Fatal intracranial arterial dissection: clinical pathological correlation

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SUMMARY The clinical pathological features of fatal arterial dissection confined to the intracranial vessels are described. Three patients with anterior circulation dissections presented with focal ischaemic neurological deficits and pathological examination of involved vessels revealed a dissection plane between internal elastic lamina and media accompanied by intravascular thrombosis. Three of four patients with posterior circulation dissections had clinical pathological features of subarachnoid haemorrhage and at necropsy had transmural dissections. In contrast to previous reports, primary vasculopathies either degenerative or inflammatory were not identified in affected vessels. The pathogenesis of intracranial arterial dissection is discussed and the clinical features are correlated with the pathological abnormalities.

Spontaneous dissection of the intracranial vessels leading to stenosis or occlusion of the vessel lumen has been recognised with increasing frequency as an important cause of focal ischaemic neurological disease.1-3 In contrast, until recently little attention has been focused on spontaneous intracranial arterial dissection as a cause of subarachnoid haemorrhage.4-9 Though the clinical137 and radiological236 features of intracranial arterial dissection have been described in detail, pathological reports are infrequent, lack detailed description610-13 and have perhaps over-emphasised the importance of unusual vasculopathies.214-16 The association of an uncommon arterial disease with an uncommon vascular event may in many instances be the actual reason for reporting the case, a pathologist or clinician being less likely to report cases of dissection where a recognisable pathological cause is not identified.17 Furthermore, as a consequence of major anatomical differences18 between the intracranial and extracranial vasculature, certain vasculopathies which have a predilection for large diameter vessels are unlikely to involve the medium and small diameter intracranial vessels.

Detailed pathological study of seven consecutive cases of fatal arterial dissection confined to the intracranial circulation was performed to establish whether or not there was an associated primary vasculopathy and to determine pathological correlates of stroke and subarachnoid haemorrhage, the two principal clinical manifestations of intracranial arterial dissection.

Patients and methods

Seven consecutive cases (1972–1983) of intracranial arterial dissection were retrieved from the neuropathology necropsy files at the University of Western Ontario teaching hospitals. At necropsy the cervical carotid and/or vertebral arteries were removed, brains had been fixed in 20% formaldehyde for a minimum seven days. The circle of Willis and its major branches were dissected off the brain after fixation. Following paraffin impregnation but before blocking individual arterial branches were sectioned at 3 mm intervals and embedded on end. Affected vessels were sectioned through the involved area at 100 μ intervals. All sections were stained with haematoxylin and eosin, PAS, Masson Trichome, Reticulin, Movats, Elastic-Van Gieson and some with Alcian Blue. The clinical and pathological findings are summarised in the table.

Case 1 Clinical data A 63-year-old previously hypertensive male developed sudden severe posterior neck pain walking up a steep incline. The pain initially decreased in intensity and a neurological examination one hour later was normal with no nuchal rigidity. Two hours later while walking down-
stairs, severe neck pain recurred and within minutes the patient was completely unresponsive with absent oculocephalic, oculovestibular, gag and corneal reflexes. The blood pressure was 230/120 mm Hg. The neck was supple and there were bilateral subhyaloid haemorrhages. Death occurred 48 hours after the onset of neck pain.

**Neuropathology** There was bi-hemispheric swelling with massive basal subarachnoid haemorrhage. The arachnoid was incised and following removal of blood a fusiform dilatation of the right vertebral artery with intramural haemorrhage was noted (fig 1). The remaining cerebral vessels were normal. Microscopy showed a crescent-shaped haematoma extending transmurally from the lumen through the adventitia destroying the internal elastic lamina and media and causing a 50% reduction in vessel calibre (fig 2). A mild acute inflammatory cell infiltrate was present along the adventitial surface. There was no evidence of a primary medial or internal elastic lamina defect at the origin of the dissection or in the remainder of the right vertebral artery or other intracerebral vessels.

