An unusually complicated case of primary Sjögren's syndrome: development of transient "lupus-type" autoantibodies following silicone implant rejection.

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The Journal of Rheumatology is a monthly international serial edited by Earl D. Silverman featuring research articles on clinical subjects from scientists working in rheumatology and related fields.
Economic Cost and Epidemiological Characteristics of Fibromyalgia

To the Editor:

The article by Robinson, et al. intimates how much the diagnosis of fibromyalgia costs. So why does The Journal continue to publish articles discussing this illegitimate diagnosis as if it really existed? Let’s help the patients by abandoning this fallacious and undefined (and undefinable) diagnostic term. Any diagnosis that’s characterized by “I am the evidence” should immediately be discounted.

GEORGE E. EHRLICH, MD, MACR, Adjunct Professor, School of Medicine, University of Pennsylvania, Adjunct Professor of Clinical Medicine, New York University, 1101-241 South Sixth Street, Philadelphia, Pennsylvania 19106-3731, USA. E-mail: g2e@mindspring.com

REFERENCES

Ms Robinson replies

To the Editor:

As my colleagues and I mention in our article, the clinical understanding of fibromyalgia (FM) is evolving, the pathophysiology is unknown, and the diagnosis is often not made correctly. While Dr. Ehrlich and others may believe that FM is not a “real” disorder, the very fact that 4699 patients had an insurance claim with an ICD-9 diagnosis of FM is obvious evidence that many physicians disagree with his opinion. By way of comparison, there was also divergence of opinion regarding the biological basis of major depressive disorder prior to the advent of effective pharmacotherapy.

The point of our article was to demonstrate that patients with insurance claims related to FM are suffering and face great burdens, which include hidden costs of disability and burden to health care systems. Published data on FM have grown considerably from the time the term was coined in 1976. Medline search of “fibromyalgia” represents a growing trend in the literature, from 114 in the 1970s, 227 in the 80s, and 1144 in the 90s, and already 658 since 2000. Patients and physicians want answers. We have a responsibility to patients to gain better understanding of FM, whether or not there is complete agreement within the clinical community about its legitimacy as an illness.

In fact, the uncertainty of the disease is even more reason to publish and gain understanding of this disorder in order to help patients. Patients with an ICD-9 code for FM represented 2.8% of the large-employer data we analyzed. Compared with overall beneficiaries, FM claimants had 2.6 times more medical claims, almost 3 times more prescriptions for study selected medications, and had 2 times the total health care costs. We concluded there is a great need for better understanding of FM.

Where better to publish these results than with the experts in the field, rheumatologists?

REBECCA ROBINSON, MS, Health Outcomes Research Scientist, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, Indiana 46285, USA.

REFERENCE

Drs. Dobkin and Bernatsky reply

To the Editor:

Dr. Ehrlich seems to advocate banishing the publication of articles pertaining to fibromyalgia (FM) in The Journal of Rheumatology. His viewpoint apparently stems from his rejection of the diagnostic label “fibromyalgia.” He, among others (e.g., Ford1, Quintner and Cohen2), purports that use of the diagnostic label contributes to the spread of misinformation and perpetuation of an epidemic. Apparently, the lack of objective evidence underlying the symptoms described by patients renders research pertaining to FM unworthy of public dissemination. Yet one could easily name many health problems whereby “the patient is the evidence,” e.g., low back pain, migraine headaches, etc. Without patients presenting their symptoms (via self-report) most clinicians would be unable to diagnose diseases with known pathology (e.g., systemic lupus erythematosus).

So why bother investigating and reporting empirical work pertaining to the syndrome defined by the American College of Rheumatology over a decade ago? First, because it is the second most common diagnosis in rheumatology clinics3. Second, because health service utilization is high, as are the costs to society and individuals with FM4. Third, because as scientists we seek to understand the nature of the syndrome (see Pillmer, et al5 and Croft4). Fourth, because as clinicians we feel compassion for other human beings who are suffering and hope to find an effective means of treating them (see Wilke6). As a clinical psychologist I cannot help but see that the term “fibromyalgia” elicits a negative reaction in many medical doctors (among others). Why does this particular syndrome bring out the worst in some otherwise competent and caring physicians? Do time pressures experienced by doctors make it harder to fit these patients into their grueling schedules? Does the lack of effective treatment make seeing them seem futile?
Even if it is true that the label “fibromyalgia” is just a new term for muscular rheumatism, or neurasthenia, or fibrositis, or that it represents a “common distress disorder”, the fact remains that up to 2% of the adult population complains of the symptoms consistent with FM. The good news is the label itself does not appear to alter health status, function, or health service utilization.

