Case Report

# Periarticular Calcinosis Associated with Anti-Jo-1 Antibodies *sine* Myositis. Expanding the Clinical Spectrum of the Antisynthetase Syndrome

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***ABSTRACT.*** We describe a 58-year-old woman who developed interstitial lung disease (ILD), polyarthritis, and anti-Jo-1 antibodies, with no clinical evidence of myositis. Despite successful treatment with corticosteroid and azathioprine for her arthritis and pulmonary condition, she developed deforming arthropathy of the hands, with periarticular calcinosis. The association of anti-Jo-1 antibodies, ILD, and periarticular calcinosis with subluxing arthropathy *sine* myositis is rare, with few cases reported. This report expands the clinical spectrum of the antisynthetase syndrome, which is broader than previously reported. (J Rheumatol 2001;28:1401–4)

*Key Indexing Terms:*
DEFORMING ARTHROPATHY
ANTI-Jo-1 ANTIBODIES
PERIARTICULAR CALCINOSIS
PULMONARY FIBROSIS

An important development in the study of connective tissue diseases was the identification of serum antibodies associated with clinically homogeneous patient subsets[1]. In polymyositis (PM) and dermatomyositis (DM), more than 80% of patients produced autoantibodies in reaction to nuclear and/or cytoplasmic antigens, and about half these patients were shown to produce myositis-specific antibodies[1]. Among them, autoantibodies acting against aminoacyl-tRNA synthetases (antisynthetase antibodies) have been shown to be strongly correlated with myositis, interstitial lung disease (ILD), Raynaud's phenomenon, fever, arthritis, and a specific dermatitis known as "mechanic's hand." This clinical spectrum constitutes the so-called antisynthetase syndrome[1,2].

It was found that 68 to 89% of patients with both myositis and ILD have antisynthetases, but occasionally patients with ILD and antisynthetase antibodies do not show myositis[3]. We describe a woman who developed subluxing arthropathy and periarticular calcifications associated with anti-Jo-1 antibodies (antihistidyl-tRNA synthetase) without overt myositis, an uncommon finding that has rarely been reported.

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## CASE REPORT

The patient was a white woman who at the age of 33 years had rashes, fever, and inflammatory polyarthritis. A diagnosis of inflammatory polyarthritis of unknown origin was made and she was treated with oral corticosteroids and parenteral gold salts. This first episode concluded after the first year of treatment without consequences, and all therapy was discontinued. She remained well until age 58, when she developed acute onset polyarthritis, fever, throat pain, and marked edema of the dorsal aspect of both hands. Examination revealed synovitis of both wrists, bilateral 2nd and 3rd metacarpophalangeal (MCP) joint arthritis, synovitis at the 2nd, 3rd and 4th proximal interphalangeal (PIP) joints of both hands, and edema of the dorsal face of the hands. Thorax auscultation showed crackles over the basal lung fields. There were no other remarkable findings, and she did not complain of past or present proximal muscle weakness. Laboratory data including antinuclear antibody test, anti-DNA, anti-Sm antibodies, anti-RNP antibodies, anti-SSA, anti-SSB, anti-Jo1, anticentromere, anti-Scl-70, rheumatoid factor, immunoglobulins, complete and differential blood count, complement proteins, urinalysis, creatine kinase, aldolase, SGOT, SGPT, LDH, and renal function tests were completely normal, apart from high readings for C-reactive protein and erythrocyte sedimentation rate. Radiographs of the affected joints were not remarkable on the initial visit. Chest radiographs showed bilateral basal pulmonary interstitial infiltrates, confirmed in a high resolution computed tomography (HRCT) scan (Figure 1), and pulmonary function studies showed moderate restrictive lung disease with a diffusing capacity of 58% compared to healthy controls matched for age, height, and sex. Bronchoalveolar lavage showed inflammatory cellularity composed predominantly of lymphocytes (> 50%), consistent with lymphocytic alveolitis. The microbiological study for habitual pathogens, fungi, and mycobacteria was negative. A muscle biopsy yielded a negative result for myositis. A diagnosis of undifferentiated connective tissue disease was made and she was given nonsteroidal anti-

