Remitting Seronegative Symmetrical Synovitis with Pitting Oedema (RS3PE) of Hands and Feet in an 83-year-old Man

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Remitting seronegative symmetrical synovitis with pitting oedema (RS3PE) was first described by McCarty et al. in 1985 (1). It is a rare clinical syndrome that occurs predominantly in elderly men and is characterized by rapid-onset symmetrical distal teno- and/or joint synovitis, marked pitting oedema over the joints involved, especially the dorsum of the hands and feet. The erythrocyte sedimentation rate (ESR) is usually high, while rheumatoid factor (RF) and antinuclear antibodies (ANA) are negative. Other characteristics include the absence of articular erosions on radiographs and a rapid response to glucocorticosteroids leading to long-term remission (1, 2). The aetiology of RS3PE is unknown. It can occur as an idiopathic phenomenon, but also in association with various types of rheumatic diseases, most frequently late-onset rheumatoid arthritis and polymyalgia rheumatica (3–5). In addition several reports have described RS3PE as a paraneoplastic syndrome seen in association with both haematological and solid malignancies (6, 7). However, this association is confounded by the advanced age of the typical patient with RS3PE (8). Furthermore, some drugs and infectious agents have been suggested as possible triggers of the syndrome, in isolated cases (9, 10). A connection between RS3PE and certain HLA serotypes has been claimed, but not verified (11, 12). Finally, elevated serum levels of vascular endothelial growth factor and matrix metalloproteinase 3 have been reported as potentially involved in the pathogenesis, or at least as possible diagnostic markers, of the syndrome (13, 14).

CASE REPORT

An 83-year-old man presented a 5-day history of gradual bilateral swelling of the hands, wrists, feet and ankles. The swelling was accompanied by morning stiffness, impaired grip function and paraesthesia of most of finger pulpas. In addition, a severe aching of the hands occurred, especially during the night. The patient had no other constitutional symptoms and no previous medical history, apart from bilateral knee arthroplasty due to arthrosis. He took no medication and was a non-smoker. He had a temperature of 38.1ºC, while other vital signs were normal. The skin showed typical urticarial dermographism. Palpation revealed swelling and moderate tenderness of the metacarpophalangeal and proximal interphalangeal joints. The hands (especially the dorsum) showed a remarkable (non-tender) pitting oedema that extended to the middle of the lower arms (Fig. 1A). In addition, the feet and ankles had marked oedema. The finger joints had a reduced range of motion (especially the distal interphalangeal (DIP) and proximal interphalangeal (PIP) joints) with reduced grip and opponens strength. Fingers 1–3 on both hands showed reduced sensibility.

Comprehensive laboratory testing was performed, and elevated values for ESR (96 [normal <30] mm/h), C-reactive protein (254 mg/l [normal <8]), alanine aminotransferase (125 IU/l [normal <70]), alkaline phosphatase (342 IU/l [normal <105]) and prostate-specific antigen (PSA) (28 ng/ml [normal <4]) were found. Furthermore, the analysis revealed a mild inflammation-associated anaemia with haemoglobin of 6.5 mmol/l [normal 8.3–10.5], low transferrin and high ferritin. Otherwise, all parameters were normal, including platelet count, blood coagulation, creatinine, glucose levels, bilirubin, albumin, RF, anti-cyclic citrullinated peptide antibody, ANA, anti-neutrophil cytoplasmic antibodies, immunoglobulins, blood culture, thyroid-stimulating hormone, uric acid and urinalysis. Ultrasound of the abdomen, followed by computed tomography of the thorax and abdomen, displayed nothing but a moderately enlarged prostate. Transrectal ultrasound-guided prostate biopsy revealed benign prostate hyperplasia. Radiographs of the hands, wrists, ankles and feet showed signs of mild arthrosis and no erosions. Further investigations showed normal findings with respect to cerebrospinal fluid analysis,

