Internal carotid artery dissection

Internal carotid artery dissection is an important cause of ischaemic stroke in those aged under 50 years. Awareness of the clinical features is crucial as they may offer the opportunity to intervene to reduce strokes occurring or recurring.

Cervical artery dissection is an uncommon but important condition, with the clinical significance primarily reflecting an associated risk of ischaemic stroke. Delays in diagnosis and treatment may therefore result in significant morbidity and mortality. Cervical artery dissection may occur in the vertebral arteries, but most commonly occurs in the extracranial internal carotid arteries (Debette and Leys, 2009). This review focuses on the clinical features of internal carotid artery dissection as well as the current approaches to management.

Epidemiology

Carotid and vertebral artery dissection account for only 1–2% of ischaemic strokes, but they are disproportionately represented in adults under 50 years of age, accounting for 10–25% of strokes in this demographic (Schievink, 2001; Debette and Leys, 2009). Furthermore, the incidence is probably underreported, as cases presenting without localizing symptoms may remain undiagnosed (Lee et al, 2006; Debette and Leys, 2009). The incidence of internal carotid artery dissection in the USA is estimated to be 1.72 per 100 000 population per year (Lee et al, 2006). Internal carotid artery dissection may occur in any age group, but is most common in the fifth decade, with the mean age of occurrence estimated at 45.8 years (Lee et al, 2006).

Pathophysiology

What is the aetiology and mechanism of internal carotid artery dissection?

Internal carotid artery dissection occurs when a mural haematoma develops in the internal carotid artery, generally divided into spontaneous or traumatic aetiologies depending upon mechanism. The mural haematoma can develop secondary to an intimal tear, or following direct haemorrhage into the arterial wall from rupture of the vasa vasorum (Debette and Leys, 2009). Haematoma expansion may occur in the direction of the intima causing luminal narrowing, or along the direction of the adventitia, resulting in pseudoaneurysm formation (Lee et al, 2006). Local symptoms and signs of internal carotid artery dissection occur secondary to haematoma expansion and compression of local structures, including sympathetic and cranial nerve fibres (Debette and Leys, 2009).

The aetiology of internal carotid artery dissection is not fully understood, with several environmental and genetic factors implicated. It is likely that spontaneous internal carotid artery dissection occurs in individuals with a multifactorial genetic predisposition that results in a constitutional weakness in the arterial wall, which is exacerbated following exposure to an environmental trigger. Spontaneous dissections may be preceded by minor trauma, frequently involving hyperextension, rotation or lateroversion of the neck. Chiropractic manipulation, practising yoga, coughing, sneezing and whiplash injuries have all been implicated in internal carotid artery dissection (Caso et al, 2005). Associations with hyperhomocysteinaemia and migraine with aura have also been reported although the mechanisms of these are not clear (Blum and Yaghi, 2015).

There is some evidence to suggest that antecedent infection predisposes to cervical artery dissection via a mechanism independent of mechanical factors (such as sneezing and coughing), which may account for the observation that there is an increased incidence of dissection in the winter (Grau et al, 1999).

While it is likely that the genetic component of internal carotid artery dissection generally reflects a multifactorial predisposition to connective tissue disease and arteriopathy, cases associated with monogenic connective tissue disease (particularly vascular Ehlers–Danlos syndrome) have been reported (Brandt et al, 2001; Debette and Markus, 2009). One multicentre study demonstrated a correlation between recurrent cervical artery dissection and connective tissue abnormalities identified on electron microscopy of skin biopsies, despite an absence of other clinical manifestations of connective

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tissue disease, suggesting that dissection may occur as part of a systemic connective tissue defect (Brandt et al, 2001).

Traumatic dissections occur after major penetrating or non-penetrating trauma, such as road traffic accidents, and the risk is increased with accompanying traumatic injuries such as facial or basal skull fractures (Debette and Leys, 2009).

What is the mechanism of stroke in internal carotid artery dissection?

