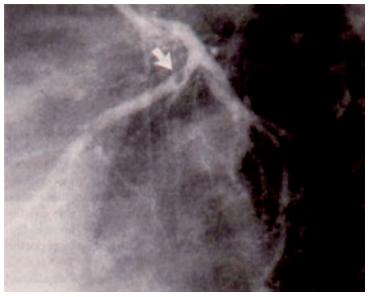
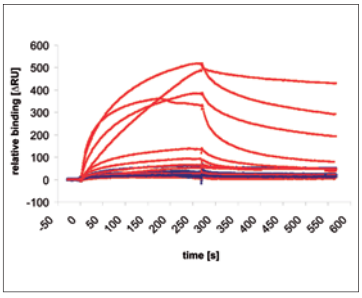
EDITION 1 – 2008

EliA™ JOURNAL





Clinical Background

Clinical Manifestations and Case Reports

The Assay

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Hughes Syndrome (The Antiphospholipid Syndrome): More Questions Than Answers

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In the following three cases are described possibly (or not) related to Hughes Syndrome (the antiphospholipid syndrome; APS), as a basis for clinical discussion. I will briefly summarise the three histories, the outcomes and possible clinical lessons from the cases.

Case 1: Low Platelets and Parkinsonism

A 55 year old housewife presented with a rapid onset of Parkinson's disease. Her only current medication was aspirin 75mg daily. Her past history was one of mild lupus (current anti-DNA negative) with chronic thrombocytopenia.

Current investigations included a normal brain MRI, platelet count 55,000 (unchanged), strongly positive IgM and IgG aCL.

What Happened Next?

Discussions included the use of steroids, immunosuppressives, a heparin trial (the favoured suggestion) and warfarin.

The patient decided against. Conventional anti-Parkinson medication has so far resulted in slight improvement only.

Discussion:

Hughes syndrome (APS) is first and foremost a neurological disease (1). From its original description in 1983, movement disorders such as chorea have been a prominent feature (2). These include cases of Parkinsonism (1). Whether this patient with aPL, thrombocytopenia and Parkinsonism meets criteria for APS is probably unimportant. What is undoubtedly important is the need for the development of investigations (e.g. SPECT, anti-neuronal antibodies) which might better define a causal link – and firmer grounds for anticoagulation.

Case 2: Ten Years On

In 1985 a 25 year old woman suffered three miscarriages. She was found to have positive aPL, and her fourth pregnancy was successfully managed at a teaching hospital with low molecular weight heparin and aspirin. She decided against further pregnancy, and was lost to follow up.

In 1995, ten years later, she suffered a recurrence of the migraine headaches she had had previously as a child and as a teenager. No diagnosis or treatment was forthcoming. In 1996, the headaches worsened, and problems of memory loss and balance became prominent. MRI showed multiple small lesions (ischemic). Other neurologic examination was inconclusive and routine blood tests were normal. In 1996, she suffered a severe hemiplegic stroke.

Discussion:

Hughes syndrome (APS) is now recognised as the commonest, treatable cause of recurrent pregnancy loss. Currently, treatment with heparin and/or aspirin is radically improving the outcome of pregnancy in aPL positive women; but what about the future? Despite 25 years of study of APS, the long term prognosis of untreated aPL positive individuals remains uncertain. Women treated successfully for aPL – related pregnancy loss deserve long term follow-up.

Case 3: Migraine and Vertigo

A 42 year old woman had a lifelong history of headaches, often migrainous. Between the ages of 35 – 40 she had had a number of episodes of "Ménière's" as well as an increase in headache. Investigated by a neurologist, she was found to be aPL positive on two occasions, negative on a third. She was started on low dose aspirin, with some improvement. At the age of 40, the headaches and migraines increased both in frequency and severity. MRI showed a few widely scattered lesions ("possibly within normal limits"). Lupus anticoagulant and anticardiolipin tests were once again negative.

What Happened Next?

Despite the negative aPL tests, a three week course of LMW heparin ("Fragmin" 10,000 units daily) was given as a therapeutic trial. With clear improvement, the patient was subsequently changed to warfarin (Coumadin). There has been sustained improvement both in the headaches and in balance. The headaches consistently return at an INR below 3.2. The patient now self-tests her INR at home and remains almost totally headache free. There have been no further episodes of vertigo.

What Is This Patient Teaching Us?

For me there are a number of lessons – or at least discussion points:

- The concept of "sero-negative APS" is, in my opinion, an important one (3). There are a number of possible explanations – one of which may be the patient such as this one with fluctuating aPL levels.
- "Ménière's" and balance problems are an under-emphasised feature of APS. The middle ear is, in some ways, an end-organ, and is subject to the ischaemia of APS.
- A "heparin trial" does have a place in the diagnosis in some patients. Despite being "soft" evidence, it is useful in situations such as that seen in this patient.
- Don't underestimate migraine – one of the cardinal features of Hughes syndrome.
- Until newer, easier anticoagulants came along, warfarin is the best we have. Self-testing of INR is, in my view as important to APS patients as insulin/sugar self-testing is in diabetics.

References:

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2. **Hughes GRV (1983)** Thrombosis, abortion, cerebral disease, and the lupus anticoagulant. Br Med J 287:1088-1089
3. **Hughes GRV, Khamashta MA (2003)** Sero-negative antiphospholipid syndrome. Ann Rheum Dis 62: 1127-1128