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OLGU SUNUMU / CASE REPORT

A Rare Case of Multicentric Reticulohistiocytosis in An Elderly Male Patient

Yaşlı Erkek Hastada Nadir Bir Multisentrik Retikülohistiyositoz Vakası

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ÖZET

Multisentrik retikülohistiyositoz (MRH), Langerhans dışı hücrelerin nadir görülen sistemik proliferatif granülomatöz bir hastalığıdır. Bu çalışmanın amacı klinik pratikte sıklıkla yanlış teşhis edilen bir multisentrik retikülohistiyositoz olgusunu sunmaktır. 74 yaşında bir erkek, altı aydır süren, sabah tutukluğu, eklem şişliği ve üst ve alt ekstremite zayıflığının eşlik ettiği artralji şikayetiyle Aralık 2022'de Romatoloji ofisine başvurdu. Fizik muayenede proksimal interfalangeal eklemlerin dorsal yüzeyinde, burun tabanında ve sağ halluks lateral yüzeyinde papüller görüldü. Ayrıca sırtta hiperemi ve proksimal ve distal interfalangeal eklemlerde, bileklerde ve dizlerde ödem tespit edildi. Laboratuvar testlerinde ESR ve ANA'nın normal sınırlar içinde olduğu görüldü. Anti-Sm, Anti-RO, romatoid faktör, Anti-CCP, HIV ve HCV testleri negatifti. Göğüs BT taramasında sağ aksiller lenf düğümünde 2,7 cm boyutunda genişleme, ateromatöz aort ve alt lobda başka değişiklikler olmaksızın dağınık atelektazili çizgiler görüldü. Abdominal ultrasonografi'de prostat büyümesi tespit edildi. Deri biyopsisinde immünohistokimyasal olarak atipik asiner proliferasyon tanımlandı. Hematoksilen-eozin boyalı cilt biyopsisinde histopatolojik olarak (Ocak 2023) yoğun bir histiyositik infiltrasyon görüldü. Histiyositlerde "buzlu cam" görünümlü eozinofilik sitoplazma görüldü. İmmünohistokimyasal olarak, S100 ve CD34 için negatif, CD68 için pozitif bulundu. Son teşhis MRH olarak raporlandı. Hastaya ilaç tedavisi uygulandı. Sonuç olarak, romatoloji pratiğinde MRH'dekilere benzer şekilde romatizmal hastalıkların (örn. dermatomiyozit ve romatoid artrit) belirti ve bulgularıyla birlikte, cilt ve eklem değişikliklerini içeren klinik semptomlar beklenmektedir. Ancak MRH'de hastalığın ilerlemesi hakkındaki bilgiler sınırlıdır. Bu yüzden, nadir görülmesi nedeniyle bu olgu sunulmuştur.
Anahtar Kelimeler: Langerhans Dışı Hücreli Histiyositoz, Patoloji, Mutisentrik Retikülohistiyositoz, Romatolojik Hastalıklar

ABSTRACT

Multicentric reticulohistiocytosis (MRH) is a rare systemic proliferative granulomatous disease of non-Langerhans cells. The aim of this study is to report a case of multicentric reticulohistiocytosis that is easily misdiagnosed in clinical practice. A 74-year-old man sought the Rheumatology office in December 2022 with a main complaint of arthralgia for six months, associated with morning stiffness, joint swelling, and upper and lower limb weakness. On physical examination, papules on the dorsal surface of the proximal interphalangeal joints, base of the nose, and lateral surface of the right hallux were observed. Hyperemia was also identified on the back, and edema of the proximal and distal interphalangeal joints, wrists and knees. Laboratory tests revealed ESR and ANA within normal limits. Tests were negative for Anti-Sm, Anti-RO, rheumatoid factor, Anti-CCP, HIV, and HCV. Chest CT-scan showed right axillary lymph node enlargement, measuring 2.7 cm, atheromatous aorta, and streaks with scattered atelectasis in the lower lobe, without other changes. On total abdominal ultrasound, prostate enlargement was detected. Immunohistochemistry of skin biopsy identified atypical acinar proliferation. Histopathology skin biopsy stained with hematoxylin-eosin (January 2023) showed a dense histiocytic infiltrate. Detail of the histiocytic component displayed “ground glass” eosinophilic cytoplasm. Immunohistochemistry was negative for S100 and CD34 and positive for CD68. Final diagnosis was MRH. The patient underwent treatment with drugs. In conclusion, clinical manifestations, including skin and joint changes, with signs and symptoms of rheumatic disorders (e.g. dermatomyositis and rheumatoid arthritis) similar to those of MRH are expected in rheumatology practice. However, knowledge about disease progression in MRH is limited. Therefore, this case report is described due to its rarity
Keywords: Non-Langerhans-Cell Histiocytosis, Pathology, Muticentric Reticulohistiocytosis, Rheumatological Diseases

