LUPUS AND MIMICS
IMPOSTERS BEWARE

Rheumatology Symposium
8th Medicine Review Course
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Dr Aisha Lateef
Division of Rheumatology
University Medicine Cluster
National University Hospital
How do you diagnose SLE?

- Positive ANA
- Positive Anti dsDNA
- Should fulfil classification criteria
- All of the above
- None of the above
SLE: A Great Mimicker

- 1001 ways to have Lupus!
  - 4/14 (1971 Criteria)
  - \( \frac{r}{n} = \frac{n!}{r!(n-r)!} \)
- 330 ways to have Lupus!
  - 4/11 (1982 Revision)
Majority of the presentations are non-specific

Remains one of the top 10 conditions where diagnosis is often delayed or missed

Be cautious: there is a real risk of over diagnosis
Some patients and presentations
Painful Scenario

- 28 year old female
- 1\(^{st}\) admission: January 2012, General Surgery

- No past medical history apart from a LSCS 2 years prior

- Now presented with:
  - Abdominal pain x 2/7
  - Nausea and vomiting x 2/7
  - Diarrhea x 2/7
Progress

- Repeated presentations for abdominal symptoms
- Treated as infectious enteritis, hyperemesis gravidarum, adhesion colic, UTI
- Developed patchy alopecia in 2\textsuperscript{nd} trimester, told “pregnancy related”
- LSCS for breech
- Post op day: intractable vomiting, abdominal distention, diarrhea
Distended small bowels with suggestion of transition at the lower abdomen associated with moderate amount of free fluid with peritoneal enhancement with suggestion of perforation peritonitis
Medical Referral

- **Further history:**
  - Recurrent admissions for abdominal pain in last year
  - No Raynaud’s, sicca, joint pains, ulcers, rash, photosensitivity
  - Rapid hair loss during pregnancy
  - No family history
  - Uncomplicated pregnancies

- **Investigations:**
  - WBC 13.2 x10⁹/L (3.4-9.6)
    - Lymphopenia
  - Albumin 20 g/L
  - UPCR 0.6G/day
  - ANA 1:640
Impression: SLE

- Lupus gut
- Borderline proteinuria (no urinary sediments)
- Alopecia
- Serology: highly positive ANA, anti dsDNA +
- Low complements
Learning Points

- Not all SLE patients present with usual symptoms of sicca / joint pain / rash / Raynaud’s

- Classification criteria for SLE have limited sensitivity

- “Incomplete SLE”
  - 57% patients with will develop SLE in a median of 5.3 years.
  - These are prone to major organ damage.
  - Early identification and treatment improve prognosis.

Doria A, Briani C. Lupus. 2008 Mar;17(3):166-70
A man with painful joints

- 32 year old male

- Presents with:
  - Joint pain for 2 months
    - Inflammatory
    - Small and large joints
  - Further History?
    - Loss of weight: 5 kg in 6 months
    - Dry mouth for few months
    - Rashes
Examination

- Physical examination
  - Afebrile, normal hemodynamics
  - Mild tenderness at MCPJs, PIPJs, wrists, knees and ankles
  - Reduced tear and saliva film
  - Diffuse erythematous rashes
Investigations

- Initial results:
  - WBC: $3.2 \times 10^9/L$ (3.4-9.6)
  - Hb: $10.5 \text{ g/dL}$ (10.9-15.2)
  - ESR: 88 mm/hr (3-9)
  - Albumin: 32g/L (38-48)
  - Creatinine: 72 mmol/L (50-90)

- What else would you like to know?
  - ANA: positive, 1: 320, speckled and homogenous
  - Rheumatoid Factor: positive, 82 IU/ml (<25)
Sufficient information for diagnosis?

- **Scenario:**
  - Young man with
    - Inflammatory polyarthritis
    - Rashes
    - Sicca symptoms
    - Weight loss
  - Labs showed
    - Bicytopenia
    - Raised inflammatory markers
    - Positive serologies
What is the diagnosis?

- SLE
- Rheumatoid Arthritis
- Sjogren syndrome
- Overlap syndrome
- None of the above
Back to Basics

- Further history:
  - Unemployed, lives alone
  - Denies current IVDU but has used it in past
  - Denies any significant family hx

- Re-examination:
  - Rashes
Further Investigations

- Anti-CCP: negative
- Anti dsDNA: negative
- Anti-Ro/La: negative
- Complements: normal
- AST/ALT: raised
Finally-------

- More investigations:
  - Anti HCV: positive
  - Viral load: high
  - Cryoglobulins: positive

- Final Diagnosis:

  *Hepatitis C with immune mediated extra-hepatic manifestations*
Extra hepatic Manifestations of Hepatitis C infection

- Wide range
- Complex incompletely understood pathogenesis
  - HCV lymphotropism
  - Chronic B cell activation
  - Antibody production
  - Progression to LPD
### Variable strength of associations

