The Coincidence of Generalized Morphea and Rheumatoid Arthritis: A case report

Sumaia Z. Hamdan [1,2,3,4*],Yousif Elnour[5], Hamdan Z Hamdan[3] , Ayat Hammad[3],[1,2]Lupe Morote

[1]Department of Rheumatology Merline Park University Hospital. Galway – Ireland EC5

[2]Department of Rheumatology & Internal Medicine University Hospital Galway. Galway – Ireland H91YR71

[3] Department of Internal Medicine.Faculty of Medicine, Al-Neelain University, Khartoum- Sudan, PO. BOX 12702.

[4]Department of Clinical Pharmacology & Therapeutics. Faculty of Medicine, Al-Neelain University, Khartoum- Sudan, PO. BOX 12702.

[5] Royal College of Surgeons in Ireland (RCSI). Dublin- Ireland D02YN77

***Correspondence**

Sumaia Z. Hamdan

Sumaia.Abuelbasher@hse.ie

drsamsom@hotmail.com

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Abstract

Morphea is an autoimmune sclerosing skin disease where abundant of subcutaneous collagen deposits result in thickening, and fibrosis.

Presentation of generalized morphea has expanded from merely isolated skin disease to association with variable systemic autoimmune disease and positive autoimmune profile in different pattern happened in systemic sclerosis. We describe a case of morphea associated with rheumatoid arthritis and a positive autoimmune profile**.**

Introduction

Morphea or localized scleroderma is a skin disorder characterized by local chronic inflammation followed by fibrotic changes in the skin and subcutaneous tissues [1]. Autoimmune activity is responsible for excessive subcutaneous collagen deposits, thickening, scarring, and fibrosis of the tissues [2].

The estimated incidence of morphea is found to be ranged from 0.4 to 2.7 per 100,000 people, however updated population based studies are limited [3,4]. Morphea affects adults and children equally, with females more susceptible to the disease than males [3,5-7].

Spectrum of sclerosing skin disorders include; systemic sclerosis (SSc), morphea and overlap syndrome [4]. Despite, morphea and SSc share the same clinical feature of skin fibrosis and identical histopathologic changes, the systemic involvement and internal organ manifestations, are extremely different [8]. Basically, Lack of internal organs involvement is characteristic of morphea [9]. However, systemic symptoms such as malaise, fatigue, arthralgias, and myalgias have been recognized in the context of morphea. Moreover, Extra- cutaneous manifestations of morphea differ from those in systemic sclerosis inform of neurological, musculoskeletal and ophthalmologic findings has been documented [5]. The highest prevalence was recognized at articular involvement [9,10].

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Joints involvement in context of generalized morphea is attributed to two different etiological mechanisms; mechanical or inflammatory. In mechanical etiology contracture of the skin overlying the joint lead to restriction and limitation of joints movement [9,11].
Inflammatory arthritis in the context of morphea reported as association with morphea in 9% of patients [2] or as part of overlap with another seropositive disease such as rheumatoid arthritis and SLE [5]. The timing of arthritis presentation in relation to skin disease could be in advance, coincident with, or following diagnosis of morphea [2].
Additionally, positive autoantibodies are associated with morphea [12]. Strong evidence supported elevated antinuclear antibody (ANA) in morphea patients [13]. Consequently, growing evidence supporting the concept that morphea is a systemic inflammatory condition is well established [14].
In this report we describe a patient who developed inflammatory arthritis with erosions preceding the onset of morphea.

Case presentation:

A 78-year- old male known hypertensive referred by his GP to Merline Park Hospital (MPH) rheumatology outpatient clinic with hands pain for two years. He had progressive restriction of both shoulder movements and elbows recently. No back or neck pain. There was no history of Raynaud's phenomenon, dysphagia, or dyspnea.

On examination, there was generalized wasting. No swollen or tender joint. There was thick sclerotic skin at level of wrists, forearms arms and shoulders bilaterally.

In addition, contractures at left elbow joint with restriction of rang of movement secondary to skin tightness. There were patchy discoloration erythematous to violaceous border and sclerotic center, oval in shape, measuring 2x3 cm over right elbow surround by sclerotic skin. No digital ulcers, calcinosis, dactylitis or telangiectasia