The vast majority of strokes associated with internal carotid artery dissection occur as a result of arterial-to-arterial thromboembolism arising from the dissected region, with most affecting the ipsilateral middle cerebral artery territory (Lucas et al, 1998; Molina et al, 2000; Benninger et al, 2004). Most of these strokes are cortical in nature, but a small proportion of patients develop lacunar infarcts, suggesting microembolism as a potential mechanism (Molina et al, 2000; Benninger et al, 2004). In contrast, approximately 5% of ischaemic strokes associated with carotid dissection occur at border zones between arterial territories, suggesting a haemodynamic mechanism in some cases (Lucas et al, 1998; Benninger et al, 2004). These border-zone infarcts may occur as a result of hypoperfusion, resulting from narrowing or occlusion of the dissected vessel, or occlusion of the ostium of a branch of the dissected vessel by the dissection flap (Blum and Yaghi, 2015).

Clinical features

Although ischaemic events such as stroke or transient ischaemic attacks may be the presenting feature of internal carotid artery dissection, there are usually preceding local symptoms (*Table 1*). Recognizing these symptoms is crucial, as it potentially allows treatment to be commenced before the development of stroke (Biousse et al, 1995). The characteristic triad of ipsilateral head, neck or face pain, partial Horner's syndrome, and subsequent cerebral (or retinal) ischaemia is infrequent, but the presence of two of these features is highly suspicious of internal carotid artery dissection (Schievink, 2001).

Table 1. Common clinical manifestations of internal carotid artery dissection

Headache
Neck pain
Eye, face or ear pain
Tinnitus
Horner's syndrome
Cranial nerve palsies (XII >XI >X)
Transient ischaemic attack
Ischaemic stroke

> **"The vast majority of strokes associated with internal carotid artery dissection occur as a result of arterial-to-arterial thromboembolism arising from the dissected region, with most affecting the ipsilateral middle cerebral artery territory"**

Local manifestations

Headache is common in internal carotid artery dissection, occurring in two thirds of cases, and is the main presenting manifestation in approximately half of all cases (Silbert et al, 1995; Schievink, 2001). It is thought to occur as a result of stimulation of pain receptors secondary to distension of the vessel wall by the mural haematoma (Debette and Leys, 2009). The headache is characteristically unilateral (ipsilateral to the dissected artery) predominantly affecting the frontotemporal area, and is most frequently described as throbbing in nature (Schievink, 2001; Debette and Leys, 2009). Onset is usually gradual, mimicking migraine, although sudden-onset 'thunderclap' headache can occur which warrants exclusion of subarachnoid haemorrhage. Neck pain occurs in a quarter of cases of internal carotid artery dissection, and this may be present in the absence of headache (Silbert et al, 1995). Pain may also be more localized, with some patients describing pain in the eye, face or ear without headache. Tinnitus is another common symptom, which may be pulsatile in nature (Biousse et al, 1995).

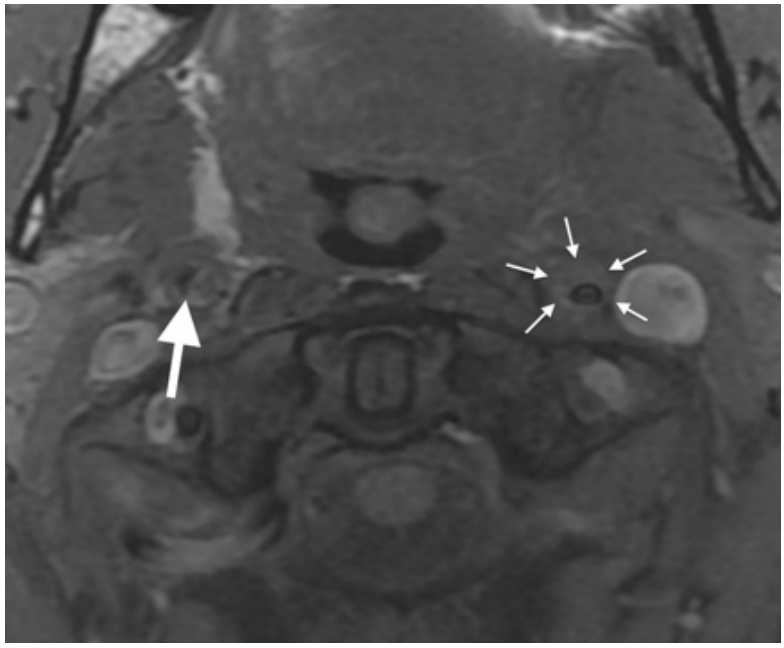
Horner's syndrome results from stretching of sympathetic fibres by the dissected internal carotid artery. Miosis and partial ptosis occur, but there is no anhidrosis as the sudomotor sympathetic fibres are found along the external carotid artery (Blum and Yaghi, 2015). When this occurs in association with headache, internal carotid artery dissection may mimic cluster headache (Silbert et al, 1995).

Occasionally, the enlarged carotid artery can result in a compressive neuropathy causing palsy of the lower cranial nerves. The hypoglossal nerve is the most frequently affected, followed by the glossopharyngeal and vagus nerves (reflecting the anatomical proximity to the internal carotid artery) (Schievink, 2001; Blum and Yaghi, 2015). Subarachnoid haemorrhage is a rare complication of internal carotid artery dissection, but may occur as a result of rupture of pseudoaneurysm complicating dissections of the intracranial portion of the artery (Debette and Leys, 2009).

Ischaemic events

The most clinically significant complication of internal carotid artery dissection is cerebral and retinal ischaemia. Completed stroke occurs in about half of patients (although estimates have been up to 95%) (Biousse et al, 1995; Schievink, 2001; Lee et al, 2006). The true incidence of stroke may be overestimated, with most

Figure 1. Axial fat-suppressed T1-weighted magnetic resonance imaging shows bilateral internal carotid artery dissections with narrowing the flow void of the right internal carotid artery (large arrows) and intramural haematoma (small arrows) surrounding the narrowed flow void of the left internal carotid artery.



studies recruiting patients from neurological or stroke centres, introducing bias towards the presence of stroke. Most completed strokes occur within the first week, but delayed stroke has been reported to occur up to 1 month later (Biousse et al, 1995). In about one third of patients, transient ischaemic attack or stroke is the inaugural manifestation (Biousse et al, 1995).

Estimates of the risk of recurrent stroke or transient ischaemic attack from internal carotid artery dissection varies from less than 1% to 15%, but the risk of recurrence is generally considered to be similar to that of symptomatic carotid stenosis (Biousse et al, 1995; Touze et al, 2003; Blum and Yaghi, 2015). The risk of recurrent stroke is greatest in the first weeks following the dissection (Touze et al, 2003).

Diagnosis and management

How is internal carotid artery dissection diagnosed?

Diagnosis of internal carotid artery dissection is based on a combination of clinical findings and radiological investigations. T1-weighted axial magnetic resonance imaging with fat suppression offers high sensitivity and specificity for detection of internal carotid artery dissection, and is considered the gold-standard diagnostic method. This allows for visualization of the mural haematoma, which manifests as a hyper-intense crescent around a narrowed lumen (*Figure 1*). This is often used in combination with magnetic resonance angiography (Provenzale, 2009).

Computed tomography angiography may be used when magnetic resonance imaging is contraindicated or unavailable, and may reveal a double lumen sign or a tapered narrowing of the dissected vessel, often said to resemble a flame (Provenzale, 2009). Ultrasonography with a combination of colour duplex and Doppler imaging offers a non-invasive technique for assessing internal carotid artery dissection, although operator dependency and poor sensitivity for intracranial dissections or those located at the base of the skull means that it should only be used as a screening method, with confirmation by computed tomography or magnetic resonance angiography.

What is the medical management of internal carotid artery dissection?

