

Letters



INSTRUCTIONS FOR LETTERS TO THE EDITOR

Editorial comment in the form of a Letter to the Editor is invited; however, it should not exceed 800 words, with a maximum of 10 references and no more than 2 figures (submitted as camera ready hard copy per Journal Guidelines) or tables and no subdivision for an Abstract, Methods, or Results. Letters should have no more than 3 authors. Full name(s) and address of the author(s) should accompany the letter as well as the telephone number, fax number, or E-mail address.

Contact. The Managing Editor, The Journal of Rheumatology, 920 Yonge Street, Suite 115, Toronto, Ontario M4W 3C7, CANADA. Tel: 416-967-5155; Fax: 416-967-7556; E-mail: jrheum@jrheum.com Financial associations or other possible conflicts of interest should always be disclosed.

“Listen to the Patient” — Anticoagulation Is Critical in the Antiphospholipid (Hughes) Syndrome

To the Editor:

The antiphospholipid syndrome (APS), first described in 1983¹, is now recognized as a major thrombotic syndrome, with clinical ramifications in almost all aspects of medicine. Affecting, almost uniquely, both veins and arteries, the clinical features range through deep vein thrombosis (DVT), chronic leg ulcers, recurrent miscarriages, headache, heart attacks, renal vein and artery thrombosis, to pulmonary embolism and even pulmonary hypertension. For the clinician, the major clinical organ to be targeted is the brain. Since the initial description of stroke as a feature of Hughes syndrome in 1983^{1,2}, it has become recognized that the syndrome is an important cause of neurological features. A number of studies have recognized that up to one in 5 “young” strokes (aged 45 or under) are associated with the (potentially treatable) syndrome — a finding with huge clinical and socioeconomic impact³.

Many patients give a history of headache and migraine, often going back to their teens. The headaches are frequently severe and daily, and sometimes associated with speech disturbance^{4,5}. Memory loss is a major feature in many APS patients — ranging from difficulty with finding the right words, to severe memory disturbance — occasionally giving rise to suggestions of Alzheimer’s³. In other patients the diverse neurological features have resulted in a differential diagnosis of multiple sclerosis — a differentiation that has often proved extremely difficult⁶.

Two clinical observations keep recurring in the case histories of patients with APS. Firstly, headache, perhaps the single most prominent symptom of APS, often disappears when anticoagulation with heparin or warfarin is started^{4,7}. Secondly, many such patients on longterm warfarin “know” when their anticoagulation is below par [i.e., when the international normalized ratio (INR) has fallen] — the headaches, memory impairment, ataxia, and even seizures reappear. In these patients, there seems to be an overwhelming argument for self-testing of INR where possible.

Case history: A 36-year-old woman complained of headaches, speech disturbance, visual impairment, lethargy, and episodes of loss of consciousness lasting up to 10 minutes. A brain scan showed numerous small, well defined white matter lesions. Blood tests revealed strongly positive anticardiolipin antibody (aCL). Her history included 3 early miscarriages 14

years earlier, 2 possible DVT, and an unproved pulmonary embolism 3 years previously. A diagnosis of Hughes syndrome (APS) was made and she was treated with warfarin, with immediate improvement in symptoms. Anticoagulation control was difficult, however, the INR fluctuating significantly.

She was certain that the symptoms (including the loss of consciousness) returned when the INR fell below a critical 2.8. With a half-day round trip to her anticoagulant clinic, and erratic INR control, she suffered 7 hospital admissions in 1999 for various thrombosis related events. She campaigned for, and received, an INR self-testing machine. By her own admission, her life has changed. Any return of headaches or other neurological feature is met with an immediate INR test and, when necessary, fine-tuning of warfarin. From 7 hospital admissions in 1999, there were none in 2000. Confidence to travel abroad has returned, and the fear of further transient ischemic attack or strokes has receded.

In this case there are a number of lessons. Recurrent miscarriage in a patient with APS may still harbor prothrombotic problems years later. Neurological features, notably headaches (or memory loss), are important. APS is an important cause of stroke. Improvement with anticoagulation can be striking. Careful INR control with warfarin is critical — indeed, many patients with brain ischemia require an INR of 3 or even more⁸. Self-testing of INR, as in the case of self-testing in diabetes, could have important medical as well as health economic benefits, especially in such a prothrombotic disorder.

Postscript: audit. The self-testing machine currently costs £300–500. This patient’s half-day visit for anticoagulation testing cost an estimated £200 per visit (she was not a wage earner). Her 7 hospital visits prior to good INR control cost an estimated £73,500. The annual cost of strokes in the UK is £2.3 billion (plus £672 million per year to caregivers). One in 5 strokes under age 45 could have the potentially treatable condition APS. In an ideal world, a potential saving of £500 million annually, and that does not count the human cost.

EDOUARD LETELLIER, MD, Visiting Research Fellow; GRAHAM R.V. HUGHES, MD, FRCP, Head, Lupus Unit, The Rayne Institute, St. Thomas’ Hospital, London SE1 7EH, UK.

We are grateful to Dr. Charles Wolfe for his advice on audit.

REFERENCES

1. Hughes GRV. Thrombosis, abortion, cerebral disease and lupus anticoagulant. *BMJ* 1983;287:1088-9.
2. Harris EN, Gharavi AE, Asherson RA, Boey ML, Hughes GRV. Cerebral infarction in systemic lupus: Association with anticardiolipin antibodies. *Clin Exp Rheumatol* 1984;2:47-9.
3. Hughes GRV. Off the beaten track: A clinician’s view. In: Khamashta MA, editor. *Hughes syndrome: antiphospholipid syndrome*. London Springer; 2000.
4. Cuadrado M, Khamashta MA, D’Cruz D, Hughes GRV. Migraine in Hughes syndrome — Heparin as a therapeutic trial? *QJM* 2001;94:114-5.
5. Cuadrado MJ, Khamashta MA, Hughes GRV. Sticky blood and headaches. *Lupus* 2001;10:392-3.
6. Cuadrado M, Khamashta MA, Ballesteros A, Godfrey T, Simon MJ, Hughes GRV. Can neurologic manifestations of Hughes (antiphospholipid) syndrome be distinguished from multiple sclerosis? Analysis of 27 patients and review of the literature. *Medicine Baltimore* 2000;79:57-8.
7. Hughes GRV, Cuadrado M, Khamashta MA, Sanna G. Headaches and memory loss: Rapid response to heparin in the antiphospholipid syndrome. *Lupus* 2001;10:778.
8. Khamashta MA, Cuadrado M, Mujic F, Taub NA, Hunt BJ, Hughes GRV. The management of thrombosis in the antiphospholipid-antibody syndrome. *New Engl J Med* 1995;332:993-7.