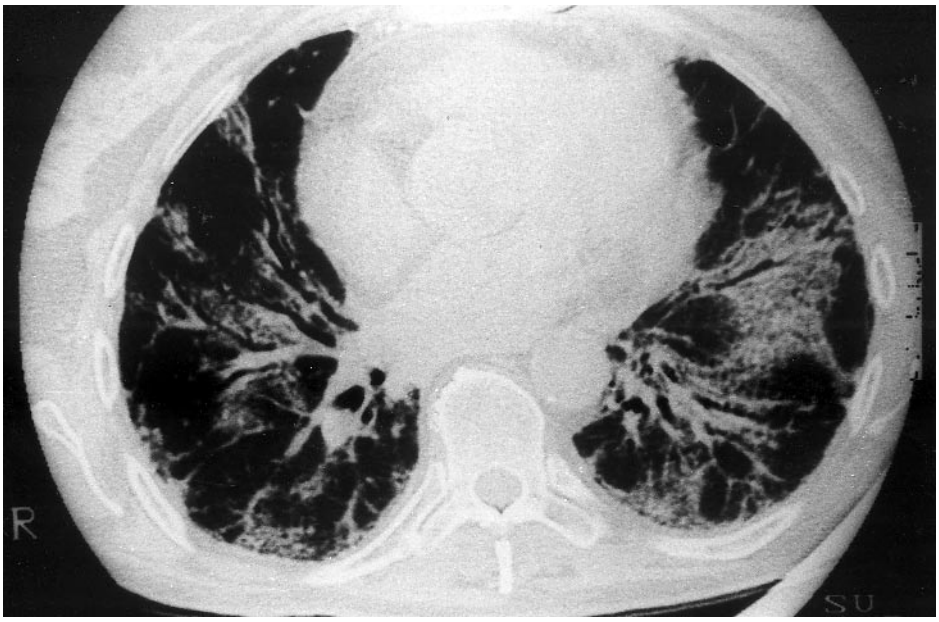


*Figure 1*. High resolution CT scan showing bilateral pulmonary fibrosis. There is increased reticulation of both lung fields and a hazy appearance suggesting active alveolar inflammation, confirmed by bronchoalveolar lavage.

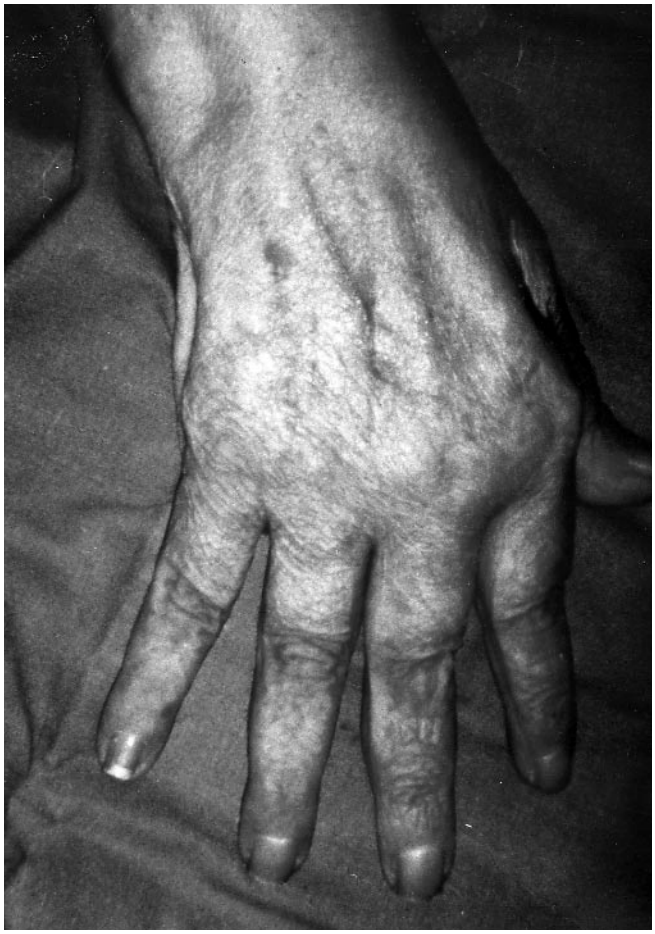

*Figure 2*. A rheumatoid arthritis-like hand with swan-neck deformities in a patient with anti-Jo-1 antibodies.

