Remitting Seronegative Symmetrical Synovitis with Pitting Edema (RS3PE): A Case Report

Tekrarlayıcı Seronegatif Pitting Ödemli (RS3PE) Simetrik Sinovit Sendromu: Bir Olgu Sunumu

Şebnem Koldaş Doğan, Birkan Sonel Tur[1], Safiye Tuncer[1], Bülent Seçkin[1]
Isparta Gülkent Devlet Hastanesi, Fizik Tedavi ve Rehabilitasyon Kliniği, Ankara
[1]Ankara Üniversitesi Tıp Fakültesi Fiziksel Tıp ve Rehabilitasyon Anabilim Dalı, Ankara, Türkiye

Abstract
Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) syndrome is a disease that affects the elderly and has a sudden onset of edema with swelling on the dorsum of the hands, synovitis on the elbows and flexor tendinitis on the fingers. Serologic tests are negative and radiographic joint destruction does not occur. Etiology of RS3PE syndrome is not known but environmental and infectious agents may play a role in its development. Being a benign syndrome responding to low dose corticosteroid and undergoing to remission in one year, RS3PE syndrome can also be associated with diseases like malignance, polimyalgia rheumatica or amiloidosis. Presented below is the case of a 63-year-old female patient with the complaint of swelling, warming and pain in her wrist, ankle and dorsum of the hands which had suddenly started 9 months previously. *(Rheumatism 2007; 22: 72-5)*

Key words: edema, seronegative, symmetrical, malignance.edema, seronegative, symmetrical, malignance.

Özet
Tekrarlayıcı seronegatif pitting ödemli (RS3PE) simetrik sinovit sendromu, sıklıkla yaşlı bireyleri etkileyen bir hastalıktır ve ellerin dorsal yüzünde şişlik, dirseklerde sinovit ve parmaklarda fleksör tendinitle birlikte ani başlangıçlı ödem ile karakterizedir. Serolojik testler negatiftir ve radyolojik eklem tahribatı görülmez. RS3PE sendromunun etyolojisi bilinmemektedir ancak gelişiminde çevresel ve enfeksiyöz ajanlar rol alabilmektedir. Düşük doz kortikosteroide cevap vermesi ve bir yılda remisyona girmesi ile benign bir sendrom olmakla beraber, RS3PE sendromu malignans, polimiyalji romatika veya amiloidozis gibi hastalıklarla da ilişkili olabilmektedir. Bu makalede 9 ay önce aniden el bileklerinde, ayak bileklerinde ve ellerin dorsal yüzünde şişlik, ısı artışı ve ağrı şikayeti başlayan 63 yaşında kadın hasta sunulmuştur. *(Romatizma 2007; 22: 72-5)*

Anahtar kelimeler: Pitting ödem, seronegatif, simetrik, malignans

Introduction

Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) is a specific type of arthritis, especially affecting the elderly (1, 2). This syndrome, which has a sudden onset and characterized by edema with swelling on the dorsum of the hands, synovitis on the elbows and flexor tendinitis on the fingers, was first defined by Mc Carthy et al. in 19851. Serologic tests are negative and radiographic joint destruction is not seen (1-8).

The etiology of RS3PE syndrome is not known, however environmental and infectious factors are known to have impact in the development of this disease (3,9-12). While RS3PE is known to be a benign syndrome responding to low dose corticosteroid and undergoing to remission in one year (3,5-8,10,12-16), it is also reported that it can associated with diseases like malignance (17-23), polimyagia rheumatica (PMR) (2,12,13,24,25) or amyloidosis (1,4,12,14). Presented below is a case of pitting edema on hands and feet characterized by symmetrical seronegative polyarthritis.

Case

FZ, a 63-year-old female patient, applied to our clinic with the complaint of swelling, warming and pain in her wrist, ankle and dorsum of the hands, started suddenly 9 months ago following a mytral valve replacement operation. The patient also had complaints of fever, weakness, limitation in her knees and difficulty in walking. She defined morning stifness lasting one hour. She told that her complaints did not decrease with nonsteroidal antiinflamatuar drug usage.

