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Chronic Hand Edema in Rheumatoid Arthritis: A Rare Extra-Articular Manifestation

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ABSTRACT

Patients with rheumatoid arthritis (RA) usually present with swelling of hands and feet due to synovitis of the small joints. Chronic edema limited to the extremities is rarely reported in the literature.

We report the case of a 55- year-old-patient, with 37 years of seropositive and deforming RA associated with Sjogren's syndrome, initially treated with corticosteroids for 17 years, currently on Leflunomide for 20 years. Her disease has been in remission for 3 years. The course was marked by the gradual onset of bilateral, symmetrical, persistent and diffuse edema in both hands for the past 20 years. It was a significant, painless and elastic infiltration of the dorsum of the hands and the fingers. The skin was tight but normal, with a positive Stemmer's sign, which suggested the lymphatic origin of the oedema. The patient flexed her fingers with difficulty. There was no infiltration of the rest of the upper nor the lower limbs. Among the extra articular signs of RA, chronic edema of the limbs remains unusual and often unrecognized. The pathophysiological mechanism is not well understood. Treatment is poorly codified. The prognosis is primarily functional.

Keywords: Rheumatoid arthritis; Hand edema; Stemmer's sign; Unilateral edema; Extra-articular manifestation

ABREVIATIONS: Hb: Hemoglobin, WBC: White Blood Cells , B.Pt: Blood Platelets, CPK: creatine phosphokinase, ANA: Anti-Nuclear Antibodies, C3, C4, CH50 complement.

INTRODUCTION

Patients with rheumatoid arthritis (RA) usually present with painful swelling of dorsum of the hands and/or feet due to synovitis of the large joints. Chronic edema limited to the extremities is rarely reported in RA. Investigating other general causes of peripheral edema is crucial, such as hypo albuminaemia, venous disease, health failure.[1-2] The results of the previous studies have suggested that such peripheral edema may be the consequence of impaired local lymph drainage, due to the extension of the inflammatory process of RA to the

lymphatic vessels.[3] Because of the rarity of published cases, we report this case observed in patient with RA who presented with distal extremity swelling of the hand's dorsum. Through our observation we discuss the different pathogenic, clinical and therapeutic options of this unusual association.

CASE REPORT

A 55-year-old housewife had a 37 years history of classical RA which was symmetrical, polyarticular (bilateral radiocarpal, MCP and IPP joints), seropositive and erosive, associated with secondary Sjogren syndrome. She was initially treated with corticosteroids for 17 years currently on Leflunomide for 20 years. Her RA was in remission for 3 years. Two years after the onset of her rheumatism, she complained of a marked edema of the hands as well as the fingers and the lower third of the forearms (Figure 1).

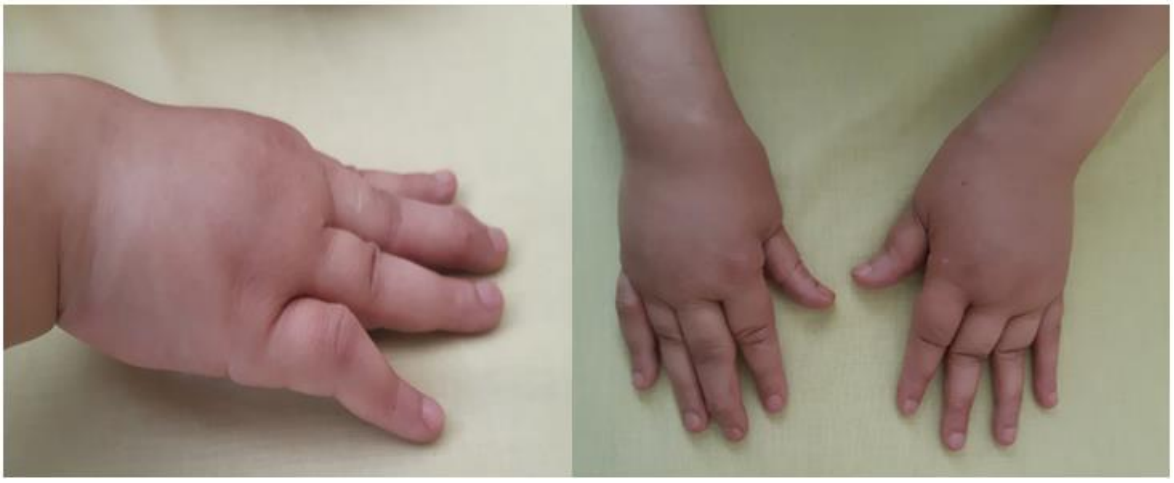

Figure 1: Dorsum of the hands edema.

Physical examination revealed bilateral and symmetrical swelling, the skin was tight, and elastic. Her hands were uncomfortable but not severely painful, underlying joints were not particularly tender. There was no edema in the lower limbs. The Stemmer's sign was positive in the upper extremities. Radiograph of the hands shows multiple bone and joint destructions (Figures 2).

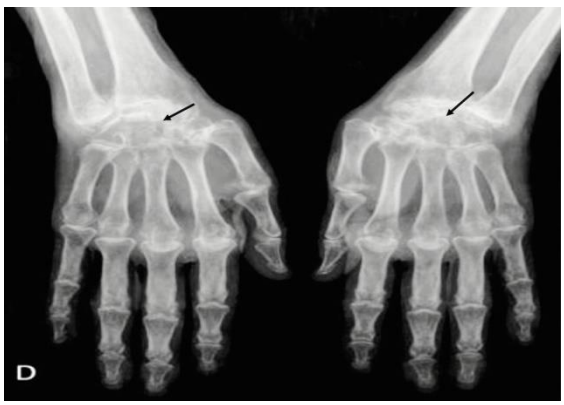

Figure 2: Radiograph of the hands : Bilateral carpite with multiple bone and joint destructions.