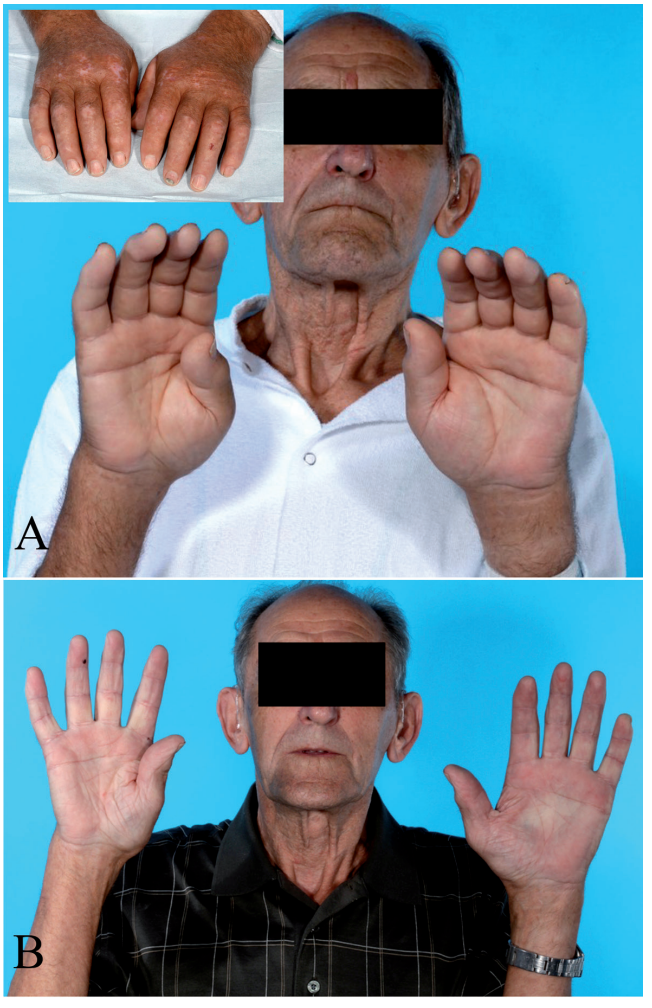

Fig. 1. (A) Marked oedema of the hands and especially the dorsal sites (insert) at the time of debut of the symptoms. (B) Almost normalized size of the hands 3 months after initiation of systemic therapy with corticosteroids.

chest X-ray, dual-energy X-ray absorptiometry (DEXA)-scan and echocardiography.

Treatment with prednisone, 25 mg daily, was initiated when obvious signs of infection and cancer were ruled out, and the pitting oedema, as well as all other symptoms, improved significantly but slowly. Approximately 7 weeks after treatment was initiated the patient experienced a deep venous thrombosis in the left leg, hence anti-coagulatic therapy, consisting of low molecular weight heparin (tinzaparin) and warfarin was instigated. Treatment with prednisone was continued, and the dose of 25 mg daily was maintained for 6 more weeks (until the oedema of the hands was resolved, Fig. 1B) before it was tapered over 2 months. All laboratory findings normalized during the course of treatment. At a clinical follow-up approximately 6 months after the initial consultation at our department only mild paraesthesia and slightly reduced sensibility of finger 1–3 persisted, while all other symptoms were completely resolved.

DISCUSSION

We present here a patient with a rapid onset of symmetric pitting oedema of both hands and feet, clinical signs of synovitis, negative rheumatoid factor, absence of radiographic bone erosions and a good response to treatment with glucocorticoid. On the basis of these findings, we diagnosed the patient with RS3PE. The data of the patient was in accordance with previously reported epidemiological characteristics of RS3PE, including high age, male gender and brisk response to glucocorticosteroids. No sign of malignancies was found. There was no indication of an association with intake of drugs and the patient did not display a history or symptoms matching an undiagnosed rheumatic disease. Thus, we conclude that the case presented here represents an isolated case of RS3PE with no underlying disease. Schaeverbeke et al. (3) suggests that RS3PE often appears to be related to late onset of several rheumatic diseases, which might take years to manifest. However, a *bona fide* pathogenetic linkage to rheumatic disease is still to be demonstrated. Russell (6) indicates that there may be a slightly elevated rate of neoplasia in patients diagnosed with RS3PE syndrome. This notion is strongly supported by Yao et al. (12), who suggest that the malignancy rate associated with RS3PE might be as high as 54%. In this report, however, the interval between onset of RS3PE syndrome and diagnosis of associated disease (cancer) is potentially very long, up to 12 years, indicating that RS3PE patients should be monitored for neoplasia with prudent age- and sex-specific surveillance for a long period of time. However, a recent study by Kimura et al. (8) fails to demonstrate an association between malignancy and RS3PE despite meticulous cancer screening, thus indicating that cancer screenings in RS3PE patients should kept at the level of age-appropriate screening protocols. The case of RS3PE presented here is, to our knowledge, only the second report of RS3PE reported from a dermatological department indicating that increased awareness of RS3PE syndrome amongst dermatologists may be warranted (15).

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