Address for Correspondence: Dr. Şebnem Koldaş Doğan, Isparta Gülkent Devlet Hastanesi Fizik Tedavi ve Rehabilitasyon Kliniği, Ankara, Turkey
Tel.: 0312 287 41 86 E-mail: sebnemkoldas@yahoo.com

Her past medical history included atrial fibrilation, pneumeunia and mytral valve replacement. Her family history was not significant. In her physical examination, mental status was normal, body temperature was 37.5°, blood pressure: 130/80 mmHg, heart rate: 75/min. In her musculoskeletal examination, there were swelling, warming and sensitivity with palpation in the metacarpophalangeal and proximal interphalangeal joints of all the digits and wrists, bilaterally and also in her ankles and left knee. There was edema in the dorsum of the hands (Figures 1 and 2). There were limitations of extension of 30° and flexion of 65° in her right wrist, extension of 45°, flexion of 60° in her left wrist and extension of 15° in her left knee. There were no other abnormal signs. The results of the laboratory tests were as follows: Hb: 9.4 g/dL, leucocyt count: 12800/mm^3, platelet count: 459000/mm^3, blood urine nitrogen: 52 mg/dL, creatinine: 2.1 mg/dL, uric acid: 7.3 mg/dL, AST: 133 UI/L, ALT: 194 UI/L, ALP: 548 UI/L, LDH: 261 UI/L, GGT: 193 UI/L, erythrocyte sedimentation rate (ESR): 100 mm/h, CRP: 88.5 mg/L, ASO: 370 UI/mL, ANA and RF: (-), beta-2 microglobulin: 8.64. In serum protein electrophoresis, albumin: 35, alpha-1 globulin: 8.9, alpha-2 globulin: 11.7, gamma globulin: 32.4. IgG: 25.7 g/L, IgA: 5.06 g/L. Cultures were negative. Tumor and hepatit markers were negative. In her hand radiographs there were narrowing between joint spaces of fifth proximal and distal interphalangeal joints but no erosive changes were observed. Knee and foot radiographs were normal. No vegetations were detected in transeusophageal ecocardiography. In abdominal USG there were minimal hepatomegally, few echo of calculus (stone) in lumen of gall bladder, ecogenic generation in size of 4 mm on the behind wall of bladder (calcified polip?, impacted crystaloid?) and minimal splenomegally. Elective operation was suggested by general surgery department for pathology of gall bladder. As a result of endoscopy of upper gastrointestinal system, benign gastric ulcers and duodenitis were diagnosed. Biopsy material taken from antroum was negative for amyloidosis. In thorax CT no interstitial involvement and malignance in lung parenchyma were detected. No pathologic results were found according to pelvic USG and vaginal smear in consultation of clinics of gynaecology for detecting malignance.

As a result, no infective disease, primarily subacute infective endocarditis, malignity, polymyalgia rheumatica (PMR) and amyloidosis were detected in scanning examination.

With these findings, the view of the patient was accepted as benign and 12.5 mg/day corticosteroid was started. In her 4 months follow up, there was remission of clinical findings and improvement in laboratory parameters (Hb: 12.3 g/dL leukocyte count: 10000/mm^3, platelet count: 320000/mm^3, ESR: 50 mm/h, CRP: 35 mg/L, albumin: 44.9, alpha-1 globulin: 10.7, alpha-2 globulin: 12.4, gama globulin: 20.1, AST: 48 IU/L, ALT: 63 UI/L, ALP: 278 UI/L, LDH: 195 UI/L, GGT: 151 UI/L) (Figure 3 and 4). The patient became independent in daily living activities. She is still being followed with the treatment of 10 mg/day corticosteroid.