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INTRODUCTION

Multicentric reticulohistiocytosis (MRH) is a rare systemic proliferative granulomatous disease of non-Langherans cells, characterized by symmetrical polyarthritis with papulonodular skin lesions with a craniocaudal distribution. MRH is a disease of unknown etiology and unpredictable course. Typically, it presents with periods of exacerbation that can vary over time, spontaneous regression despite some joint and dermatological involvement. Internal organs can also be involved, causing pleural and pericardial effusion. On histology, a dense histiocyte infiltrate, containing typical multinucleated cells at the site of the lesion, is identified. The prevalence of MRH is not fully known, and approximately 300 cases worldwide have been reported to date. Several case reports have demonstrated an association between MRH and malignancies, such as lung and breast cancer. The diagnosis of MRH requires a clinical, radiological, and histopathological approach. Treatment is challenging due to the lack of knowledge about the etiology (1–4).

The aim of this study is to report a case of multicentric reticulohistiocytosis that is easily misdiagnosed in clinical practice.

CASE

A 74-year-old man arrived at the Rheumatology office in December 2022, complaining of arthralgia for six months on the proximal interphalangial joint (PIP), distal interphalangial joint (DIP), and wrists, elbow, and knees, associated with morning stiffness, joint edema, and weakness in the upper and lower limbs. The patient reported cutaneous papules on the extensor surface of the hand and nail fold joints; hyperemia on the dorsal region; and asthenia in the upper and lower limbs. He lost 12 kg in 6 months, complained of insomnia and denied fever, lung and intestinal symptoms, alcoholism, and smoking. Prior history included systemic arterial hypertension, diabetes mellitus, glaucoma, and benign prostatic hyperplasia. Metformin 500 mg, losartan 50 mg, and glibenclamide 5 mg were used. Prednisone had also been prescribed 20 mg for four months.

On physical examination, papules on the dorsal surface of the PIP, base of the nose and lateral side of the right hallux were observed. Hyperemia on the back and edema of the PIP and DIP joints, wrist and knees were also identified, as shown in Figures 1 and 2.

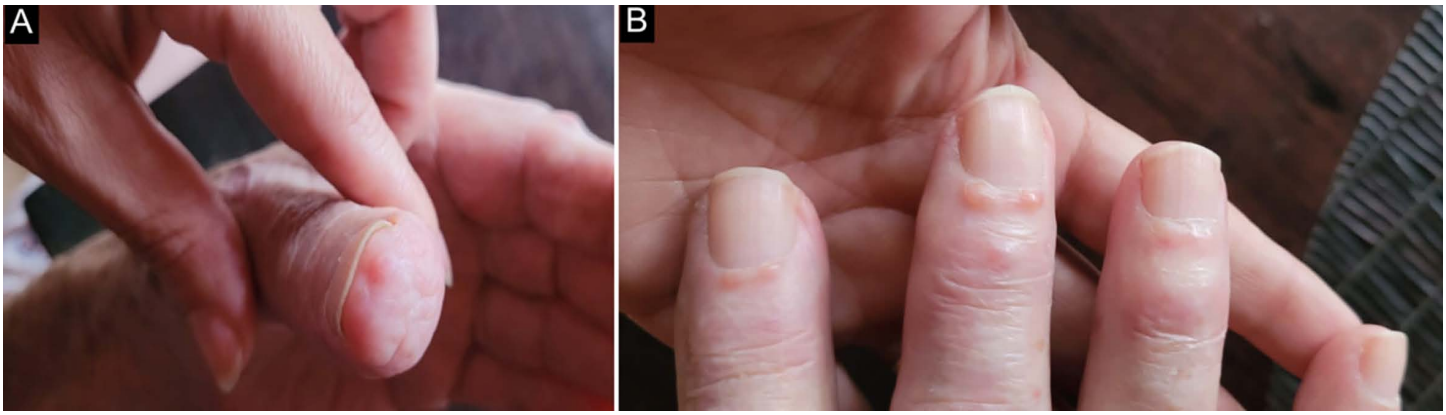

Figure 1 (A, B). Papules of the nail fold region observed at first consultation.