inflammatory drugs and 15 mg/day prednisone, but only a partial response was achieved. Thus parenteral gold salts were added to her previous treatment. She remained almost asymptomatic for a year, but it was necessary to discontinue this therapy due to mucositis and proteinuria related to the gold salts. A few days later, her pulmonary status worsened, causing shortness of breath on exertion and nonproductive cough with an associated worsening in gas exchange, so the steroid dose was increased to 1 mg/kg/day and 150 mg/day azathioprine (AZA) were also added. She again remained symptom-free for the next 18 mo, and then AZA was stopped. She is now being treated with 10 mg/day prednisone and her pulmonary status is stable, but despite excellent symptomatic control of her condition, over the last 2 years she has developed a deforming arthropathy with swan-neck deformities (Figure 2), boutonnière deformity of the 5th right finger, and periarticular-intraarticular calcifications at several levels in both hands, but without overt erosions (Figure 3), as well as in the shoulders. She has also developed ligamentous ossification affecting the anterior common vertebral ligament (Figure 4). In addition, her immunological profile has changed with the appearance of antiextractable nuclear antigen antibodies and anti-Jo-1 antibodies, while other laboratory data (as above) remain in the normal range.

## DISCUSSION

Anti-Jo-1 is the most common of a group of anticytoplasmic-amino-acyl-tRNA-synthetase enzymes and is itself directed against histidyl-tRNA synthetase, an enzyme that catalyzes the binding of the amino acid to its cognate transfer RNA during protein synthesis[1]. Due to the cytoplasmic locations of the antigens to which they are directed, such autoantibodies are often found in patients who are ANA negative[1], as in our case.

Antisynthetase antibodies, which include anti-Jo-1, anti-PL7, anti-PL12, anti-OJ, and anti-EJ, occur in the sera of 25 to 40% of adult patients with PM/DM, and have been related to the development not only of myositis but also of ILD, fever, arthritis, Raynaud's phenomenon and so-called "mechanic's

