Connective Tissue Disorders: 
My Aching Joints

Eddie Needham, MD, FAAFP

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Eddie Needham, MD, FAAFP

Program Director/Academic Chairman, AdventHealth Winter Park Family Medicine Residency, Florida; Clinical Professor, University of Central Florida College of Medicine, Orlando; Clinical Associate Professor, Florida State University College of Medicine, Tallahassee

Dr. Needham has been a program director for 16 years. In 2017, he received the Gold Level Program Director Recognition Award from the Association of Family Medicine Residency Directors (AFMRD) for his years of leadership and experience. He has been a requested speaker at the AAFP’s annual Family Medicine Experience (FMX) for 10 years, as well as speaking for both the Georgia Academy of Family Physicians and the Florida Academy of Family Physicians for more than 15 years. Dr. Needham practices full-service family medicine, providing care from “conception to resurrection.” In October 2018, he received the AAFP’s Chair of the Year Award for his leadership of the Care of Cardiovascular Conditions Live Course. He was recognized as the Florida AFP’s 2013 Full-Time Florida Family Physician Educator, as well as the Georgia AFP’s 2007 Teacher of the Year. It is his joy and passion to teach students of medicine the wonders of the human body and spirit.
Eddie Needham, MD, FAAFP

Biography

- Practices “conception to resurrection” family medicine
- Taught family medicine for two decades
- Joy and passion to teach the wonders of the human body and spirit.
- Married for 31 years with five grown children
- Adventure:
  - Rigors of triathlons, soccer, and volleyball
  - Wonder and surprise of fishing
  - Mountain top experiences with friends

Learning Objectives

1. Identify the major symptoms and risk factors for the connective tissue disorders dermatomyositis, scleroderma and systemic lupus erythematosus, including age, race, family history and gender.

2. Differentiate between dermatomyositis, scleroderma, and systemic lupus erythematosus and other conditions that present with similar symptoms; provide an appropriate diagnosis and/or suggest additional testing when necessary.

3. Establish protocols for patients diagnosed with dermatomyositis and polymyositis to evaluate for malignancy at diagnosis, followed by long-term surveillance.

4. Counsel patients on treatment regimens to manage symptoms including combinations of immunosuppressant and/or anti-inflammatory medications, diet, lifestyle, and follow-up appointments.

5. Establish protocols to recognize and manage possible complications associated with connective tissue disorder treatment.
Audience Engagement System

**Step 1**

**Step 2**

**Step 3**

CME001 (PBL) Acute and Chronic Heart Failure
Location: Room 113A
Date: Thursday, Sep 28, 10:10 AM
Duration: 1 hour
Credit Hours: 1

Faculty:
Ford D. N., PhD (114)
Michael Mullen, MD (114)

1. Practice applying new knowledge and skills gained from Acute and Chronic Heart Failure research through collaborative working with peers and expert faculty.
2. Identify strategies that foster optimal management of acute and chronic heart failure within the context of...

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General Comments re: CTD (Connective Tissue Diseases)

• Pattern recognition is invaluable in assessing for potential CTDs
• Women are affected much more frequently than men for almost all CTDs
• Most CTD patients should be managed with the help of a rheumatologist when prescribing immunomodulators or biologic agents
Patient Case

• 37 yo female presents with progressive shortness of breath.
• Has given birth to 7 healthy children previously without difficulty.
• Other complaints include:
  • Knee and elbow pain
  • Patchy hair loss
Patient Case

- Labs of note:
  - ANA (+) at 1:320
  - Platelet count of 96
  - WBC 3.5
  - Lymphocyte count of 1200
- Exam notable for bilateral pleural effusions

Poll Question #1

37 yo female with dyspnea, arthralgias, (+) ANA, mild pancytopenia, and pleural effusion. What is the most likely diagnosis?