#### HCV-related rheumatic diseases in the setting of HCV syndrome

<table>
<thead>
<tr>
<th>HCV Syndrome</th>
<th>Strength of association between HCV and diseases</th>
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<tbody>
<tr>
<td><strong>Rheumatic diseases</strong></td>
<td>high</td>
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<tr>
<td>Mixed cryoglobulinemia</td>
<td><strong>Sicca syndrome</strong></td>
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<td>Others</td>
<td>Hepatitis HCC</td>
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</table>

Other Infectious Diseases

- **Viral:**
  - HIV
  - Hepatitis B
  - Parvovirus B19
  - Infectious mononucleosis (Epstein-Barr Virus)

- **Bacterial:**
  - Lyme’s disease
  - Tuberculosis
  - Syphilis (secondary)
  - Infective Endocarditis
Take Home message

- Chronic Infections can mimic AI diseases
- Serologies can be misleading
- Look at the clinical picture
- Employ tests when indicated, but remember to treat the patient, not the test
- Consider infection associated rheumatic/autoimmune syndromes when the presentation is not typical
Rashes and Lumps

- 35 year old female from India
- Presents with 2 month history of:
  - Intermittent fever
  - Weight loss
  - Rashes
  - Hand pain
  - Lumps in the neck
Investigations

- Seen by her GP and labs done
  - WBC: 3.2 x10⁹/L (3.4-9.6)
  - Hb: 9.5 g/dL (10.9-15.2)
  - ESR: 110 mm/hr (3-9)
  - Albumin: 28g/L (38-48)
  - ANA: positive
  - Anti dsDNA: 28 (<25)
  - Complements: low

- Prescribed steroids but has not started yet
What will you suggest?

- Start Steroids
- Add immunosuppressnats
- Biopsy the rash
- Biopsy the lymph node
Etiology?

- Induced Sputum: negative for TB

Next Step
- Lymph node biopsy

Diagnosis?
- Small Lymphocytic Lymphoma
Lymphadenopathy is common in SLE
Reported in 25-67% of patients
However, watch out if:
- Generalized lymphadenopathy
- Concomitant hepato-splenomegaly
- B symptoms

Autoantibodies:
- Be aware of low specificity
Refractory Rashes

- 44 year old female
- 2 years history of recurrent rashes
  - Erythematous, scaly, extensor surfaces
Progression

- Treated as psoriasis
  - Topical steroid creams
  - Phototherapy
  - Methotrexate
  - TNF inhibitors

- 3 months later:
  - Presented with
    - Inflammatory joint pain
    - New onset feet swelling
    - Pleuritic chest pain
Is it Psoriatic arthritis?

- **Examination**
  - Pitting pedal edema bilaterally
  - Inflamed MCP and MTPJs

- **Investigations**
  - RF, CCP negative
  - ESR 84 mm/hr (5-15)
  - Urine dipstick: protein 2+
  - Normal serum creatinine and liver enzymes
What else would you like to consider?

- Pneumonia with psoriatic arthritis
- MTX Pneumonitis
- Amyloidosis
- Drug induced Lupus
Clinical Picture

- Middle aged woman
- Long standing rashes
- New onset synovitis, proteinuria, ILD
- After use of TNF inhibitors
- Further Investigations: ANA positive

- Diagnosis: Drug Induced SLE
Drug Induced Lupus (DIL)

- First case report in 1945
- More than 90 drugs and recombinant therapeutic agents have been associated with DIL
- It is estimated that 10–15% of patients diagnosed with SLE are drug induced
- Factors influencing the development of DIL:
  - Gender, age, and genetic predisposition
  - Structure of the inciting drug
  - Rate of metabolism as determined by acetylator status
<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Definite</th>
<th>Possible</th>
<th>Suggested</th>
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<tbody>
<tr>
<td>High risk</td>
<td>Hydralazine</td>
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<td>Procainamide</td>
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<td>Moderate risk</td>
<td>Quinidine</td>
<td>Sulfadiazine</td>
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<td>Isoniazid</td>
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<td>Low risk</td>
<td>Methyldopa</td>
<td>Carbamazepine</td>
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<td>Chlorpromazine</td>
<td>Propylthiouracil</td>
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<td>Penicillamine</td>
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<td>Very low risk</td>
<td>Minocycline</td>
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<td>Ethosuximide</td>
<td>Gold salts</td>
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<td>Phenytoin</td>
<td>Penicillin, Streptomycin, Tetracycline,</td>
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<td>Primidone</td>
<td>Ciprofloxacin, Rifampicin, Nitrofurantoin Cefuroxime,</td>
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<td>Trimethadione</td>
<td>Cefepime</td>
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<td>Valproate</td>
<td>Phenylbutazone</td>
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<td>Dipheylhydantoin</td>
<td>Estrogens, Oral contraceptives, Danazol.</td>
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<td>Zonisamide</td>
<td>Lithium</td>
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<td>Methimazol</td>
<td>Para-aminosalicylic acid</td>
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<td>Atenolol</td>
<td>Ibuprofen</td>
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<td>Timolol</td>
<td>Diclofenac, Benoxaprofen, Mesalazine</td>
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<td>Pindolol</td>
<td>Reserpine</td>
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<td>Oxprenolol</td>
<td>Griseofulvin</td>
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<td>Propranolol</td>
<td>Clonidine</td>
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<td>Labetalol</td>
<td>Hydroxiurea</td>
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<td></td>
<td>Acebutolol</td>
<td>Interferons (others than IFN alpha)</td>
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<td>Metoprolol</td>
<td>Gemfibrosil</td>
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<td>Hydrochlorothiazide</td>
<td>Allopurinol</td>
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<td>Terbinafine</td>
<td>Quinine</td>
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<td>Minoxidil</td>
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<td>Simvastatin</td>
<td>Calcium channel blockers</td>
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<td>Fluvastatin</td>
<td>Enalapril, Lisinopril</td>
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<td>Pravastatin</td>
<td>Amiodarone, Spironolactone</td>
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<td>Fluorouracil</td>
<td>Interleukin-2</td>
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<td>Clobazam, Clozapine</td>
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<td>Tocainide</td>
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<td>Etanercept, Infliximab</td>
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<td>Adalimumab, Certolizumab pegol</td>
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<td>Zafirlukast</td>
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<td>Omeprazol, Esomerezol</td>
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Clinical Picture

