Review

Diagnosis and management of vertebral artery stenosis

G.C. CLOUD and H.S. MARKUS

From the Division of Clinical Neuroscience, St George’s Hospital Medical School, London, UK

Introduction

Approximately one-quarter of ischaemic strokes involve the posterior or vertebrobasilar circulation.1 Stenosis of the vertebral artery can occur in either its extra- or intracranial portions, and may account for up to 20% of posterior circulation ischaemic strokes.2–6 Stenotic lesions, particularly at the origin of the vertebral artery, are not uncommon. In an angiographic study of 4748 patients with ischaemic stroke, some degree of proximal extracranial vertebral artery stenosis was seen in 18% of cases on the right and 22.3% on the left.7 This was the second most common site of stenosis after internal carotid artery stenosis at the carotid bifurcation. Such stenotic lesions are now potentially treatable by endovascular techniques.8

In marked contrast with carotid artery stenosis, the optimal management of vertebral artery stenosis has received limited attention, and is poorly understood. This partly reflects difficulties in imaging the vertebral artery adequately, and limited surgical treatment options. Recent improvements in imaging and the arrival of vertebral artery angioplasty, however, have opened up new opportunities for intervention in this disease.

We review vertebral artery anatomy, what is known of the natural history of vertebral artery disease, the role of imaging in the diagnosis of vertebral artery stenosis, and treatments for vertebral artery stenosis.

Anatomy

The vertebral artery arises from the supraposterior aspect of the first part of the subclavian artery. In 6% of cases, the left vertebral artery arises directly from the aortic arch. Unlike the internal carotid artery, which is an almost direct extension of its parent vessel the common carotid artery, the vertebral artery branches almost at right angles to its feeding vessel. The vertebral artery, being 3–5 mm in diameter, is of much smaller relative calibre than the subclavian, with only a small amount of subclavian blood flow normally being directed into each vertebral. These differences in anatomy may well reflect in dissimilar flow dynamics between the origins of the carotid and vertebrobasilar cerebral circulations, with a consequent predilection to forming a different type of atherosclerotic plaque. Plaque disease at the vertebral artery origin has been thought to be ‘smoother’ and less prone to ulcerate with secondary thrombus formation.9 Differences between carotid and vertebral artery plaque morphology have been inferred from angiographic appearances, but there are few published pathological data to support this.10

Anatomically, the vertebral artery can be divided into three extracranial parts and an intracranial portion (Figure 1). Part one is from the origin to the point at which it enters the transverse foramina of either the fifth or sixth cervical vertebra. During the second part, it courses within the intervertebral foramina until exiting as the third part behind the atlas and heading towards the foramen magnum. The final intracranial part begins as it pierces the dura and arachnoid mater at the base of the skull, and ends as it meets its opposite vertebral artery to form the midline basilar artery at the level of the

Address correspondence to Dr G.C. Cloud, Division of Clinical Neuroscience, St George’s Hospital Medical School, Cranmer Terrace, London SW17 ORE. e-mail: g.cloud@sghms.ac.uk
© Association of Physicians 2003
medullopontine junction. In its extracranial portion the vertebral artery gives small spinal branches to the periosteum and vertebral bodies and muscular branches to the deep surrounding muscles of the region. The short fourth intracranial part gives off major anterior and posterior spinal arteries to the medulla and spinal cord, minute penetrating vessels to the medulla and its largest branch—the posterior inferior cerebellar artery (PICA), which supplies a small portion of the dorsal medulla and cerebellum. Occasionally this PICA branch is absent, and collateral vessels then feed the lateral medulla. As it enters the skull, the vertebral artery wall shows marked change, with a reduction in the thickness of the adventitial and medial layers, and a reduction of elastic fibres in the media and external elastic lamina.11

In up to 15% of the healthy population, one vertebral artery is atretic (<2 mm diameter) and makes little contribution to basilar artery flow. Lesser degrees of asymmetry are also frequent. The left vertebral is dominant in approximately 50%; the right in 25% and only in the remaining quarter of cases are the two vertebral arteries of similar calibre. These variations have little or no clinical significance, unless there is associated vertebral artery origin or proximal subclavian artery stenosis.

