ORIGINAL RESEARCH PAPER

Internal Medicine

A CASE OF REMITTING SERONEGATIVE SYMMETRICAL SYNOVITIS WITH PITTING OEDEMA ASSOCIATED WITH LIVER ABSCESS

KEY WORDS: Puffy hands, Pitting edema, RS3PE, Rheumatoid

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ABSTRACT

Remitting seronegative symmetrical synovitis with pitting oedema is a rare rheumatic syndrome which is easily missed due to lack of clinical vigilance and because its mimics (rheumatoid arthritis, spondyloarthropathy, polymyalgia rheumatica) are substantially more common. It is known to present alone or in association with rheumatic diseases, malignancies and infections. We report a case which presented with acute synovitis and pitting oedema of both hands during the clinical course of liver abscess. He had elevated inflammatory markers and negative rheumatoid factors. There was no radiological evidence of bony erosion. Ultrasound scan of hands showed evidence of extensor tenosynovitis. He had a dramatic response to low dose steroids with no further recurrence on follow up. This case signifies the importance of awareness of this rare condition among clinicians and its association with infectious conditions such as liver abscess.

INTRODUCTION

Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) presents with an acute onset of marked pitting edema on the dorsum of both hands and/or feet and symmetrical distal synovitis. It is characterized by rheumatoid factor (RF) seronegativity and absence of articular erosion radiologically. Excellent response to low dose steroids is seen which induces long term remission. It occurs more frequently in elderly males with male: female ratio of 4:1[1]. Another important characteristic is its association with rheumatological diseases, malignancies and infectious conditions such as tuberculosis, parvovirus B19, Streptobacillus moniliformis, Escherichia coli, Campylobacter jejuni, and Mycoplasma pneumoniae.[2,3]

Case Report

A 60 year old gentleman presented to the outpatient department with acute onset of swelling on dorsum of both hands, pain in all proximal interphalangeal, metacarpophalangeal and both wrist joints and inability to make a fist since one and half month. He did not complain of early morning stiffness and had no pain or swelling of feet. He did not have any similar episodes in the past. He had no history of pain in and around shoulder or hip. He had no history of pain or bluish discoloration of finger tips on exposure to cold. He had a history of solitary abscess in right lobe of liver managed in another hospital two months back; pig tail drainage of pus was done and antibiotics were administered for a month. Microbiological or serologic diagnosis were not obtained. He presently complained of altered bowel habits since last 15 days but denied any complaint of fever, jaundice or right upper quadrant pain. He was a chronic alcoholic but claimed abstinence over last two months. He had diabetes and hypertension since last 12 years for which he was presently on metformin 500 mg twice daily and telmisartan 40 mg once daily. On examination, there was pitting oedema on dorsum of both hands and tenderness over proximal interphalangeal, metacarpophalangeal and wrist joints. These joints also had limited range of motion. Rest of the systemic examination was unremarkable. Blood investigations were as in Table 1.

Table 1: Investigations

Investigations	Values
Haemoglobin	10.2 g/dl
Total leukocyte count	4.40 x 10^9/L
MCV	101.6 Fl
Platelet count	110 x 10^9/L
CRP	6.23 mg/L
ESR	110 mm 1st hour
Total Bilirubin	0.43 mg/dl
AST	36 U/L
ALT	39 U/L
ALP	113 U/L
GGT	66.5 U/L
Total serum protein	7.6 g/dl
Albumin	4.2 g/dl
Globulin	3.4 g/dl
A/G Ratio	1.24
Serum Creatinine	1.10 mg/dl
Serum Urea	20.04 mg/dl
Sodium	140 mmol/L
Potassium	4.2 mmol/L
Chloride	103.2 mmol/L
HbA1c	6.5 %
TSH	4.61
HIV -1 & 2	Non Reactive
HBsAg	Non Reactive
HCV	Non Reactive
RA Factor	Negative
Anti CCP antibody	Negative
ANA (immunofluorescence)	Negative

MCV – Mean corpuscular volume, CRP – C-reactive protein, ESR – Erythrocyte sedimentation rate, AST – Aspartate transaminase, ALT – Alanine transaminase, ALP – Alkaline phosphatase, GGT – Gamma glutamyl transpeptidase, A/G ratio – Albumin globulin ratio, HbA1c – Glycosylated hemoglobin, TSH – Thyroid stimulating hormone, HIV – Human immunodeficiency virus, HBsAg – Hepatitis B surface antigen, HCV – Hepatitis C virus, RA Factor – Rheumatoid arthritis factor, anti CCP antibody – anti cyclic citrullinated peptide antibody, ANA – Anti nuclear antibody

His urine and stool routine examination was normal with Urine

Albumin creatinine ratio of 20 mg/g. Electrocardiography and 2-D Echocardiography were normal. On X-ray of both hands there was no evidence of articular surface erosion. Diffuse thickening of synovial sheath of extensor and flexor tendons of bilateral hands with peritendinous mild fluid collection was noted in Ultrasound scan of both hands. No obvious raised vascularity was noted in color doppler – findings suggestive of tenosynovitis.