Discussion

Mc Carthy et al. firstly described RS3PE syndrome with 10 cases characterized by symmetrical synovitis in peripheral joints and pitting edema on the dorsum of the hands, primarily affecting elderly (1, 2). Etiology of the RS3PE syndrome is unknown but environmental factors or infectious agents are known to have impact in the development of this disease (3, 9-12). In the literature, clinical and laboratory criteria for RS3PE syndrome can be classified as following: onset at an advanced age (age $\geq$ 65 years), negative RF and ANA tests, symmetrical polysynovitis involving wrists, metacarpophalangeal, interphalangeal, tarsal, metatarsophalangeal joints, tenosynovitis of the flexor and extensor joints of the hands, pitting edema of the involved joints, morning stiffness, rapid response to corticosteroid treatment and exclusion of other pathologies (4, 7, 8). There can be systemic signs like fever and weakness in RS3PE syndrome but radiographic joint destruction is not observed. Because of the pitting edema on the dorsum of the hands, RS3PE syndrome can often be confused with many diseases, such as rheumatoid arthritis (RA), seronegative arthropaties (psoriatic arthritis, Reiter's syndrome, ankilozan spondylitis,

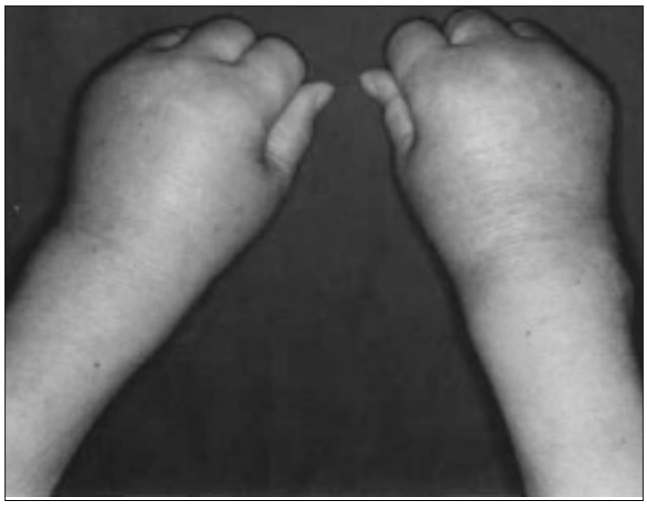

Figure 1.

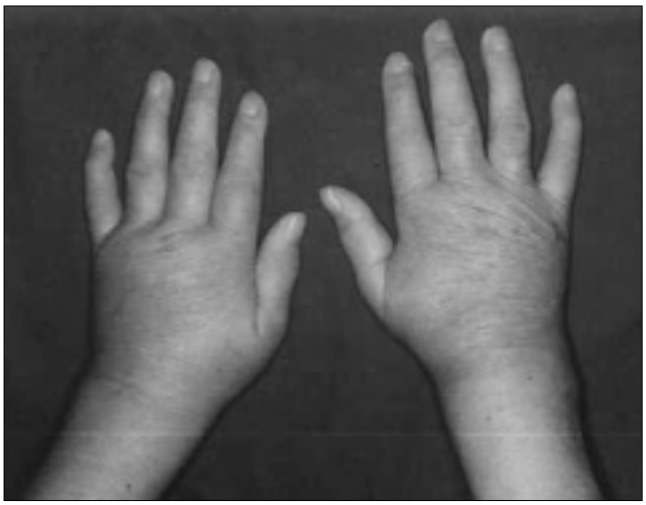

Figure 2.

enteropathic arthropathies), chondrocalcinosis, reflex sympathetic dystrophy syndrome (RSDS), connective tissue diseases (systemic lupus erythematosus, scleroderma, mixed connective tissue diseases) and panarteritis nodosa (PAN) (12,14,26). RS3PE syndrome can reportedly be related to diseases like malignity, polymyalgia rheumatica or amyloidosis (1-3, 9-14, 17-25).