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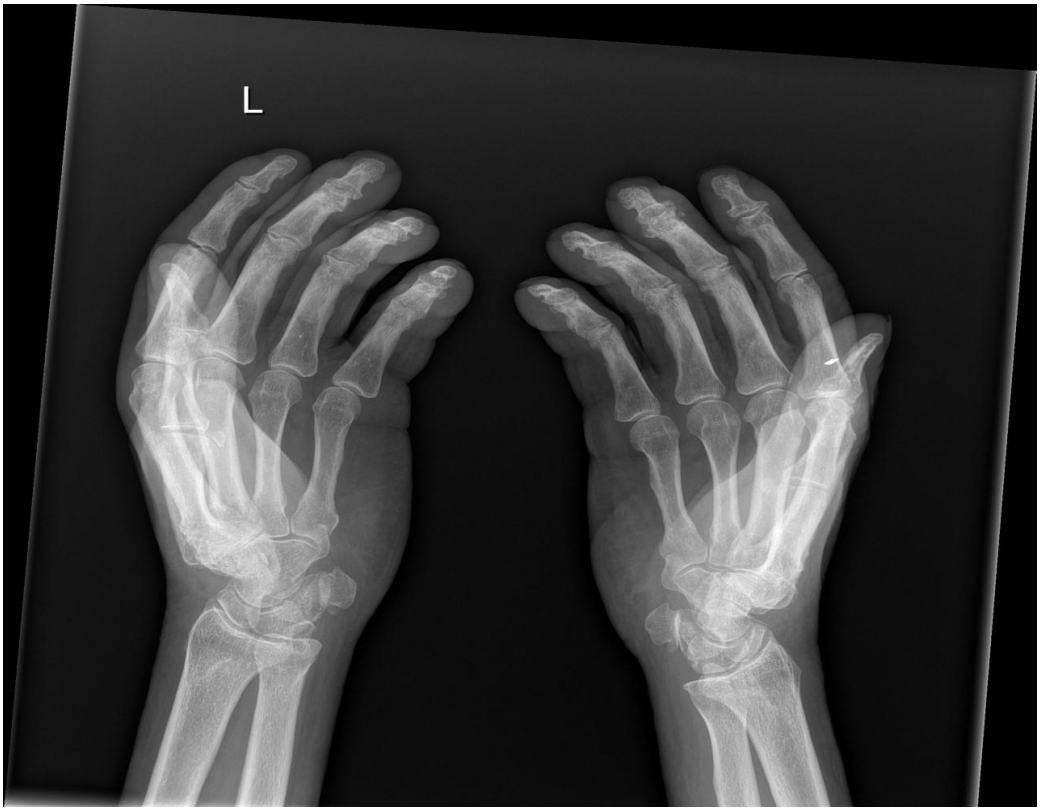
His inflammatory markers were elevated. For instance, C-reactive protein (CRP) was 154 mg/L and erythrocytes sedimentation rate (ESR) 51mm/hr. Furthermore, he has positive rheumatoid factor (RF) 59 iu/mL (0-14), anti-cyclic citrullinated peptide antibodies (ACPA) 340 (0-20 EU/mL), whereas antinuclear antibodies (ANA) was weak positive. The rest of serological screening were negative including systemic sclerosis profile and myositis panel.



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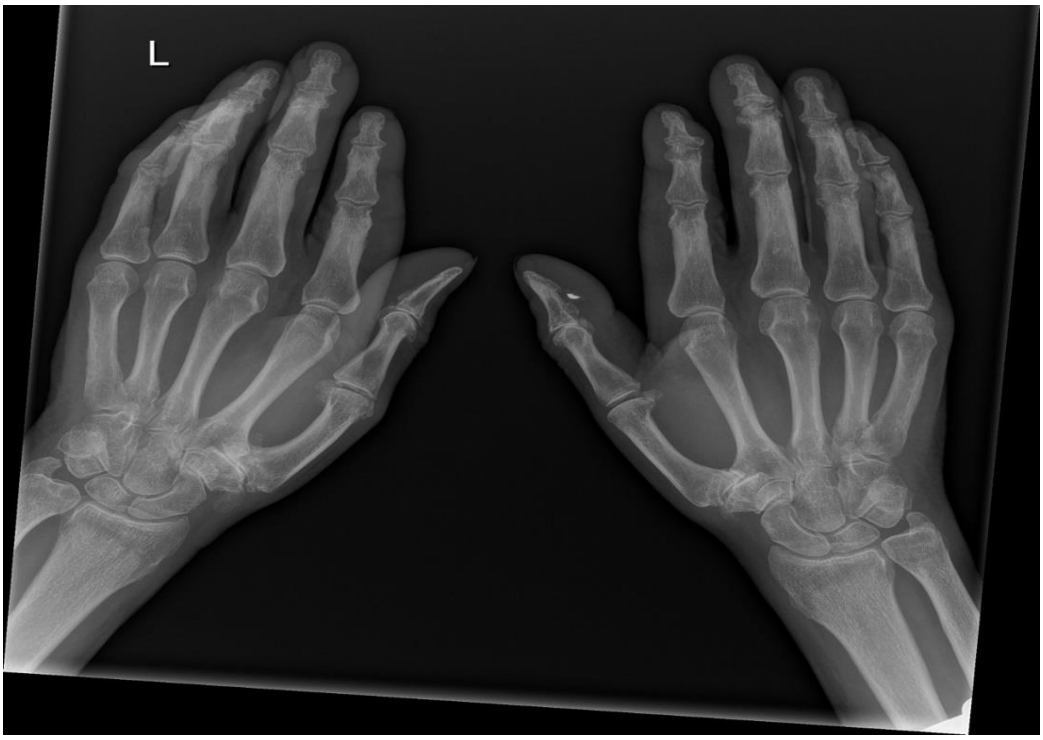

