A therapeutic dilemma: atrial fibrillation, transient ischaemic attacks and an unruptured intracranial aneurysm

AJ Larner, EL Rose, PRD Humphrey

INTRODUCTION

Atrial fibrillation (AF) is a risk factor for cerebrovascular ischaemic events: 5% of patients suffer a first stroke or transient ischaemic attack (TIA) per year, and following an initial embolism the stroke recurrence rate is more than 10% per year. Systematic reviews of randomized controlled trials show that anticoagulation with warfarin reduces the relative risk of stroke by almost two-thirds; absolute risk reductions are 2.7% and 8.4% for primary and secondary stroke prevention respectively (Koudstaal, 2000). However, these benefits must be balanced against an increased risk of cerebral haemorrhage (0.3% per year *vs* 0.1% per year in placebo group). Consensus guidelines recommend anticoagulation be used in patients with AF, either persistent or paroxysmal, at risk of stroke unless there are specific contraindications (Gorelick et al, 1999). Nonetheless, anticoagulation is underused: in some studies only one quarter to one half of patients who might benefit from warfarin received it, principally because of concerns about safety, specifically monitoring the international normalized ratio (INR; Sudlow et al, 1998). This paper presents a patient illustrating the therapeutic dilemma posed in balancing the benefit:risk ratio of stroke prevention *vs* haemorrhagic risk.

CASE REPORT

Within 1 month, a 69-year-old right-handed man had three episodes of weakness of sudden onset affecting the left arm and face, followed by complete recovery within 10 minutes to 2 hours. He was a non-smoker, but had been diagnosed with hypertension 4 months earlier, treated with bendrofluazide. The neurological examination was normal, but he was in atrial fibrillation (ventricular rate >100/min) with a blood pressure of 160/70 mmHg. There were no carotid bruits. Transthoracic echocardiogram, carotid doppler ultrasonography and computed tomography (CT) of the brain were all normal. A diagnosis of transient ischaemic attacks (TIAs) was made, probably caused by emboli of cardiac origin. He was commenced on sotalol (40 mg twice daily) to attempt to prevent further attacks of atrial fibrillation. The use of anticoagulation was also considered.

In the past medical history, an episode of right-sided weakness of sudden onset, lasting 5 hours with complete recovery, had occurred 8 years earlier. CT brain scan at that time showed a high density lesion in the left internal capsule; it was not possible to decide whether this was haemorrhage into an infarct or a primary intracerebral haemorrhage from a left middle cerebral artery aneurysm. Cerebral angiography showed a small saccular aneurysm close to the trifurcation of the right (sic) middle cerebral artery. This lesion was thought incidental to the clinical history and, because of its size, surgery was not advised. Interval magnetic resonance angiography 3 and 6 years later showed no change in aneurysm size (<2 mm) and management remained conservative.

Despite the evidence supporting anticoagulation to prevent stroke in patients with atrial fibrillation, it was initially thought that this treatment would be contraindicated by the presence of an unruptured intracranial aneurysm. However, in the absence of evidence specific to this clinical situation (see discussion), the available data suggested that benefits of anticoagulation (stroke prevention) outweighed (haemorrhagic) risk in this patient. These issues were discussed with the patient who decided to opt for anticoagulation. Close monitoring to maintain an international normalized ratio between 2.0 and 2.5 was the aim. After 12 months of follow up the patient remained well with no further TIAs and no complications.

DISCUSSION

Since the prevalence of AF is around 2–5% of the population over 60 years of age, and of unruptured intracranial aneurysm (ICA) around 3.6–6% (Wardlaw and White, 2000), then by chance alone the two conditions should coexist in 7.2/10 000 population (taking the lowest estimates of prevalence); if there are shared aetiological factors, the concurrence rate might be greater. Hence the current case scenario is unlikely to be uncommon. Despite this, the authors know of no specific evidence to assist decision making in this management dilemma: no randomized controlled trial of anticoagulation in patients with AF, TIAs and ICA has been published.

Risk factors which increase stroke rate in AF, including increasing age, prior cerebral ischaemia (stroke or TIA), systemic hypertension, congestive heart failure and diabetes mellitus, have been used in the CHADS2 (congestive heart failure, hypertension, age, diabetes mellitus and stroke) scoring system to classify stroke risk in AF (Gage et al, 2001). With a CHADS2 score of three, this patient falls within a category where anticoagulation is considered a better choice than aspirin to reduce stroke risk (as for any patient with previous TIA or stroke; Gage et al, 2001).