There were no signs of hypothyroidism or heart, lung, liver, or kidney disease or tumoral syndrome, in the clinical assessment.

Biological tests were normal, especially the inflammatory syndrome (sedimentation rate, C- reactive protein and serum protein electrophoresis) and the blood counts. Muscle's enzymes and the immunological balance were within the normal ranges (anti-nuclear antibodies, C3, C4, CH50 fractions and complement C1-inhibitor).

Medical imaging such as the thoracic standard and scan X-rays, the ultrasound of the soft tissues and the axillary hollow, echocardiography , arterial and venous doppler of the affected limb and echo-mammography appeared normal.

The diagnosis of secondary lymphedema associated with RA was retained in the absence of clinical evidence of general causes of edema, the positivity of Stemmer's sign and the painless peripheral edema. The hand edema was permanent, causing only a functional impairment.

No change was observed after changing disease-modifying antirheumatic drugs, intra-articular steroid injections, or low-dose systemic corticosteroids.

Table: Resultats of laboratory tests

Laboratory tests	Results	References
Blood counts	Hb : 12g/dl	12 – 16 g/dl
	WBC: 5030 µL	4000 – 10 000 µL
	B.Plt : 220 000 µL	150 000- 400 000 µL
Protein c reactive	4.5/ mg/l	< 6 mg/l
Sedimentation rate	23mm/1^{s} h	
CPK	96 UI/l	20 – 200 UI/l
ANA	< 1/80	< 1/80
C3	0.9 g/l	0.8-1.6 g/l
C4	0.5 g/l	0.2-0.5 g/l
CH50	50 g/l	25 – 100 g/l

DISCUSSION

Chronic peripheral edema is unusual extra-articular feature of RA, often diagnosed clinically.[4] It does not appear to be correlated with the positivity of rheumatoid factor nor with the activity of the disease.[4-5] In this case, edema persisted although the remission of RA. The upper limbs are affected more often than the lower limbs, and it usually appears many years after the onset of the disease, though cases of early manifestation have been reported like our patient. Bilateral forms are also possible but rare.[6-7]

The pathogenesis of edema is not well known. The most mentioned theory is thrombotic obstruction of lymphatics by fibrin and other degradation products of coagulation (FDP) during RA, leading to persistent inflammation and lymphangitis. This destruction and obstruction of lymphatic vessels impair lymphatic

drainage.[8] This assumption finds these bases in the observation of Minari C. et al., in their series of RA patients with lymphedema, 66% had a marked increase of FDP concentration.[9]

A further mechanism, which could explain the onset of edema in RA, is the increase of capillary filtration and permeability during acute joint inflammation with excess lymph production. It was reported that the increased capillary permeability in patients with RA and lymphedema, lead to increased leakage of the liquids into the extracellular compartment in addition of reduced lymph clearance in subcutaneous tissue.[10] That cause seemed likely in our patient because of the early onset of the edema, during the high disease activity.

These two mechanisms could be associated, as demonstrated by Kiely et al.[11], they have proposed that the inflammatory response associated with acute synovitis may, through increased capillary filtration, overwhelm the normal capacity of the lymphatic system, or directly cause lymphangitis, resulting in lymphatic impairment and subsequent edema.

The diagnosis of rheumatoid lymphedema is mainly clinical based on the infiltrated, swollen, painless and tense aspect of the extremities with variable functional impotence.[3]
Most reports include lymphographic studies, and we also regard lymphography as valuable to reveal obstruction of the deep lymphatic channels.[5-11] Since there is no specific therapy of lymphedema aside from pathogenetic hypothesis and of the chronicity of the edema, we decided not to perform such an invasive and unpleasant examination.

Regression of peripheral edema, whether spontaneous or under treatment, is rarely observed and chronicity is often the rule.[4] However, several complications may occur; in particular disability and joint limitations, also when involving lower limbs, chronic skin ulcers with bacterial infections can appear and modify by this fact the prognosis. In fact, 11 out of 36 patients in the series by Seitz CS et al. of chronic leg ulcers in RA had an underlying secondary chronic lymphedema.[12]

Treatment of lymphedema is controversial and is often disappointing. It is known that treatment of the underlying RA is not effective.[13] Also, it seems that edema to not respond to diuretics, corticosteroid or other drugs.[14]

Some cases, reported that Etanercept reduced the lymphedema in patients with RA, but evidence of the benefits of this treatment is insufficient in the literature.[15] Surgery may be adopted as therapeutic option to restore lymphatic flow combined with physical treatment.[16]

The corner stone of the management of edema is physical treatment of the affected limb, such as massage, manual lymph drainage, exercises and multilayer short stretch bandages.[17] The patient described in this case report adopted this option to reduce her disability.

CONCLUSION

Peripheral and chronic edema of the limbs remains an exceptional extra-articular manifestation of RA. Often misunderstood and neglected, it impacts functional prognostic and daily activity of RA patients. Although physical methods take a place of choice in this indication, therapy is not codified and need multidisciplinary approaches.

Conflicts of interest: None.

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