Figure 1: Degenerative changes in both first carpometacarpal joints

Degenerative changes in interphalangeal joints

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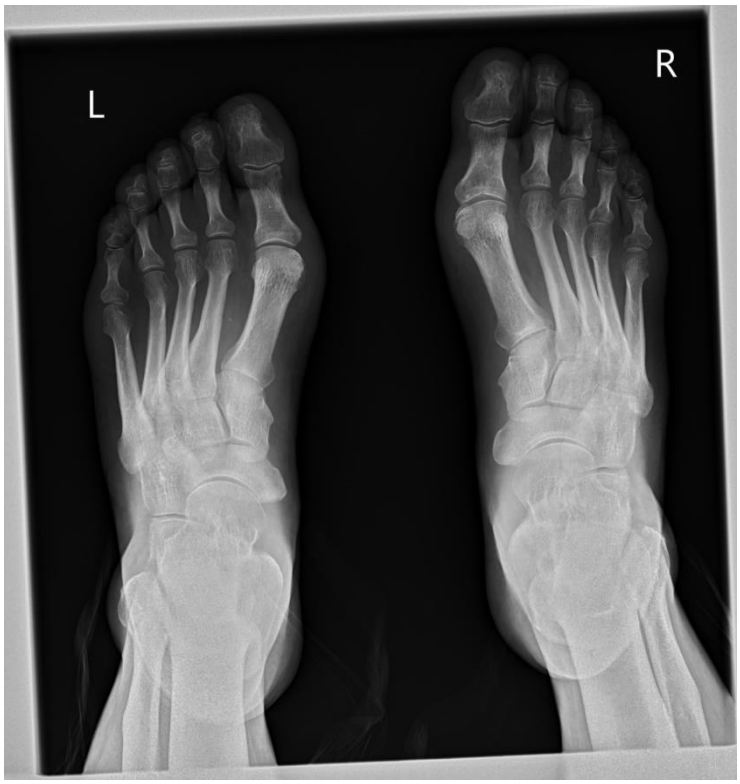

Figure 2: Mild Hallux valgus deformity bilaterally, Marginal erosion in the heads of the little toe metatarsals bilaterally and in the proximal phalanx of the left great toe.

Chest radiograph was normal. Pulmonary function test and echocardiography were insignificant. Screening for malignancy including, CT Thorax abdomen and pelvis, tumor markers were normal.

Based on EULAR Criteria for diagnosis of rheumatoid arthritis (RA) 2010 he scored 6/10. In view of his hand's joints pain, duration of symptoms, significant both inflammatory and serological markers he was diagnosis as rheumatoid arthritis.

Outcome:

On 14th October, 2021, methotrexate 10 mg/week was initiated. Three months later on follow up visit the patient showed excellent response to methotrexate (MTX) in the form of improved

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joints pain and skin stiffness. The plan was made to increase MTX dose to 15 mg/week and review him pending the result of skin biopsy.

Skin biopsy revealed mild atrophic epidermis, overlying a thickened papillary reticular dermis with loss of adenexal structures which seam replaced by extensive area of collagen. Along with minimal patchy of superficial and deep chronic inflammatory infiltrate. Sclerosing dermatitis with mild superficial and deep perivascular inflammatory infiltrate extending to suncutis and fascia. Biopsy shows scleroderma.

In two months his followup showed much improvement to MTX and the plan was to continue on current dose MTX. The diagnosis of localized scleroderma (Morphea) in association with rheumatoid arthritis was established.