**Case 2**

**Clinical data** A 48-year-old previously well, normotensive female had a two-week history of severe intractable occipital headache, aggravated by coughing. This was most severe in the morning and was associated with vomiting, blurred vision, dysarthria, episodic weakness and sensory impairment of the right arm and two days before admission, a left facial palsy. Positive findings on examination included reduced pain sensation in the V1, V2 and V3 distribution on the left, a diminished left corneal reflex, a left central facial palsy, a mild right upper monoparesis and diminished pain sensation in the left extremities. Gait was broad based and ataxic and the patient was unable to sit without support. Computed tomography did not show intracerebral haemorrhage. The patient was heparinised. Twenty hours later she was unconscious with decerebrate posturing and absent oculocephalic and oculovestibular reflexes and she died four hours later.

**Neuropathology** There was extensive recent infarction of the right basis pontis and right superior cerebellar peduncle. At the level of the middle cerebellar peduncles, virtually all of the basis pontis, an extensive area of the right cerebellar hemisphere and a small area of white matter in the left cerebellar hemisphere were infarcted. Both occipital lobes and the right thalamus showed foci of recent haemorrhagic infarction. There was an area of old (3–4 weeks) infarction in the left occipital lobe. The rest of the brain and the spinal cord were normal. The anterior circulation vessels were patent, free of thrombus and did not show atheroma. The basilar artery was mildly dilated and occluded from the origin of the anterior inferior cerebellar arteries to the bifurcation. In addition the proximal segments of both posterior cerebral arteries and both superior cerebellar arteries were occluded (fig 3). Microscopy demonstrated complete occlusion of the mid-basilar segment by an organising haematoma. A dissection plane extended between internal elastic lamina and media and an area of haemorrhage denoted the origin of the dissection site. Occasional internal elastic lamina gap defects were noted close to the dissection site but the remaining cerebral vessels were unremarkable.

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**Table 1** Fatal Intracranial dissection; summary-clinico-pathological features

<table>
<thead>
<tr>
<th>Case No</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Contributory factors</th>
<th>Clinical presentation</th>
<th>Artery</th>
<th>Subarachnoid haemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>63/M</td>
<td>Vigorous walk</td>
<td>Neck pain</td>
<td>Vertebral (R)</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>48/F</td>
<td>Heparin</td>
<td>Occipital headache</td>
<td>Basilar</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>46/F</td>
<td>—</td>
<td>Occipital headache</td>
<td>Basilar</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>38/F</td>
<td>Tug of war</td>
<td>Collapse</td>
<td>Carotid (L)</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>20/M</td>
<td>Cerebral trauma</td>
<td>Hemiplegia</td>
<td>Carotid (R)</td>
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<td></td>
</tr>
<tr>
<td>6</td>
<td>31/F</td>
<td>Raking leaves</td>
<td>Hemiplegia</td>
<td>Carotid (R)</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>18/M</td>
<td>Cerebral trauma</td>
<td>Hemiplegia</td>
<td>Carotid (R)</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

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**Fig 1** Schematic representation of vascular territory involved by dissection. Area A is shown in fig 2. (Circle viewed from below)
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**Case 3**

**Clinical data** A 46-year-old mildly hypertensive (170/90 mm Hg) female developed sudden severe occipital headache associated with a right hemiparesis and dysarthria six weeks prior to death. The CSF was bloody and angiography demonstrated basilar trunk narrowing with an atypical mid-segment berry aneurysm. Over the following seven days the hemiparesis gradually improved, there was no recurrence of headache and apart from horizontal diplopia and a right central facial nerve palsy, the patient was well.

**Neurosurgical findings** At operation 39 days later a left temporal bone flap was reflected and the tentorium divided to expose the basilar artery. A fusiform red-purple swelling extended along the basilar artery from the origin of the anterior inferior cerebellar artery to the superior cerebellar artery and was recognised as a dissection. The affected basilar artery segment was mobilised and wrapped with cotton gauze. Post-operatively the only deficit was a mild right hemiparesis. However, on the third post-operative day, the patient became unconscious with fixed dilated pupils and absent brain stem reflexes. She died on the sixth post-operative day.

