



THE SIGNIFICANCE AND INCREASING IMPORTANCE OF IgA ANTIPHOSPHOLIPID ANTIBODIES

Measuring serum levels of specific antiphospholipid antibody isotypes is an important tool for evaluating the risk of thromboembolic disease and/or diagnosing the antiphospholipid syndrome (APS). It is a common practice in many clinical laboratories to measure and report only IgG and IgM antiphospholipid antibodies. In the early 1990s, Corgenix researchers (Lopez LR et al. *Am J Clin Pathol* 1992;98:449-454) investigated the clinical correlation of IgG, IgM and IgA anticardiolipin (aCL) antibodies in a group of female SLE patients selected for a history of thrombosis. In this group, over half of the 43 pregnancies presented by these patients resulted in fetal loss, compared to an SLE control group with only 1 spontaneous abortion in the 13 pregnancies recorded. In the selected SLE patients, a strong correlation was seen between IgA aCL antibodies and thrombosis. The addition of the IgA aCL determination to the classical IgG and IgM assays increased the number of patients testing positive for anticardiolipin antibodies by 31.6%. These results confirmed previous reports of the association of IgA aCL antibodies with thrombosis and fetal loss in SLE patients.

In 1998, Wilson et al. (*Arthritis Rheum* 1999;42:1309-1311) reviewed the published scientific literature on the significance of IgA antiphospholipid antibodies and presented their findings at the 8th International Symposium on Antiphospholipid Antibodies held in Sapporo, Japan. Wilson concluded that IgA aCL antibodies are common in SLE, and in many studies, these antibodies were associated with thrombosis. In addition, experimental work also suggested that IgA aCL antibodies are as prothrombotic as the IgG and IgM isotypes.

Antiphospholipid antibodies are a heterogenous group of autoantibodies directed to phospholipid-protein complexes or to proteins (cofactors) in the absence of phospholipids. These proteins (i.e. B2GPI) are thought to play an important role in the development of thrombosis in APS. Several recent studies on the clinical significance of anti-B2GPI antibodies in APS have shown that these antibodies are more specific for thrombosis than aCL antibodies, and many clinical laboratories now include assays for these antibodies as part of their diagnostic panel for APS. What is the clinical significance of IgA anti-B2GPI antibodies? Do IgA

anti-B2GPI antibodies measured by ELISA support current IgG and IgM anti-B2GPI determinations? Corgenix in-house studies show a high prevalence (67%) of IgA anti-B2GPI antibodies in SLE patients with a history of thrombosis compared to 11% in SLE controls. Furthermore, 77.8% of Primary APS patients had high serum levels of IgA anti-B2GPI antibodies.

Other publications on IgA anti-B2GPI antibodies from independent groups support our findings. Fanopoulos et al. (*J Rheumatol* 1998;25:675-680) reported the frequency of IgA aCL and anti-B2GPI antibodies in patients with SLE and APS. High levels of IgA anti-B2GPI antibodies were found in 58% of SLE patients compared to 2% of blood donors. There was a statistically significant higher frequency along with elevated levels of IgA anti-B2GPI antibodies in SLE patients with APS compared to those without. Moreover, the highest antibody levels were observed with IgA anti-B2GPI compared to aCL and other isotypes of anti-B2GPI. They concluded that the sensitivity of the anti-B2GPI antibody test for APS is significantly increased by measuring IgA in addition to IgG and IgM isotypes. More recently, Greco et al. (*Lupus* 2000;9:33-41) tested prospectively for aCL and anti-B2GPI antibodies in a large group of patients with "anticardiolipin associated" diseases. In patients previously positive for aCL, 44% were positive for aCL on repeat testing, and 58% were positive for anti-B2GPI. In patients with APS, 48.6% were positive for aCL and 64% were positive for anti-B2GPI. Overall, IgA anti-B2GPI was the most frequent isotype found (60.9%). The results confirm that high serum levels of IgA anti-B2GPI antibodies are frequently found in patients with SLE and APS, and the determination of this antibody isotype may provide valuable serologic information in the evaluation of antiphospholipid antibodies.

