

Remitting seronegative symmetrical synovitis with pitting edema (RS3PE): a paraneoplastic syndrome? A new case

Sirs,

In 1985, McCarty *et al.* described a series of 10 patients over 65 years of age with a sudden-onset joint syndrome characterized by symmetrical and seronegative synovitis (S3) associated to pitting edema (PE). The course was benign and remitting (R) in response to low-dose corticosteroids (1). Since then, RS3PE has generated considerable interest due to its still uncertain significance (2-10). Accordingly, some authors have questioned whether this syndrome is a specific disease (2), since it can be associated with or represent the onset of other rheumatic disorders in elderly patients, such as rheumatoid arthritis, spondyloarthropathy, connective tissue diseases, polymyalgia rheumatica, sarcoidosis, vasculitis, relapsing polychondritis, or various infections. RS3PE can even behave as a paraneoplastic syndrome (2-9).

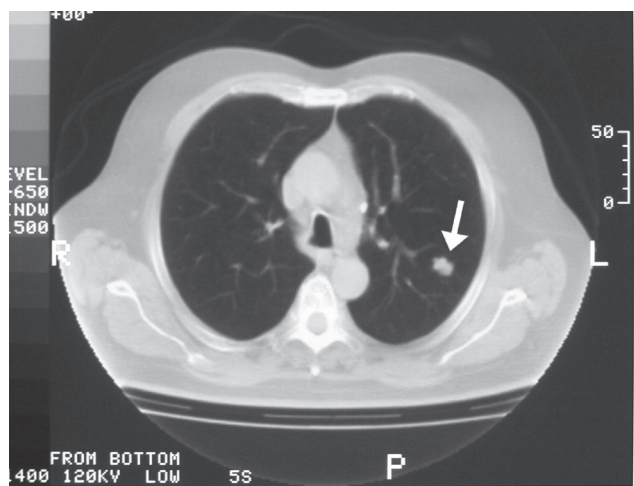
Clinical case

A 72-year-old male presented without antecedents of interest other than the smoking of 25-40 cigarettes/day since 14 years of age.

The patient consulted the rheumatology clinic with a three-month history of pain and swelling in the hands and feet, with scant response to NSAID therapy prescribed by his general practitioner. There were no other symptoms except tiredness throughout the day.

Examination revealed pain in response to palpation and swelling of the wrists, metacarpophalangeal joints, proximal interphalangeal joints, ankles and tarsal region bilaterally and symmetrically, with pitting and diffuse edema. The patient was unable to form a complete fist, and presented limited mobility of the aforementioned joints. There were no skin lesions, and cardiopulmonary auscultation and abdominal examination proved normal, with no palpable adenopathies. The following results were obtained: normal complete blood count, erythrocyte sedimentation rate 70 mm in the first hour, negative rheumatoid factor, negative autoantibodies, nonspecific HLA, negative hepatitis B and C virus serology, and biochemical and urine parameters without alterations. The x-ray study of the hands and feet showed an increased soft tissue component. RS3PE syndrome was diagnosed and treatment was started in the form of 12.5 mg of prednisone in a morning dose. Three weeks later the patient showed no symptomatic improvement and the prednisone dose was increased to 15 mg. The study was completed with tumor markers

Fig. 1. CT of the chest showing a pulmonary nodule in the left upper lobe. No adenopathies are seen.



and angiotensin converting enzyme assay, which proved normal. The chest x-rays showed the presence of a solitary node in the left upper lung lobe. In view of this finding, high-resolution chest CT was carried out, confirming the presence of the node, without adenopathies or other alterations (Fig. 1). Bone scintigraphy and abdominal-pelvic ultrasound showed no evidence of metastatic disease.

A left upper lobectomy was performed, without complications. A pathological study showed the presence of a poorly differentiated large-cell carcinoma of a squamous nature. Following surgery and during 14 months of follow-up, the patient has shown no further episodes of joint symptoms.

In 1993, Roldán *et al.* (3) described the first association of RS3PE with non-Hodgkin lymphoma, and since then different solid and hematological tumor processes have been related with the previous, simultaneous or posterior development of RS3PE. Tumor secretion of certain proinflammatory cytokines has been proposed as a pathogenic mechanism underlying this association (4). The search for an occult neoplasm in a recently diagnosed patient is not necessary. Indeed, abnormal signs or symptoms identified at history or in the clinical examination, particularly the presence of systemic manifestations or a lack of response to low-dose corticosteroids, suggest a paraneoplastic origin of the syndrome, and only treatment of the tumor will prove effective in such cases (5). A recent report suggests the need for long-term, or even lifetime, follow-up of these patients, because a neoplasm may occur some time after diagnosis of this syndrome (9).

It is too soon to speak of a paraneoplastic RS3PE syndrome. The association between RS3PE and the neoplasm in our patient may have been a coincidence, since both diseases affect the same group of patients. Case-control and multicenter studies are needed to determine the true significance of this association.

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References

1. MC CARTY DJ, O'DUFFY JD, PEARSON L: Remitting seronegative symmetrical synovitis with edema, RS3PE syndrome. *JAMA* 1985; 254: 2563-7.
2. SCHAEVERBEKE T, FATOUT E, MARCE S *et al.*: Remitting seronegative synovitis with pitting edema: disease or syndrome? *Ann Rheum Dis* 1995; 54: 681-4.
3. ROLDAN MR, MARTÍNEZ F, ROMÁN J *et al.*: A non-Hodgkin's lymphoma: initial manifestation (letter). *Ann Rheum Dis* 1993; 52: 85-6.
4. SIBILLA J, FRIES S, SCHAEVERBEKE T: Remitting seronegative symmetrical synovitis with pitting edema (RS3PE): a form of paraneoplastic polyarthritides. *J Rheumatol* 1999; 26: 115-20.
5. PAIRA S, GRAF C, ROVERANO S, ROSSINI J: Remitting seronegative symmetrical synovitis with pitting edema: a study of 12 cases. *Clin Rheumatol* 2002; 21: 146-9.
6. TUNC SE, ARSLAN C, AYVACIOGLU NB *et al.*: Paraneoplastic remitting seronegative symmetrical synovitis with pitting edema (RS3PE syndrome): a report of two cases and review of the literature. *Rheumatol Int* 2004; 24: 234-7.
7. CANTINI F, SALVARANI C, OLIVIERI I: Paraneoplastic remitting seronegative symmetrical synovitis with pitting edema. *Clin Exp Rheumatol* 1999; 17: 741-4.
8. OLIVE A, DEL BLANCO J, PONS M, VAQUERO M, TENA X: The clinical spectrum of remitting seronegative symmetrical synovitis with pitting edema. The Catalan Group for the study of RS3PE. *J Rheumatol* 1997; 24: 333-6.
9. RUSSELL E: Remitting Seronegative Symmetrical Synovitis with Pitting Edema Syndrome: followup for neoplasia. *J Rheumatol* 2005; 32: 9.
10. OIDE T, OHARA S, OGUCHI K *et al.*: Remitting seronegative symmetrical synovitis with pitting edema (RS3PE) syndrome in Nagano, Japan: clinical, radiological, and cytokine studies of 13 patients. *Clin Exp Rheumatol* 2004; 22:91-8.