Case Report

Remitting Seronegative Symmetrical Synovitis with Pitting Edema Associated with Acute Myeloid Leukemia

NICOLE CHIAPPETTA and BARRY GRUBER

ABSTRACT. Remitting seronegative symmetrical synovitis with pitting edema (RS_3PE) almost exclusively affects elderly men and can occur independently or may be associated with a vast array of clinical conditions including underlying malignancy. Patients present with a polyarthritis similar to rheumatoid arthritis. We describe a case of an elderly man presenting with RS_3PE who developed acute myeloid leukemia. It is important for clinicians to be aware of this possibility and initiate appropriate investigations, particularly if systemic symptoms are prominent, to detect an occult malignancy at a potentially earlier stage. (J Rheumatol 2005;32:1613–4)

Key Indexing Terms:
RS_3PE ACUTE MYELOID LEUKEMIA SYNOVITIS

Remitting seronegative symmetrical synovitis with pitting edema (RS_3PE) was first described by McCarty, *et al* in 1985[1]. Almost all individuals affected are elderly men who present with a polyarthritis similar to rheumatoid arthritis. RS_3PE can occur independently or may be associated with a vast array of clinical conditions including underlying malignancy, both hematologic and solid tumors. We describe a case of an elderly man presenting with RS_3PE, who developed acute myeloid leukemia (AML). This is the first reported case of RS_3PE presenting as a paraneoplastic syndrome associated with AML.

CASE REPORT

An 82-year-old man presented to the Emergency Department with a 48-hour history of bilateral hand swelling and pain. He had a history of coronary heart disease requiring double vessel coronary bypass surgery 6 months prior to presentation. His review of symptoms was negative except for a 13.6 kg weight loss following his surgery.

Massive bilateral pitting edema encompassing the dorsum of his hands and synovitis of his wrists was noted on examination. A diagnosis of RS_3PE was rendered and 10 mg prednisone daily was initiated. The patient had a rapid clinical response with resolution of his symptoms within one week of starting therapy. Initial laboratory evaluation including chemistry, urine analysis, liver function tests, rheumatoid factor, and antinuclear antibodies were within normal limits. The patient's complete blood count (CBC) showed a leukocyte count of 6,800 (with normal differential), platelets of 170,000, and hemoglobin of 14.7 g/dl. Erythrocyte sedimentation rate (ESR) was 122 mm/h. Considering the possibility of an underlying occult malignancy, the patient was evaluated with a prostate specific antigen, colonoscopy, chest radiograph, and computed tomography scans of the abdomen and pelvis. All tests were within normal limits.

Three months after initial presentation, the patient was maintained on prednisone 10 mg daily, as attempts to taper his dose resulted in recurrent pitting edema of his hands. At 3 months, a CBC showed a leukocyte count of 48,000 and platelets of 20,000. (CBC one month before was within normal limits.) The patient was admitted to hospital and a bone marrow biopsy revealed acute myeloid leukemia. He was started on chemotherapy, but expired 3 weeks into his treatment secondary to underlying sepsis.

DISCUSSION

RS_3PE was first described by McCarty in 1985[1]. Ten patients reported symmetrical synovitis predominantly involving the wrists and flexor digitorum tendon sheaths associated with marked pitting edema of the dorsum of both hands[2]. The majority of these patients were older men, average age 69.5 years. They were consistently rheumatoid factor negative. ESR ranged from 14 to 104, average 49.5 mm/h. All but one patient had morning stiffness greater than one hour. The average duration from presentation to diagnosis was 1.9 months. Radiographic imaging of the hands and wrists failed to demonstrate erosions in these patients[3].

In 1997, Olive, *et al*[4] proposed diagnostic criteria based on 27 patients with clinical presentation consistent with RS_3PE: (1) bilateral pitting edema of both hands; (2) sudden onset of polyarthritis; (3) age > 50 years; and (4) seronegative rheumatoid factor. Polyarthritis involves the metacarpophalangeal joints, proximal interphalangeal joints, wrists, shoulders, elbows, knees, and ankles in decreasing frequency. Elevation of acute phase reactants, persistent rheumatoid

From the Department of Rheumatology, Stony Brook University Hospital, New York, New York, USA.

N. Chiappetta, DO; B. Gruber, MD, Director of Rheumatology, Stony Brook University Hospital.

Address reprint requests to Dr. N. Chiappetta, Department of Rheumatology, Stony Brook University Hospital, T-16, Room 040 Nicholls Road, Stony Brook, New York, USA, 11794.
E-mail: nchiappetta@optonline.net

Accepted for publication April 4, 2005.

factor seronegativity, and edema responsive to low dose corticosteroids have consistently been observed[5]. Absence of erosive disease on radiographic analysis differentiates RS_3PE from rheumatoid arthritis. The etiology of edema in RS_3PE is unknown, but recent magnetic resonance imaging studies suggest that marked extensor tenosynovitis is responsible[4].

The occurrence of RS_3PE as a paraneoplastic syndrome has been described[1,2,5,6]. Systemic signs and symptoms (weight loss, anorexia, fever) and poor response to corticosteroids are clinical characteristics suggesting that RS_3PE may represent a paraneoplastic syndrome[5]. Olive, *et al*[4] discuss 2 patients who developed hematologic malignancies, one with T cell lymphoma and the second with myelodysplastic syndrome. Olivieri, *et al*[3] summarized 20 case reports of individuals with RS_3PE as the first manifestation of a solid or hematologic malignancy. In 12 of the 20 patients, diagnosis of RS_3PE preceded the onset of malignancy with a median of 2 months; in 4 patients it was concomitant with, and in 2 patients it was subsequent to, diagnosis of cancer. Fifteen of the 20 patients presented with solid tumors, adenocarcinoma being the most common histologic type. These tumors originated in the prostate, stomach, colon, endometrium, and pancreas. Hematologic malignancies have also been described: the 5 remaining patients developed chronic lymphocytic leukemia or non-Hodgkin's lymphoma.

In summary, diagnosis of RS_3PE in the elderly has been associated with underlying malignancy, either concomitant with or preceding diagnosis. It is important for clinicians to be aware of this possibility in order to detect an occult malignancy at a potentially earlier stage. An appropriate investigation may be justified particularly if systemic symptoms are prominent.

REFERENCES

1. McCarty DJ, O'Duffy JD, Pearson L, Hunter J. Remitting seronegative symmetrical synovitis with pitting edema. RS3PE syndrome. JAMA 1985;254:2763-7.
2. Cantini F, Salvarani C, Olivieri I, et al. Remitting seronegative symmetrical synovitis with pitting oedema (RS3PE) syndrome: a prospective follow up and magnetic resonance imaging study. Ann Rheum Dis 1999;58:230-6.
3. Olivieri I, Salvarani C, Cantini F. RS3PE syndrome: an overview. Clin Exp Rheumatol 2000;18 Suppl 20:S53-S55.
4. Olive A, Del Blanco J, Pons M, Vaquero M, Tena X. The clinical spectrum of remitting seronegative symmetrical synovitis with pitting edema. J Rheumatol 1997;24:333-6.
5. Ekenel M, Yavuz S, Karti S, Direskeneli H, Akoglu T. Remitting seronegative synovitis with pitting edema associated with chronic lymphocytic leukemia. Clin Rheumatol 2000;19:247-8.
6. Sibilia J, Friess S, Schaeverbeke T, et al. Remitting seronegative symmetrical synovitis with pitting edema (RS3PE): a form of paraneoplastic arthritis? J Rheumatol 1999;26:115-20.