‘A’ for ANA (Antinuclear Antibody)

What is ANA?

These are antibodies that the immune system makes against the cellular components in the nucleus-including proteins, DNA, RNA, and nucleic acid-protein complexes -which are helpful in the diagnosis of autoimmune diseases.

When to send ANA in clinical practice?

When there is a clinical context for autoimmune disease, most common being,

- Pyrexias of unknown origin (PUO)

  Nonspecific /constitutional symptoms (fatigue or chronic tiredness, muscle weakness, joint symptoms dizziness, weight loss)

  Mucocutaneous manifestations (Hard palate ulcers, Rashes, skin tightness, Raynaud’s phenomenon, brittle hair or hair loss, alopecia)

  Dry eyes and/or mouth, salivary gland enlargement

  Unexplained proteinuria / neuropsychiatric features (specially girls)

Other indications

- Young child < 7 years with Oligo/ Polyarticular JIA to predict higher risk for chronic anterior uveitis
- Children presenting with Autoimmune Hemolytic anemia

- Chronic ITP, Evans syndrome (Autoimmune hemolytic anemia with thrombocytopenia),Unexplained thrombotic episodes (Secondary APLA)
- Child on anti-tubercular therapy (AKT) develops SLE like features

Which method is ANA to be done by?

An ANA screen is the first test to be ordered. Even prior to an ANA test, the clinical examination and the nature of the complete blood counts, inflammatory markers, renal & liver functions, serum complements and other initial tests can offer a “pre- test probability “ of autoimmune connective tissue disease.

ANA screens are commercially available by ELISA or by Immunofluorescence (IFA) **Doing an ANA by IFA is the recommended test as ELISA is associated with higher incidence of false positives and false negatives.**

Is the ANA screen the same as the ANA profile/ANA Blot?

- An ANA screen is the first recommended test which depending on clinical context and the intensity of titre can suggest the likelihood of a connective tissue disorder (CTD). The pattern of positivity can also suggest the nature of CTD- eg. Homogeneous, speckled, centromere etc.
- An ANA profile/ Blot subsequently looks at the individual extracted nuclear antibodies against which the ANA is directed which is useful along with clinical picture to decide what kind of CTD would be the likely diagnosis.
- Doing an ANA profile/ANA Blot right away before/ without an ANA screen is not helpful because on its own it has little diagnostic relevance and is also a much more expensive test.

Is every ANA positivity significant for a diagnosis of CTD?

- From a variety of studies looking at blood donors etc, it’s clear that there is inherently a false positive rate of 4-15% of ANA in the general population.
- Many labs consider 1:160 as a significantly positive titre. The rate of false positivity reduces at higher titres, but even at titres of 1:160, there can still be close to 4% false positivity.

- ANA is a test therefore that has a moderate specificity but a high sensitivity (currently almost 100%) for the diagnosis of SLE. This means that in a reliable lab a FANA (Fluorescent ANA) test that is negative almost completely rules out SLE but a positive test has to be interpreted in the light of the entire clinical picture to validate its significance.
- ANA can be false positive in conditions like malignancies , lymphoproliferative disorders, autoimmune thyroiditis ,autoimmune hepatitis ,biliary cirrhosis , inflammatory bowel disease ,drugs etc
- ANA is useful ONLY for diagnosis and not for followup - there is no merit in repeating it to see if it has become negative after treatment

Take home messages

- **Clinical settings decide when to send ANA since the pretest probability determines the significance of the ANA test.**
- **ANA by Indirect Immunofluorescence (IFA) is the recommended method to test.**
- **ANA screen must be ordered first, not ANA profile/Blot.**
- **ANA Blot to be ordered only if ANA tests significantly positive.**
- **ANA is for diagnosis, not follow up.**

NEXT COMING B- BIOLOGICS

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