Rheumatology - Interpretation of Laboratory Results

Jim Croker
Rheumatologist
Tamworth

Rheumatoid factor

- antibody versus IgG
- various antibody classes
  - IgM, IgG, IgA
- IgM rheumatoid factor is the class usually measured

Nephelometry to detect rheumatoid factor

- sample from patient mixed with solution with IgG bound to substance
- rheumatoid factor in sample binds to the IgG
- this is picked up as change in turbidity of the fluid
- reported as continuous variable

Specificity of rheumatoid factor

- rheumatoid arthritis
- connective tissue disorders
  - Sjögren’s syndrome, SLE, cryoglobulinaemia, vasculitis
- infections
  - bacterial - endocarditis
  - mycobacterial - TB, leprosy
  - spirochaetal - syphilis, Lyme disease
  - viral - rubella, CMV, IM, influenza
  - parasitic
- inflammatory disease
  - sarcoidosis, periodontal disease, pulmonary interstitial disease, liver disease
- hypergammaglobulinaemic purpura
- autoimmune hepatitis
- normal people

Rheumatoid arthritis

- ~70% of patients are seropositive (for rheumatoid factor)
- ~30% of patients will be seronegative (for rheumatoid factor) throughout course
  - some patients initially labelled as seronegative RA will later be reclassified eg to psoriatic arthritis
- generally patients with high titre rheumatoid factor have a worse prognosis
  - joint disease
  - extra-articular features

Anti-CCP antibodies

- antibodies to cyclic citrullinated peptides
- specificity
  - rheumatoid arthritis
    - more specific than rheumatoid factor
  - TB
  - in rheumatoid arthritis
    - between 50% and 70% of patients have anti-CCP antibodies
    - generally patients with high titre anti-CCP antibodies have a worse prognosis
Statistics

• 2 x 2 tables
• sensitivity (a/a+c) – looks at those with disease
• specificity (d/b+d) – looks at those without disease
• positive and negative predictive value – looks at the test

For the clinician

• history, examination
• provisional diagnosis (and differential diagnosis)
• perform test (if needed)

For the clinician

• if the test is positive
  – ask in what other conditions does a positive test occur
  – this relates to the specificity of the test
  – the more specific the test for a certain disease, the higher the positive predictive value eg antibodies to dsDNA in lupus
• if the test is negative
  – ask whether the disease can occur if the test is negative
  – this relates to the sensitivity of the test
  – the more sensitive the test for a certain disease, the higher the negative predictive value eg ANA in lupus

Again for the clinician

• when the test result becomes available, go back and put the result in clinical context (prior probability)
• need to remember that quoted values for sensitivity and specificity come from defined groups of patients
  – the sensitivity will vary depending on the particular spectrum or severity of patients included in the disease present group
  – the specificity will vary depending on the particular controls included in the disease absent group

Synovial fluid analysis

• request
  – cell count
  – micro
    • cells
    • crystals
    • gram stain
  – culture and sensitivity

Synovial fluid analysis

• crystals
  – urate
    • negatively birefringent
  – calcium pyrophosphate
    • positively birefringent
Synovial fluid analysis

- white cell count
  - normal < 200/cmm
  - non-inflammatory 200 to 2,000/cmm
  - inflammatory > 2,000/cmm

Uric acid levels

- do not correlate well with gout
- can have elevated uric acid level and never develop gout
- can have a normal uric level and be in the middle of a severe attack of polyarticular gout
- do not treat asymptomatic hyperuricaemia

ANA

- antibodies in blood that bind to nuclei of cells in laboratory
- occur in connective tissue disorders, other diseases and in normal people
  - not specific for SLE
  - a positive test does not necessarily indicate a diagnosis of SLE
- occur in nearly every patient with SLE
  - very sensitive test for SLE
  - a negative test makes a diagnosis of SLE very unlikely

ANA – lab report

- titre eg 1 in 640
- staining pattern eg homogeneous, speckled, rim, nucleolar and centromere
  - the centromere pattern is quite specific for scleroderma with limited skin involvement (CREST variant of scleroderma)
  - others patterns are nonspecific

Antibodies to dsDNA

- highly specific for SLE
- in SLE
  - occur in ~ 50% of patients
  - high titres correlate with active disease and lupus nephritis

ENA

- antibodies to extractable nuclear antigens
- to further define a positive ANA
- antibodies to
  - SSA – SLE or Sjogren’s
  - SSB – SLE or Sjogren’s
  - Sm - SLE
  - RNP - MCTD
  - Jo-1 - polymyositis
  - topoisomerase 1 - scleroderma
  - etc
**ANCA**

- antineutrophil cytoplasmic antibodies
  - antibodies that bind to the cytoplasm of neutrophils in the laboratory
- patterns
  - diffuse cytoplasmic staining (cANCA)
  - perinuclear staining (pANCA)
- specific antibodies
  - antibody to proteinase 3
  - antibody to myeloperoxidase

**ANCA**

- general relationships
- cANCA
  - proteinase 3
  - Wegener’s granulomatosis
- pANCA
  - myeloperoxidase
  - microscopic polyarteritis, Churg-Strauss syndrome and renal limited vasculitis

**HLA B27**

- genetic marker
- type 1 MHC molecule
- occurs in ~ 10% of normal population
- occurs in ~ 90% of patients with ankylosing spondylitis
- occurs in ~ 60% to 80% of patients with reactive arthritis (hospital series) but less frequently in community studies

**ESR**

- measures the rate at which red cells fall through plasma
- determined by the plasma concentration of certain proteins including fibrinogen
- a non-specific marker of inflammation

**CRP**

- protein produced by the liver in response to cytokine stimulation
- a non-specific marker of inflammation