OLGU SUNUMU CASE REPORT

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Remitting Seronegative Symmetrical Synovitis with Pitting Edema

Tekrarlayıcı Seronegatif Pitting Ödemli Simetrik Sinovit

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ABSTRACT Remitting seronegative symmetric synovitis with pitting edema (RS3PE) is a rare clinical syndrome characterized by abrupt onset of pitting edema on the dorsum of the hand and associated synovitis. The etiology of RS3PE syndrome is unknown and it affects the elderly with a benign course which responds dramatically to low dose of corticosteroid treatment. The serological tests are negative and radiographic joint destruction does not occur in this condition. The diagnosis of RS3PE is not easy, as it is always hindered by the lack of definite diagnostic criteria and presence of other much more common rheumatological disorders that mimic it. RS3PE syndrome can emerge as a musculoskeletal symptom of a paraneoplastic syndrome. Herein we present a case report diagnosed with RS3PE in order to draw attention to RS3PE in patients presenting with pitting edema on dorsum of the hand.

Keywords: Tenosynovitis; edema; ultrasound; RS3PE

ÖZET Tekrarlayıcı seronegatif gode bırakan ödemli simetrik sinovit [Remitting seronegative symmetrical synovitis with pitting edema (RS3PE)], sinovit ile ilişkili ve el dorsumunda ani başlangıçlı gode bırakan ödem ile karakterize nadir görülen bir klinik sendromdur. RS3PE sendromunun etiyolojisi bilinmemektedir ve düşük doz kortikosteroid tedavisine dramatik olarak cevap veren iyi seyirli bir süreç ile yaşlıları etkilemektedir. Serolojik testler negatiftir ve bu durumda radyografik eklem harabiyeti meydana gelmez. RS3PE tanısı kolay değildir, çünkü her zaman kesin tanı kriterlerinin olmaması ve onu taklit eden diğer çok daha yaygın romatolojik bozuklukların varlığı nedeniyle engellenir. RS3PE sendromu, paraneoplastik bir sendromun kas-iskelet sistemi semptomu olarak ortaya çıkabilir. Burada el dorsumunda gode bırakan ödemli hastalarda RS3PE tanısına dikkat çekmek için RS3PE tanılı bir olgu sunulmaktadır.

Anahtar Kelimeler: Tenosinovit; ödem; ultrason; RS3PE

Remitting seronegative symmetric synovitis with pitting edema (RS3PE) is a rare clinical entity with acute onset and benign course. Although it can coexist with rheumatological and neoplastic diseases, the etiology is unknown and it responds dramatically to corticosteroid treatment.[1] The diagnostic criteria include bilateral pitting edema of hands, sudden onset of polyarthritis, age >50 years, and negativity for rheumatoid factor (RF).[1,2] A sudden onset of pitting edema of the hand is associated with synovitis of the wrist-hand joints, and tendon sheaths. Shoulder, knee, ankle and elbow joints can also be affected.[2] Herein, we present a case report with RS3PE syndrome in order to draw attention clinicians to clinical and differential diagnosis of RS3PE disease.

CASE REPORT

A 74-year-old female patient admitted with the complaints of swelling, pain and stiffness on upper extremities for the last four weeks. She had a history of upper respiratory tract infection occurred a few weeks

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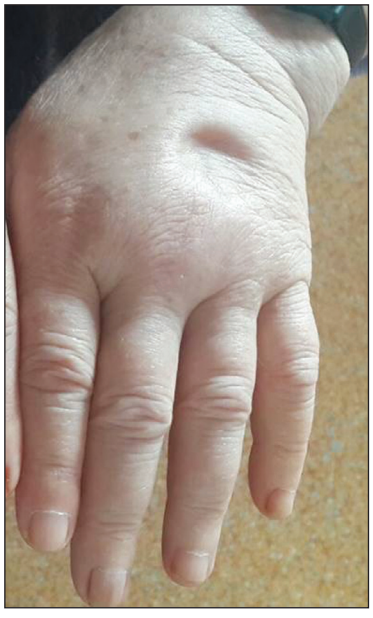

FIGURE 1: Apparent pitting edema on the patient's left hand.

before the onset of swelling. She had difficulty making fists, but did not report any erythema, warmth and shoulder/hip pain, except morning stiffness lasting half an hour. She had no history of trauma, fever, night sweats, weight loss, systematic disease or malignancy. Her family history was not significant for any disease.