Considering haemorrhagic risks of anticoagulation, although ICA is recognized to predispose to intracranial haemorrhage, it is not among recognized predictors of intracranial haemorrhage related to oral anticoagulant

Dr AJ Larner is Consultant Neurologist and **Dr PRD Humphrey** is Consultant Neurologist at the Walton Centre for Neurology and Neurosurgery, Fazakerley, Liverpool L9 7LJ, and **Dr EL Rose** is Consultant Cardiologist at Halton General Hospital, Runcorn, Cheshire

Correspondence to: Dr AJ Larner

therapy (e.g. intensity of anticoagulation, increasing age, hypertension, prior ischaemic stroke, leukoaraiosis; Hart, 2000). Hence, warfarin does not seem to induce arterial wall rupture. Occasional reports of anticoagulant-related intracranial haemorrhage with subsequent discovery of an underlying ICA have appeared, although bias against reporting such events seems highly likely. However, such bleeds may simply reflect the natural history of ICA: the risk of spontaneous haemorrhage from a small ICA is around 0.05% per year (The International Study of Unruptured Intracranial Aneurysms Investigators, 1998). Hence, there is currently no evidence that anticoagulation increases the risk of bleeding from an unruptured ICA (although clearly it increases the risk of complications from any bleed which does occur).

A study of patients with extracranial carotid artery disease and incidental ICA (Kappelle et al, 2000) provides data of possible relevance to clinical decision making in this case. A subgroup of 90 patients from the prospective North American Symptomatic Carotid Endarterectomy Trial had incidental unruptured ICA, most <10 mm in diameter, of whom 32 underwent carotid endarterectomy with perioperative heparin anticoagulation without prior aneurysm clipping. Only one patient suffered a subarachnoid haemorrhage, 6 days after uncomplicated surgery, but postmortem found no evidence of aneurysm rupture. Hence, perioperative anticoagulation with heparin did not increase risk of aneurysm rupture in these patients.

Despite the evidence supporting the use of anticoagulation to prevent stroke in patients with AF (Koudstaal, 2000) the authors initially thought this would be contraindicated in this patient by the unruptured ICA. However, upon consideration of the available data, the benefit:risk ratio for anticoagulation in this patient was deemed favourable (Gage et al, 2001). Specifically, the relative risk reduction of almost two-thirds for stroke prevention greatly outweighed the risks of haemorrhage. Whether the haemorrhagic risks of anticoagulation (0.3% per year) and of spontaneous ICA rupture (0.05% per year) are independent, additive, or multiplicative, is not apparent from the literature. In general, therefore, any patient in AF who suffers a stroke with recovery, or TIA, for no other reason, and who has a small unruptured ICA, should be anticoagulated. **HM**

Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ (2001) Validation of clinical classification schemes for predicting stroke. Results from the National Registry of Atrial Fibrillation. *JAMA* **285:** 2864–70

Gorelick PB, Sacco RL, Smith DB et al (1999) Prevention of a first stroke. A review of guidelines and a multidisciplinary statement from the National Stroke Association. *JAMA* **281:** 1112–20

Hart RG (2000) What causes intracerebral hemorrhage during warfarin therapy? *Neurology* **55:** 907–8

Kappelle LJ, Eliasziw M, Fox AJ, Barnett HJM for the North American Symptomatic Carotid Endarterectomy Trial Group (2000) Small, unruptured intracranial aneurysms and management of symptomatic carotid artery stenosis. *Neurology* **55:** 307–9

Koudstaal PJ (2000) Anticoagulants for preventing stroke in patients with non-rheumatic atrial fibrillation and a history of stroke or transient ischemic attacks. *Cochrane Database Syst Rev* **2:** CD000185

Sudlow M, Thomson R, Thwaites B, Rodgers H, Kenny RA (1998) Prevalence of atrial fibrillation and eligibility for anticoagulants in the community. *Lancet* **352:** 1167–71

The International Study of Unruptured Intracranial Aneurysms Investigators (1998) Unruptured intracranial aneurysms – risk of rupture and risks of surgical intervention. *N Engl J Med* **339:** 1725–33

Wardlaw JM, White PM (2000) The detection and management of unruptured intracranial aneurysms. *Brain* **123:** 205–21