Case Report

Remitting Seronegative Symmetrical Synovitis with Pitting Edema Associated with Subcutaneous *Streptobacillus moniliformis* Abscess

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ABSTRACT. We describe an 84-year-old woman who developed remitting seronegative symmetrical synovitis with pitting edema (RS_3PE) associated with a subcutaneous abscess of the hand due to *Streptobacillus moniliformis*. Polyarthritis and edema were relieved after therapy with corticosteroids. We review the association of RS_3PE to different rheumatologic, neoplastic, or infectious diseases. (J Rheumatol 2001;28:1696–8)

Key Indexing Terms:
REMITTING SERONEGATIVE SYMMETRICAL SYNOVITIS WITH PITTING EDEMA
RS_3PE SYNDROME *STREPTOBACILLUS MONILIFORMIS*

Remitting seronegative symmetrical synovitis with pitting edema (RS_3PE) is a form of seronegative polyarthritis first described by McCarty, *et al*[1]. The main characteristics are pain and joint swelling of the hands and feet together with pitting edema, affecting mostly elderly people living in rural areas. Recent reports emphasize the nonspecific nature of this entity rather than a syndrome that can represent the initial form of different rheumatic diseases[2]. Occasionally it has been associated with sarcoidosis and solid or hematologic malignancies[3-5]. We have found no cases associated with infectious diseases. We describe a patient presenting with a polyarthritis resembling RS_3PE syndrome coincidental with a subcutaneous abscess due to *Streptobacillus moniliformis*.

CASE REPORT

An 84-year-old woman living in a rural community in Spain was admitted to our hospital after 5 days of pain and swelling affecting both hands, knees, and feet accompanied by pitting edema and severe functional impairment of the hands. No evidence for pelvic or shoulder girdle involvement was found. There was no fever, malaise, rash, systemic complaints, or recent viral disease. The history was unremarkable except for moderate hypertension. Examination showed symmetrical swelling of both hands (especially the wrists) accompanied by pitting edema, swelling of the knees, and an erythematous, warm and fluctuating area over the volar aspect of the right wrist. The rest of the examination was unremarkable.

Laboratory analyses showed a white blood cell count of 15,000/mm^3 (91% granulocytes, 4% lymphocytes) and erythrocyte sedimentation rate (ESR) of 67 mm/h. Renal, liver, and thyroid function tests were within normal limits. Serum electrophoresis was normal. Rheumatoid factor (RF) and antinuclear antibodies were negative. C-reactive protein (CRP) was elevated to 206 mg/l. Low values of C3, 64 mg/l, and C4, 1.5 mg/l, were found. Arthrocentesis of the left knee yielded 10 ml of inflammatory synovial fluid with 40,000 cells/mm^3, with no crystals under polarized light microscopy. Blood, synovial fluid, and urine cultures were negative. Direct puncture of the abscess of the right wrist disclosed a purulent fluid, which on gram staining revealed numerous neutrophils and thin and poorly staining gram negative rods. After 48 h incubation, gram negative bacilli with pleomorphic filamentous morphology, characteristic bulbous swelling arranged in chains, and tangled clumps grew on solid media (Figure 1). Incubation on sheep agar showed small smooth, grayish and not hemolytic colonies. No growth occurred on chocolate agar or liquid media supplemented with hemoglobin. The organism was catalase and oxidase negative, indol production and urease activity negative, and nitrate was not reduced to nitrite. The isolate was inhibited by penicillin, vancomycin, erythromycin, tetracycline, gentamicin, and sodium polianethol sulfonate and resistant to trimethoprim/sulfamethoxazol, colistin, nalidixic acid, and norfloxacin. The organism was identified as *S. moniliformis*. No acid-fast bacilli were encountered at Ziehl-Neelsen stain and Löwenstein-Jensen culture. Arthrocentesis of the right wrist disclosed a few synovial drops where no bacteria were identified. Radiographs showed osteoarthritic changes over the proximal and distal interphalangeal joints of the hands and the knees. Chondrocalcinosis was absent. Indomethacin 50 mg qid and amoxicillin-clavulanate were initiated, but the symptoms did not improve and on the 7th day, treatment with deflazacort 30 mg/day was instituted with frank improvement. The abscess drained spontaneously. When the patient was questioned again, she remembered a rat bite on the left foot some days before the start of the complaints. Corticosteroids were tapered.

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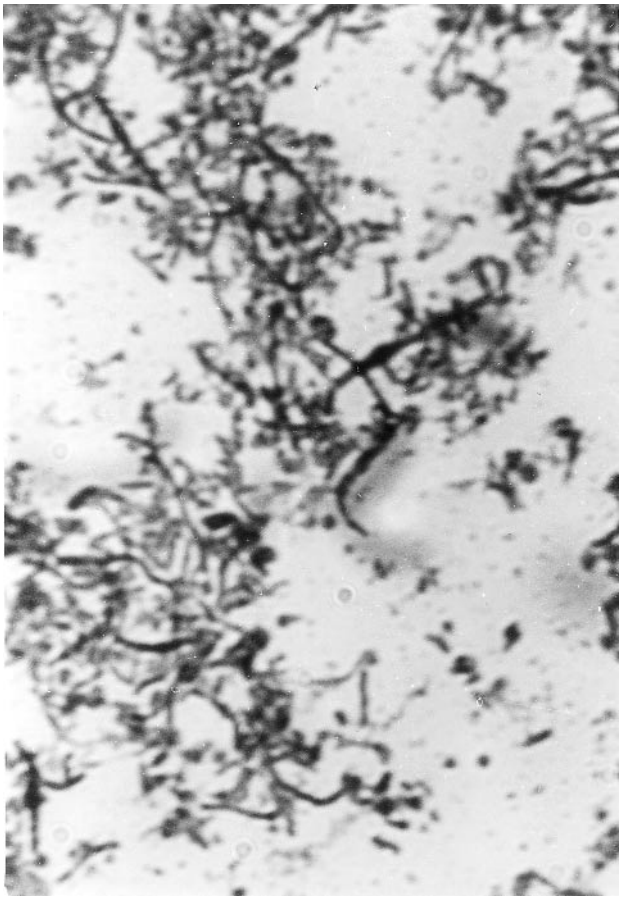