Discussion

Up to date this is the first case report to document seropositive RA in association with generalized morphea. The concept of morphea as a systemic disease and immunologically mediated, associated with other different autoimmune disorders is documented in consensus in literature.[5,9]. Not only that but also, coexistence of inflammatory arthritis with generalized morphea is reported a long time ago [1]. A study done earlier stated that co-existing inflammatory arthritis in 20.8% of morphea patients Kasheml.[16]. Another review highlights association of sacroiliitis, generalized synovitis, and inflammatory arthritis with morphea [17]. Furthermore, studies investigated molecular and genetic component of morphea patient illustrated morphea is immunogenetically distinct and alleles in morphea are associated with conditions such as rheumatoid arthritis (RA) and other autoimmune conditions [18]. Population based studies indicate patients with RA have increased risk of morphea, implicating a common susceptibility allele [18] and shared HLA types with RA. [ ] All of these evidence are in line with our case.

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Presence of autoantibodies in case of morphea contribute to the higher frequency of co-existing inflammatory arthritis [2,20]. Moreover, it has direct implication in disease subtypes, damage extent, and relapse potential and responding to treatment [13].

Rheumatoid factor (RF), which is typically associated with adult rheumatoid arthritis, is reported in 16% of morphea patients [4, 14]. Another study explored rheumatoid factor (RF) isotypes level in patients with morphea versus level in normal controls. It showed IgM RF, IgG RF and IgA RF were positive in 30%, 21%, and 7% of the morphea patients, respectively. Furthermore, the levels of IgM RF were higher in the patients with generalized morphea and directly correlate with disease severity and the extend of skin sclerosis [20].

The presence of antinuclear antibody ANA is also found in morphea patient [21-22] with greater frequency than expected in comparison to a healthy population [13]. Study done previously showed positive ANA (titer ≥1:160) in 39% (35/89) of those tested [5]. Adults had a higher frequency of ANA positivity with 53% (19/36) testing positive as compared to 30% (16/53) of children.[5]. Other evidence reports up to 50% of patients morphea patient shown elevated antinuclear antibody (ANA) [13].

Anti-cyclic citrullinated peptide antibody (ACPA) is the most useful and specific autoantibodies in diagnosis of rheumatoid arthritis (RA). To date no any published study or case report explore ACPA in morphea patient. However, Coexistence of RA and morphea reported in published evidence showed seropositive arthritis (RF and ACPA) in advanced to skin disease. Their experience found difficulties in control of arthritis with conventional synthetics disease modified anti rheumatic medications (csDMARDs) and start on biological agent etanercpt. At the time the patient had satisfactory remission for arthritis he developed morphea. Anyhow, the authors attributed the morphea as adverse effects for etanercept rather than coexistence with rheumatoid arthritis. However, various cutaneous manifestations has been reported as TNF inhibitors side effects [23, 24] but paucity of evidence support morphea as TNF inhibitors side effects [25].

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Limited reference explore ACPA in SSc patients.ACPA is found in 11.5% SSc patients. Further, patient with ACPA positive are more susceptible to arthralgia [26]. Other study showed significant arthritis connected with the presence of ACPA antibodies in SSc patient [27].

The onset of arthritis in our case preceding onset of morphea. However, documented evidence report (37.5%) patients had morphea lesions in advanced clinical arthritis, and (37.5%) had arthritis before the appearance of morphea while (25%) patients had both morphea and arthritis at the time of diagnosis [2].

The mainstays of treatment for active generalized morphea are corticosteroids and methotrexate [17]. Our patient showed excellent response and improvement to systemic steroid in combination with MTX therapy in small doses, both skin and joint disease simultaneously. Although the evidence reported the reverse and there is agreement about difficulties of treatment of morphea and arthritis when coexist in variable degree of extend. However, Satisfactory response to MTX alone or in combination with corticosteroid for skin disease in generalized morphea is reported. In contrast, concomitant arthritis showed poor response to first line systemic treatment and majority of the patient required escalation to second for line systemic treatment [2]

Second-line medications options including Cs DMARD such as sulfasalazine, leflunomide, hydroxychloroquine. Refractory condition needs escalation to biologic DMARD such as TNF inhibitors, abatacept, tocilizumab, and rituximab [28] as well as MMF [19, 29, 30].

Conclusion:

This case and the reviewed literature endorse that morphea is systemic disease. Co-existence of inflammatory arthritis with morphea can happen in advance, simultaneously or followed skin disease in variable period. Presence of autoantibodies in morphea anticipated severity of skin disease in addition to development RA or any other autoimmune disease depends on autoantibodies profile.

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Treatment of morphea in case of seropositive autoantibodies shows variable response and outcomes regarding arthritis and morphea. Our experience showed excellent control for both arthritis and skin disease with first line combination of steroid and MTX.

Screening for malignancy especially in elderly with new onset morphea should be considered.

It is the time to adopt holistic approach in assessment and management of morphea patient including modification in the focus of merely skin disease to comprehensive systemic disease and exploring patient autoantibodies profile for early disease control and satisfactory outcome.

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