**Neuropathology** The immediate cause of death was brain stem compression caused by haemorrhagic venous infarction of the left temporal lobe, secondary to thrombotic occlusion of the anastomotic vein of Labbé with superim-
posed diffuse ischaemic encephalopathy. An old, (4–5 weeks) 1 cm diameter area of cystic infarction was present in the left basis pontis. The basal meninges showed extensive haemosiderin staining. When the surgical gauze was removed, a 5 mm long segment of ecchymosis was noted to involve the mid-basilar trunk (fig 4). Microscopy showed a transmural dissection plane extending from the lumen through the internal elastic lamina and media to the adventitia with, in addition, rostral and caudal extension (figs 5, 6). In the caudal segment, the dissection doubled back creating the false impression of two distinct dissection zones. The media showed moderate to severe myofibroblast proliferation (fig 7) but this change was confined to the immediate vicinity of the dissection plane and was not seen in the unaffected segments of the basilar artery or in any of the remaining cerebral vessels. The cleavage plane was patent and free of thrombus. Occasional foci of intramural haemosiderin deposition were observed. The basilar internal elastic lamina showed occasional small gap defects (fig 8) close to and remote from the point of origin of the dissection. There was no evidence of either atheroma or other primary vasculopathy involving any of the remaining cerebral vessels.

Case 4
Clinical data A 38-year-old previously well normotensive mother of four while standing quietly in her kitchen suddenly cried out, fell to the ground and was noted to have flexed arms, extended legs, and absence of speech. One hour later in hospital the patient opened her eyes in response to commands but shortly thereafter showed a rapidly deteriorating level of consciousness progressing to complete unresponsiveness. Computed axial tomography demonstrated mid-brain and pontine infarction. There was no improvement and death occurred eleven days following onset of symptoms.

Neuropathology Extensive subarachnoid blood clot was dissected off the ventral surface of the brain stem to expose a fusiformly enlarged and echymotic basilar artery. Bilateral tonsillar herniation was accompanied by upward transtentorial mid-brain herniation. There was extensive haemorrhagic infarction of the left crus cerebri and substantia nigra with more diffuse haemorrhagic infarction of the basis pontis and pontine tegmentum bilaterally. The haemorrhage extended into and completely obliterated the fourth ventricle. Furthermore, the patency of the cerebral aqueduct was severely compromised by the oedematous and infarcted mid-brain. There was moderate dilatation of both lateral ventricles. Microscopy showed obliteration of the basilar lumen (fig 9) by an organising haematoma which extended transmurally through the internal elastic lamina and media to the adventitia where it was continuous with the subarachnoid haemorrhage. A light acute inflammatory cell infiltrate was present in the adventitia.
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Fig 6 Composite photomicrograph showing origin of dissection (A), extensive myofibroblast proliferation surrounding patent false lumen (B) and large organised intramural haematoma extending to adventitia (arrow) (C). Elastic Van Gieson (A, C) Haematoxylin/eosin (B).
adjacent to the dissection site. A small atheromatous plaque was noted at the origin of the dissection. In the distal basilar segment, the dissection plane involved only the innermost media. The remaining cerebral vessels were normal.

Case 5
Clinical data A 20-year-old male collapsed during a tug-of-war game and was noted to have a right-sided weakness. One hour later he was drowsy but responsive with sensory dysphasia and a dense right hemiplegia. The blood pressure was 150/90 mm Hg and the pulse 100 per minute and regular. Four hours later he became more drowsy with dilated and poorly responsive left pupil but improved following mannitol infusion. On the third hospital day however he showed a decreased level of consciousness, a dilated and unresponsive left pupil and bilateral papilloedema. Twenty-four hours later cardiac arrest occurred and resuscitation was unsuccessful.

Neuropathology The brain showed marked bithemispheric swelling greater on the left side where, in addition, there was uncal herniation. There was an extensive area of infarction in the distribution of the left middle and anterior cerebral arteries involving the frontoparietal region and extending medially to involve the basal ganglia. Secondary mid-brain and pontine haemorrhages were present. The entire right internal carotid, both vertebral and the left cervical carotid arteries were patent but the left intracranial carotid artery was completely occluded from the distal intracavernous segment through the bifurcation, into the A1 and M1 segments of the anterior and middle cerebral arteries respectively (fig 10). Microscopic examination of multiple segments of the occluded area showed a dissecting haematoma between the media and internal elastic lamina which forced the internal elastic lamina into the lumen (fig 11) thereby severely compromising the patency of the supraclinoid segment; a large intimal/inal elastic lamina tear identified the origin of the dissection. Although the haematoma diminished in size distally the terminal segment of the left internal carotid artery and proximal A1 and M1 segments were occluded by thrombus. There was no evidence of atheroma or other primary medial or internal elastic lamina disease in these or in matched contralateral intracerebral vessels.

Case 6
Clinical data A 31-year-old female while raking leaves suddenly developed severe right-sided headache associated with left sided weakness and repeated clonic move-
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Figure 10  Schematic representation of internal carotid artery dissection in longitudinal and cross section. Origin of dissection (A) is shown in fig 11. (Circle viewed from below)

Figure 11  Coiled interrupted end of internal elastic lamina at origin of dissection lying free within vessel lumen. Elastic Van Gieson.

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Patient 5

by continuous oral estrogen therapy. Twenty-four hours after admission the patient became more drowsy with an enlarging, poorly responsive right pupil, did not improve following dexamethasone and mannitol and died 72 hours after the onset of headache.

Neuropathology  The immediate cause of death was massive, recent, bland hemispheric infarction in the distribution of the right internal carotid artery with uncal herniation and secondary mid-brain haemorrhages. There was occlusion of the ipsilateral internal carotid artery extending from the supraclinoid segment through the bifurcation to involve the A1 and M1 segments (fig 12). The cervical and cavernous segments were normal as were the remaining cerebral vessels. Microscopy showed vascular occlusion of varying severity by a partly organised dissecting haematoma which extended between internal elastic lamina and media (fig 13), forcing the internal elastic lamina into the vessel lumen. The origin of the dissection was identified in the distal carotid segment where the haematoma communicated freely with the lumen through a large intimal/elastic tear. There was no evidence of atheroma or other primary vasculopathy in the affected or other intracranial arteries.

Case 7

Clinical data  An 18-year-old previously well male suffered severe thoracoabdominal trauma during a motor vehicle accident but was neurologically intact when examined both before and after surgical evacuation of large retroperitoneal and pelvic haematomas. However, twenty

Fig 12  Schematic representation of internal carotid artery dissection showing origin of dissection (A) and intramural haematoma (B) which tapers distally (C) and (D). (Circle viewed from below)
hours after admission he demonstrated a mild left hemiparesis and an enlarging right pupil, both improving following mannitol infusion. Angiography failed to demonstrate filling of the right internal carotid artery beyond the syphon. Fourteen hours later the patient's level of consciousness deteriorated, the right pupil was dilated and unresponsive and there was decerebrate posturing of the left extremities. Death occurred two hours later.