Figure 1. Pleomorphic filamentous bacilli with characteristic bulbous swelling arranged in chains and tangled clumps on gram stain (× 1000).

Eight months later, she remains asymptomatic and complement levels are within normal ranges.

DISCUSSION

RS_3PE is a rheumatic syndrome of acute onset characterized by the simultaneous advent of pain and symmetrical pitting edema of the back of the hands and sometimes the feet. Asymmetrical cases have been reported[6]. Occasionally it is accompanied by fever and asthenia. Large synovial discharges are usually not found. It is most frequent among elderly white men living in rural communities with seasonal incidences in the spring and autumn[1]. Laboratory studies show an increase of acute phase reactants such as CRP and ESR, sometimes accompanied by moderate anemia. RF is negative. In cases where synovial fluid analysis was carried out, leukocyte counts were usually low. Radiographic findings include edematous appearance of soft tissues and osteopenia. Bone erosions are absent. Magnetic resonance imaging discloses pronounced extensor tenosynovitis[7]. Lymphoscintigraphy studies show normal lymphatic function[8]. The treatment is corticosteroids, with disappearance of the edema in one month and complete remission in 18 months. Etiology is not known; studies for *Borrelia burgdorferi* or retroviral etiology have been negative[9]. It has been associated with HLA-B7[10]. Initially considered as a separate entity, today some authors believe it to be a syndrome that can represent the initial form of various diseases including polymyalgia rheumatica, rheumatoid arthritis, seronegative spondyloarthropathy, and rarely sarcoidosis and Horton's arteritis[2,4]. Association with carcinoma, lymphoma, and myelodysplastic syndromes with complete remission after tumor excision has been described. Tumor derived interleukin 6 has been implicated in the pathogenesis of tumor associated cases[5].

Streptobacillus moniliformis is an uncommon human pathogen contracted from exposure to rodents. Nasopharyngeal carriage rates in wild and laboratory rats range from 50% to 100%. Rat bite fever is an uncommon infectious disease produced in most cases by *S. moniliformis* (a pleomorphic, gram negative bacillus), and in a small number of cases by *Spirillum minus* (a spirochetal specimen). The disease affects mainly laboratory workers, inhabitants of infested areas, and children. The term rat bite fever encompasses 3 distinct clinical disorders caused by 2 organisms: (1) spirillary rat bite fever ("sodoku") caused by *S. minus*, with local reaction at the site of the rodent bite or scratch, characterized by induration, tenderness, or ulceration; (2) streptobacillary rat bite fever produced by *S. moniliformis*; and (3) Haverhill fever, produced by *S. moniliformis* after ingestion of milk or water contaminated by the excretions of infected rats[11]. In rat bite fever caused by *S. moniliformis,* after an incubation period of 1–20 days patients typically present fever, chills, headaches, arthralgia-arthritis, and papulomacular rash. Infrequent complications include endocarditis, meningitis, pneumonia, and numerous organ abscess formations[12]. Septic arthritis has been described. In these cases leukocyte counts in synovial fluid are high, in contrast to sterile arthritis, in which they are usually lower[13-17].

Diagnosis is based on culture of the microorganism. Once grown, its typical morphological appearance and growth characteristics on culture make it relatively easy to establish diagnosis. The organism is a non-encapsulated, non-motile, non-acid fast, highly pleomorphic, gram negative bacillus. Fluorescent acridine orange staining may be useful in detecting *S. moniliformis* in cases in which the gram stain appears negative[18]. Differential diagnosis includes Lyme disease, mountain fever, leptospirosis, and secondary syphilis. Most cases resolve spontaneously or with treatment usually with penicillin (5–7 days of intravenous penicillin followed by oral penicillin for 7 days). Fatal cases have been described[19].

Our patient developed a polyarthritis resembling those of RS_3PE that improved shortly after corticosteroid institution. In addition to polyarthritis, a subcutaneous abscess due to *Streptobacillus moniliformis* was encountered. The patient

remembered a rat bite on the foot a few days before, but no lesion at the site was seen on admission. She had no fever, rash, or malaise as typically encountered in rat bite fever. It was not possible to identify the bacilli on synovial fluid from the knee and the wrist after a long incubation period. Low serum complement values seen at first suggested an immune mediated response to infection. We have not found a case of RS_3PE accompanying an infectious agent but this case supports the tendency to consider the RS_3PE syndrome as the initial manifestation of various rheumatic, neoplastic, or other conditions.

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