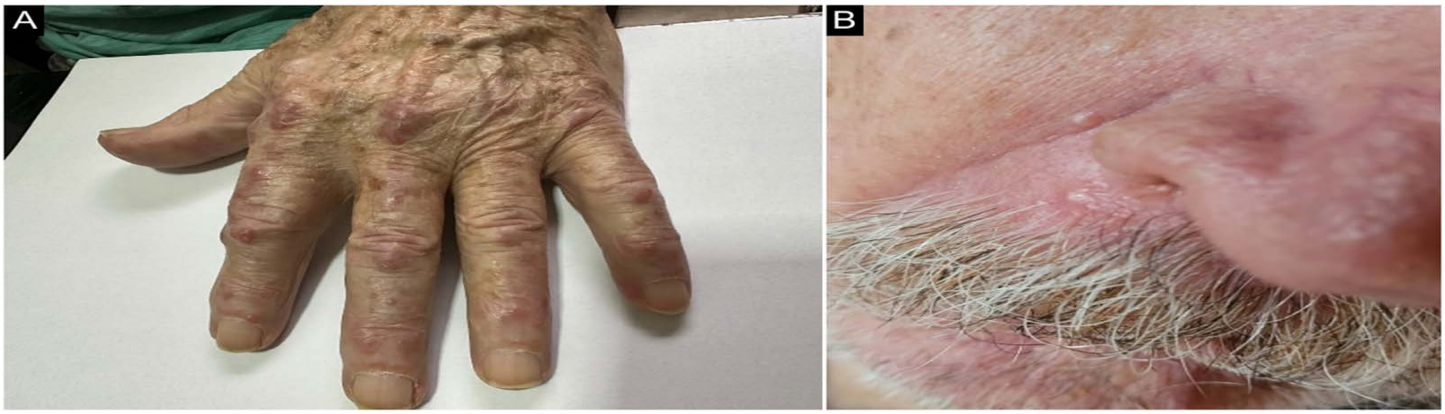

Figure 2. The patient had cutaneous papules on the extensor surface of the PIP and DIP joints (A) and base of the nose (B).

Laboratory tests revealed erythrocyte sedimentation time (ESR) and anti nuclear antibody (ANA) values within normal limits. Tests were negative for rheumatoid factor, Anti-Sm, Anti-Ro, Anti-CCP, HIV, and HCV. Chest tomography showed right axillary lymph node enlargement, measuring 2.7 cm, atheromatous aorta, and streaks with scattered atelectasis in the lower lobe, without other changes. On total abdominal ultrasound, prostate enlargement was identified. A skin biopsy with immunohistochemistry detected atypical acinar proliferation. Histopathological analysis of skin biopsy stained in hematoxylin-eosin (January 2023) showed dense histiocytic infiltrate in the skin (Figure 1A). Detail of the histiocytic component displayed a "ground glass" eosinophilic cytoplasm (Figure 1B). Immunohistochemistry study of the skin was