Late onset RA or seronegative arthropathies can be confused with RS3PE syndrome like in this patient. RA is similar to RS3PE syndrome with some clinical findings and symptoms. RS3PE syndrome is distinguished from RA as it is remitting, there is no joint destruction and negative serologic tests like this patient (12, 14). Especially pitting edema rarely occurs in RA often unilaterally and generally in seropositive RA (4, 5, 8).

Remitting seronegative symmetrical synovitis with pitting edema can also be confused with PMR. Salvarani et al. reported that prevelance of swelling with pitting edema in distal extremities in PMR was 8 % in a retrospective study of 245 cases (25). Both of the disease are seronegative, are seen at an advanced age, response to low dose corticosteroid dramatically. But PMR is often seen in females and RS3PE syndrome is in males. However, RS3PE is also reported in males (3). The case presented here, there was no pain and stiffness in her neck, shoulder and pelvic girdle and she has peripheral joint symptoms, so we excluded the diagnoses of PMR (3, 8, 25). Like in this case dramatic response to low dose corticosteroid can be observed in RS3PE and PMR but not in RA (3, 5-8, 10, 12-16).

Chondrocalcinosis also is in relation with pitting edema but asymmetric involvement, chondrocalcinosis in radiographs and crystals in the joint fluid make us to diagnose chondrocalcinosis (1, 8). In this patient, because of the symmetry of the edema and the absence of findings except of degenerative changes in radiographs chondrocalcinosis wasn't considered. Reactive arthritis such as Retiter's syndrome and psoriatic arthritis were discarded because of absolutely asymmetric involvement ans sausage toes and fingers.

Puffy edema can also be seen in amyloidal arthropathy but this is progressive and irreversible (1). In this patient, because of remission of complaints with low dose corticosteroid treatment and negativity dying result of amyloidosis biopsy material taken from gastric antrum, we didn't consider the diagnosis of amyloidosis.

Remitting seronegative symmetrical synovitis with pitting edema is a benign arthritis that can be remission with low dose corticosteroid therapy. Russel et al. reported that they received dramatic response by adding 10 mg/day prednison to the treatment in 6 cases from a series of 13 cases (3). Chaouat and et al. in 3 out of 4 cases and Parisier in 2 cases observed resolving of edema with low dose steroid in 6-18 months (4, 15). Finnel also emphasized that good response to low dose corticosteroid in his reported 3 cases (12).

As well as the reported benign forms of RS3PE syndrome responding to low dose corticosteroid, there are also paraneoplastic forms as a primary or secondary manifestation of a neoplastic period without response to corticosteroid (17-22, 27). In all of these patients, RS3PE is an indirect manifestation of the tumour and started shortly before and after the malignance (19). Firstly in 1989, non-hodgkin lymphoma related with RS3PE syndrome was reported (21). Paraneoplastic RS3PE is often in relation with solid tumours and hystological types are adenocarcinoma. In a retrospective study of Sibilia et al. 6 cases with adenocarcinoma were reported. Additionally, the mean survival after discovery of polyarthritis is 11 months (20). According to the all reported cases, the response of corticosteroid was poor in most of the cases. The existence of systemic symptoms (fever, anorexia, weight loss) and poor response to corticosteroid remind us paraneoplastic RS3PE (19).

In the case presented here because of the existence of systemic symptoms, malignance were investigated with detailed clinical and laboratory examination and no pathologic signs were detected. She is being followed with low dose corticosteroid for 7 months.

In conclusion, this patient is accepted as benign with these findings on the other hand it should be kept in mind that this clinic entity can be found together with malignance, polymyalgia rheumatica, infection and amyloidosis as well as being benign and more detailed investigations should be made in patients with these kinds of findings.

