Antinuclear Antibody

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GLMS April 2020 CME

Patient 1

- 20 year old Samoan female, with ANA 1:1280
- Presents with 8 mths history of joint pains in the hands, feet, knees
- EMS 10 minutes
- Fatigue, rash, chest pains

Patient 2

- 40 year old female caucasian with 6 year history of arthralgia of wrist, elbows, shoulders and back pain
- ANA 1:160
- Hair loss
- Previous hyperactive thyroid, received radioactive iodine in 1990

Patient 3

- 47 year old caucasian female with a 5 year history of generalised arthralgia and myalgia
- Distant history of rash and long standing hair fall
- ANA 1:320
- Long standing headaches

Patient 4

- 38 year old Indian female with 1 year history of arthralgia and myalgia
- Significant fatigue
- Some weight gain
- ANA 1:80

Patient 5

- 72 year old Caucasian with a years of low back pain and knee pain (previous knee joint replacement)
- ANA 1:320 and raised ESR
- Dry mouth and occasional mouth ulcers
- Also seeing orthopaedics for knee pain

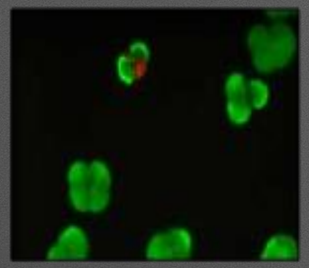
How are they tested?

- Enzyme immunoassay (EIA) or enzyme linked immunosorbent assay (ELISA)
- Indirect fluorescent antibody (IFA). The gold standard
- Fluorescent pattern reviewed

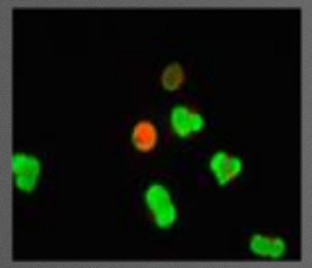
- WDHB
- CMDHB
- Labtests
- ADHB (Lab plus)

Patterns

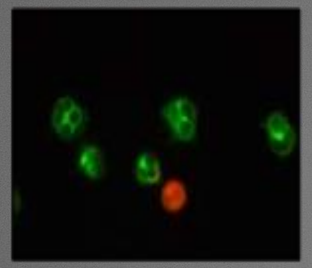
- Homogenous - ass/w SLE, mCTD, drug-induced lupus, autoimmune hepatitis
- Nucleolar - ass/w polymyositis and scleroderma
- Centromere - Associated with CREST syndrome (Calcinosis, raynauds, eosphageal dysfunction, sclerodactaly, telangiectasia)
- Speckled - SLE, CTD, chronic inflammatory disease, Sjogren’s



P-ANCA
with positive ANA



P-ANCA
with negative ANA



C-ANCA

- P-ANCA staining pattern can also be produced by other antibody
- Anti-nuclear antibodies (ANA) in the sample can stain the nuclei of the neutrophils. In some cases, especially anti-DNA antibodies, the staining can resemble a P-ANCA pattern.

Ds-DNA

For routine detection of autoantibodies against dsDNA

1. Enzyme immunoassays, (EIA) or enzyme-linked immunoabsorbent assay (ELISA)
2. FARR assay (radioimmunoassay)(RIA) - Gold standard
3. Crithidia luciliae immunofluorescence test. (CLIFT)

- ds-DNA
- ds-DNA
- ds-DNA at LabPlus (ADHB)

Dealing with a positive ANA…

- Pre-test probability
- ANA testing is sensitive but not specific
- Prevalence of low titre ANA is about 13% in young and healthy individuals (20-60 years old)
- Healthy older population can up to 30%
- More common in females
- Can be influenced by
  - Autoimmune thyroid disease,
  - Autoimmune liver disease,
  - Infections,
  - Malignancies

Sensitivity of ANAs in rheumatic disease:

- SLE 95-100%
- Scleroderma 60-80%
- mCTD 100%
- Polymyositis/Dermatomyositis 61%
- Rheumatoid Arthritis 52%
- Sjogrens syndrome 40-70%
- Discoid lupus 15%

Sensitivity of ANA in non-rheumatic diseases:

- Hasimoto’s thyroiditis 46%
- Grave’s disease 50%
- Autoimmune hepatitis 100%
- Primary autoimmune cholangitis 100%
- Primary pulmonary hypertension 40%

Picking the patients for testing…

- What's the pre-test probability???