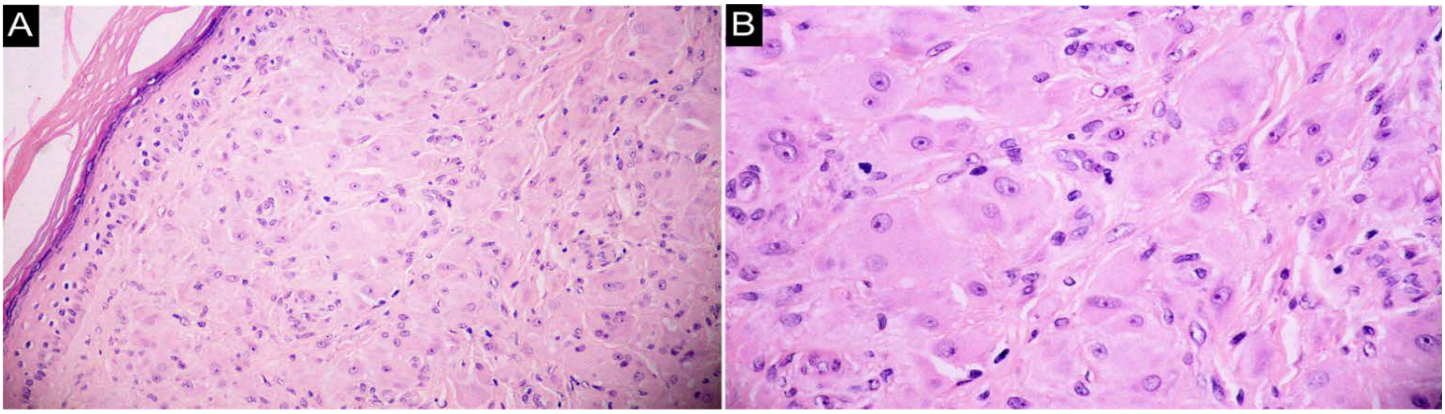

Figure 3. Histopathology of skin biopsy stained in hematoxylin-eosin. (A): 200x Magnification. (B): 400x Magnification.

negative for S100 and CD34 and positive for CD68. The final diagnosis was MRH. The patient initiated treatment with methotrexate 15 mg, increasing the dose to 20 mg after one month. Folic acid and risedronate were given and prednisone was maintained.

On telemedicine reassessment on February 17, 2023, the patient reported continuous pain on the metatarsophalangeal joints, wrist, elbow, and right shoulder; knee pain and redness. His weight had stabilized at 61 kg and he denied cough, fever or urinary changes. On physical examination, he presented limited flexion of his fingers and rotation of his right shoulder, knee arthritis, and a right armpit lymph node. He was emaciated, eupneic, acyanotic, and had papular skin lesions on his fingers. Management included maintenance of prednisone 20mg, with initiation of celecoxib and tramadol 2x/day. The patient remains under rheumatological care to monitor disease progression and therapeutic efficacy.

The patient authorized the publication of this case and signed the Free and Informed Consent Form (FICF).

DISCUSSION

MRH is a rare, severe, multisystemic disease that corresponds to an inflammatory response to stimuli of unknown origin. The most frequently affected age group is 43 years old. Caucasian women between the fifth and sixth decades of life are more commonly affected, as described in the literature. In contrast, this case report shows a 74-year-old male patient. The condition is marked by severe polyarthritis and mucocutaneous eruptions. Histopathology reveals histiocytes with a "ground glass" appearance, PAS-positive cytoplasm and resistant diastasis due to the autophagy-lysosomal pathway (5–8).

The severity of the disease lies in disfiguring lesions on the face and mutilating arthritis that affect up to 45% of cases, resulting in the loss of quality of life. The entity can be classified in the group of non-X histioses, along with juvenile and adult xanthogranulomas; and benign cephalic and sinus histiocytosis, for example. Before the term multicentric reticulohistiocytosis was coined in 1954 by Goltz and Laymon, many other terms were used to characterize this nosocomial entity. However, MRH is differentiated from other reticuloendothelial diseases and its systemic nature has been defined (6,7). In 1969, 33 patients were studied by Barow and Holubar and malignancies were associated with 15% of cases. Other diseases such as diabetes mellitus, tuberculosis (active phase) and thyroid disorders, as well as autoimmune disorders were also associated with MRH. It has been hypothesized that MRH is a paraneoplastic condition. However, progression of MRH is not linked to cancer itself and does not change when the latter is excluded. Among members of the same family, there is a 12% association with MRH manifestations, invalidating the hypothesis of a hereditary cause (8).

The natural history of the disease is marked by periods of flare-ups and remissions of subcutaneous nodules. There

are periods of improvement interspersed with worsening of arthritis, which can be disabling. Arthritis is the most prominent disease manifestation, occurring in up to 45% of cases. Onset is usually insidious and progressive. Involvement of distal interphalangeal joints can lead to the "accordion hand" deformity, which is also found in rheumatoid arthritis and psoriatic arthritis (6).