Physical examination revealed pitting edema (+++) on both hands, extending to the elbow regions and mild tenderness (Figure 1). Stemmer sign was positive on the left side which was also colder than the other side. Laboratory tests including complete blood count, liver/kidney/thyroid function tests, tumor markers and C-reactive protein were all normal, except for a mild increase in erythrocyte sedimentation rate (26 mm/hour). While RF, anti-CCP, Anti-dsDNA, and ENA panel were all negative, antinuclear antibody (ANA) was positive 1/320 (in speckled granular pattern).

Bilateral hand radiographies revealed joint space narrowing on right 2nd interphalangeal joint. Echocardiography, Doppler imaging, and axillary/abdominal ultrasonographic imaging were all normal. Ultrasound imaging (US) showed mild effusion within the radiolunate joint, and subcutaneous edema surrounding the extensor tendons indicating tenosynovitis (Figure 2). The patient was prescribed prednisolone 5 mg/daily with the diagnosis of RS3PE. Corticosteroid dose was reduced gradually after four weeks and ceased at the end of 8th week. The patient's edema disappeared completely at the end of the first month (Figure 3).

DISCUSSION

RS3PE, a rare elderly-onset rheumatic syndrome, is clinically characterized by pitting edema of both hands, negative RF, absence of radiographic erosions,

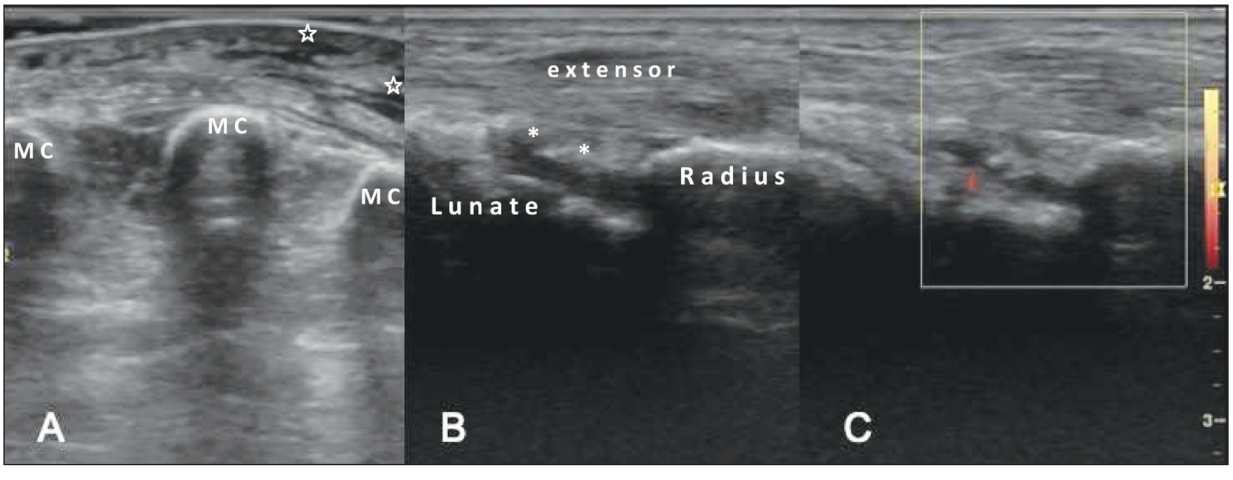

FIGURE 2: Axial (A) and longitudinal (B) ultrasonographic views show effusion within the radiolunate joint (asterisks) and diffuse edema of the subcutaneous tissue (stars), surrounding the extensor tendon. Power Doppler imaging (C) reveals no active inflammation.
MC; Metacarpal head.

