CASE REPORT

Stroke and patent foramen ovale: intervene or wait

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SUMMARY

A 33-year-old woman presented to the emergency department with an acute left partial anterior circulation ischaemic stroke. Thrombolysis was not administered due to a rapidly improving National Institutes of Health Stroke Scale (NIHSS) score and she was thereafter given appropriate treatment for secondary prevention. CT and MRI demonstrated a left basal ganglia infarct with haemorrhagic transformation. Initial investigations revealed no evidence of atrial fibrillation or large vessel disease. Further investigation with transthoracic, bubble contrast and transoesophageal echocardiogram all indicated the presence of a grade 1 tunnel-shaped patent foramen ovale (PFO) with some aneurysmal interatrial septum. No other cause for her stroke was found. There is no current evidence to support the routine use of percutaneous PFO closure in prevention of stroke or transient ischaemic attack. National guidelines advise transcatheter closure of PFO should only be considered for patients with recurrent cryptogenic stroke on optimal medical management.

BACKGROUND

Patent foramen ovale (PFO) is found in 27% of cases in autopsy studies. This anatomical variant of the interatrial septum is found to decrease with increasing age.¹ Stroke and cryptogenic stroke have been associated with PFO. Up to 40% of cryptogenic ischaemic strokes are found to have concurrent PFO in one-third of patients.^{2–5}

Patients with cryptogenic stroke and PFO are at low risk of having recurrent cerebrovascular events.

Official advice regarding the management of PFO-associated cryptogenic stroke has remained inconclusive for a long time. Recommendations to offer closure with a percutaneous device are often made to such patients, but it is not known whether this intervention reduces the risk of recurrent stroke.

CASE PRESENTATION

A 33-year-old right-handed Caucasian woman, working full time as a waitress, presented to the emergency department with a sudden onset of right-sided facial droop, right-sided weakness and slurred speech associated with headache.

There was a medical history of gestational diabetes and she was not prescribed any regular medicines. There was no family history of stroke or transient ischaemic attack (TIA). The patient was a current smoker with a 17 pack-year history and no personal history of alcohol or illicit drug use.

Examination revealed a temperature of 37.0°C, heart rate 88 bpm regular, blood pressure 113/66 mm Hg, SpO₂ 96% on air, respiratory rate 13 breaths/min and capillary blood glucose of

7.0 mmol/L. Cardiovascular examination was unremarkable. There was a mild expressive dysphasia, right facial nerve palsy sparing the forehead, right upper and lower limb weakness (Medical Research Council grade 2/5 in all modalities) and impaired finger–nose coordination on the right side.

Her speech impairment and limb weakness resolved entirely during the course of her 5-day admission to hospital, although there was a residual right facial droop on discharge.

INVESTIGATIONS

ECG showed sinus rhythm. Twenty-four hour ECG monitoring did not show paroxysmal atrial fibrillation. Full blood count, and renal and liver function tests were normal, serum C reactive protein <2 mg/L, serum thyroid-stimulating hormone 1.25 mU/L, plasma glucose 5.2 mmol/L, plasma homocysteine 10.1 µmol/L, serum total cholesterol 4.2 mmol/L, serum triglyceride 2.0 mmol/L, serum high-density lipoprotein (HDL) cholesterol 1.0 mmol/L, calculated low-density lipoprotein cholesterol 2.3 mmol/L, serum cholesterol/HDL ratio 4.2 mmol/L, anticardiolipin screen negative for IgG, IgM & IgA, antinuclear antibody negative, erythrocyte sedimentation rate 16 mm/h, total creatine kinase 75 U/L, lupus anticoagulant negative, antithrombin III activity normal, protein C activity normal, activated protein C (APC) resistance normal, prothrombin time normal, free protein S antigen normal and factor V Leiden PCR not indicated as APC resistance was not shown.

CT of the brain (figure 1A and B) showed a hypo attenuating region in the left basal ganglia just superior to a hyper attenuated left middle cerebral artery segment representing acute ischaemia.

MRI of the brain (figure 2) showed an acute left basal ganglia infarction with haemorrhagic transformation.

Transthoracic echocardiogram with bubble contrast (figure 3) showed normal cardiac chambers and good function. The interatrial septum looked highly mobile, which indicated the possible presence of a PFO.

Transoesophageal echocardiogram (figure 4) confirmed grade 1 tunnel-shaped PFO with some aneurysmal interatrial septum.

DIFFERENTIAL DIAGNOSIS

Seizure and hemiplegic migraine.

TREATMENT

The patient's National Institutes of Health Stroke Scale (NIHSS) score was initially 9 but was rescored at 4 during the prethrombolysis assessment and therefore she was not a candidate for thrombolysis. The high dose of aspirin was

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Figure 1 (A) Axial slice from unenhanced CT of the head demonstrating early ischaemic change in the left basal ganglia (black arrow). (B) Axial slice from unenhanced CT of the head demonstrating left middle cerebral artery hyperdensity (black arrow).

discontinued due to haemorrhagic transformation. The patient was subsequently started on vascular protection: clopidogrel 75 mg daily, simvastatin 40 mg daily and omeprazole 20 mg daily.

OUTCOME AND FOLLOW-UP

The patient was referred to a tertiary centre for percutaneous closure of PFO.

DISCUSSION

Contention remains regarding the agreed management of patients with PFO and cryptogenic stroke. This is because there are no trials comparing medical treatment (antiplatelet and anticoagulation), percutaneous closure of PFO and surgical closure of PFO. The current national stroke guidelines

recommend the prescription of an antiplatelet agent as secondary prevention for patients with PFO and cryptogenic stroke.⁶

Mas *et al*⁷ concluded that the risk of recurrent stroke in patients given aspirin and diagnosed as having PFO with cryptogenic stroke was comparable to patients without a PFO. A meta-analysis of five retrospective cohort studies has shown warfarin to be superior to aspirin in preventing recurrent stroke in this patient group.⁸

However, this is in contrast to findings from the PFO in Cryptogenic Stroke Study (PICSS), which found no difference in the incidence of recurrent stroke in patients with PFO taking either aspirin or warfarin.⁹

The CLOSURE 1 Trial researchers randomised patients with cryptogenic stroke or TIA to best medical treatment or treatment with endovascular closure. Taking into account various confounding factors including selection bias, time-lag bias and drop-out bias, it found no significant difference in outcomes between the two research arms.¹⁰

The RESPECT Trial researchers randomised patients with cryptogenic stroke to medical therapy or closure of PFO. The primary intention-to-treat analysis showed no statistically significant benefit with closure. However, it did demonstrate that closure was superior to medical therapy in the as-treated analysis with a statistically significant difference in stroke events per 100 patient-

Figure 2 Axial slice from MRI of the brain with T2-weighted imaging and turbo spin echo sequence showing an acute left basal ganglia thrombotic stroke with haemorrhagic transformation (black arrow).

Figure 3 Transthoracic echocardiogram (apical four-chamber view) with bubble contrast demonstrating a stream of microbubbles filling the left ventricle following systemic venous injection (white arrow).

Figure 4 Transoesophageal echocardiogram: (bicaval view, left atrium at top and right atrium below, septum) showing grade 1 tunnel-shaped patent foramen ovale with some aneurysmal interatrial septum (white arrow).

years (0.39 in closure group compared with 1.45 in medical therapy group). PFO closure does no harm and may do some good, reducing risk from about 1–2% per year to 0.5–1%.¹¹

As per the current advice from national guidelines, it is suggested that transcatheter closure of PFO should only be considered for patients with recurrent cryptogenic stroke on optimal medical management.⁶

A few studies have found varied results with direct closure of PFO. Dearani *et al*¹² showed that 92.5% of 91 patients were

free of stroke/TIA 1 year after direct closure of PFO, and 83.4% were event free after 2 years.

Homma *et al*¹³ found that 19.5% of 28 patients treated with surgical closure had recurrent events (stroke/TIA) at 13-month follow-up.

The management of patients with cryptogenic stroke and PFO remains a challenge. There is a lack of clear evidence regarding superiority of either medical or invasive treatment. Is it acceptable to expect patients to wait for a second and potentially devastating stroke before closing their defect?

On the basis of current evidence, patient perspective is the key. Our patient was not prepared to wait to have another stroke or TIA (on maximum vascular protection) to have PFO closure, hence she was referred to a tertiary centre for percutaneous closure of PFO.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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Learning points

- The significance of patent foramen ovale (PFO) in the aetiology of stroke and transient ischaemic attack (TIA) is a controversial topic with ongoing research into its optimal management.
- PFO closure is a low-risk procedure and may provide significant benefit for patients with cryptogenic stroke.
- Patients with a confirmed PFO suffering from cryptogenic stroke or TIA can be referred for evaluation of endovascular treatment and this decision should be strongly influenced by patient choice.
- We suggest that these patients should be studied as part of a national database.
- Further randomised controlled trials are needed to strengthen the evidence base.

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