Contrast enhanced computed tomography of thorax showed a calcified nodule in left upper lobe. Contrast enhanced computed tomography of whole abdomen showed a hypodense lesion in segment VII of right lobe of liver (~15 cc) likely suggestive of residual liver abscess. Pus aspiration was not possible under ultrasound guidance. Two samples of blood culture were sterile. Entamoeba histolytica serology test was not available in our hospital hence, could not be done. ACR-EULAR 2010 RA criteria score was calculated to 7 – joint involvement: > 10 joints involved (+5), Serology: negative RA Factor and anti CCP antibody (0), Acute phase reactants: abnormal CRP or abnormal ESR (+1), Duration of symptoms: ≥ 6 weeks (+1). Oral prednisolone 20 mg once daily, etoricoxib 90 mg once daily, oral metronidazole 800 mg thrice daily was initiated which resulted in dramatic improvement of symptoms with complete resolution of joint pain and swelling over dorsum of hands within two weeks. Repeat ESR and CRP levels showed reducing trend – 34 mm and 1.1 mg/L respectively. Prednisolone was continued for one more week after which it was stopped. Patient has been on follow up over last six months with no recurrence of symptoms. This rapid resolution of symptoms with low dose steroids with no further recurrence in the absence of radiological evidence of articular surface erosion confirms the diagnosis of remitting seronegative symmetrical synovitis with pitting edema. Ultrasound scan of whole abdomen was repeated after three weeks of oral antibiotics which did not show any residual abscess.

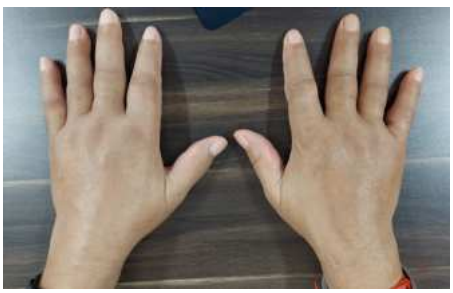

Fig. 1: Pitting edema on dorsum of both hands and wrist

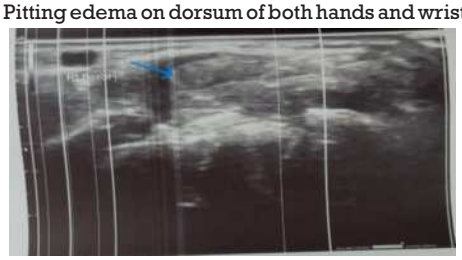

Fig. 2: Ultrasound showing tenosynovitis of right forearm flexors (blue arrow)

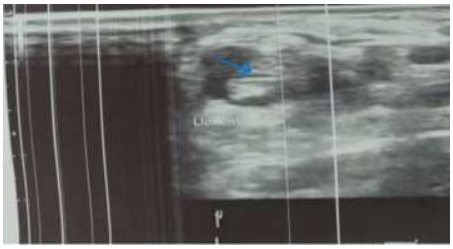

Fig. 3: Ultrasound showing tenosynovitis of left forearm extensors (blue arrow)

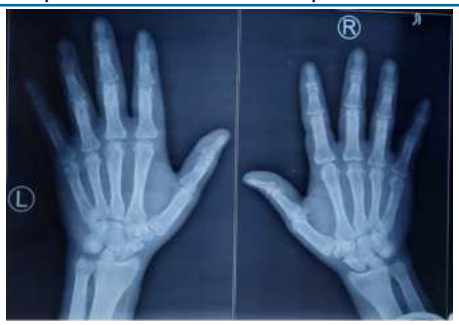

Fig. 4: X -ray of both hands and wrist showing no evidence of erosive arthritis

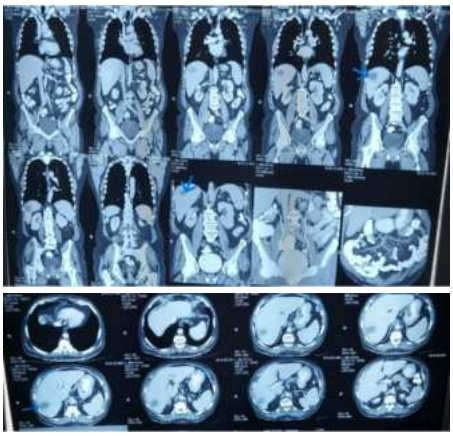

Fig. 5: Contrast enhanced computed tomography of thorax and abdomen showing residual liver abscess in segment VII of right lobe of liver (blue arrows)

