Symptomatic vertebrobasilar artery stenosis treated with enoxaparin

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Intracranial artery stenosis is a major cause of stroke worldwide, and is more prevalent in Asian, African and Hispanic populations.[1,2] It is defined as stenosis of an intracranial vessel of at least 50%, and can be diagnosed non-invasively using magnetic resonance angiography (MRA), computed tomography angiography (CTA), or transcranial doppler. In the warfarin vs aspirin for symptomatic intracranial stenosis randomized controlled trial (WASID),[3] warfarin was associated with more adverse events and provided no benefit over aspirin. A recent Cochrane Review found that endovascular angioplasty/stenting was associated with higher complication rates than best medical management.[2] Thus, intensive therapy with antiplatelets, statins and antihypertensives are the mainstay of treatment. Despite these measures, stroke recurrence rates remain high at 12.2% per annum.[4] Symptomatic vertebrobasilar stenosis is associated with a higher rate of stroke recurrence than anterior circulation stenosis.[5] A *post hoc* analysis of the WASID trial suggested that warfarin may be more effective in this subgroup of patients.[5] There is clinical equipoise on the best treatment strategy for patients with recurrent events despite best medical management. Here, we present two haemodynamically stable patients with vertebrobasilar stenosis, and with recurrent events on intensive medical therapy.

Case one

A 79-year-old New Zealand European female with a history of hypertension on amlodipine 10mg once daily (OD) presented with two episodes of transient diplopia and left hemiparesis. On arrival, neurological examination was unremarkable. Blood markers were unremarkable with a C-reactive protein of 3.2mg/L and normal complete blood count. CT and CTA of the brain demonstrated an irregular stenotic distal right vertebral artery (Figure 1a). Aspirin (300mg loading, 100mg OD thereafter), clopidogrel (300mg loading, 75mg OD thereafter) and atorvastatin 80mg OD were initiated. Two days later, she had a recurrence of her symptoms. Brain imaging excluded acute infarction or hemorrhage, but persistent vertebral stenosis. Antiplatelets were discontinued and she was started on a heparin infusion adjusting as per activated partial thromboplastin time, switching to therapeutic enoxaparin (1.5mg/kg/day) the following day. We continued this treatment for one month, before switching to aspirin and clopidogrel for a further two months, then clopidogrel monotherapy. She remained asymptomatic two years later.

Case two

An 87-year-old New Zealand European lady presented with transient diplopia and left hemiparesis. Past medical history notable for hypertension. On arrival, she was neurologically intact. MRA brain demonstrated a critically stenosed/occluded basilar artery (Figure 1b) and a small right occipital lobe acute infarct. She was commenced on clopidogrel and aspirin (as per the regimen described earlier) and atorvastatin 80mg OD. Four days later, she deteriorated with dysarthria, hemiparesis, and tongue deviation. CT brain imaging was unremarkable. She was started on intravenous heparin for 24 hours, then switched to subcutaneous enoxaparin (1.5mg/kg/day). She remained neurologically stable and follow-up brain imaging three weeks later demonstrated improved flow within the basilar, however distal vertebral plaques persisted (Figure 1c). During this time her hemiparesis improved, and at time of discharge three weeks later was independently mobile with a walking frame. She was switched to clopidogrel and aspirin, and remained asymptomatic four months later.

Discussion

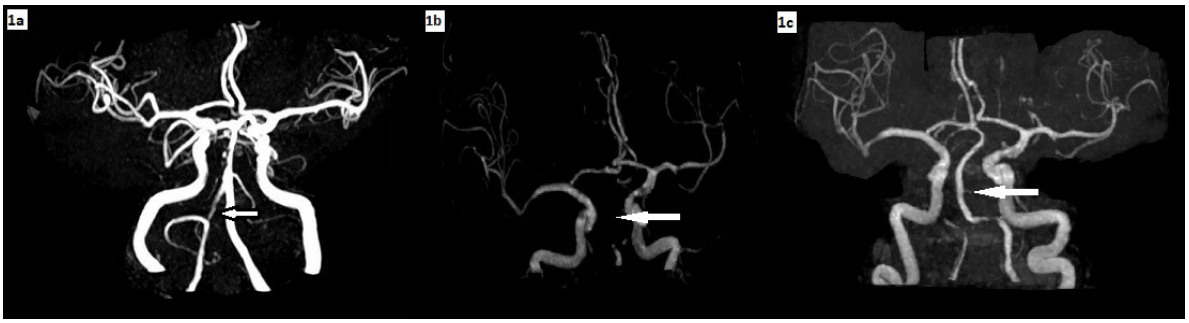
Here we present two patients with vertebrobasilar stenosis failing intensive medical therapy who responded favourably to therapeutic anticoagulation. Anti-Xa monitoring was not required, in accordance with guidelines.[6] Based on our experience, we have found this approach to be highly effective in

preventing recurrent stroke without major bleeding events.[7,8] Intracranial stenting remains a treatment option in patients refractory to medical therapy.

Patients presenting acutely with vertebrobasilar occlusion should be considered for treatment with intravenous thrombolysis and/or clot retrieval. The recently presented randomised control trial Endovascular Treatment for Acute Basilar Artery Occlusion trial (ATTENTION) demonstrated lower rates of disability and mortality with the latter.[9] In those ineligible for hyperacute treatments, heparinisation has a role.

Although WASID found that anticoagulation was ineffective in intracranial stenosis, our two patients seem to have responded well to the introduction of heparin. We used a short duration of anticoagulation thereby firstly, preventing further artery to artery embolisation while allowing plaque stabilisation to occur and secondly, minimising the risk of bleeding from chronic anticoagulation. Patients in the warfarin arm in WASID were in therapeutic range less than two thirds of the time.[3] Using standard dosing enoxaparin in our patients (after unfractionated heparin in first 24 hours) we would expect effective anticoagulation. Treatment with direct oral anticoagulation may be equally efficacious and investigation in larger trials is warranted.

Figure 1: a) CT angiography demonstrating critical stenosis of the right distal vertebral artery; **b)** MR time of flight angiography demonstrating absence/poor flow in the basilar artery; **c)** Improving after three weeks of anticoagulation revealing a residual stenosis of the distal left vertebral artery.



COMPETING INTERESTS

Nil.

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