Extracranial vertebral artery stenosis

The extracranial vertebral artery is affected by several pathological processes that cause stroke. The commonest is atherosclerotic disease—the main focus of this review—but others include vertebral artery dissection, fibrous banding in the neck, extrinsic compression in its second and third parts due to trauma of the cervical vertebrae or osteophytic impingement and compression, and vasculitis, most commonly giant-cell arteritis.

Post-mortem findings have shown atherosclerotic stenosis at the vertebral artery origin in cases of cerebrovascular death. Furthermore, atherosclerotic disease at the first part of the vertebral artery is commonly associated with similar disease in the internal carotid artery.12,13 However, there have been very few pathological specimens from in vivo cases, as endarterectomy for vertebral stenosis is rarely performed, and bypass surgery does not yield specimens. Despite the possible differences in plaque appearance between extracranial vertebral and internal carotid artery disease,10 it is generally considered that the two sites share a common pathogenesis, with stroke resulting from formation of emboli at the site of atherosclerotic plaque.14

Haemodynamic stroke, however, is less commonly due to vertebral artery stenosis,9 because both vertebral arteries feed into one basilar artery. Also, in contrast to the ICA, the vertebral artery gives off numerous branches in the neck, therefore facilitating a considerable collateral blood supply, which often reconstitutes the distal artery after occlusion at the origin.

There are no population-based prevalence data for extracranial vertebral artery stenosis. Studies to date have been of small numbers in specialist cohorts.15 The largest published series are from the New England Medical Centre posterior circulation stroke registry.16 Of 407 patients who were symptomatic from either posterior circulation stroke or transient ischaemic attack (TIA) or both, 80 (20%) were found to have >50% stenosis of the first part of the vertebral artery. Posterior circulation stroke was defined by imaging studies and vertebro-basilar TIA was diagnosed by experienced stroke neurologists using Caplan’s criteria.17 Stenosis was demonstrated either by conventional or magnetic resonance angiography (MRA). Just under half (37/80) had an occluded vertebral artery, and 15% (12/80) had bilateral involvement. A quarter (22/80) of these cases also had intracranial vertebral artery or basilar disease, which may have been the cause of symptoms. In almost half the patients (38/80),
however, the vertebral origin stenosis was the only identified cause of stroke, suggesting that vertebral artery stenosis was the cause of at least 10% of registry events. The risk factor profile for these patients was similar to that of anterior circulation stroke, and the mean age for the group was 62.5 years. The distribution of ethnicity was similar to that of the registry as a whole, but there was a preponderance of men in the group with vertebral artery origin stenosis. No follow-up data have been published in this group to date.

Unlike carotid disease, the prognosis of symptomatic vertebral artery stenosis is unknown. The only published prospective series of vertebral artery stenosis is from the Cleveland Clinic,\textsuperscript{18} and included predominantly asymptomatic cases. This was a prospective collection of 96 cases of angiographically-proven vertebral artery stenosis of $\geq 50\%$, of which 89 had stenosis at the origin, and eight had intracranial vertebral or basilar artery disease. Cases of occlusion or those who underwent operative procedures, presumably on symptomatic grounds, were excluded. Five-year follow-up suggested a modest overall increased stroke rate of 5.25% per annum, but only 18 had posterior circulation symptoms at time of angiography. The majority had in fact presented with anterior circulation symptoms, and 74 had an associated $>50\%$ internal carotid artery stenosis, 52 of whom underwent carotid endarterectomy. Perhaps unsurprisingly, the survival rate of the entire group was related to their carotid artery and concomitant cardiac disease. Only two of the 23 strokes seen during follow-up were in the posterior circulation, and in both cases there was co-existing basilar artery stenosis at the time of presentation. None of the isolated extracranial vertebral artery stenoses developed posterior circulation infarction.