DISCUSSION

RS3PE was first described by McCarty et.al in 1985 with a case series of 10 elderly patients who presented with acute onset of symmetrical synovitis and pitting oedema of distal extremities.[1] A retrospective study done by Olive et al. in 1997, wherein they evaluated 27 cases with RS3PE and established the following diagnostic criteria for the disease:[4]

- Clear pitting oedema on both hands.
- Polyarthritis with acute onset.
- Age above 50.
- Negative rheumatoid factor.

Absence of erosive arthritis radiologically and dramatic response to low dose corticosteroids are characteristic.[5,6] It is postulated that pitting oedema of distal extremities which is more commonly observed on the dorsum of both hands giving boxing glove appearance occurs as a result of local reaction.[1,4] Ultrasound and MRI can demonstrate prominent extensor tenosynovitis in the forearms and hands, with lesser amounts of flexor tenosynovitis and synovitis of the metacarpophalangeal and proximal interphalangeal joints.[7] Russell et al.[8] reported in their series with 13 cases that the patients responded dramatically to 10 mg/day prednisolone treatment. If they relapse or fail to respond, an underlying malignancy or an alternative diagnosis must be considered. This subgroup of patients with paraneoplastic RS3PE may also require significantly higher doses of steroids to show signs of improvement.[9] RS3PE in the presented case was based upon the following: male gender and age of 60 years, acute onset of symmetric pitting oedema over dorsum of both hands with limited range of motion of wrist, metacarpophalangeal and proximal interphalangeal joints, demonstration of tenosynovitis of extensor tendons of hands on ultrasound and absence of articular erosion on radiographs, negative RA factor and most importantly dramatic response and remission with low dose corticosteroids which was sustained over last six months. Etiopathogenesis of RS3PE is still unsettled. Some studies suggest vascular endothelial growth factor (VEGF) may play a role in oedema formation. Associations with HLA,

malignancy, infections and rheumatologic diseases have also been cited.[10] Our case was associated with liver abscess – microbiological diagnosis could not be attained. On literature review, we did not find any other case report where RS3PE was reported to be associated with liver abscess.

Despite a clear diagnostic criteria, differential diagnosis is very difficult. Important differentials to consider include hypoalbuminemia, volume overload, deep vein thrombosis of upper limbs, seronegative rheumatoid arthritis, polymyalgia rheumatica, amyloid arthropathy, psoriatic arthropathy, crystal arthropathy, late-onset spondyloarthropathies, Reiter syndrome, and mixed connective tissue disease. Seronegative RA also has a late onset but disease activity measures, radiographic progression and remission rates are similar to seropositive RA and it requires intensive treat-to target therapy with DMARDs and do not typically respond to low dose of corticosteroids. [11] Remitting, seronegative, symmetric synovitis with pitting edema is most frequently confused with polymyalgia rheumatica (PMR) since both are seronegative, are seen in older ages and respond to corticosteroids. Salvarani et al. [12] found pitting edema of distal extremities in 8% of the cases in their study examining 245 cases with PMR diagnosis. It is mostly seen in women, requiring long-term steroid treatment and showing relapse and recurrence more frequently. Progressive swelling and non-recovery with treatment in amyloid arthropathy, typical skin findings in psoriatic arthritis, and determination of chondrocalcinosis radiologically and crystals in synovial fluid in crystal arthropathy are useful distinctions. Reiter syndrome is differentiated by asymmetric stiffness with conjunctivitis and urethritis and asymmetric pitting oedema in lower limbs; late-onset spondyloarthropathies are differentiated by asymmetric pitting oedema with sacroiliitis; and mixed connective tissue disease is differentiated by Raynaud's phenomenon and ANA positivity in high titre. [1,4,6] These were not seen in our case.

CONCLUSION

In conclusion, although its diagnostic criteria are clear, RS3PE is a syndrome with a benign course, the differential diagnosis of which is very difficult. It is found to be associated with infections, rheumatologic or neoplastic diseases; the diagnosis of RS3PE can sometimes precede these associations.[13] Hence, it is imperative to carefully investigate them for these conditions. Correct recognition and patient follow-up after diagnosis are important. It ultimately remains a diagnosis of exclusion. Thus, awareness of this rare syndrome amongst clinicians is important.

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