Publication of the Month

September 09/08: Anti-alpha Fodrin in Sjögren's Syndrome

Sjögren's syndrome (SS) is a chronic inflammatory disease of unknown cause characterized by diminished lacrimal and salivary gland secretion, but non-exocrine manifestations are also frequent. The disease occurs as a primary pathologic entity (primary Sjögren's syndrome = pSS) or in association with rheumatoid arthritis or other connective tissue disorders (secondary Sjögren's syndrome = sSS). The most prevalent serological markers are the "classical" Sjögren's syndrome antibodies to SS-A (also called Ro) and SS-B (also called La).

In 1997 Haneji et al found that 41 of 43 pSS-patients and 5 of 8 sSS-patients had antibodies to the human cytoskeletal protein α-fodrin, whereas neither of the control patients with SLE or RA nor healthy blood donors were positive. Different studies were made to confirm these data – more or less successfully. The authors of the following study assessed the diagnostic utility of measuring α-fodrin antibodies of the IgG and IgA isotype and compared it to that of the classical IgG anti-Ro/La antibodies in a large cohort of patients with pSS:

Locht H, Pelck R, Manthorpe R
Diagnostic and Prognostic Significance of Measuring Antibodies to α-Fodrin compared to Anti-Ro-52, Anti-Ro-60, and Anti-La in Primary Sjögren's Syndrome
J Rheumatol 2008; 35: 845–849

Sera from 321 patients with pSS (according to Copenhagen criteria), of which 205 fulfilled the new American-European 2002 consensus criteria were tested. Specificity was determined using control groups consisting of healthy blood donors (n = 76), SLE patients (n = 108), and patients with RA (n = 95). The distribution of individual antibodies is shown in the table:

Antibodies	Sensitivity, Copenhagen Criteria, n = 321	Sensitivity, EU/US Criteria, n = 205	Specificity n = 279
IgA anti-α-fodrin	32%	35%	88%
IgG anti-α-fodrin	31%	37%	94%
IgG anti-Ro52	38%	60%	92%
IgG anti-Ro60	26%	42%	93%
IgG anti-La	20%	32%	97%
IgA or IgG anti-α-fodrin	45%	50%	85%
IgG anti-Ro52 or Ro60 or La	43%	69%	91%

In the cohort of SLE patients, 25 of 108 (23%) had either Ro52, Ro60 or La antibodies; one in the RA group was positive (1%); and none of the blood donors. IgA or IgG anti-α-fodrin was found in 24 (23%) SLE patients, 14 (15%) RA patients, and 4 (5%) blood donors. Interestingly, anti-Ro52 was the most sensitive marker for pSS. Internal organ damage and hematological abnormalities were closely associated with the presence of anti-La. To compare frequencies of anti-Ro/La between pSS patients fulfilling the Copenhagen versus the EU/US consensus criteria makes virtually no sense as determination of these autoantibodies is one of the items included in the EU/US criteria. Thus, it is not surprising that the sensitivity of anti-Ro/La was considerably higher when these criteria were applied.

The authors conclude that the diagnostic sensitivity or specificity for pSS could not be improved by the use of IgG or IgA anti-α-fodrin antibodies. The traditional anti-Ro/anti-La were slightly superior.