PATTERNS OF ARTHRITIS: LAB AND OTHER TESTING

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Objectives

• Present several patterns of arthritis
• Where lab and imaging fit into various patient presentations
• Benefits and pitfalls related to lab testing
Patterns of arthritis

- Non-inflammatory (OA, trauma, mechanical problem)
- Inflammatory
  - Monoarthritis
  - Oligoarthritis
  - Polyarthritis
How do we determine the presence of inflammation?

- Cardinal findings of inflammation
  - Warmth
  - Erythema
- Joint swelling
  - Palpation
  - Appearance
- Imaging
- Inflammatory markers
  - ESR
  - CRP
How do we determine the presence of inflammation?

**Physical:** cardinal signs of inflammation (erythema, warmth) – limited utility because mostly associated with crystals and infection

**Inflammatory markers:** ESR, CRP
If very high (in elderly), may suspect polymyalgia rheumatica or giant cell arteritis
But, may be normal in some cases with low grade inflammation.
And, in some cases, it is not possible to figure out why these tests are abnormal.

Inflammation: “You can observe a lot just by watching” – Yogi Berra

- Joint swelling (fluid or synovial thickening)
  - Compare one side to the other
  - Joint fluid (knee is most accessible) – WBC > 2000
- Synovitis – soft tissue thickening around joints (small joints of hands/wrist/toes because of infiltrated synovium) which is tender to firm palpation, sometimes subtle

- Bony hard enlargement suggests osteoarthritis (but there may also be superimposed synovitis)
Inflammation: Imaging

- Radiography
  - May show soft tissue thickening (not specific)
  - May show fluid in knee, elbow, ankle
  - May show erosions (= inflammatory process)
  - May show evidence of crystal deposition
- MRI – not typically done for detection of synovitis but demonstrates synovial thickening
  - SI joints (in x-ray neg spondyloarthritis) may show bone marrow edema which may help establish dx of spondyloarthritis
- Power Doppler Ultrasound – potential hope for the future for visualizing synovitis, but requires technical expertise

Evaluation of inflammatory polyarthritis involves…

- Pt demographics: younger vs older, habits
- Pattern
  - Acuity, other related sxs
  - Symmetrical
  - Asymmetrical (especially if oligoarthritis)
- The rest of the physical
  - If the patient reports pain only in certain places, are those the only joints you should check?
  - Careful examination for any skin/nail findings
- Use of serological tests
- Possibly, joint fluid
Hand pain

- 42 y/o Caucasian woman with a history of hand pain and swelling for 2 months
- PMH: HTN
- SHx: smokes 1 PPD
- Fhx: negative for arthritis
- ROS: difficulty with hand function
- PE: joint swelling and tenderness in wrists, MCPs 2-3, PIPs 2-4
Screening tests for suspected inflammatory polyarthritis

- Rheumatoid factor
- CCP
- ANA
- ESR
- CRP

INITIAL SCREENING SEROLOGIES

- RF + ANA -
- RF + ANA +
- RF - ANA +
- RF - ANA -
INITIAL SCREENING SEROLOGIES

- **RF + ANA -**: RA
- **RF - ANA +**: ?
- **RF + ANA +**: RA, Rhupus?
- **RF - ANA -**: Seroneg RA

Anti-cyclic citrullinated peptide, “CCP”

- May be seen in early RA (which may be RF-)
- Positive in some cases of RF negative RA
- Same sensitivity as RF but more specific
  - (25% false + RF w/Hep C)
- Better correlation with overall disease severity
### INITIAL SCREENING SEROLOGIES

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<th>RF</th>
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<td>RF - CCP - ANA - Seroneg RA</td>
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### Next steps

- Lab: RF neg, CCP 3 (<1), ANA 1.4 (nl < 1), ESR 45, CRP 3
- X-ray – sl degenerative change at the base of the thumb; soft tissue swelling in MCPs/PIPs
- Dx: RA
- Start methotrexate 10-15 mg/wk (after baseline labs, Hep B, C testing), and CXR
Criteria for RA

- Old set of criteria did not include CCP and would be more likely to miss early RA
- Newer criteria (2010) more complicated
  - Includes CCP
  - Scoring system
  - Potentially allows the diagnosis of RA with only 1 involved joint
  - May diagnose some pts with RA which is not sustained

Why RA?

- Most common chronic inflammatory arthropathy (1%)
- Fairly symmetric
- At least 4 joints for 6 weeks
- Wrists, MCPs, PIPs
- CCP and/or RF
- X-rays?
• 35 y/o Caucasian woman presents with 4 wk history of hand pain and swelling.
• PMH: unremarkable
• SH: married, 2 young children, no illicits
• ROS: no fever or rash; ROS negative
• PE: sl swelling and tenderness in wrists, MCPs 2-3, PIPs 2-4
• Next steps?
Next steps

• Lab:
  • RF neg
  • CCP neg
  • ANA neg
  • ESR 40
  • CRP 2
• X-rays: no erosions, sl soft tissue swelling
Diagnostic possibilities

- Seronegative RA?
  - Criteria for RA require arthritis for 6 weeks
- Viral
  - Parvovirus B19
  - Hep B, C, HIV
  - Others (Chikungunya virus may appear in this country)
- Psoriatic
  - RA-type

Case management

- Check parvovirus serologies
- If arthritis is persistent, consider a DMARD trial (e.g. hydroxychloroquine 200 mg bid for 2 months)
Hand pain

• 28 y/o Caucasian woman c/o 2 months of hand pain and swelling
• PMH: unremarkable
• Shx, Fhx, ROS: non-contributory
• PE: exam confirms swelling
Labs

- RF –
- CCP –
- ANA 1:320
- ESR 38
- CRP 2.4
- CBC: WBC 3.6
- Other labs normal

Additional labs

- Anti-dsDNA antibodies – 45% (<10)
- Anti- Smith – neg
- Anti-SSA, SSB – neg
- Anti-RNP – neg
- Complements – normal

DX:?
Dx: Lupus with arthritis

- This form of lupus may remain predominantly joint-centric and in some pts may be difficult to treat.
  - May cause joint deformities
- But, may evolve to include other systems – heart, lung, renal, CNS, skin, etc.

When to order an ANA

- When you suspect a “connective tissue disorder” (polyarthritis, Raynaud, finger thickening/skin tightness, sicca syndrome, myositis)
- Derm: discoid rash, photosensitive rash, malar
- Card-pulm: pericarditis, unexplained pleural effusion (pleuritis), infiltrates
- Renal: glomerulonephritis, proteinuria
- Neuro: polyneuropathy, unexplained CNS changes, transverse myelitis
When to order an ANA

- Unexplained fevers
- Hematologic changes
  - Leukopenia
  - Thrombocytopenia
  - Hemolytic anemia
- Unexplained thrombosis
  - Anti-cardiolipin antibodies
  - Lupus anticoagulant

POSITIVE ANAs IN RHEUMATIC DISEASES

- SLE > 99%
- DRUG INDUCED LUPUS > 99%
- SCLERODERMA 75-90%
- SJOGREN SYNDROME 75-90%
- RA 30-50%
- POLYMYOSITIS 30-50%
**ANA: SEROLOGICAL CLARIFICATION**

( DNA, Smith, RNP should not be ordered if ANA is negative)

- **Anti-DNA** – SLE
- **Anti-Smith** – SLE
- **Anti-RNP (ribonucleoprotein)** – MCTD if RNP is sole abnormality and other compatible findings
- **Anti-SSA (Ro)** – Sjogren’s syndrome, SLE, other
- **Anti-SSB (La)** – Sjogren’s syndrome, SLE

**Other:**
- Raynaud’s alone – anti-centromere (limited scleroderma)
- Raynaud’s + skin tightening – anti-Scl-70, Anti-RNA polymerase III
- Myositis – anti-Jo-1 (anti-synthetase syndrome)

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**When not to order an ANA**

- Chronic widespread pain (fibromyalgia)
  - It is not necessary to make sure the ANA is negative to diagnose fibromyalgia
- Chronic fatigue
- Osteoarthritis
- Illnesses unlikely to be related to autoimmune process
- Confusing situations
FALSE POSITIVE ANAs

DRUGS

procainamide, hydralazine, quinidine, penicillamine, anti-TNF agents, phenytoin, others

DISEASES

chronic liver disease, immune lung diseases, etc.