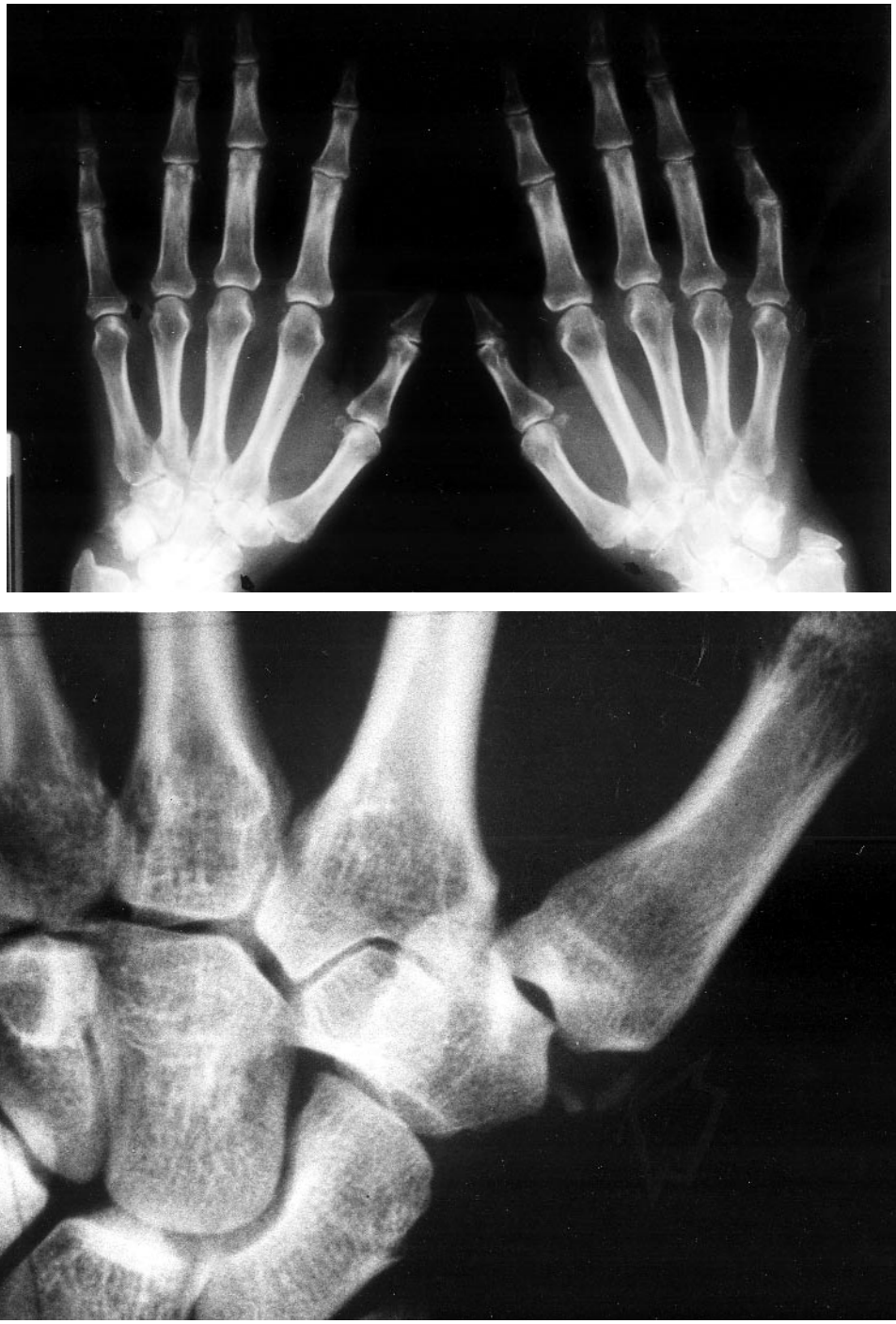

*Figure 3*. A. Microcalcinosis present at multiple levels, but clearly visible at the MCP and PIP joints of the 4th left finger, DIP of the 5th left finger, radial border of the left radiocarpal joint, radial border of the right trapezium, and MCP joint of the 5th right finger. B. A more detailed view showing the base of the thumb with calcifications that affect the radial border of the trapezium.

hand" (antisynthetase syndrome)[1]. On the other hand, articular symptoms often occur early in the disease course of PM/DM. They are usually mild and clear up soon after the introduction of corticosteroid therapy, but on rare occasions patients with PM/DM develop a deforming arthropathy that has been associated with anti-Jo-1 antibodies[4].

In larger series, almost all patients with ILD and myositis have antisynthetases (mainly anti-Jo-1), the association of such antibodies only with myositis without ILD — or the opposite, ILD *sine* myositis — being quite rare[1,3-5]. Because individual patients may not demonstrate all the clinical features conforming to the antisynthetase syndrome, it can