These and several other studies have shown that some patients with antiphospholipid antibodies may present only the IgA isotype. These findings lead to the recommendation to test for IgA antibodies in the routine laboratory screening of antiphospholipid antibodies, and to look specifically for IgA antibodies in patients with clinical manifestations suggestive of the APS but with normal levels of IgG and IgM antibodies.

THE READER RESPONSE

Q: Our laboratory would like to begin offering all three isotypes (IgG, IgM and IgA) in our anti-cardiolipin antibody panel, but our billing department says that we can only bill for a single isotype? Any suggestions?

A: This was clarified in a recent publication by the American Medical Association (AMA), CPT Changes 2001, An Insider's View, on page 167: 86147 Cardiolipin (phospholipid) antibody, each Ig class. As stated in the Rationale paragraph (which explains why the change occurred), "CPT code 86147 was revised to specify 'each Ig class' to allow reporting of each class of Ig antibody ordered (eg. IgG, IgM and IgA). Frequently, multiple class determinations of cardiolipin antibodies measurements are necessary."

Similarly, CPT code 86146 Beta 2 Glycoprotein I antibody also applies for each Ig class tested (IgG, IgM and IgA.)

Thus, if your laboratory is running all three isotypes (or Ig classes) of anti-cardiolipin or anti-B2GPI antibodies, your billing department can use the same CPT code to bill for all three isotypes and you will be reimbursed for all three.

READER ANNOUNCEMENTS

- The following paper, based on studies conducted at **Corgenix**, was recently accepted for publication in *American Clinical Laboratory*, where it will appear in the April 2002 issue:

Clinical performance (sensitivity and agreement with thrombosis) of four antiphospholipid antibody assays. LR Lopez, AM Whittier, KJ Dier, DO Taylor, TR Buckner, LW Olsen and CA Fink.

This work is unique, as **Corgenix** is the only company to feature FDA-cleared assays for the detection of four antibodies associated with the anti-phospholipid syndrome (aCL, aPS, aB2GPI and aPT).

- The **Biennial Meeting of the International Association for the Study of the Liver (IASL)** and the **37th Annual Meeting of the European Association for the Study of the Liver (EASL 2002)** will meet consecutively in Madrid, Spain, from April 15 – 21, 2002. **Corgenix** invites you to stop by our booth (#31, floor C) during the exhibition to learn more about Hyaluronic Acid (HA) as a serological marker for liver disease.

READER PRODUCT FEATURE

REAAADS IgA Anti-Beta 2 Glycoprotein I Semi-Quantitative Test Kit

For *In Vitro* Diagnostic Use

Assay format -	96-well microtiter plate (8 x 12 strips) with breakaway wells
Sample matrix -	Human serum
Sample dilution -	1:50
Antigen -	Purified human Beta 2 Glycoprotein I
Conjugate -	Horseradish peroxidase (HRP) / goat anti-human IgA
Chromogenic substrate -	TMB (single component)
Stopping solution -	0.36 N Sulfuric acid
Assay incubations	
Sample -	15 min @ room temperature
Conjugate -	15 min @ room temperature
Substrate -	10 min @ room temperature
Wavelength -	450 nm
Clinical specificity -	95%
Clinical sensitivity -	Autoimmune population: 27%
Product number:	039-001 IgA aB2GPI
Also available:	037-001 IgG aB2GPI 038-001 IgM aB2GPI

READER ANNOUNCEMENTS (cont.)

- Corgenix** is pleased to announce that the Hyaluronic Acid (HA) Test Kit, our first product to bear the CE Mark, will be available for distribution outside the U.S. in April. While CE marking will not become mandatory in Europe until December, 2003, **Corgenix** anticipates that all of our *in vitro* diagnostic products will be CE-marked well in advance of the deadline.

REMINDERS

- Digestive Disease Week (DDW)**, at the Moscone Center in San Francisco, CA, May 19-22, 2002, where **Corgenix** will present information on HA (booth #2906).
- The 4th Annual Symposium and Wet Workshop on Hemostasis and Thrombosis** the Marriott Hotel in Indianapolis, IN, May 23-24, 2002.

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