**Intracranial vertebral stenosis**

Intracranial vertebral artery stenosis in the fourth segment of the vertebral artery often also involves the basilar artery, and is more strongly associated with brainstem infarction than extracranial vertebral artery stenosis. It has mainly been reported in symptomatic patients and is thought to be more common in Japanese, Chinese and Black Americans than in Caucasians.\textsuperscript{19,20} In the Cleveland Clinic follow-up series of 44 patients with distal vertebral or basilar artery stenosis, 38 were symptomatic for posterior circulation disease.\textsuperscript{21} Of these, only 16 had vertebral artery disease alone, and in two cases the extracranial vertebral artery was also involved. However, over six years of follow-up, there was a greater incidence of posterior circulation TIA, stroke and death, compared to the extracranial vertebral artery group, with an overall stroke rate of 7% per annum.

In a prospective, non-randomized trial of aspirin against warfarin for secondary prevention in intracranial posterior circulation artery stenosis of $\geq 50\%$,\textsuperscript{22} 37/68 cases involved the vertebral artery. The overall stroke rate associated with lone intracranial vertebral artery stenosis (31/68 cases) was 13.7% per annum, at a median follow-up of 13.8 months. The recurrent stroke rate in the territory of the stenotic vertebral artery was lower, at 7.8% per annum. The warfarin group had a lower recurrent stroke rate, but the numbers were small, and treatment was not randomized, making definite conclusions on the efficacy of warfarin difficult.

The New England Medical Centre posterior circulation registry identified 75 cases of severe symptomatic intracranial vertebral artery occlusive disease, and suggested that the prime site of disease is distal to the origin of PICA.\textsuperscript{23} Bilateral intracranial vertebral artery disease was also common (42/430 patients in the registry).\textsuperscript{24} Embolism from cardiac sources and extracranial vertebral artery stenosis was found to be the commonest cause of ‘proximal’ posterior circulation stroke (medullary and PICA cerebellar territory stroke).\textsuperscript{25} Those cases with concomitant basilar disease and distal posterior circulation were associated with poor outcome, and unlike the smaller Cleveland clinic series, the distribution of the stenosis did seem to have a prognostic significance.

**The role of imaging in diagnosis**

The gold standard for diagnosing vertebral artery stenosis remains Digital Subtraction Angiography (DSA), although this has a small morbidity and associated mortality.\textsuperscript{26–28} Stenosis at the vertebral artery origin can still be missed with standard arch views, because of superimposition of the subclavian artery over the first segment of the vertebral artery and additional oblique views are required.

The initial non-invasive investigation of choice for extracranial vertebral artery disease is ultrasound,\textsuperscript{29} and some part of 80–90% of all vertebral arteries can be insonated.\textsuperscript{30} By using Doppler ultrasound alone, however, the artery origin can only be imaged in up to 60% of subjects.\textsuperscript{31} This can be improved to over 80% by incorporating the use of colour Doppler flow imaging.\textsuperscript{32} More recent series using power Doppler imaging in combination with colour flow techniques, have shown an advantage over conventional techniques in terms
of sensitivity for detecting significant stenosis, which approaches 100% in some studies, without reducing specificity. Improved accuracy in estimation of flow velocities, may achieved by taking readings from both low (C5-6) and high (C1-2) cervical regions. Even so, the technique, like all ultrasound imaging, is highly user-dependent.

Transcranial Doppler ultrasound (TCD) can be used to detect intracranial vertebral artery stenosis with a sensitivity of as high as 80%, and a specificity of 80–97% when compared with DSA. However, the degree of stenosis is underestimated in over half of the cases, and occlusion of vessels may be missed. Another potential use of TCD is the detection of emboli from a stenosis, and many studies have detected asymptomatic embolization in patients with symptomatic carotid stenosis. However, there have been no such studies involving vertebral artery origin atherosclerotic stenosis, although TCD has been used for monitoring during percutaneous transluminal angioplasty (PTA) of vertebral stenosis.

Helical or spiral computerized tomography angiography (CTA) is able to image the extracranial vertebral artery without the risks associated with catheter angiography, but its use has not been fully validated against DSA. In one promising study of 24 patients with symptoms of vertebrobasilar ischaemia, CTA visualized the vertebral origin in all cases, and was able to detect all the extracranial vertebral artery stenotic lesions found by DSA. In addition, it was thought to confer further diagnostic benefit in differentiating between ‘kinked’ and truly atherosclerotic stenosed vessels. In another study, of 14 lesions seen on DSA in patients with acute posterior circulation ischaemic stroke, 13 were detected by CTA, but only seven of these 13 could be reported as definite stenosis or occlusion. The same study of 103 posterior circulation strokes found a less good correlation between CTA and Doppler.