- Usually milder disease
  - Arthralgias, myalgias, fevers, and serositis are more common in DIL
  - Rashes (malar rash, discoid rash), photosensitivity, and oral ulcers occur less frequently in DIL
  - Renal and central nervous system disease rarely
  - Exceptions have been reported
  - Antibodies: mostly ANA and anti histones
A Gut Feeling

- 51 Chinese Female
- Systemic lupus erythematosus x 5 years
  - Recent flare (autoimmune hepatitis, pneumonitis, cytopenias)
  - Treated with high dose prednisolone (0.6mg/kg/day)
- Latest prescription
  - Mycophnolate mofetil 2.5g daily
  - Hydroxychloroquine 200mg
  - Prednisolone 10mg
A Gut Feeling

- **Presents with**
  - Fever x 2/52, daily, no night sweats
  - LOW 2-3kg over past 1/12
  - LOA with epigastric discomfort
  - Intermittent Cough

- **Physical examination**
  - Temp: 38°C
  - Small supraclavicular lymph nodes
  - Tender right IF region
Investigations

- TW 7.05 x10⁹/L
- Hb 11.3g/dL
- Plt 221 x10⁹/L
- ESR 102mm/hr
- CRP 63mg/L
- C3 75mg/dL (85-185)
- C4 12mg/dL (10-50)
- Anti-dsDNA 39 IU
- Albumin 33 (38-48)
- AST 23 (10-50)
- ALT 35 (10-70)
# Other Investigations

## AFB smear
- **Sample Origin**: Sputum, Induced
- **Request status**: Completed
- **Visual Aspect**: 
- **Acid fast bacilli**: not seen on direct smear

## TB molecular
- **Sample Origin**: Sputum, Induced
- **Request status**: Completed
- **Visual Aspect**: 
- **Molecular comment**: Positive for Mycobacterium TB complex
- **Rifampicin resist**: not detected (RpoB mutation not detected)

This result was obtained using the GeneXpert test. This test has the following accuracy in the detection of active pulmonary tuberculosis. These standards are applicable to sputum and not to other specimens.

- **Smear +ve patients**
  - Sensitivity 87% - 100%
  - Specificity >99%

- **Smear -ve patients**
  - Sensitivity 64% - 71%
  - Specificity >98%

The test has the following estimated accuracy in the detection of Rifampicin resistance.
- **Sensitivity 95%**
- **Specificity >98%**
CT Abdomen

Cecal wall thickening

4.00 mm
Diagnosis – Disseminated TB in SLE

- Disseminated pulmonary TB + abdominal infection (presumed ileocecal tuberculous enteritis)

- Prevalence of TB in SLE patients reported between 3.6 to 11.6%
- Up to 52.4% of patients with SLE have extra-pulmonary TB
Take Home Message

- Be aware of high risk of infections in SLE patients
- Fever can still be a sign of infection in immunosuppressed patients
- Do not assume it is a flare of autoimmune disease
- Treat both if co-existing:
  - *Immunosuppressive therapy is permitted with appropriate microbiological treatment (risk vs benefit)*
Other Mimickers

- Rheumatological disorders
  - Vasculitis - multi-system inflammatory condition
  - Still’s disease
  - Overlap Syndrome

- Dermatologic conditions
  - Rosacea
  - Polymorphous light eruption

- Endocrine disorders
  - Autoimmune thyroid disease
Questions?

Thank you