Who’s Jo?  
Lab Tests Every Chest Radiologist Should Know.

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Introduction:
Thoracic imaging findings are illustrated for pulmonary diseases that can be associated with specific laboratory tests. The goals of this exhibit are to familiarize the radiologist with these laboratory tests and the key imaging and clinical findings associated with these diseases.

Selected Markers:

Galactomanin (GM)
• A cell-wall component released by Aspergillus species during hyphal growth
• Angioinvasive aspergillosis (Fig.1) occurs in immunosuppressed patients and has a very high mortality.
• Early diagnosis is challenging because of nonspecific clinical and radiographic findings and poor yield of cultures.
• Serum GM detection is a moderately useful screening tool to diagnose angioinvasive aspergillosis.
• Bronchoalveolar lavage GM assay more sensitive 90% and specific 94%(1).

Perinuclear Anti-Neutrophil Cytoplasmic Antibody (p-ANCA)
• Elevated in 40-90% of patients with microscopic polyangiitis (MPA) (2)
• p-ANCA immunofluorescence testing is less specific for MP than ELISA test for myeloperoxidase (MPO) antibodies
  • MPA is a small vessel nongranulomatous necrotizing vasculitis
  • Clinical prodrome of fever and weight loss
  • Rapid development of glomerulonephritis
  • Most common cause of pulmonary renal syndrome
  • Pulmonary findings of diffuse alveolar hemorrhage (Fig. 2) that, when repetitive, can lead to fibrosis.

Classical-Anti-Neutrophil Cytoplasmic Antibody (c-ANCA)
• Highly specific for Wegener granulomatosis, now designated, ANCA-associated granulomatous vasculitis, elevated in 85-90% of patients (3).
• c-ANCA immunofluorescence testing less specific than ELISA testing for the specific antibody involved in ANCA-associated granulomatous vasculitis: proteinase 3 antibodies (anti-PR3).
• ANCA associated granulomatous vasculitis:
  • Medium vessel nercrotizing vasculitis
  • Adults 30-60 years-old presenting with nasal or oral inflammation
  • Abnormal urine sediment
  • Imaging findings include randomly distributed pulmonary nodules, which often cavitate when >2 cm, ground-glass opacity, and airway wall thickening and stenosis (Fig 2).

Jo-1 Antibody
• Antibody targeting aminoacyl-transfer RNA synthetase implicated in polymyositis/dermatomyositis.
• Only present in 25-30% of patients, but highly specific and important prognostically with regard to lung disease (4).
• Dermatomyositis/Polymyositis:
  • Middle aged individuals who present with symmetric proximal muscle weakness with markedly elevated creatine kinase levels.
  • 35-40% will have ILD, but it accounts for 60% of mortality
  • When Jo-1 Ab present, pulmonary fibrosis occurs in 70% (5)
  • Imaging findings are typical of NSIP (Fig. 4) with ground-glass opacity in 92%, reticulation and bronchiectasis in 88%; honeycombing in 16%

Adenosine Deaminase (ADA) and Quantiferon Gold
• ADA is an enzyme that promotes the proliferation and differentiation of T lymphocytes in the presence of live intracellular micro-organisms (TB).
• Testing pleural fluid for ADA is a minimally invasive, inexpensive test for tuberculous pleurisy.
• Pleural fluid ADA has a high sensitivity (90-100%) and specificity (89-100%) for TB (6).
• With the low prevalence of TB in the United States, the positive predictive value is only 15%, but the test has a good negative predictive value and can be used for screening.
• For latent TB testing, Interferon gamma release assays (Quantiferon Gold) are replacing tuberculin skin testing because of increased accuracy. In this test, monocytes from blood are exposed to TB antigens and interferon gamma levels are measured (Fig. 5).

Vascular Endothelial Growth Factor-D (VEGF-D)
• VEGF-D induces the formation of lymphatics, promotes the spread of tumor cells to lymph nodes, and is elevated in patients with lymphangioleiomyomatosis (LAM).
• Diffuse thin-walled lung cysts in the presence of clinical tuberous sclerosis complex or renal angiomyolipomas on CT is diagnostic of LAM.
• 50% of sporadic LAM patients do not have angiomyolipomas appreciable by CT and historically require biopsy for diagnosis.
• Serum VEGF-D levels > 800 pg/mL are highly sensitive and specific for LAM in a patient with cystic lung disease and may obviate the need for biopsy (7).

Anti-nuclear Antibodies (ANA)
• Anti-nuclear antibodies are associated with systemic lupus erythematosus (SLE), rheumatoid arthritis, scleroderma and Sjögren syndrome.
• Two specific anti-nuclear antibodies are useful in the diagnosis of SLE:
  1. Ds-DNA antibodies have a 70% sensitivity and 97% specificity for SLE. Titers fluctuate with disease activity.
  2. Sm antibodies have a 30% sensitivity and 96% specificity for SLE (8).
• Patients with SLE present with a variety of pulmonary findings:
  1. Pleurisy and pleural or pericardial effusion 40-65%
  2. Acute lupus pneumonitis 4%
  3. Chronic interstitial pneumonitis 3-13%
  4. Pulmonary artery hypertension 4-40%
  5. Antiphospholipid syndrome and pulmonary embolism (8)

Granulocyte-Monocyte Colony Stimulating Factor (GM-CSF)
• GM-CSF antibodies have been detected in blood and in bronchoalveolar lavage (BAL) fluid in patients with pulmonary alveolar proteinosis (PAP).
• Lin et al. detected anti-GM-CSF antibodies in both blood and BAL fluid samples of 12 of 13 patients with idiopathic PAP patients and were unable to detect GM-CSF in the blood or BAL fluid from 35 patients with other pulmonary diseases, 3 patients with secondary PAP, or in 30 healthy individuals (9).
• As the diagnosis of idiopathic PAP is often one of exclusion, and GM-CSF assay may assist in diagnosis.
• Quantitative anti-GM-CSF antibody levels in BAL may also be useful in predicting prognosis (9).

Conclusion:
As electronic medical records become more common, radiologists have easy access to detailed histories, physical exam findings, and laboratory values. Knowledge of certain laboratory values as well as the presentation of pulmonary diseases may help the radiologist make a specific diagnosis when imaging findings are nonspecific.

References: