Clinico-pathological conference
edited by H.M. Moutsopoulos

Rheumatoid resorptive arthropathy

P.V. Voulgari, S.C. Efremidis[1], A.A. Drosos

Department of Internal Medicine and [1]Department of Radiology, Medical School, University of Ioannina, Ioannina, Greece.

Paraskevi V. Voulgari, MD, Attending Rheumatologist; Stavros C. Efremidis, MD, Professor of Radiology; Alexandros A. Drosos, MD, FACR, Associate Professor of Medicine/Rheumatology.

Please address correspondence and reprint requests to: Prof. Alexandros A. Drosos, MD, FACR, Department of Internal Medicine, Medical School, University of Ioannina, GR 451 10 Ioannina, Greece.

Clin Exp Rheumatol 1999; 17: 474-6.

Key words:
Rheumatoid arthritis, resorptive arthritis, psoriatic arthritis, scleroderma arthropathy.

Case presentation
(P.V. Voulgari)
The patient was a 42-year-old, single woman with a six-year history of symmetrical polyarthritis. She presented to our outpatient Rheumatology Clinic with a poor grip. During the preceding years, as a result of an emotional disturbance, she had refused to visit any physician or to receive medication for her arthritis. Clinical examination revealed hypermobility of the finger joints. The digits appeared shortened and excessive skin folds were present. The phalanges could be inserted into one another and then be pulled out into abnormally long extensions (telescope-like action). A small subcutaneous nodule was also present over the extensor surface of the second digit of the right hand (Fig. 1). No signs of psoriasis were found.
Laboratory evaluation showed a hemoglobin (Hb) value of 9.1 gr/dl with features of anemia of chronic disease (low serum iron and normal ferritin levels). The C-reactive protein (CRP) was 42 mg‰ (normal value: < 6 mg‰) and the erythrocyte sedimentation rate (ESR) was 65 mm/hr. Serum rheumatoid factor (RF) was positive at a titer of 1/640 (latex fixation test). Finally, HLA-typing revealed HLA A2-28, B12-17, DR4-2 alloantigenes.

Radiological findings
(S.C. Efremidis)
Hand and wrist radiographs showed severe erosive arthropathy affecting the wrists, metacarpophalangeal (MCP), and proximal interphalangeal (PIP) joints bilaterally. More specifically: 1) the carpal bones of the right wrist were completely resorbed and the distal ulna presented a whittled appearance; 2) there were severe resorptive changes with whittled metacarpals and sublaxations of the MCP joints; and 3) there were extensive erosive changes in the PIP joints. Osteopenia was also present (Fig. 2).

Differential diagnosis
(A.A. Drosos)
The differential diagnosis in this case included an aggressive untreated rheumatoid arthritis (RA), psoriatic arthritis (PSA) and scleroderma resorptive ar-

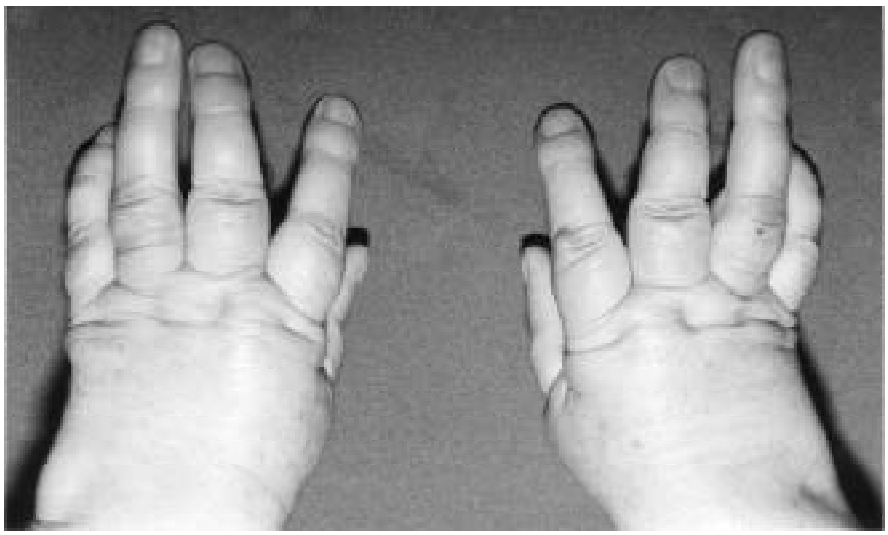

Fig. 1. Excessive skin folding in both hands and a rheumatoid nodule over the extensor surface of the second digit of the right hand.

