

Update on the Approach to Rheumatic Disorders for the Allergist/Immunologist

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Outline

- Laboratory assays that might be used by allergists
- Allergic or adverse reactions to rheumatic therapies
- Rheumatic diseases that are likely to present to the allergist/immunologist

Overview

- Essential for confirming suspected diagnoses
- Less effective for excluding a suspected diagnosis
- Terminology sometimes confusing
- Methodologies are susceptible to error

Statistics

- “Lies, damn lies and statistics”
- Sensitive assays are useful screening tests
 - Increased false positive
 - Enhanced negative predictability
- Specific assays are useful confirming tests
 - Increased false negative
 - Enhanced positive predictability
- Generally, sensitivity and specificity are inversely related

Tests to be Discussed

- Acute phase reactants
- Autoantibodies
- Complement measurements
- Immune complex assays

Acute Phase Reactants

- Most useful
 - Erythrocyte sedimentation rate
 - C reactive protein
 - Platelet count
- Regulated by
 - IL-1
 - IL-6
 - Tumor necrosis factor (TNF)

Erythrocyte sedimentation rate

- Useful inexpensive test
- Depends upon production of fibrinogen
- Affected by RBC number and morphology
- Tends to be slow to rise and fall, 3-7 days
- Normal value increases with age, approximately half of age in years, if female add 10

Quantitative C-Reactive Protein

- Precisely quantitated
- Not dependent on RBCs
- Changes within hours of a change in stimulus

Typical Case Presentations

- Urticaria versus urticarial vasculitis
- Atypical pruritus
- Unusually ill appearing patient with upper airway complaints or findings
- Cough or asthma with systemic complaints
- Multi-organ or multi-system findings or complaints

Autoantibodies

- Antinuclear antibody (ANA)
 - Smith antibody
 - Anti-Ro and anti-La (ENA antibody)
 - dsDNA antibody
- Antineutrophil cytoplasmic antibody
- Antithyroid antibodies
- Antimitochondrial antibody
- Others

Other Autoantibodies

- Thyroglobulin and thyroid peroxidase
- Glutamic acid dehydrogenase
- Acetylcholine receptor, GQ1b, GM1, GD1a
- Smooth muscle, mitochondrial, ANA
- Parietal cell
- *Saccharomyces cerevisiae*
- I, i, CD47, Duffy, Pr
- Liver/kidney microsomes or cytosol proteins

Antinuclear antibody

- Useful screening test but not specific
- Titers helpful initially, low titers almost always of no significance
- Consider antihistone antibodies if drug-induced lupus or drug “allergy” a consideration
- SLE cannot be diagnosed with ANA alone

Other “lupus” antibodies

- Double-stranded DNA (ds-DNA) and Smith antibody very specific for SLE
- Anti-Ro or -La occur in cutaneous lupus and Sjogren’s syndrome/disease
- Centromere pattern of ANA typical of CREST syndrome
- RNP antibody more common with mixed connective tissue disease
 - More likely to develop PHBP and SOB or interstitial pulmonary fibrosis

Antineutrophil cytoplasmic antibody (ANCA)

- Two patterns
 - Cytoplasmic
 - Perinuclear
- Not related to ANA
- Cytoplasmic
 - Wegener's granulomatosis
- Perinuclear
 - Chrug Strauss vasculitis
 - Microscopic polyangiitis

Other autoantibodies

- Anti-SCL 70
 - Scleroderma with lung involvement
- Antimitochondrial antibody
 - Primary biliary cirrhosis, which may present as pruritus
- Rheumatoid factor
 - Not specific, may suggest immune complexes
- Anti-citrullinated polypeptide
 - More specific, less sensitive than RF

Immune complex assays

- No generally reliable test
- Most useful for allergists is cryoglobulins
 - urticarial vasculitis
- Interpretation of other studies difficult
 - C1q binding
 - RAJI cell assay
 - Polyethylene glycol precipitation (PEG)

Complement assays

- CH 50 best screening assay for deficiency
 - C4 has 2 alleles on each chromosome so may be deficient with mild decrease or normal CH50
- C4 generally more useful than C3 In monitoring
- C2 most common deficiency associated with autoimmune disease but any “early” deficiency a consideration

Adverse or allergic reactions to rheumatic therapies

- Aspirin or NSAIDs
 - Urticaria
 - Asthma/Nasal polyp
- Embrel
- Rituximab

Rheumatic conditions likely to present to allergist/immunologist

- Wegener's granulomatosis
- Temporal arteritis/Giant cell arteritis
- Churg Strauss Vasculitis
- Sjogren's syndrome
- CREST or MCTD
- RA (eosinophilic pleural effusion)
- Lupus anticoagulant
- Ankylosing spondylitis (Crohn's disease)