Neuropathology There were bilateral smear-type subdural haematomas over both cerebral convexities. The immediate cause of death was massive recent, bland, hemispheric infarction in distribution of the right middle cerebral artery with associated sub-falcal and uncal herniations and secondary brain stem haemorrhages. The cervical segment of the right internal carotid artery showed adventitial haemorrhage related to direct arterial puncture during angiography but the lumen was not compromised. The intima displayed occasional fatty streaks but was otherwise normal. The internal carotid artery was occluded from the syphon distally through the bifurcation into the proximal A1 and M1 arterial segments (fig 14). Microscopy showed complete occlusion of the aforementioned vessels by thrombus. The adventitia and media of the supraclinoid carotid segment were extensively infiltrated by polymorphonuclear leucocytes and also showed loss of the intima and internal elastic lamina over a wide area with the lateral margins of the intact internal elastic lamina rolled back into the lumen. The occluding haematoma was intimately associated with the medial inflammatory exudate at the dissection origin. The remainder of the circle of Willis was unremarkable and in particular no defects were noted in the internal elastic lamina nor was there evidence of atheroma or a primary vasculopathy.

Discussion

The clinical features of the seven patients are fairly typical, reflecting a younger at-risk population (mean age of 37-7 years) though the slight excess of females is contrary to the cumulative experience. Headache or neck pain was present in four patients and showed regional localisation to the area of the involved vessel, a finding similar to that reported by others; the pain is usually attributed to stretching of pain sensitive nerve fibres in the affected vessel. Of interest, in some patients the pain may precede the onset of stroke or haemorrhage by several days suggesting early non-occlusive dissection. The finding of focal intramural haemosiderin (case 3) is suggestive of previous intramural haemorrhage or dissection.

The clear separation of patients into two groups based on the clinical presentation of a focal ischaemic event (cases 5, 6, 7) and subarachnoid haemorrhage (cases 1, 3, 4) reflects the underlying vascular pathology. In the first group the dissection plane lay between the internal elastic lamina and media, a dissecting haematoma of variable age pushed the elastic lamina into the lumen where occlusion was usually completed by superimposed thrombosis. An intimal/elastic lamina tear was
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always demonstrable but required extensive serial sectioning of the affected vessel. In the second group, when subarachnoid haemorrhage was the primary manifestation of intracranial dissection, the cleavage plane extended transmurally from the lumen through intima, elastic lamina and media to the adventitia. This finding contrasts with previous reports which have suggested that the dissection plane lies within media or adventitia,\textsuperscript{7,21} does not communicate with the lumen\textsuperscript{7,10,19,20} and that subarachnoid haemorrhage originates from vasa vasorum or from areas of neovascularisation which have developed in response to medial necrosis.\textsuperscript{22} It is generally accepted that intracranial vessels do not have vasa vasorum\textsuperscript{18} and furthermore it is extremely unlikely that haemorrhage from small low pressure adventitial vessels could cause extrinsic compression and partial obliteration of a high pressure, large diameter intracranial vessel such as the basilar\textsuperscript{23} or vertebral artery (cases 2, 4). We believe that all intracranial dissecting haematomas originate within the vessel lumen and extend through intima and elastic lamina into media for a variable distance. The subsequent course of the dissection is determined by several factors which may include systolic blood pressure, vessel location and presence of underlying vascular disease. It is noteworthy that all anterior circulation dissections (cases 5, 6 and 7) presented with focal ischaemic events whereas three (cases 1, 3 and 4) of four posterior circulation dissections had subarachnoid haemorrhage strongly suggesting a role for local anatomical factors in determining the transmural extent of the dissection. Review of reported cases of dissection causing subarachnoid haemorrhage shows similar findings with approximately 80% involvement of the posterior circulation vessels.\textsuperscript{6}