NORMALS

5-15% positive depending on age and test method
20-30% positive in relatives of persons with SLE

Hand pain

- 75 y/o Caucasian woman c/o pain her hands and wrists for years, gradually getting worse.
- Rx OTC NSAIDs with limited benefit
- PMH: HTN, Back pain
- Meds: lisinopril
- Fhx: + for OA
- PE: PIPs and DIPs have bony hard enlargement to a moderate degree
- Several PIP joints are “angulated”
- Several PIPs and DIPs are tender to palpation
Labs

- RF –
- CCP –
- ANA –
- ESR, CRP nl
- X-rays: OA (osteophytes and sclerosis) of most PIP and DIP joints with irregularity of joint margins and cystic changes
“Gull wing” deformity
“Inflammatory” osteoarthritis

- It is estimated that about 5% of persons with hand OA have a more severe form of arthritis with more joint damage and pain than in usual hand OA
- Lab results unremarkable
- Some response to Plaquinil 200 mg bid (6 mg/kg/d)
- For many, frustrating because not responsive to treatment

Hand pain

- 73 y/o Caucasian woman has had mild hand pain for years but is now having more pain in her wrists (variably) and MCP joints
- PMH: HTN, DM
- Meds: Amlodipine, metformin
- s/p bilat TKRs
- PE: wrists – tender and sl puffy; MCPs several TTP and sl puffy; DIPs have OA changes
Labs

RF –
CCP –
ANA –
ESR, CRP –
CPPD arthropathy

- Low grade CPPD associated inflammatory arthropathy
- AKA “Pseudo-RA” pattern of CPPD arthropathy
- Treatment: Colchicine 0.6 mg qd or bid
Another hand pain

- 72 yo Caucasian male with pain in several fingers on and off for several months
- PMH: GPA (in long term remission), HTN, CKD, OA, Gout
- Meds: Lisinopril, allopurinol, occ oxycodone for severe pain
- PE:
Lab:

- RF-
- CCP-
- ANA-
- ESR 30
- CRP 1.2
- Creat 2
- Uric acid 7.1

Analysis

- Not the pattern expected in RA, SLE, viral arthritis
- OA is present – possible inflammatory OA
- Gout – is uric acid at target?
- Can gout appear in this chronic (non-attack) form?
- Could it be CPPD crystal arthritis?
- Other:
  - spondyloarthropathy
More hand pain

- 42 y/o Caucasian woman c/o pain and swelling in several fingers for about 4 months.
- PMH: Borderline HTN
- SH: no drug use
- ROS: AM stiffness in hands

- PE: R 2\textsuperscript{nd} DIP enlarged and TTP
L DIP 4 has similar changes
**PATTERNS OF PSORIATIC ARTHRITIS**

*10-15% of persons with psoriasis get arthritis*
- Polyarthritis - oligoarthritis, polyarthritis (RA-like)
- DIP joint involvement with nail changes
- Dactylitis (“sausage” digit)
- Arthritis mutilans (severe joint destruction)
- Spondylitis
Definitions, Extra-axial Lesions, and the Role of HLA-B27: Summary

- **Definition**
  - SpAs are inflammatory diseases that include AS, ReA, psoriatic arthritis, enteropathic arthritis, and uSpA

- **Extra-axial manifestations**
  - Common; may involve many different systems

- **Role of HLA-B27**
  - Although most people with SpA are HLA-B27+, most people who are HLA-B27+ do not have SpA

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**Enthesitis**

![Image of enthesis](image)
### DISEASE ASSOCIATED WITH HLA-B27

- **ANKYLOSING SPONDYLITIS**
- **REACTIVE ARTHRITIS**: GI infection; GU infection
  (formerly known as Reiter’s Syndrome)
- **PSORIATIC SPONDYLITIS**
- **SPONDYLITIS WITH IBD**
- **iritis**
- **UNDIFFERENTIATED SPONDYLOARTHITIS**
Polyarthritis – other etiologies

- Hemochromatosis – MCP OA-like changes
- Vasculitis – other features usually predominant
- Sarcoidosis – may be more a periarthritis, LE
- Severe allergic reactions (periarthritis)