The optimal treatment strategy in internal carotid artery dissection remains a subject of debate, and current practice varies between centres, although recent studies have helped inform the decision between antiplatelet or anticoagulant management. A randomized feasibility study comparing the efficacy and safety of anticoagulation (unfractionated heparin or low-molecular weight heparin followed by warfarin) and antiplatelet agents (one or a combination of aspirin, dipyridamole or clopidogrel) found no significant difference between the two approaches, with 2% of the antiplatelet group and 1% in the anticoagulation group experiencing subsequent ipsilateral stroke or death (odds ratio 0.335, confidence intervals 0.006–4.233, P=0.63) (Markus et al, 2015). Adverse event rates in this study were low with one report of major bleeding (subarachnoid haemorrhage) and two of minor bleeding in the anticoagulation group, and no bleeding events in the antiplatelet group. There is a theoretical possibility that anticoagulation carries a greater risk of mural haematoma expansion and recurrent dissection, but this has not been shown to be clinically significant (Machet et al, 2013).

Because recurrence of ischaemic events is an infrequent occurrence, any definitive study into the relative efficacy of anticoagulation or antiplatelet regimens will need to have a very large study population. In the absence of definitive evidence for the optimal treatment strategy, decisions must be made on a case-by-case basis. In large strokes antiplatelet agents may be favoured to avoid the risk of haemorrhagic transformation associated with anticoagulation. Likewise, in cases of intracranial arterial dissection, when pseudoaneurysm formation may be complicated by subarachnoid haemorrhage, antiplatelet agents may be preferred. Conversely, anticoagulation may be preferred if a thrombus is detected in the arterial lumen, or if there are multiple embolic infarcts ipsilateral to the dissected vessel (Engelter et al, 2007).

Anticoagulation is usually continued for 6 months, although optimal treatment duration has not been established. This is often followed by secondary prevention with antiplatelet agents in the long term (Debette and Leys, 2009).

Acute stroke in the setting of internal carotid artery dissection is managed in the same manner as acute

ischaemic stroke of other aetiology. Although there is a theoretical risk that thrombolysis with recombinant tissue plasminogen activator may increase the mural haematoma, it is generally considered safe in internal carotid artery dissection, and should not be withheld unless there is another contraindication (Georgiadis et al, 2006). As with other aetiologies of ischaemic stroke, optimization of the cardiovascular risk profile is also important with use of cholesterol-lowering agents, and blood pressure and glycaemic control as indicated.

Is there a role for endovascular treatment in internal carotid artery dissection?

Endovascular treatment with stent placement has been used in some cases of acute ischaemic stroke complicating spontaneous and traumatic internal carotid artery dissection, with some studies suggesting that clinical outcomes and safety are comparable to those of thrombolytic therapy (Haussen et al, 2016). It is also important to consider a possible false lumen resulting from the dissection and the risk this may pose with intra-arterial catheter insertion. However, experience in this area is limited and it is unclear in which patients endovascular therapy would be of benefit, so further studies are necessary before this is recommended above optimal medical treatment.

Conclusions

Internal carotid artery dissection is an important condition to diagnose and treat, as it carries a high risk of completed ischaemic stroke. It is important to have a high index of suspicion for internal carotid artery dissection when cerebral or retinal ischaemic events occur in young patients, or in any stroke accompanied by headache, neck or face pain or Horner's syndrome. Radiological diagnosis is best made with T1-weighted magnetic resonance imaging with fat suppression, accompanied by magnetic resonance angiography, although computed tomography angiography may also be used. The optimal treatment strategy is yet to be established, and the choice of antiplatelet or anticoagulation therapy should be made on a case-by-case basis. **BJHM**

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KEY POINTS

- Internal carotid artery dissection is an important cause of ischaemic stroke, particularly in individuals below 50 years of age.
- Ischaemic stroke typically occurs as a result of thromboembolism.
- Clinical features preceding ischaemic stroke may include headache, neck pain, and localized compressive effects leading to Horner's syndrome.
- T1-weighted axial magnetic resonance imaging with fat suppression is the imaging modality of choice to confirm dissection.
- There is currently equipoise between antiplatelet and anticoagulant therapy in dissection, although features including presence of thrombus or size of infarct may influence the decision.

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