A. Rheumatoid arthritis
B. Systemic lupus erythematosus
C. Wegener’s granulomatosis
D. Sarcoidosis
Lupus Erythematosus Prep

Systemic Lupus Erythematosus (SLE)

- SLE is a systemic inflammatory autoimmune disease with protean manifestations.
- Female: male incidence of 9:1
- Typically affects women of child bearing years
- US prevalence of 0.1% (1 per 1000)
- More prevalent and severe among blacks and Hispanics
SLE

• Estimated survival rates of 96% at 5 years, 93% at 10 years, and 78% at 15-20 years.
  • Previously, 50% at 5 years in the 1950’s

• Major causes of mortality is premature coronary artery disease with a 50 fold increase over general population.

• Increased risk of osteoporosis
  • From disease and drugs (steroids)
  • 3 months of prednisone 5mg/day or more → DEXA

SLE

• The diagnosis is clinical
• (+) ANA – not always helpful
• Must have 4 of 11 diagnostic criteria
• Lab tests cannot substitute for pattern recognition in the history and physical by the physician!
SLE Diagnostic Criteria

• Mucocutaneous signs – 4 of them
• Brain – neurologic involvement
• Lab – (+) ANA
• Lab – other immune criteria
• Arthritis – nonerosive (vs Rheumatoid Arthritis)
• Serositis
• Hematologic disturbances
• Renal disease

Mucocutaneous Signs

• Malar rash
  • Spares the nasolabial folds
• Discoid rash
  • Erythematous, raised, scaling plaque, central scar
  • Follicular plugging
• Photosensitivity
• Aphthous ulcers
  • Usually painless
Neurologic involvement

- Seizures
- Psychosis
- Of note, 80% of patients will have some form of cognitive impairment by 10 years after diagnosis.


Lab

- (+) ANA
  - 90% of patients with SLE have a (+) ANA
- Negative at < 1:40 serum dilutions
- Indeterminate at 1:40 – 1:160
- Clearly positive at > 1:320
Lab

- False (+) RPR
- Prolonged PTT (Lupus anticoagulant)
- (+) Anti-Smith antibodies
- (+) Anti-double stranded DNA antibodies
- (+) Anticardiolipin antibodies
- (+) Lupus erythematosus cell prep

Arthritis and Serositis

- Nonerosive polyarthritis
  - 2 or more joints
  - Tenderness
  - Swelling
  - Effusion
    - Consider arthrocentesis
- Serositis affecting the pleura or pericardium
  - Rub or effusion, EKG with pericarditis, pleurisy
Hematologic Involvement

- Leukopenia < 4000 WBCs
- Lymphopenia < 1500
- Thrombocytopenia < 100
- Hemolytic anemia
  - Schistocytes, look at the blood smear
  - Elevated total and indirect bilirubin
  - Decreased haptoglobin

Renal involvement

- Proteinuria > 0.5 grams/day
- > 3+ protein on dipstick
- Cellular casts indicative of renal disease
  - RBC casts suggest glomerulonephritis
  - Tubular casts suggest inflammation of the tubules
Clinical Manifestations of SLE

American College of Rheumatology
Slide Set
Poll Question #2

Which of the following is not a cause of an elevated ESR?

A. Acute gout flare
B. SLE/Lupus
C. Polymyalgia rheumatica
D. Fibromyalgia
Etiologies of elevated ESR > 100mm/hour

- Acute gout
- Polymyalgia rheumatica/temporal arteritis
- Rheumatoid arthritis
- SLE
- Infections:
  - Osteomyelitis, Subacute bacterial endocarditis, deep tissue abscess
- Cancer:
  - Carcinoma, leukemia, lymphoma, multiple myeloma


Diagnostic Tests for CTDs

- Antinuclear antibodies (ANA)
  - SLE, scleroderma, Sjogren’s, poly-/dermatomyositis, mixed CTD
- Anti-SSA (Ro), Anti-SSB (La): SLE and Sjogren’s syndrome
- Anti-Jo-1: Polymyositis
- ANCA (antineutrophilic cytoplasmic antibodies)
  - Wegener’s (c-ANCA) and vasculitides (p-ANCA)
  - Confirm Wegener’s with antiproteinase 3 Ab
  - Confirm vasculitis with antmyeloperoxidase Ab
- Anti-ribonucleoprotein (Anti-RNP): Mixed CTD
- Antitopoisoenmerase Ab (anti-Scl-70): diffuse scleroderma
- Anti-centromere antibodies
  - Limited scleroderma, CREST syndrome
Tests specific for SLE

