Fibromyalgia: Friend or Foe

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Fibromyalgia: syndrome (not disease) characterized by chronic musculoskeletal aches, pains, and stiffness; pain on digital palpation, but articular pathology absent

American College of Rheumatology (ACR) criteria (1990):
- FM — history of chronic widespread pain (CWP) for ≥3 mo in all 4 quadrants of body and in ≥11 of 18 tender point (TP) sites on digital palpation when 4 kg pressure applied; myofascial pain syndrome (MPS) — involves 1 to 3 quadrants; includes regional pain syndromes; if untreated, sometimes progresses to FM; more common in men; much better prognosis than FM; digital TP sites — 10 in upper back and neck; 4 in buttocks; 4 in lateral epicondyles and anserine bursa of knees

Revised ACR criteria (2010): FM diagnosed if CWP present based on widespread pain index (includes number of painful body regions; symptom severity scale includes fatigue, waking unrefreshed, cognitive symptoms, and symptoms that last ≥3 mo); no examination of TPs; 1990 and 2010 criteria both valid

Epidemiology: FM affects 2% to 5% of adult population (CWP diagnosed in 10%-20%) in United States; majority 35 to 60 yr of age; 90% women; FM most common subset of CWP

Triggers of FM and related conditions: include infectious diseases, physical trauma, psychologic stress, peripheral pain syndromes, hormonal abnormalities, drugs, vaccinations, and catastrophic events (eg, war)

Signs and symptoms: widespread pain with TPs (100%); generalized weakness reported but muscle strength normal; unrefreshing sleep; fatigue (in majority but not all patients); morning stiffness; tension headaches; painful periods; irritable colon or urinary syndrome; sleep — 85% of patients with FM have sleep abnormality resulting in α-wave intrusion into δ-wave sleep or upper airway resistance patterns; leads to decreased production of melatonin and growth hormone while sleeping; RLS — seen in 10% to 15% of patients with FM; cytokines — levels normal and cannot be measured in serum; however, studies in vitro show cytokine dysregulation; glial cells in spinal cord show to influence cytokine production (opiates stimulate cytokine production by glial cells, leading to hyperalgesia; therefore, narcotics contraindicated in management of FM); pain processing augmented

Comorbidities: 45% of patients have posttraumatic stress disorder; 45% of young women have some type of severe psychosocial distress; 10% have bipolar disorder

Differential diagnosis: numerous pseudo-FM syndromes; rule out autoimmune disease, cancer, substance abuse, malnutrition, bipolar disorder, early stages of multiple sclerosis or myasthenia gravis, low thyroid or high parathyroid levels, vitamin D deficiency, and infection

Treatment: patient education most important component; adherence to therapy also important; multidisciplinary approach

5. Interpret ANA test results in relation to SLE.

Faculty Disclosure

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Factors that promote development of SLE: include environmental factors and susceptibility genes; defect in clearance of apoptotic cells thought to cause activation of innate and adaptive immune systems, resulting in production of autoantibodies and immune complexes, which ultimately leads to tissue damage

Types of lupus erythematous (LE): cutaneous LE (if chronic, discoid LE); SLE (majority of patients); drug-induced LE; crossover or overlap syndrome and/or mixed connective tissue disease; “incomplete lupus”

Signs and symptoms: arthralgias; arthritis; myalgias; rashes (most commonly in sun-exposed areas); photosensitivity; alopecia; aphthous ulcers; Raynaud phenomenon; unexplained fever; extreme fatigue; pleurisy; edema in legs or around eyes; lymphadenopathy; dry eyes and mouth

Musculoskeletal features: malar rash over cheeks and bridge of nose (nasolabial folds spared); subacute cutaneous LE (polycyclic annular rash with central clearing; occurs in photosensitive areas); discoid LE causes scarring; aphthous ulcers often painless; alopecia extremely common; if unsure whether rash related to SLE, ask dermatologist to do biopsy (should include involved and uninvolved skin); negative test helpful in ruling out SLE

Vascular features: Raynaud phenomenon seen in ≤60% of patients with SLE; nailfold capillaroscopy can be done with dermatoscope or ophthamscopel; abnormal, dilated capillary loops often seen in patients with connective tissue disease

Musculoskeletal features: arthralgias most common presenting symptom; symmetric polyarthritis of small joints seen (definitities not fixed; no underlying erosive disease); inflammatory tendinitis; not all joint pain in SLE related to arthritis (eg, with hib pain, consider other causes such as avascular necrosis or osteoporosis with fracture)

Serious complications: seen in ≤50% of patients with SLE; include nephritis, involvement of CNS, hematologic abnormalities, and vasculitis; patients with SLE have 7- to 10-fold increased risk for coronary heart disease and stroke