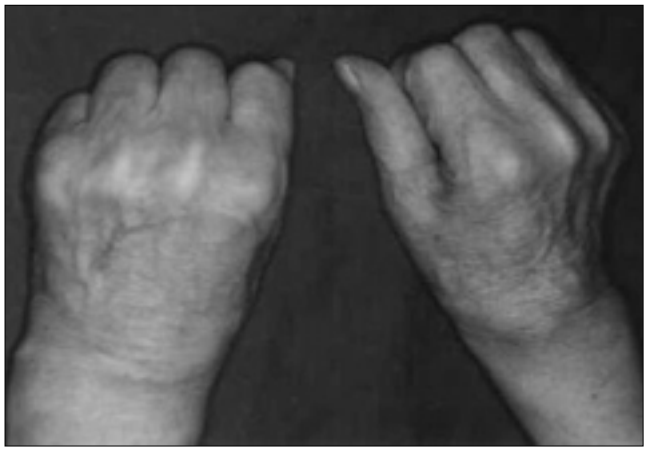

Figure 3.

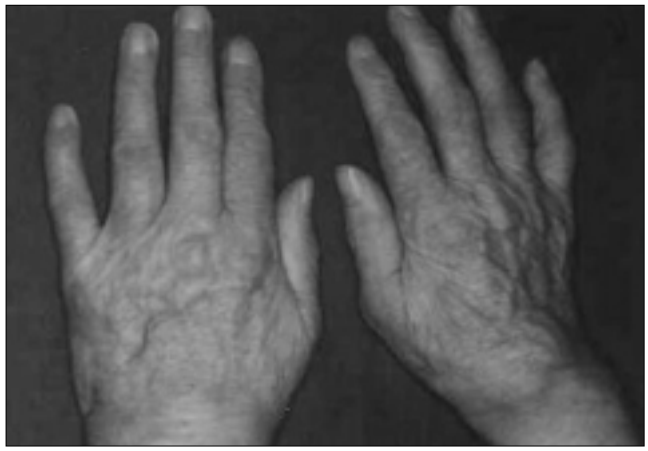

Figure 4.