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REFERENCES

Letters

An Unusually Complicated Case of Primary Sjögren’s Syndrome: Development of Transient “Lupus-type” Autoantibodies Following Silicone Implant Rejection

To the Editor:

We describe the appearance of transient “lupus-type” autoantibodies (anti-Sm and anti-RNP) with no clinical evidence of systemic lupus erythemato-sus (SLE), concurrent with the rejection of a silicone wrist implant inserted 4 years previously, in a woman with a 15 year history of primary Sjögren’s syndrome (pSS) who had been followed for 8 years. In addition, she had had persistent cytopenia (leukopenia and thrombocytopenia) as well as a monoclonal gammapathy. Progression of pSS to serological and then to clinical SLE has previously been documented in one patient only. In our patient these autoantibodies might have been precipitated by silicone implant rejection. The sudden occurrence of wrist pain combined with appearance of the lupus-type autoantibodies makes this probable. After surgical removal of the implant, these autoantibodies disappeared, without progression to clinical SLE. The controversial effect of silicone implant rejection on the emergence of a different pattern of autoimmunity is briefly discussed.

A 61-year-old Caucasian woman had been diagnosed with hypothyroidism at age 40. Since 1985, she had complained of increasing dryness of the mouth and eyes and recurrent submandibular gland swellings. Dental caries, pyelitis, cystitis, and bronchitis necessitated repeated courses of antibiotics. Gammaglobulin injections (Beniglobin; Germany) were given for 3 months. She was also given steroids (prednisone 10 mg daily), chloroquine (Nivaquine), methotrexate (MTX), and sulfasalazine. MTX and steroids were discontinued in 1996. Schirmer’s test was dry (positive) bilaterally (<5 mm) and submandibular adenopathy was present. An initial mild hypogammaglobulinemia with a monoclonal peak in the mid-gammaglobulin region was detected. The serum M component was 21 g/l and serum gammaglobulin was 5 g/l (normal 6–15 g/l), confirmed by repeated estimations. Immunofixation for IgG was high positive. The gammaglobulin was of the IgG lambda type. Bone marrow showed plentiful megakaryocytes and granulocyte precursors with mild prominence of plasma cells (9%), some of which were morphologically abnormal with large, definite nucleoli. Bence-Jones proteinuria and cryoglobulins were not detected. Serum gammaglobulin concentrations were reported as normal at 8 g/l two years later.

The erythrocyte sedimentation rate remained persistently elevated (70–90 mm/h). Antinuclear antibodies were constantly demonstrated (1:160 to 1:640, speckled pattern) as were antibodies to Ro and La. Rheumatoid factor was found in 1999 (Rose-Waaler positive); rheumatoid factor Latex was 108.8 IU/ml (normal 0–39). Antibodies to dsDNA by ELISA (confirmed by immunodiffusion and Western blot) were negative. Antibodies to dsDNA by C.Pathida luciliae were negative. Antibodies titers to parvovirus and to hepatitis C were negative.

Persistent leukopenia and thrombocytopenia were present. The platelet counts fluctuated to as low as 117 × 10^9/l, and the white blood cell count to as low as 2.70 × 10^9/l (normal 4–12.0). Neutropenia as low as 0.59 × 10^9/l was detected.

Two years later, a lower limb lymphocytic vasculitis was diagnosed. In early 2002, she complained of severe pain in her right wrist, without preceding trauma. Antibodies to dsDNA by ELISA were initially detected, but on repeat testing by immunofluorescence (C. luciliae), they proved to be negative. ELISA (confirmed by immunodiffusion and Western blot) detected antibodies to Sm at a titer of 1:5120. Antibodies to RNP were also detected by immunoblotting. The appearance of both these antibodies was transient. Radiographs at this time showed advanced cystic degeneration of carpal bones and fragmentation of the wrist implant (Figure 1). An excision arthroplasty was performed. The pain subsided and repeated immunological testing over the next year showed total disappearance of the lupus-type autoantibodies. Laboratory investigations for measurement of antismic tone antibodies could not be undertaken at this time.

HLA testing found the patient to be A24, 11, DR15, 17, B7, 50, and C2, 7.

The progression of pSS to serological and then to clinical SLE has previously been documented by Satoh, et al., who described a 69-year-old Japanese woman with pSS who developed anti-Sm antibodies after a stable course of 9 years, followed by clinical SLE. Lupus associated autoantibodies (although not to Sm and RNP) following silicone breast implants have also been reported.