Controversy exists concerning the nature and frequency of underlying vasculopathies which would predispose the intracranial vasculature to dissection. A wide variety of diseases including atherosclerosis,\textsuperscript{9} fibromuscular dysplasia,\textsuperscript{16,24} cystic medial necrosis,\textsuperscript{20} intimal fibroelastic aberrations\textsuperscript{24,4} and moyamoya disease\textsuperscript{11,14,25} have clearly been responsible for dissection in some well documented instances. We were unable in an unselected consecutive necropsy series to provide conclusive evidence of an associated vasculopathy. Others have shown a similar absence of underlying vascular disease in spite of careful and detailed examination.\textsuperscript{7,19,20,22,23,26,27} Our series though small lacks the bias inherent in isolated case reports and compiled case reports published as review articles.\textsuperscript{1} Some of the published photomicrographs purporting to show fibromuscular dysplasia\textsuperscript{24} are unconvincing and more likely represent partial healing of the involved vessel characterised by florid myofibroblast proliferation. Such changes were observed in case 3 and the diagnosis of fibromuscular dysplasia was briefly entertained but the myofibroblast proliferation was confined to the immediate area of dissection, was not apparent remote from the dissection site and was not seen in other intracranial vessels. Furthermore, the long interval (39 days) from onset of symptoms to death clearly points towards healing with attempted resolution as the most likely explanation for the observed change.

In the absence of a primary vasculopathy it has been suggested\textsuperscript{4} that dissection might arise as a result of vessel wall weakening due to congenital gap defects in the internal elastic lamina. A careful biophysical analysis\textsuperscript{28} of the size and distribution of elastic lamina gap defects in intracranial vessels has shown that over 80% of normal vessels contain round or ellipsoid defects of which almost 50% may be enlarged. Furthermore, enlargement of the fenestrations is accompanied by a reduced ligament efficiency whereby the intervening intact elastic tissue has to bear an increased load resulting in increased stress per unit area and leading to further elastic degeneration. Gap defects were noted in patients 2 and 3 and may have contributed to the progression of dissection but whether isolated gap defects alone are sufficient to initiate dissection especially given their very high frequency and the relative rarity of intracranial dissection is unknown.

It is difficult to ignore the temporal relationship of dissection to physical exercise\textsuperscript{5,10,25,29,30} and it is tempting to speculate that perhaps a transient rise in cerebral perfusion pressure during severe physical stress accompanied by a minor defect in the elastic lamina could initiate dissection which as already mentioned would then extend for a variable distance through the vessel wall or perhaps even remain undiagnosed and heal spontaneously. Although spontaneous resolution of dissection has been documented infrequently,\textsuperscript{20,26} and case 5 of Drake \textit{et al.},\textsuperscript{6} it is possible that non-occlusive subclinical dissection is more common that hitherto realised.

Trauma, either direct to the cervical carotid artery or in association with cervical manipulation is a common cause of extracranial arterial dissection and though uncommonly associated with intracranial arterial dissection is being recognised with increasing frequency, particularly in the posterior fossa where relatively minor trauma to the skull base or neck may produce massive basal subarachnoid haemorrhage.\textsuperscript{31} However, it is difficult to determine from the reported cases whether the involved vessels have undergone traumatic laceration, traumatic dissection or both. Similarly, traumatic anterior circulation dissection\textsuperscript{2,14,25,32,33} may follow a relatively mild
head injury and frequently there is a delay of several hours before symptoms are manifest.
Pathological examination usually reveals subintimal dissection involving the supraclinoid carotid segment and extending for a variable distance into the middle cerebral artery, the most likely mechanism of dissection involving acceleration induced shear forces between the mobile supraclinoid and fixed intracavernous segments. Occasionally the involved vessel may reveal evidence of a vasculopathy.

Although anticoagulation is recommended in the management of intracranial dissection it is noteworthy that case 2 in our series, case 7 of Drake’s series and one other other case showed clinical deterioration following heparinisation. We were unable to define the pathological correlate of our patients’ deterioration but there was no evidence of subarachnoid haemorrhage or haemorrhagic infarction. It is possible that a small area of mural haemorrhage noted at the dissection site compromised an already severely stenosed but still patent lumen. Hochberg’s patient developed a haematoma within a large haemorrhagic infarct whilst Drake’s patient refused further investigation. Surgery is clearly the treatment of choice for posterior fossa dissections and in the absence of any evidence implicating anticoagulants in the progression of the dissection itself, conservative management with anticoagulants is still the recommended treatment.

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