- SLE occurs in 15-50/100,000
- 95% females
- Peak age 15-50 years old

CTD symptoms…

- Oral ulcers
- Hair loss
- Photosensitive rash
- Raynauds
- Pleurisy
- Inflammatory arthritis/arthralgia
- Sicca symptoms
- Others
  - Reflux

Systemic symptoms

- Fatigue +/- muscle weakness
- Weight loss
- Night sweats
- Fevers

ANA negative with positive dsDNA

- ANA negative lupus is very rare
- dsDNA is specific to lupus (97%) but sensitivity 30-70%
- Occurs in 40-85% in patients with SLE
- Associated with renal disease in patients with SLE
- Prevalence can be dependant on the assay.
  - FARR assay showed 0% in healthy older population.
- Laboratory false positive
  - 3% of patients with multiple medical issues has raised dsDNA

SSA ab/Ro antibody

- 50% of SLE and 75% of Sjogrens syndrome
- Associated with cutaneous lupus and ILD
- Anti-Ro and La can often be seen Sjogren’s syndrome with accompanying sicca symptoms
- Women of child bearing age
  - 1-2 % of congenital heart block and 10% neonatal lupus

DFS70 ab

- Occasionally reported under ANA testing
- Speckled and homogenous ANA patterns will be checked
- No association with autoimmune disease
- Cannot be requested separately

Patient 1 continued…

- A recap 10 years down the line…
- Positive dsDNA, centromere pattern, smRNP
- Diagnosed initially with undifferentiated CTD/SLE, started on Prednisone and Hydroxychloroquine
- 5 years after diagnosis she developed cryptogenic organising pneumonia
- At 6 years, class 2 lupus nephritis
- At 7 years, lupus enteritis
- Immune suppression related recurrent UTI and shingles
- Last year recurrent cough, wheeze, SOBOE
- Now on HCQ 400mg, Mycophenolate 1g BD, prednisone 5mg and doing well…

Patient 2 continued…

- Inflammatory back pain, MRI spine showed L3/4 disc disease
- Inflammatory arthralgia
- Besides ongoing hair loss, no other CTD symptoms
- ANA remained 160 to 320, mildly low C4 and long-standing mild neutropenia
- Possible undifferentiated CTD, trialled on HCQ
- Side effects to HCQ with skin pigmentation, headaches, nausea
- Lifestyle change and feeling better
- ANA remains the same 3 years from presentation and renal function and MSU are stable…monitor…

Patient 3 continued

- No CTD symptoms, multiple trigger areas with no synovitis
- Diagnosed as primary fibromyalgia and was discharged in 2014
- Re-referred this year with rising ANA 1280, ongoing arthralgia, increase of oral ulcers
- Low complements, neutropenia and leucopenia
- No renal involvement
- SLE, started on HCQ

Patient 4 continued

- No CTD symptoms
- Stressful job as a teacher and helping her husband’s business
- Multiple trigger points
- Poor sleep and fatigue
- Inflammatory markers, renal fucntion, MSU is bland
- No help with amitryptilline,
- Discharged on Gabapentin and referral to MDT

Patient 5 continued…

- Degenerative changes on her spine X-ray, non-inflammatory symptoms
- No CTD symptoms, renal function and MSU clear
- On amitryptilline, likely contributing to dry mouth
- MGUS being monitored
- R) TKJR infected

Take home message…

- Back to basics of history
- Take in account pre-test probability, this helps to interpret a positive ANA
- Sometimes, time will tell…

Additional tests

- MSU - microscopic haematuria, urinary casts
- Urine Protein creatinine ratio
- Complements
- ESR
- Antiphospholipid screen
- Hepatitis screen
- Autoimmune liver screen
- Thyroid autoab
- Cryoglobulins
- Serum protein electrophoresis

Thank you for listening!