Other accompaniments of pSS in our patient, such as leukopenia and thrombocytopenia and indeed neutropenia (reported in 10% of patients with pSS), although previously reported, are also uncommon. In our
patient it was initially combined with a mild hypogammaglobulinemia, distinctly rare in this disorder, which might have been related to previous therapy with immunosuppressives such as MTX, thus possibly adding to her predisposition to recurrent infections. Garcia-Carrasco, et al recently investigated the frequency of hypogammaglobulinemia in a group of Spanish patients with SS, and found 8% had low IgG levels. These investigators also found evidence of previous parvovirus infection in 35%. As the hypogammaglobulinemia in our patient was transient, it is possible that it may have been drug induced. However, the frequency of infections seemed not to decrease following normalization of the gammaglobulin levels, and because of this, the infections may have been related to the underlying SS itself (because of mucosal abnormalities seen in this condition), combined with the neutropenia and not because of immunosuppression from drugs or the hypogammaglobulinemia. Another explanation might be an occult polymorphonnuclear cell dysfunction or abnormality of T cell subsets.

There was a persistent monoclonal gammopathy and a diagnosis of monoclonal gammopathy of undetermined significance was also made. According to several authorities, this may be predictive for the future development of myeloma.

Monoclonal gammapathies have also infrequently been documented in association with SS. However, Sugai, et al studied 12 Japanese patients with pSS and found a large variety of monoclonality in their group, while Broginni, et al in 358 patients with SS found this to be present in 6% of patients.

Our patient, in addition, also had hypothyroidism. She thus represents another example of the “mosaic of autoimmunity” as described by Shoenfeld and Isenberg. The question arises as to the relationship of the silicone implant leakage and its probable rejection and the transient development of these autoantibodies. This case is not dissimilar to our report of a 45-year-old woman who, upon inhalation of a polyclonal lymphocyte-activating factor, developed 6 different autoimmune diseases associated with a panoply of autoantibodies. The combination of an environmental factor and a genetic predisposition is therefore well known as leading to an overt autoimmune disease.

In our case the silicone may have acted as an “adjuvant”. Indeed, injections of silicone to MRL/lpr strains of mice have been followed by increased titers of SLE autoantibodies as well as cytokine changes. Illnesses resembling rheumatoid arthritis, SLE, and SS, termed “siliconosis,” following silicone breast augmentation have been reported, as well as a fibromyalgia/chronic fatigue syndrome.

Infections such as mycobacterial, gram-negative, and specifically Epstein-Barr virus are also known to be associated with the emergence of SLE related autoantibodies and even overt SLE.

The transient appearance of these antibodies simultaneous to the silicone transplant rejection, and their disappearance with its speedy removal, makes a strong case for not considering such transplants in patients with preexisting autoimmune disease or diathesis.

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Book review


This handbook is part of a series called Fast Facts, Indispensable Guides to Clinical Practice, which focuses on providing pocketbook synopses of diseases. Previously published Fast Facts topics have included “Osteoporosis” and “Soft Tissue Rheumatology.” The authors of this text are experts in their field and provide an overview of rheumatoid arthritis. The resulting reference is a concise yet comprehensive review of RA.

There are 10 chapters, including sections on Aetiology, Clinical Features, and Investigation. However the authors have elected for their first chapter to concentrate on normal joint anatomy, which suitably provides the reader with some fundamental tools to approach the chapter on Pathogenesis. There is up to date information on treatment, including a section on Management with Biological Response Modifiers. Despite the acknowledged purpose of being a quick reference text, the reader will be pleasantly surprised to find a chapter devoted to assessment of rheumatic disease activity. Well organized tables, figures, and pictures complement the easy to read text. Each chapter aptly concludes with a summary of the pertinent points as well as key references for those who wish to do further detail.

This is a well organized and thorough review that is appropriately directed to medical students and residents as well as family practitioners.

Bindu Nair, MD, FRCP, Assistant Professor of Medicine, University of Saskatchewan, Saskatoon, Saskatchewan S7N 0W8, Canada.

Correction

Østergaard M, Peterfy C, Conaghan P, et al. OMERACT rheumatoid arthritis magnetic resonance imaging studies. Core set of MRI acquisitions, joint pathology definitions, and the OMERACT RA-MRI scoring system. J Rheumatol 2003;30:1385–6. Page 1386, column 2, line 4, should read: Bone edema. Bone edema is scored 0–3 by the volume of edema: 0, no edema; 1, 1–33% of bone edematous; 2, 34–66%; 3, 67–100%. We regret the error.