Magnetic resonance imaging (MRI) used alone can detect intracranial vertebral artery disease, but it is best used in combination with magnetic resonance angiography (MRA) to assess both extra and intracranial vertebral arteries. Review of the New England Medical Centre registry experience comparing MRA with DSA, showed that MRA has a higher sensitivity for detecting basilar stenosis than either extracranial or intracranial vertebral artery disease. Sensitivity was 100%, for two independent observers identifying 12 stenoses in 39 basilar arteries. In the 62 patients with extracranial vertebral stenosis, the origin of the vertebral artery was not always well demonstrated, resulting in lower sensitivity results. Intracranial vertebral artery stenosis sensitivity was the least impressive, and lesions were missed, particularly at the junction between the intracranial and extracranial vertebral artery portions. An important pitfall with MRA is an over-reporting of occlusion in cases of high-grade stenosis. This is because time-of-flight MRA relies on flow-related enhancement to depict vessels, and therefore provides information about flow characteristics; low flow can appear as an absent vessel. Signal-to-noise ratio can be improved by the addition of contrast agents, and contrast-enhanced MRA appears promising. Reports to date have concentrated on carotid artery disease, but there is also a suggested improvement over conventional MRA in detecting lesions at the origin of the extracranial vertebral artery. However, there is a specific problem of imaging the vertebral artery origins due to coil design limitations and decreased signal at the spatial limits of the coil. This lack of signal could exacerbate the problems with differentiating low flow due to high grade stenosis and occlusion, and is not necessarily helped by the use of contrast.

**Treatment**

**Medical treatment**

Medical treatment alone has been the standard treatment for posterior circulation stroke, although other than for cardioembolic causes, this has tended to ignore the specific pathophysiological process underlying the event. To date, there have been no randomized trials of the use of different antiplatelet therapies or anticoagulation against antiplatelet therapy, in known cases of extracranial vertebral artery atherosclerotic stenosis. Similarly, there have been no completed randomized trials in intracranial vertebral artery stenosis, although there is one small retrospective, non-randomized study. This compared anticoagulation with warfarin to an INR of 1.6–1.8 with aspirin 325 mg, in cases of symptomatic, major intracranial artery, 50–99% angiographically-proven stenosis. Results of an ongoing prospective randomized trial between warfarin and aspirin in major intracranial artery stenosis are awaited.

**Surgical treatment**

Surgery for vertebral artery stenosis can be performed either by endarterectomy or reconstruction. Endarterectomy for atherosclerotic stenosis at the origin and proximal extracranial vertebral artery has been performed via a supravacuicular incision since the early 1960s, with variable success rates.
procedure is technically difficult, due to poor access to the vessel origin and many surgeons have resorted to clavicular osteotomy to improve this. Complications including lymphoceles, fistulas, vocal cord paralysis and pneumothorax are all well recognized. Similar problems with access exist for endarterectomy of intracranial vertebral artery stenosis, which usually involves a limited suboccipital craniotomy. Although a technically feasible operation, success rates are poor, and revascularization is the preferred surgical treatment in suitable cases.47,48

Reconstruction for extracranial vertebral artery stenosis involves transposition of the vertebral artery, usually to the common or internal carotid artery,46,49 but has also been reported with transposition to the subclavian and thyrocervical trunk arteries. Endarterectomy of the carotid or vertebral artery is often performed at the time of the transposition procedure. Results of 369 extracranial vertebral artery reconstructions (252 proximal, 117 distal) from Berguer’s group,46,50,51 found a low combined stroke and death rate for proximal reconstruction, of less than 2% and cumulative patency rates of 92% at 10 years follow-up. For distal extracranial vertebral artery reconstruction a combined stroke and death rate of approximately 6% and cumulative patency rates of 80% were found at 5 years, which is similar to that in standard extracranial carotid endarterectomy. Seventy percent of patients who had undergone distal extracranial vertebral artery reconstruction, however, were dead at 5-year follow-up, mainly from cardiac disease. Of the survivors, 97% were 'stroke-free' at similar follow-up. In addition, the complications of surgery were considerable, with an incidence of Horner’s syndrome of 10% following extracranial reconstruction and a similar frequency of post-operative lymphoceles. In distal vertebral artery reconstruction, thrombosis of the transposed vessel and a need for urgent vein grafting was seen in 11% of cases. Other series have described vocal cord paralysis and phrenic nerve injury as other notable complications.52 Transposition surgery for intracranial vertebral artery stenosis has also been reported, although the numbers of cases are less and the success rates not as high in terms of resolution of symptoms of vertebrobasilar ischaemia, while complications are higher.53,54