- Anti-double-stranded DNA antibodies
  - Present in 60% of SLE patients
- Anti-Smith antibodies
  - Present in 40% SLE patients
- C3 and C4 complement levels
  - Decrease with activity of SLE, esp. lupus nephritis
Tests specific for Rheumatoid Arthritis

- Rheumatoid factor
  - IgM antibody
  - Can be elevated in other conditions than RA
- Anticyclic citrullinated peptide antibodies

SLE Treatment

- NSAIDs
  - Can be used early in SLE treatment
  - Effective for arthralgias and serositis
  - Avoid with lupus nephritis and renal insufficiency
  - Avoid Cox-2 inhibitors in patients with an increased risk of CVD
Poll Question #3

Which of the following non-selective NSAIDs is least likely to cause GI irritation/bleeding?

A. Ibuprofen
B. Indomethacin
C. Meloxicam
D. Naproxen

NSAIDs and risk of GI bleed

2010 meta-analysis of relative risk of bleeding or perforation with NSAID use. Overall risk was increased fourfold

Celecoxib RR = 1.4  Indomethacin RR = 5.1
Ibuprofen RR = 2.2  Ketoprofen RR = 5.1
Diclofenac RR = 3.6  Piroxicam RR = 8.0
Meloxicam RR = 4.2  Ketorolac RR = 14.5
Naproxen RR = 4.6

SLE treatment

• Steroids
  • High dose steroids can be used to manage severe disease episodes
  • May serve as bridge therapy until slow-acting drugs become effective
  • Low dose (5mg daily) can be used in the treatment of mild SLE
  • Topical steroids for localized skin manifestations
  • Intra-articular steroids for joint disease
    • Rule out septic arthritis first

SLE treatment

• Hydroxychloroquine
  • All SLE pts should be on hydroxychloroquine unless not tolerated
  • Requires 6-12 weeks to show benefit.
  • Can be combined with NSAIDs for mild disease
    • Cutaneous manifestations and arthralgias

SLE treatment - Other immunomodulatory drugs

- Methotrexate – some benefit
- Mycophenolate mofetil (Cellcept)
- Cyclophosphamide
  - Historically used for lupus nephritis
- Biologics – belimumab and rituxamb (off label)


Scleroderma
(Systemic Sclerosis)
Scleroderma

- A chronic condition characterized by fibrosis of the skin and internal organs
- Raynaud’s phenomenon is present in most patients at some stage of the disease
- Prevalence between 20-250 patients per $10^6$
- Women have a 5 fold increased risk
- Survival of 78% at 5 years, 55% at 10 years, 37% at 15 years, and 27% at 20 years
- 60% of patients die from pulmonary disease
Scleroderma

• Major criterion is symmetric sclerosis
  • Skin thickening
• Minor criteria
  • Sclerodactyly – thickening/tightening of the fingers
  • Digital pitting or loss of finger tip pad substance
  • Bilateral basilar pulmonary fibrosis

Scleroderma

• 2 forms of the disease
• Limited
  • Morphea – localized thick, hardened skin patches
  • Linear scleroderma – bands of hard skin
  • CREST syndrome
  • Systemic sclerosis sine scleroderma
• Diffuse
CREST syndrome

- Calcinosis
- Raynaud’s phenomenon
- Esophageal dysmotility
- Sclerodactyly
- Telangiectasia

Lab testing

- Most patients have a (+) ANA
- Nucleolar pattern is present in 30%
- Anti-topoisomerase-1 Ab (Scl-70) are associated with diffuse scleroderma
  - Present in 40% of patients
- Anti-centromere Ab are present in 75% of patients with limited scleroderma and CREST
Routine monitoring every 6 months