Nodules can range from a few millimeters to 2 cm, with a craniocaudal progression. Cutaneous lesions that acquire a convalescent nature on the face are referred to as leonine facies. As described in this case report, MRH prefers the hands, juxta-articular areas, and face. Anal and genital mucous membranes are spared, unlike the lips, gums, and nasal septum (7). On histopathology, lymphocytes and giant cells are replaced by fibrosis, with the presence of fibroblasts. On immunohistochemistry, similar to this case study, the marker for Langerhans cells S100, for example, dermal dendrocytes type I (Factor XIIIa) and type II CD34 were negative. The test was positive for the monocyte/macrophage marker CD68, which occurs in around 100% of cases in the literature (8). Therefore, with the evidence above, it can be concluded that MRH has a probable monocyte-macrophage origin (CD45+, CD68+). It originates from a histiocyte between dermal and articular tissues. The main differential diagnoses, apart from psoriatic and rheumatoid arthritis, are lepromatous leprosy, disseminated xanthomas, and fibroxanthomas, tumor stage of mycosis fungoides, cutaneous lymphomas, and cutaneous sarcoidosis (7).

Internal organs, such as the heart (causing pericardial effusion, and heart failure); pleura, and lungs can be affected (8). The course of the disease is usually five to eight years until facial involvement and joint limitation occur. Nevertheless, a combination of methotrexate, cyclophosphamide, steroids, and other immunomodulators has proven effective for disease remission. It is worth highlighting that anti-TNF agents can be added to treat resistant MRH. Once the diagnosis of MRH is made, it is also necessary to screen for cancer, since around 1/3 of patients metachronously and synchronously develop cancer (6). A study has shown that approximately one-third of analyzed patients (n = 24) had autoimmune disorders, and about twenty-five percent of these patients had an associated malignancy (9). It is important to note that this disease can mimic and even coexist with rheumatic conditions. Patients may seek rheumatology or dermatology consultations, and inadvertently be diagnosed with rheumatoid arthritis or dermatomyositis, potentially resulting in misdiagnosis or missed underlying cancers.

In conclusion, clinical manifestations, including skin and joint changes, with signs and symptoms of rheumatic disorders (e.g. dermatomyositis and rheumatoid arthritis) similar to those of MRH are expected in rheumatology practice. However, knowledge about disease progression in MRH is limited. Therefore, this case report is described due to its rarity. Furthermore, specialists need to know the importance of early detection of the disease by clinical examination and histopathology, differentiating MRH from other rheumatic diseases.

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REFERENCES

1. Rezuș E, Burlui MA, Cardoneanu A, et al. Multicentric Reticulohistiocytosis Exhibiting Positive HLA-B*07 and HLA-B*08: A Case Report. Medicine (Kaunas) 2020;56(9):456.
2. Farokhi A, van Vugt RM, Hoekzema R, et al. Multicentric reticulohistiocytosis: a case report. BMC Res Notes 2018;11(1):647.
3. Baek IW, Yoo SH, Yang H, et al. A case of multicentric reticulohistiocytosis, Mod Rheumatol 2017;27(1):165-8.
4. Tajirian AL, Malik MK, Robinson-Bostom L, et al. Multicentric reticulohistiocytosis, Clin Dermatol 2006;24(6):486-92.
5. Barrow MV, Sunderman FW Jr, Hackett RL, et al. Identification of tissue lipids in lipoid dermatoarthritis (multicentric reticulohistiocytosis). Am J Clin Pathol 1967;47(3):312-25.
6. Barrow MV. The nails in multicentric reticulohistiocytosis. (Lipoid dermato-arthritis). Arch Dermatol 1967;95(2):200-1.
7. Luz FB, Gaspar NK. Multicentric reticulohistiocytosis. An. Bras. Dermatol 1999;74(5):497-503.
8. Mariotti EB, Corrà A, Lemmi E, et al. Multicentric Reticulohistiocytosis Associated with an Early Form of Systemic Lupus Erythematosus: A Case Report of a Rare Disease, with Mini Review of the Literature. J Clin Med 2022;11(21):6529.
9. Sanchez-Alvarez C, Sandhu AS, Crowson CS, et al. Multicentric reticulohistiocytosis: the Mayo Clinic experience (1980-2017). Rheumatology (Oxford) 2020;59(8):1898-905.