References

1. Mc Carty DJ, O'Duffy JD, Pearson L, Hunter JB. Remitting seronegative symmetrical synovitis with pitting edema RS3PE syndrome. JAMA 1985; 254: 2763-7.
2. Jones JP. Rheumatoid Arthritis: The Clinical Picture: Koopman WJ editor. Arthritis and Allied Conditions. A Textbook of Rheumatology. 14th edition. Pennsylvania: Williams and Wilkins, 2001: 1179.
3. Russel EB, Hunter JB, Pearson L, Mc Carty DJ. Remitting, seronegative, symmetrical synovitis with pitting edema-13 additional cases. J Rheumatol 1990; 17: 633-9.
4. Chaouat D, Le Parc JM. The syndrome of seronegative symmetrical synovitis with pitting edema (RS3PE syndrome): A unique form of arthritis in the elderly? Report of four additional cases. J Rheumatol 1989; 16:1211-3.
5. Sattar MA. Remitting seronegative symmetrical synovitis with pitting edema in young adults: a subset of rheumatoid arthritis or a distinct syndrome? Br J Rheumatol 1990; 29: 479-81.
6. Özoran K, Ataman Ş, Aydıntuğ O, Tülek N, Düzgün N. Remitting seronegative symmetrical synovitis with pitting edema: an adult case with excellent prognosis. Rheumatol Int 1994; 13: 215-6.
7. Olive A, Del Blanco J, Pons M, Vaquera M, Tenax and the Catalan Group. The clinical spectrum of remitting seronegative symmetrical synovitis with pitting edema. J Rheumatol 1997; 24: 333-6.
8. Olivo D, D'Amore M, Lacava R, Rossi MG, Gareri P, Fiorentini C, et al. Benign edematous polysynovitis in the elderly (RSPE syndrome). Clin Exp Rheumatol 1994; 12: 669-73.
9. Michaels RM, Hochman RF. Remitting seronegative symmetrical synovitis with pitting edema (letter). JAMA 1986; 255: 2444-5.
10. Russel EB, Mc Carty DJ, Schwab J, Hanel D, Komorowski R, Stransky G, et al. RS3PE syndrome: No evidence for retroviruses. J Rheumatol 1994; 21: 1105-6.
11. Zatuchni J. Remitting seronegative symmetrical synovitis with pitting edema (letter). JAMA 1986; 255; 2444.
12. Finnel JA, Cuesta IA. Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) syndrome: A review of the literature and a report of three cases. J Foot Ankle Surg 2000; 9: 189-96.
13. Cimmino MA, Silvestri E, Garlaschi G. Remitting seronegative symmetrical synovitis with pitting oedema (RS3PE) as recurrence of aborted PMR. Ann Rheum Dis 2001; 303.
14. Olivieri I, Salvarani C, Cantini F. Remitting distal extremity swelling with pitting edema: A distinct syndrome or a clinical feature of different inflammatory rheumatic diseases? J Rheumatol 1997; 24: 249-52.
15. Pariser KM, Canoso JJ. Remitting seronegative (A) symmetrical synovitis with pitting oedema- Two cases of RS3PE syndrome. J Rheumatol 1991; 18: 1260-2.
16. Cantini F, Salvarani C, Olivieri I, Benozzi L, Macchioni L, Nicolli L, et al. Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) syndrome: a prospective follow up and magnetic resonance imaging study. Ann Rheum Dis 1999; 58: 230-6.
17. Tada Y, Sato H, Yoshizawa S, Kimura H, Kitamura M, Kusaba T, et al. Remitting seronegative symmetrical synovitis with pitting edema associated with gastric carcinoma. J Rheumatol 1997; 24: 974-5.
18. Goldenberg K, Rozenbaum M, Rosner I, Naschitz J, Kotler C. Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) secondary to non-Hodgkin's lymphoma. Clin Exp Rheumatol 1998; 16: 767-8.
19. Cantini F, Salvarani C, Olivieri I. Paraneoplastic remitting seronegative symmetrical synovitis with pitting edema. Clin Exp Rheumatol 1999; 17: 741-4.
20. Sibilia J, Friess S, Schaeverbeke T, Maloisel F, Bertin P, Goichat B, et al. Remitting seronegative symmetrical synovitis with pitting edema (RS3PE): A form of paraneoplastic polyarthritis? J Rheumatol 1999; 26: 115-20.
21. Ethiopia A, Bell D. Gastric carcinoma in association with remitting seronegative symmetrical synovitis with pitting edema. J Rheumatol 1999; 26: 1203-4.
22. Cobeta-Garcia JC, Domingo-Morera JA, Martinez-Bungui J. RS3PE syndrome chronic lymphoid leukemia. Clin Exp Rheumatol 1999; 17: 266-7.
23. Genovese MC. Musculoskeletal syndromes in malignancy: Kelley N, Ruddy S, Harris E, Sledge C editors. Textbook of Rheumatology. 6th edition. Philadelphia: WB Saunders Company, 2001: 1596.
24. McCarty DJ. Comparison of polymiyalgia rheumatica and remitting seronegative symmetrical synovitis with pitting edema syndrome: comment on the article by Salvarani et al. Arthritis Rheumatism 1996; 39: 1931-2.
25. Salvarani C, Gabriel S, Hunder GG. Distal extremity swelling with pitting edema in polymyalgia rheumatica. Arthritis Rheumatism 1996; 39: 73-80.
26. Billey T, Navaux F, Lassoued S. Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) as the first manifestation of periarteritis nodosa. Report of a case (letter). Rev Rhum Mal Oste'oartic 1995; 62: 53-4.
27. Rolden MR, Martinez F, Roman J, Tornes A. Non-Hodgkin's lymphoma: initial manifestation. Ann Rheum Dis 1993; 52: 85-6.