ACR criteria for classification: include skin, systemic, and laboratory criteria; 4 of 11 needed for classification; only 1 in 3 patients diagnosed with SLE fulfills criteria

Diagnosis: made by antinuclear antibody (ANA) testing; methods vary but gold standard immunofluorescence assay (IFA) using human epithelial type 2 (Hep-2) or other cell tumor line; ANA testing in many reference laboratories done with enzyme-linked immunosorbent assay (ELISA) or coated beads; therefore, always specify testing be done with IFA; Interpretation of ANA test: 32 million people in United States have elevated ANAs; ≤1 million have SLE; but 98% of patients with SLE have positive ANA test; ANA has appropriate sensitivity but lacks specificity for SLE; positive ANA test does not confirm diagnosis of SLE, but negative test suggests another diagnosis

Recommendations for ANA testing in primary care setting: always test for ANA using IFA; population screening with ANA yields more false-positive than true-positive results; usefulness of ANA test to confirm SLE depends on pretest probabilities; low-titer ANA positivity should be viewed in clinical context

Autoantibodies more specific for SLE: anti-double stranded (ds) DNA present in ≤50% of patients with SLE and highly correlated with kidney disease; anti-Smith (Sm) antibody present in ≤25% of patients with SLE; other autoantibodies found in SLE include anti-Ro/La, antiphospholipid, and antihistone

Development of autoantibodies before clinical onset of SLE: study of >30 million serum specimens from 5 million military service personnel; samples from 130 participants before diagnosis of SLE; ANAs present in ≤80% of these patients before any clinical disease activity; anti-dsDNA and anti-Ro/La present in ≤50%; authors found antibodies present years before diagnosis; 3 stages — no symptoms or antibodies; positive titer but “benign” antibodies; increase of pathogenic antibodies (anti-Sm; anti-dsDNA) and clinical onset of
symptoms; testing healthy patients may identify individuals with benign autoantibodies; unknown how many will progress to clinical illness, what factors predict progression, and what can be done to prevent progression

Role of rheumatology: optimize referrals so timely diagnosis can be made among carefully prescreened patients; ANA should only be drawn if autoimmune process suspected after taking good history and performing physical examination; rheumatologists can interpret autoantibody testing in context of medical history and may order additional confirmatory tests

Differential diagnosis: other autoimmune disorders, infections, malignancies, neurologic disorders, hormonal imbalance (eg, thyroiditis) can mimic SLE.

Full ANA panel vs ANA test as screen: if autoimmune disease suspected, start with ANA testing by IFA as screen; not useful to order full panel as few patients with connective tissue disease have negative ANA test

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Suggested Reading

1. Identify the incorrect statement about fibromyalgia (FM).
   (A) Diagnosis requires history of chronic widespread pain for \( \geq 6 \) mo
   (B) Must occur in all 4 quadrants of body
   (C) Affects 2% to 5% of adult population in United States
   (D) Majority of patients are 35 to 60 yr of age

2. Fatigue is a presenting symptom in 100% of patients with FM.
   (A) True (B) False

3. About 50% of patients with FM also have ______ and vice versa.
   (A) Reflex sympathetic dystrophy (C) Functional bowel disease
   (B) Lyme disease (D) Chronic fatigue syndrome

4. Which of the following is considered the most important component of treatment of FM?
   (A) Physical therapy (C) Psychiatric therapy
   (B) Pharmacotherapy (D) Patient education

5. Which of the following drugs approved by the Food and Drug Administration for treatment of FM may be a better choice for a patient with depressed mood?
   (A) Duloxetine (B) Milnacipran (C) Pregabalin

6. No evidence supports the use of ______ in the treatment of FM.
   (A) Dopaminergic agents (C) Serotonin-norepinephrine reuptake inhibitors
   (B) Opiates (D) Tricyclic antidepressants

7. Which of the following is the most common musculoskeletal symptom of SLE?
   (A) Arthritis (C) Arthralgia
   (B) Myalgia (D) Inflammatory tendonitis

8. Patients with SLE have 7- to 10-fold increased risk for:
   (A) Coronary heart disease and stroke (C) Painful aphthous ulcers
   (B) Raynaud phenomenon (D) Nephritis

9. Only ______ patients diagnosed with SLE fulfill the American College of Rheumatology criteria for the disease.
   (A) 2 out of 3 (B) 1 out of 2 (C) 1 out of 3 (D) 1 out of 4

10. Antinuclear antibody testing is indicated when SLE is suspected. Always request that the reference laboratory test with:
    (A) Coated beads (B) Immunofluorescence assay
    (C) Enzyme-linked immunosorbent assay (ELISA)

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