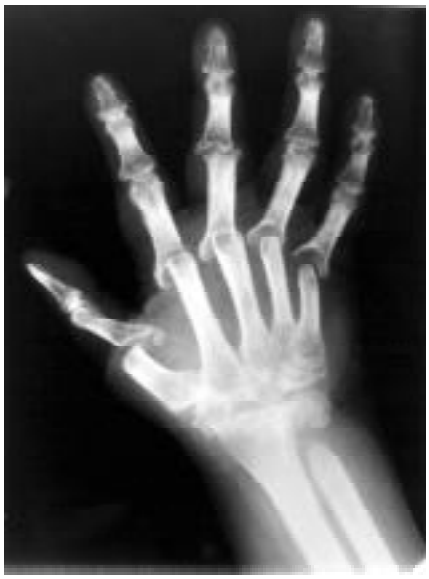

Fig. 2. Close-up view of the right hand x-ray demonstrates: (i) resorption of the carpal bones and a pencil-like deformity of the distal ulna; (ii) resorptive changes of the metacarpophalangeal joints with whittling and sublaxations; and (iii) erosive findings of the proximal interphalangeal joints.

thropathy. Reliable differentiation between RA and PSA in this patient was based on the absence of psoriatic rash and the absence of resorptive changes at the distal interphalangeal (DIP) joints, with the characteristic pencil-in-cup deformity (1). In addition, the presence of RF and the subcutaneous nodule favored the diagnosis of RA. The absence of Raynaud's phenomenon and skin changes despite her long-standing arthritis, as well as the absence of acrosclerosis, erosive changes of the distal tufts, or resorption of the soft tissues of the fingertips, and finally the absence of subcutaneous calcifications, ruled out the possibility of scleroderma as the underlying cause of the disease in this patient (1).

The common radiological findings in RA consist of fusiform soft tissue swelling, juxta-articular osteoporosis, diffuse joint space loss and marginal subchondral bony erosions. The most serious result of rheumatoid involvement of the hand is resorptive arthropathy, defined as severe resorption of the bone that begins at the articular cartilage and spreads along the diaphysis of the involved phalanges.

Erosive damage in RA patients is known to occur early in the course of the disease (2). Factors which may influence disease progression and erosive changes are: RF, rheumatoid shared epitope, the levels of acute phase response proteins (APR), early treatment with disease modifying antirheumatic drugs (DMARDs) and the effectiveness of drug therapy.

It is generally accepted that high titers of RF are associated with more severe disease and with the presence of extra-articular manifestations (EAM) including rheumatoid nodules (3). The APR, measured either directly by the determination of CRP concentrations or indirectly by the ESR, is a sensitive and objective indicator of both the activity and the extent of synovial inflammation (4). Studies have shown that persistent reductions in ESR and CRP values are accompanied by the slow progression of radiological lesions (5).

The association between human leukocyte antigen (HLA) class II genes and RA is well established. Many studies have demonstrated that RA is associated with the DRB1-encoded alleles HLA-DR4 and HLA-DR1 (6). Weyand *et al.* reported that the severity of RA, as defined by the EAM and destructive arthritis, was correlated with the "dose" of the rheumatoid epitope (7). In contrast, Boki *et al*. showed that only a minority of Greek RA patients carries the rheumatoid epitope and that DR4 is not associated with disease severity in these patients (8, 9).

DMARDs have been shown to be effective in suppressing synovitis and in delaying radiological disease progression in recent-onset RA (10). In addition, it seems that even in patients with established RA the early introduction of DMARDs is more effective than delayed treatment with second-line agents (11-13). Other factors which may influence the progression of RA are listed in Table I (14, 15).

Our patient suffered from a very severe form of RA. There were many contributing factors which led to the above described catastrophic resorptive changes: the long-standing untreated disease; the presence of EAM, like rheumatoid nodules and anemia of chronic disease; the high titers of RF; the high levels of APR; and finally the presence of rheumatoid epitope, indicating an unfavorable prognosis and outcome.

Final diagnosis

Resorptive rheumatoid arthritis.

Patient follow-up

(A.A. Drosos)

The patient was started on methotrexate (10 mg/week) and prednisone (7.5 mg/day). After two months of treatment substantial clinical and laboratory improvement was noted.

