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CME CREDIT

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Arthralgias, myalgias, facial erythema, and a positive ANA: not necessarily SLE

A single positive laboratory result does not justify potentially harmful therapy

Physicians, whether generalists or specialists, frequently see patients with vague musculoskeletal complaints and intermittent rashes who are thought to have a connective tissue disease. Often, systemic lupus erythematosus (SLE) is diagnosed on the basis of a history of these manifestations (without confirming them objectively by physical examination) and on a positive antinuclear antibody (ANA) titer.[1–3] When such a diagnosis is made, a physician may then be tempted to prescribe medications such as corticosteroids or antimalarials, which may have little impact on the disease course, can cause harmful side effects, and should be reserved for patients with clearly defined SLE who have organ system involvement.

In the case below I outline two different scenarios for a patient with musculoskeletal complaints and a positive ANA titer, as an illustration of the points made above.

CASE STUDY: DOES THIS PATIENT HAVE SLE?

A 30-year-old Caucasian woman, mother of two children ages 4 and 2, presents for evaluation of arthralgias, myalgias, fatigue, stiffness, and a faint malar rash; these symptoms have been present for approximately 18 months but have worsened over the last few months. She describes herself as previously healthy; as a matter of fact, she used to be physically very active, practicing aerobic exercises or swimming at least 1 hour, 6 days a week.

This pattern changed dramatically after her first child was born; she returned to work as an elementary school teacher 2 months postpartum but did not resume her structured exercise program. After her second child was born, she decided to stay home and take care of her children, thinking that by so doing she could balance her daily activities better and find time to go back to exercising. However, she never felt like exercising. Rather, she usually felt tired, achy, and unable to sleep soundly at night even after the baby was sleeping through the night. In addition, she felt quite stiff in the morning and needed about half an hour to limber up.

The patient's hands and fingers became painful and "swollen"—it became difficult for her to remove her rings, which she finally stopped wearing. She also noticed a facial rash after sun exposure. She tried taking over-the-counter analgesics and "arthritis" compounds,

TABLE

FIBROMYALGIA OR LUPUS? TWO SCENARIOS

History	30-year-old Caucasian woman with a history of arthralgias, myalgias, morning stiffness, fatigue, and facial erythema	
	Scenario 1	**Scenario 2**
Physical examination	Negative	Facial erythema Synovitis Oral ulcers
Routine laboratory test results	Normal complete blood count Normal thyroid-stimulating hormone level Normal urinalysis	Anemia Thrombocytopenia Leukopenia Lymphopenia Normal thyroid-stimulating hormone level Mild hematuria Mild leukocyturia Mild proteinuria
Initial serologic test results	Antinuclear antibody titer 1:160 (normal 1:40)	Antinuclear antibody titer 1:160
Further laboratory tests indicated	None	Serum creatinine level Anti-DNA titer Anti-Smith titer Serum complement level 24-hour protein excretion Renal biopsy (possibly)
Diagnosis	Fibromyalgia	Systemic lupus erythematosus with kidney involvement
Treatment	Symptomatic	According to organ-system involvement
Prevention	Healthy behaviors	Healthy behaviors
Follow-up	Reassessment by specialist only if new symptoms ensue	Management in conjunction with specialist or specialists

One third of patients with SLE have fibromyalgia–like symptoms

but these did not help. Finally, she seeks the help of a physician.

There is nothing else of importance in the patient's present illness, medical history, or review of symptoms. She has a distant cousin with "lupus," but does not know any details. With this history, we have two possible clinical scenarios.

First scenario: no objective signs

The patient is mildly overweight, in no acute distress, and has normal vital signs. The physical examination reveals nothing abnormal except for tenderness elicited over the trapezius and the cervical and lumbar paraspinal muscles; specifically, there are no rashes, oral ulcers, or synovitis. The white blood cell count is 5.2×10^9/L with 30% lymphocytes, 5% monocytes, and 65% polymorphonuclear leukocytes; the hematocrit is 38%, and the platelet count is normal. An antinuclear antibody (ANA) test is positive at a 1:160 dilution, with a homogenous pattern (normal: negative at a 1:40 dilution). The thyroid-stimulating hormone level is normal. A fresh urine specimen is obtained and is normal (TABLE).

Second scenario: objective signs, abnormal laboratory values

The patient is thin and appears to be in some pain; the vital signs are normal except for a heart rate of 100 per minute. She has mild

facial erythema, two oral ulcers on the hard palate, and tenderness and minimal swelling over the metacarpophalangeal and proximal interphalangeal joints of both hands. The white blood cell count is 3.2×10^9/L with 10% lymphocytes, 10% monocytes, and 80% polymorphonuclear leukocytes; the hematocrit is 31%, and the platelet count is 415×10^9/L. The ANA titer is 1:160, homogeneous pattern. The thyroid-stimulating hormone level is normal. A fresh urine specimen shows trace protein, 2 to 4 red blood cells per high-powered field, and 4 to 5 white blood cells per high-powered field.