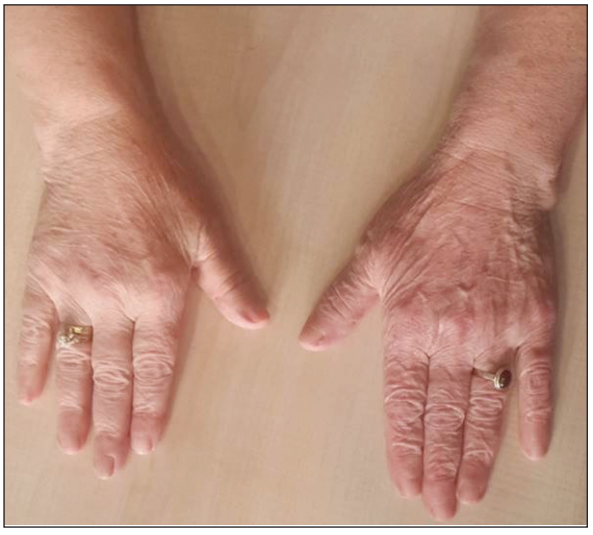

FIGURE 3: Normal view of the patient's hands after one-month duration of corticosteroid treatment.

dramatic response to glucocorticoids, and a good prognosis.[3-8] Although RS3PE was initially assumed to be a strain of rheumatoid arthritis (RA), currently it is recognized as a distinct syndrome.[4,6,8] The etiology of the disease is still not well known. RS3PE is generally more common in men than in women. The pitting edema often occurs in the hands, rarely it also may occur in the feet. On the other hand the obvious pitting edema in RS3PE patients is commonly caused by extensor tenosynovitis, which is usually symmetrical, but rarely can be unilateral.[9]

The pathogenetic mechanisms of the disease and its relationship with neoplasm are still issues to be addressed. A systematic review evaluating 331 RS3PE cases from 121 articles, determined the ratio of concurrent malignancy rate as 16.31%.[7] The pathogenesis of RS3PE may involve increased level of vascular endothelial growth factor (VEGF), based on limited data.[4,8] Recently, it has been shown that US can be used to distinguish patients with RS3PE from patients with late onset RA.[3] Compared to late onset RA, mild but more extensive articular synovitis and more frequent synovial effusion were observed in the RS3PE. In addition, although tenosynovitis of carpal extensor tendons was similar, peritendinitis of digital extensors and subcutaneous edema were found to be more frequent in the RS3PE group.[3] Subcutaneous edema may be caused by spread of extensive synovitis to extra-articular tissue and capillary permeability facilitated by VEGF. Our patient's having mild synovial effusion, extensor tenosynovitis and subcutaneous edema in the US evaluation were also compatible with RS3PE syndrome rather than late-onset RA.

Differential diagnosis of RS3PE comprises RA, complex regional pain syndrome, polymyalgia rheumatica (PMR), reactive arthritis, psoriatic arthritis, crystal and amyloid arthropathies. Nevertheless, lymphedema should also be considered**.** Malignancy can develop before, during or after this syndrome.[6] Therefore, paraneoplastic syndromes should also be eliminated and monitored in the follow-up. The clinical findings of our patient met the diagnostic criteria for RS3PE, in addition non-existence of erosion in x-rays, negativity of anti-CCP as well as quick response to low dose of steroids have supported our diagnosis of RS3PE. The ANA positivity in low titration was previously reported in some RS3PE patients.[3] Nevertheless, a mild to moderate acute phase response may be present in laboratory tests, but RF serology is commonly negative.[10] Patients diagnosed as RS3PE with normal acute phase reactants were also presented in some previous studies.[4,5] The presence of normal acute phase reactant and the localized dorsal hand edema provided exclusion of PMR in the differential diagnosis of our case.

Complex regional pain syndrome generally progresses with unilateral involvement and was not considered in clinical diagnosis because of findings such as full range of motion, normal hand radiography, absence of an initiating event/trauma/injury, absence of dystrophic changes in skin and nail, absence of sensory changes including hyperesthesia, allodynia.

The differential diagnosis of RS3PE is not easy, as it is frequently hindered by the lack of definite diagnostic criteria and presence of other rheumatological disorders that can mimic it. RS3PE syndrome can also emerge as a musculoskeletal symptom of a paraneoplastic syndrome. We suggest that clinicians should be aware of this rare but easily treatable syndrome in patients with bilateral upper extremity edema.

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