Endovascular treatment
Surgery has been performed less frequently in recent years for cases refractory to medical treatment. This is because there is now a growing literature of case series suggesting that endovascular intervention, with percutaneous transluminal angioplasty (PTA) and stenting, is a safe and effective treatment for extracranial vertebral artery atherosclerotic stenosis, especially at the vertebral artery origin.55–63 As the technique has evolved from coronary endovascular intervention, there has been a trend for treatment with expandable wall stents as a primary procedure (Figure 2). Some early reports where PTA alone was performed for VA origin stenosis were associated with a marked incidence of restenosis, comparable to that seen in PTA of ostial renal artery stenosis, partly due to vessel wall recoil.64,65 Restenosis rates between different series are difficult to compare, due to the differing techniques used to image the extracranial vertebral arteries during follow-up, both within and between series. From the coronary literature, there is some suggestion of improved rates of patency and restenosis in stented vessels, and also diminished rates of thromboembolism when stents are used.66,67 This reduction in thrombus formation and thromboembolism is thought to be due to a
protective layer of fibrous and neo-intimal tissue growing over the stent mesh and covering the atherogenic tissues of the vessel wall. A further advantage of primary stenting is a reduced rate of intimal dissection at the time of the procedure. To date, the series with primary deployment of stents to stenotic lesions of 50% or more in the extracranial vertebral arteries, have shown high levels of technical success of 98–100% in improving the angiographical appearance of the stenosis. There have been no major reported complications with the procedure: no intra-operative deaths and no strokes related to posterior circulation disease on current short-term (range 6–25 months) follow-up reports. The frequency of peri-operative posterior circulation TIA has been reported as being between 0 and 3%. However, these results are from series of selected cases, and data from randomized controlled trials are required. Until then, the use of such intervention is likely to remain largely experimental.

The same can be said of endovascular intervention for intracranial vertebral artery stenosis. The condition itself, which is frequently associated with concomitant basilar artery stenosis, carries a greater stroke risk than extracranial vertebral artery stenosis—some 17 times the expected stroke rate of a normal population matched for age and sex. However, intervention with PTA and stenting for such lesions has only been reported in isolated small case series of patients. Intracranial stenting as reported seems to be a more technically difficult procedure than endovascular extracranial intervention, and the balance of benefit and risk is more uncertain. Best treatment for intracranial vertebral artery stenosis remains controversial because of uncertainty about benefits of PTA and the lack of acceptable surgical alternatives, while optimal anti-thrombotic management for intracranial stenosis is also unclear. In practice, such intervention is only being recommended as for surgery, in selected cases in specialist centres, after ‘best’ medical treatment has failed.

Conclusion

Vertebral artery stenosis is an important aetiology of posterior circulation stroke. Improvements in non-invasive imaging are providing better anatomical information about vertebral artery occlusive disease. This should allow an improved understanding of the natural history of this disease process in terms of its liability to cause disabling stroke and death. Until the natural history is clearer, it is difficult to evaluate specific medical treatments and interventions fully, although endovascular intervention with primary stenting for extracranial vertebral artery stenosis is a promising potential treatment.

Acknowledgements

GC is a Clinical Research Fellow funded by the Stroke Association.

References

Vertebral artery stenosis


74. Chimowitz MI. Angioplasty or stenting is not appropriate as first-line treatment of intracranial stenosis. Arch Neurol 2001; 58:1690–2.