WITHOUT OBJECTIVE SIGNS, SLE IS UNLIKELY

Before examining the laboratory data and attempting to interpret the positive ANA study, we first need to know the pretest probability that this patient indeed has SLE. In the first scenario, we essentially have subjective manifestations, none of which could be corroborated objectively. In addition, the routine laboratory test results are normal. Thus, the pretest probability of SLE is less than 1%, and the posttest probability, although higher, is still low—approximately 5%.[4]

To conclude that this patient has a mild form of lupus, "incomplete" lupus, or "variant" lupus is, in my view, not only erroneous but detrimental for the patient and physician alike. The patient may go on to learn more about this disease and be frightened by what she finds out, given that the available literature does not, by and large, distinguish mild from severe SLE. She may also have her health insurance terminated or new insurance denied because she has a "serious" medical condition.

The physician may lose objectivity about this patient's primary complaints and may feel compelled to use inadequate and potentially toxic therapies. In this situation, obtaining additional serologic tests in the hope that they will aid in diagnosing lupus with more certainty is plainly wrong. In our first scenario, the pretest probability of lupus increases to only 20% if an anti-dsDNA study is positive.[4,5]

OBJECTIVE SIGNS INCREASE THE PROBABILITY OF SLE

The second scenario is dramatically different: there are objective physical findings (granted, these are few), and the laboratory tests demonstrate anemia, leukopenia, lymphopenia, thrombocytosis, hematuria, leukocyturia, and proteinuria. In short, there is enough evidence of an ongoing active inflammatory process to make the pretest probability of lupus quite high—70% to 80%. A positive ANA study reaffirms this possibility, raising the posttest probability to nearly 100%.[4]

At this point, an anti-dsDNA study is not needed for diagnosis, but it certainly will be informative for adequate patient management and is clearly indicated (as may be other tests, such as complement levels, 24-hour urinary protein excretion, a baseline serum creatinine, and even a renal biopsy). This patient's fibromyalgia-like symptoms do not rule out the diagnosis of SLE, since up to one third of patients with SLE may have such symptoms,[6,7] although the basis for this clinical association is poorly understood.

HYPOTHESIS: FIBROMYALGIA-LIKE, ANA-POSITIVE SYNDROME IS COMMON, DISTINCT FROM SLE

Patients like the one in the first scenario often go to specialists for a second opinion; unfortunately, both the patient and the referring physician are often unwilling to accept diagnoses other than SLE. Indeed, in a study published in 1995,[8] we described a subset of patients referred to our center with the diagnosis of SLE whose main symptoms were similar to those of the patient in the first scenario. Although these complaints suggest SLE, if all of them cannot be objectively validated (and not just one of them), this diagnosis is highly unlikely. Rather, these symptoms and tenderness bilaterally above and below the waist suggest the diagnosis of fibromyalgia, a condition much more frequent than SLE not only in the general population but in the practices of generalists and specialists alike.[9]

Without objective signs, the posttest probability of SLE is only 5%

We called this condition "fibromyalgia-like, ANA-positive syndrome" and are convinced that it is very common among middle-aged Caucasian women. Some rheumatologists may disagree, believing that such patients have mild SLE and should be treated with antimalarials to prevent a "flare" of the disease. These physicians may be influenced by a relatively recent Canadian study demonstrating flare-ups of the disease upon discontinuation of antimalarials in patients with inactive SLE.[10,11] However, I agree with

Matteucci,[12] who commented at that time that patients like ours cannot be compared with the ones from the Canadian study,[11] since in fact they do not have SLE and no one has shown that antimalarials prevent the development of full-blown lupus in patients with "preclinical" lupus (if indeed we accept this as a possible diagnosis for patients like the one described in the first scenario).

MANAGEMENT

Regardless of the clinical scenario, the management is challenging. First, one should honestly discuss with the patient the differences between fibromyalgia and SLE and their possible association, the rationale for the use of different drugs, and the possible disease course and outcomes. In the first scenario, judicious use of tricyclic antidepressants is indicated; in the second scenario, a definite treatment plan can be made only after the nature and extent of organ-system involvement is defined, particularly of the kidney. In both scenarios, we would recommend:

- A sustained and structured exercise program.
- Avoidance of narcotic analgesics.
- Acquisition of healthy behaviors (eg, improved diet, more regular sleep patterns).
- Elimination of unhealthy habits (eg, smoking cessation, moderate alcohol consumption).
- Education and counseling.

However, which aspects to emphasize should be an individualized decision. ■

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