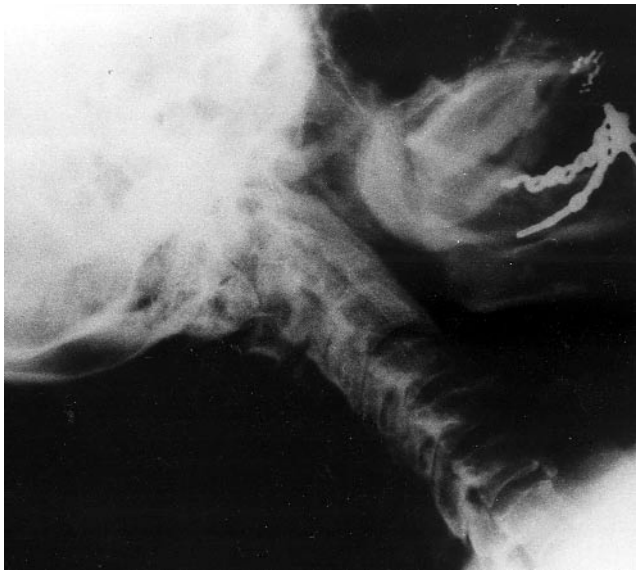

*Figure 4*. Lateral view of the cervical spine showing ossification (rather than calcinosis) of the common anterior vertebral ligament at the level of C5-C6 disc space. There is no disc space narrowing and degenerative changes are almost absent, therefore this image should not be confused with degenerative changes or diffuse idiopathic skeletal hyperostosis (DISH).

be difficult to recognize the syndrome before obtaining a positive test for one of the defining antisynthetase antibodies[4]. Friedman, *et al*[3] describe 10 patients (from a series of 170 with PM/DM) with antisynthetases whose clinical picture was dominated by ILD in the absence of clinically evident myositis despite followup for as long as 13.5 years. They found only 2 cases of arthritis in their small series, but gave no further details. That work emphasizes the rarity of our finding of anti-Jo-1 with ILD without evidence of myositis. Another striking aspect of our case was the development of a rapidly, although only slightly, deforming arthropathy, very similar to a rheumatoid hand (Figure 2), despite successful therapy for ILD and synovitis. Oddis, *et al*[4] report that 12 out of 21 anti-Jo-1 positive patients with PM developed inflammatory polyarthritis at some time during their disease course, and 4 of these 12 patients developed a subluxing arthropathy similar to that found by us and others[6,7]. Nonetheless, their cases had the triad of myositis, ILD, and anti-Jo-1, while our case lacked myositis.

Since 1976, when Bunch, *et al*[8] gave the first description of a deforming arthropathy associated with PM/DM, probably no more than 20 new cases have been added to the literature. However, the prevalence of this condition may be underestimated if we consider that with longterm followup a greater proportion of anti-Jo-1 positive patients with PM/DM may develop joint deformities[4]. Additionally, our patient also showed periarticular and intraarticular calcifications located at both hands and shoulders, something found rarely by others. Cohen, *et al*[9] describe a patient with probable mixed connective tissue disease, ILD, polyarthritis, periarticular calcinosis, anti-Jo-1 antibodies, and joint destruction due to osteolysis. Kazmers, *et al*[7] report a case of anti-Jo-1 positive DM, erosive polyarthritis, and periarticular calcinosis identified as hydroxyapatite, and more recently, Citera, *et al*[10] added a new case of apatite deposition in anti-Jo-1 positive PM with deforming arthritis. Thus although calcinosis is considered rare in adult PM, patients with anti-Jo-1 antibodies appear to be a high risk subgroup for this complication[4]. Another notable finding in our case was ligamentous ossification affecting the anterior vertebral ligament at the cervical spine, an image not previously reported in anti-Jo-1 related conditions, although of course it could be merely a concurrent disease.

In summary, the deforming arthropathy associated with periarticular calcinosis is part of the clinical spectrum of antisynthetase syndrome. It normally appears when other characteristics of the syndrome are already present, such as ILD and myositis, although it remains a very rare condition when one of these 2 elements (ILD or myositis) is absent. Thus, our case of anti-Jo-1 related subluxing arthropathy, periarticular calcinosis, and ILD *sine* myositis confirms that the clinical spectrum of the antisynthetase syndrome is broader than previously reported.

Additionally, the specificity of anti-Jo-1 is not as apparent as originally thought, and the antibody may be found in a wider spectrum of patients. There may not be an "antisynthetase syndrome" but the antibody may be associated with a variety of clinical manifestations.

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