• Complete blood count
• Creatinine level
• ESR
• Urinalysis
• ECG
• Echocardiogram
• PFTs: +/- DLCO to check for fibrosis

Clinical manifestations of Scleroderma
Raynaud’s Phenomenon

- “WBC”
- White
- Blue
- Carmine (Red)
- This is the order of color change with Raynaud’s Phenomenon
Scleroderma Treatment

• Arthralgias can be treated with:
  • NSAIDs, hydroxychloroquine, MTX, azathioprine, or mycophenolate
• Inflammatory episodes: steroids
• Any patient with scleroderma and HTN should be on an ACEI to preserve renal function
• Esophageal disease/reflux: PPI
• Pulmonary Disease: Cyclophosphamide

Scleroderma Treatment

• Raynaud’s phenomenon:
  • Calcium channel blockers: extended-release
    • Nifedipine or amlodipine
  • IV iloprost (prostacyclin analogue – vasodilator)
  • Sildenafil (phosphodiesterase inhibitor leading to vasodilation)
Patient Case

• 47 yo male with three year history of progressive weakness.
• He has trouble brushing his hair or reaching over his head.
• MRI brain and spine normal 3 years ago
• 6’ 5” male sitting in NAD
• Can’t get out of a chair without leaning far forward; cannot raise arms past 90 degrees

Poll Question #4

47 yo male with shoulder girdle weakness and normal brain MRI. Most likely diagnosis?

A. Poliomyelitis
B. Polymyositis
C. Statin myopathy
D. Cushing’s syndrome with steroid myopathy
Polymyositis

Patient Case

• Patient with similar complaints with:
  • Erythematous plaques on the dorsal MCPs and PIPs of both hands
  • Erythematous patches and plaques on the upper eyelid
Dermatomyositis

Gottron’s papules
and
Heliotrope rash

Findings in both DM and PM

• Elevations in muscle enzymes
  • CPK, muscle aldolase, LDH, AST, ALT
• Symmetric proximal muscle weakness
• Characteristic EMG findings
• (+) anti-Jo-1 antibodies
• Muscle biopsy demonstrating active inflammation
• Additionally in DM
  • Heliotrope rash and Gottron’s papules
DDx for proximal muscle weakness

- DM/PM
- Polymyalgia rheumatica
- Temporal arteritis
- Endocrinopathy
  - Thyroid
  - Cushing’s disease
  - Parathyroid
- Infections
  - Toxoplasma, trichinosis
  - Viral
- Glucocorticoid myopathy
- Statin myopathy
- Neurologic disorders
  - Myasthenia Gravis
  - Eaton-Lambert
  - Amyotrophic lateral sclerosis
- Muscular dystrophies
- Myopathies
- Electrolyte disturbances
Dermatomyositis

• Both DM and PM increase the risk of cancer, DM>PM
  • 3 fold increase in RR in DM; 2 fold increase with PM
  • 70% of cancers are peritoneal adenocarcinomas
• Recommend age appropriate cancer screening for patients (C-scope pts > 50 yo, etc...)
• In higher risk patients, consider CT Chest, Abdomen, Pelvis

DM/PM treatment

• Initial high dose steroids to placate the inflammatory myopathy: 60-80mg daily
  • Wean down over ~ 1 year
• Steroid sparing agents:
  • Azathioprine
  • Methotrexate
  • Hydroxychloroquine

Practice Recommendations

1. The astute history and physical exam is vital when a CTD is suspected. (Pattern recognition). (SORT C)
2. Order studies only as indicated, avoiding the “immune panels” that can give false (+) tests. (SORT C)
3. Work closely with a rheumatologist, when available, in diagnosing and treating our patients. (SORT C)
4. Consider hydroxychloroquine in all patients with SLE. (SORT A)
Thank you for your attention

Contact information:
Eddie.Needham.MD@AdventHealth.com

Questions