilol 1954; 69: 717-31.
9. Weber FP, Freudenthal W. Nodular non-diabetic cutaneous xanthomatosis with

hypercholesterolemia and atypical histological features. Proc R Soc Med 1937; 30: 522-6.

10. Selmi C, Greenspan A, Huntley A, Gershwin ME. Multicentric reticulohistiocytosis: a critical review. Curr Rheumatol Rep. 2015; 17:36.
11. Goodman WT, Barrett TL. Histiocytoses. In: Bolognia JL, Schaffer JV, Cerroni L, editors. Dermatology. 4th ed. China: Elsevier Saunders; 2018. p. 1627-8.
12. Rapini RP. Multicentric reticulohistiocytosis. Clin Dermatol 1993; 11: 107-11.
13. Tajirian AL, Malik MK, Robinson-Bostom L, Lally EV. Multicentric reticulohistiocytosis. Clin Dermatol 2006; 24: 486-92.
14. Hsiung SH, Chan EF, Elenitsas R, Kolasinski SL, Schumacher HR, Werth VP. Multicentric reticulohistiocytosis presenting with clinical features of dermatomyositis. J Am Acad Dermatol 2003; 48: S11-4.
15. Gianotti F, Caputo R. Histiocytic syndromes: a review. J Am Acad Dermatol 1985; 13: 383-404.
16. Tan BH, Barry CI, Wick MR, et al. Multicentric reticulohistiocytosis and urologic carcinomas: a possible paraneoplastic association. J Cutan Pathol 2011; 38: 43-8.