Acknowledgments

The authors wish to thank Mrs. E. Horti for her secretarial assistance.

References

1. BROWER AC: *Arthritis in Black and White.* 2nd ed., Philadelphia, W.B. Saunders; 1997.
2. FUCHS HC, KAYE JJ, CALLAHAN LF, NANCE EP, PINCUS T: Evidence of significant radiographic damage in rheumatoid arthritis within the first 2 years of disease. *J Rheumatol* 1989; 16: 585-91.
3. WOLFE F, SHARP JT: Radiographic outcome of recent-onset rheumatoid arthritis. A 19-year

Table I. Factors determining the progression of rheumatoid arthritis.

Early	Disease onset with symmetrical polyarthritis
	Systemic manifestations (low grade fever, fatigue)
	Increased ESR, CRP
	Positive RF
	Presence of the "rheumatoid epitope" (DR4, DR1)
Later	Polyarticular involvement
	Increased morning stiffness
	RF > 1/160
	Anemia
	Thrombocytosis
Definitive	Presence of rheumatoid nodules
	Early radiological erosions of hand x-rays

ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; RF: rheumatoid factor.

study of radiographic progression. *Arthritis Rheum* 1998; 41: 1571-81.

4. MALLYA RK, DE BEER FC, BERRY H, HAMILTON EDW, MACE BEW, PEPY SMB: Correlation of clinical parameters of disease activity in rheumatoid arthritis with severe concentrations of C-reactive protein and erythrocyte sedimentation rate. *J Rheumatol* 1982; 9: 224-8.
5. DAWES PT, FOWLER PD, CLARKE S, FISHER J, LAWTON A, SHADFORTH MF: Rheumatoid arthritis. Treatment which controls the C-reactive protein and erythrocyte sedimentation rate reduces radiological progression. *Br J Rheumatol* 1986; 25: 44-9.
6. WINCHESTER R, DWYER E, ROSE S: The genetic basis of rheumatoid arthritis: the shared epitope hypothesis. *Rheum Dis Clin North Am* 1992; 18: 761-83.
7. WEYAND CM, HICOK KC, CONN D, GORONZY JJ: The influence of HLA-DRB1 genes on disease severity in rheumatoid arthritis. *Ann Intern Med* 1992; 117: 801-6.
8. BOKI KA, PANAYI GS, VAUGHAN RW, DROSOS AA, MOUTSOPOULOS HM, LANCHBURY SS: HLA class II sequence polymorphisms and susceptibility to rheumatoid arthritis in Greece: The shared HLA-DRβ epitope hypothesis accounts for only a minority of Greek RA patients. *Arthritis Rheum* 1992; 35: 749-55.
9. BOKI KA, DROSOS AA, TZIOUFAS AG, LANCHBURY JS, PANAYI GS, MOUTSOPOULOS HM: Examination of HLA-DR4 as a severity marker for rheumatoid arthritis in Greek patients. *Ann Rheum Dis* 1993; 52: 517-9.
10. BUCKLAND-WRIGHT JC, CLARK GS, CHIKANZA IC, GRAHAME R: Quantitative microfocal radiography detects changes in erosion area in patients with early rheumatoid arthritis treated with myocrisine. *J Rheumatol* 1993; 20: 243-7.
11. WEINBLATT ME: Rheumatoid arthritis: Treat now, not later ! (Editorial). *Ann Intern Med* 1996; 104: 773-4.
12. VAN DER HEIDE A, JACOBS JWG, BIJLSMA JWJ, *et al.*: The effectiveness of early treatment with "second line" antirheumatic drugs. A randomized, controlled trial. *Ann Intern Med* 1996; 124: 699-707.
13. ABU-SHAKRA M, TOKER R, FLUSSER D, *et al.*: Clinical and radiographic outcomes of rheumatoid arthritis patients not treated with disease modifying drugs. *Arthritis Rheum* 1998; 41: 1190-5.
14. ERHARDT CC, MUMFORD PA, VENABLES PJ, MAINI RN: Factors predicting a poor life prognosis in rheumatoid arthritis. An eight year prospective study. *Ann Rheum Dis* 1989; 48: 7-13.
15. PINCUS T, CALLAHAN LF: What is the natural history of rheumatoid arthritis ? *Rheum Dis Clin North Am* 1993; 19: 123-51.