Systemic Sclerosis Antibodies

Indications for Ordering

Comprehensive evaluation of systemic sclerosis (SSc)

Test Description

Panel includes
- Nuclear Antibody (ANA) by IFA, IgG
  - Semiquantitative IFA
  - Reports centromere pattern
- Centromere Antibody, IgG
  - Semiquantitative multiplex bead assay
- Scleroderma (Scl-70) (ENA) Antibody, IgG (anti-topoisomerase)
  - Semiquantitative multiplex bead assay
- RNA Polymerase III Antibody, IgG
  - Semiquantitative ELISA
- Fibrillarin (U3 RNP) Antibody, IgG
  - Qualitative immunoblot assay
- PM/Sc1-100 Antibody, IgG by Immunoblot
  - Qualitative immunoblot assay
- RNP (U1) (Ribonucleic Protein) (ENA) Antibody, IgG
  - Semiquantitative multiplex bead assay

Tests to Consider

Typical testing strategy

Initial testing
- CBC with platelet count and automated differential
- Anti-nuclear antibody (ANA) by IFA
  - Confirmatory or secondary testing based on one or more of the following
    - ANA IFA patterns with three main patterns observed (centromere, nucleolar, and speckled patterns)
    - Clinical presentation
    - Ethnicity

Primary tests

Systemic Sclerosis Comprehensive Panel 2013325
- Indicated when suspicion for SSc is high and patient presents with features of overlap syndrome
- Individual tests in panel (may also be ordered separately)
  - Scleroderma (Scl-70) (ENA) Antibody, IgG 0050599
  - RNP (U1) (Ribonucleic Protein) (ENA) Antibody, IgG 0050470
  - Centromere Antibody, IgG 0050714
  - Nuclear Antibody (ANA) by IFA, IgG 0050639
  - Fibrillarin (U3 RNP) Antibody, IgG 2012173
  - PM/Sc1-100 Antibody, IgG by Immunoblot 2003040
  - RNA Polymerase III Antibody, IgG 2001601

Systemic Sclerosis Panel 2012057
- Indicated for patients with distinct features of SSc
- If ANA IFA is positive and SSc-specific markers are negative, testing for other markers associated with SSc or connective tissue disease based on observed ANA IFA pattern(s) is performed
- Negative results do not rule out SSc
  - If negative and suspicion for SSc is strong, consider testing for U3 RNP (fibrillarin), PM/Sc1-100, U1RNP, Th/Tho, or other connective tissue disease autoantibodies based on patient’s clinical presentation
- Individual tests in panel (may also be ordered separately)
  - Nuclear Antibody (ANA) by IFA, IgG 0050639
  - Scleroderma (Scl-70) (ENA) Antibody, IgG 0050599
  - RNA Polymerase III Antibody, IgG 2001601

Related tests

- Anti-Nuclear Antibody (ANA), IgG by IFA with Reflex by IFA Pattern 2008467
- Myositis Antibody Comprehensive Panel 2010851
- Connective Tissue Diseases Profile 0051668

Disease Overview

Incidence – 3-20/million

Age of onset – peak onset 20-30 years

Sex – M<F, 1:3-8

Ethnicity – overall slight increase in prevalence for African Americans compared to Caucasians
  - 10-fold increase in Choctaw Indians
Symptoms

• Dermatologic
  o Digital ulcers
  o Hair loss
  o Sclerodactyly
  o Abnormal nailfold capillaries
  o Raynaud phenomenon
  o Skin thickening
  o Telangiectasia

• Gastrointestinal
  o Gastroparesis/constipation
  o Esophageal dysmotility
  o Gastroesophageal reflux disease
  o Malabsorption

• Pulmonary
  o Pulmonary hypertension leading to interstitial fibrosis

• Musculoskeletal
  o Arthralgias/myalgias
  o Arthritis
  o Myopathy (usually proximal)

• Cardiovascular
  o Conduction abnormalities (eg, arrhythmias)
  o Myocardial fibrosis
  o Pericarditis
  o Valvular abnormalities

• Otorhinolaryngologic
  o Sicca syndrome

• Renal
  o Glomerulonephritis
  o Scleroderma renal crisis

Diagnostic issues

• Autoimmune connective tissue diseases may present with similar features, particularly early in disease, making diagnosis difficult

• ANA IFA patterns may help define diagnostic pathways
  o Most patients with SSc will have at least one of the following antibodies, and ordering tests for only these three antibodies is adequate for initial evaluation (van den Hoogen, 2013)
    ▪ Centromere
    ▪ Scl-70
    ▪ RNA polymerase III

• The presence of SSc-specific antibodies may help predict disease phenotype
  o Calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia (CREST) syndrome
    ▪ Antibodies against centromere are most common
  o Diffuse cutaneous SSc
    ▪ Antibodies against Scl-70 and RNA polymerase III are most common

• Antibody patterns may differ by ethnicity
  o Testing for less commonly associated SSc antibodies (eg, U3-RNP, PM/Scl, and Th/To) may be appropriate when results for antibodies commonly associated with SSc are negative.
    ▪ Antibodies against U3-RNP are most common in African Americans
    ▪ Th/To and PM/Scl are more common in Caucasians with limited SSc

Test Interpretation

Clinical sensitivity

• Sensitivity for ANA by IFA for SSc ranges from 90-95%
• Sensitivity for individual SSc-specific marker is dependent on ethnicity

Results

Reports ANA patterns (including centromere)
  o If positive, pattern and titers are reported

Limitations

• Negative antibody test result does not exclude SSc
  o 5-10% of SSc patients are ANA IFA negative
• Panel does not include Th/To
• The multiplex bead assay detects antibodies targeting the centromere protein B of the centromere complex

Reference