Basilar artery aneurysm with autonomic features: an interesting pathophysiological problem

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Abstract
Unruptured cerebral aneurysms often present with neuro-ophthalmological symptoms but ocular autonomic involvement from an aneurysm of the posterior circulation has not previously been reported. A patient is described with a basilar artery aneurysm presenting with headache and unilateral autonomic symptoms. After angiographic coiling of the aneurysm there was a near complete resolution of these features. The relevant anatomy and proposed mechanism of autonomic involvement of what may be considered—from a pathophysiological perspective as a secondary trigeminal-autonomic cephalgia—is discussed (J Neurol Neurosurg Psychiatry 2001;71:805–808)

Keywords: trigeminal autonomic cephalgia; cluster headache; trigeminovascular system

Although the most common presentation of a cerebral aneurysm is with subarachnoid haemorrhage, unruptured cerebral aneurysms may present with headache or other symptoms, in particular neuro-ophthalmological features. These usually large, symptomatic aneurysms are important to detect as, unlike small (<10 mm) aneurysms, which have an annual rupture rate of 0.05%, those with a diameter greater than 25 mm have an annual rupture rate of 6%.1,2 The neuro-ophthalmological features depend on the size and location of the aneurysm relative to the visual pathways and other cranial nerves.1 However, autonomic features from a basilar artery aneurysm have not previously been described and have some interesting physiological implications for the trigeminal-autonomic syndromes.

Case report
A 61 year old woman presented with a 30 month history of a left sided headache. The headache started suddenly, was localised above the left eye and radiated occipitally, occurring for 3 to 14 days each month but with a residual background pain. For the year before presentation the pain had become daily, associated with left nasal stuffiness, tearing and reddening of the eye, and drooping of the eyelid. She had noticed blurring of vision in the left eye for 4 months. Compound analgesics, ergotamine with caffeine, and 50 mg amitriptyline at night had not relieved the pain.

She had a medical history of hypertension controlled on enalapril. Her mother had had headaches but the patient had no personal history of headaches. On examination there was a left sided ptosis, conjunctival injection, and lacrimation (fig 1). Direct and consensual pupillary responses to light and the accommodation reflex were normal. Pupillography was not performed. External ocular movements were normal with no diplopia. Fundoscopy was normal. She had no other neurological signs apart from a mild, long standing “no-no” head tremor. Her blood pressure was 120/80. Brain CT without contrast showed a large basilar artery aneurysm (fig 2) the location of which was confirmed on CT angiography as lying between the left superior cerebellar artery and the left posterior cerebral artery (fig 3). The aneurysm was successfully occluded with angiographic coil embolisation. By day 5 after embolisation the lacrimation, nasal stuffiness, and conjunctival injection had resolved, the

Figure 1 Patient before embolisation showing left sided ptosis (with permission).
blurred vision and headache improved but ptosis persisted. Three months after embolisation she had only infrequent mild daily headache and the ptosis was less than on initial presentation. A repeat angiogram showed some compaction of the coils but an increase in the size of the neck compared with the previous angiogram. It is planned to repeat the angiogram at intervals in the future.

Discussion
We describe a patient who presented with headache in association with cranial autonomic symptoms manifested clinically by nasal stuffiness, lacrimation and conjunctival injection (parasympathetic activation), and ptosis (sympathetic inactivation). We consider these symptoms to be secondary to the basilar artery aneurysm because there are anatomical pathways that would explain these features, and symptoms improved after coiling of the aneurysm.

This combination of autonomic features, which may also include rhinorrhea, forehead and facial sweating, meiosis, and eyelid oedema, are prominent in some primary headache disorders, the pain of which is mediated via the trigeminovascular system. These disorders include cluster headache, paroxysmal hemiantria and SUNCT (short lasting neuralgiform headache with conjunctival injection and tearing) syndrome, which may be collectively described as trigeminal autonomic cephalgias. A lesser degree of parasympathetic activation is not uncommonly seen in migraine and may be accompanied by cranial release of vasoactive intestinal polypeptide (VIP). However, autonomic activation from structures supplied by C1/C2 has only rarely been described in humans and presents an interesting pathophysiological challenge in terms of explaining the mechanisms at work in this patient’s clinical presentation.

The sensory innervation of the pain producing intracranial vascular structures of the forebrain is by trigeminal nerve afferents whereas those below the tentorium cerebelleri are innervated mainly by branches of the C2 dorsal root. Trigeminal nerve afferents relay via the trigeminal nucleus caudalis in the caudal medulla and in neurons of the dorsal horns at C1 and C2, the trigeminocervical complex. Efferents from the trigeminocervical complex synapse in the superior salivatory nucleus. Stimulation of these pain producing structures in experimental animals leads to c-fos expression, activation of neurons, in the superior salivatory nucleus. Parasympathetic fibres pass from the superior salivatory nucleus via the greater petrosal nerve component of the facial nerve to the sphenopalatine ganglion to mediate the parasympathetic features associated with trigeminally mediated pain. Efferent nitric oxide and VIP containing fibres from the sphenopalatine ganglion also produce vasodilation of both cerebral and extracerebral arteries, including the meningeal arteries that are served by trigeminal afferents. These connections complete a positive feedback loop for the exacerbation of vasodilatation and pain in primary headache disorders—the trigeminovascular reflex. In addition, parasympathetic mediated vasodilatation of the internal carotid artery may injure the surrounding plexus of sympathetic fibres en route to the eye and forehead. Thus trigeminal activation can cause simultaneous parasympathetic activation and sympathetic inactivation, probably accounting for the autonomic features seen in the trigeminal autonomic cephalgias.

How might cervical inputs entrain cranial parasympathetic neurons? Indeed, there have been previous reports of structures with a cervical innervation—for instance, lesions produced from the lateral medullary syndrome, to trigger headache syndromes with cranial autonomic symptoms similar to cluster headache. This can be explained by convergence of afferent trigeminal and C2 afferents at the level of the trigeminocervical complex. In experimental animals stimulation of structures innervated by the trigeminal nerve, such as the superior sagittal sinus and middle meningeal

![Figure 2](image2.png) **Figure 2** CT without contrast showing the large aneurysm of the basilar artery.

![Figure 3](image3.png) **Figure 3** Pre-embolisation CT angiogram showing aneurysm lying between superior cerebellar artery and posterior cerebral artery.
Basilar artery aneurysm with autonomic features

artery, activates neurons in the trigeminocephalic complex. Similarly, stimulation of the greater occipital nerve, a branch of C2, leads to activation of neurons in the very same regions. It has also been shown that stimulation of the greater occipital nerve in rats leads to ipsilateral conjunctival injection, tearing, and ptosis in one third of animals. Thus an anatomical pathway exists whereby C2 activation may trigger efferent neurons from the trigeminocephalic complex, including those to the superior salivatory nucleus that mediate parasympathetic activity.

Neuro-ophthalmological symptoms from intracranial aneurysms are many and varied, depending on anatomical site and size and include visual loss, diplopia from III or VI nerve palsies, Horner’s syndrome, and symptoms from midbrain or pontine involvement. Visual loss may be caused by compressive injury to the optic nerve or chiasm from aneurysms of the anterior communicating, or the supraclinoid carotid artery. Diplopia is most commonly caused by a third nerve palsy from a posterior communicating artery aneurysm, but can also be caused by third nerve compression from cavernous, carotid, or basilar artery aneurysms or, more rarely, by sixth nerve compression of a vertebral artery aneurysm. Although we report sympathetic inactivation from a basilar aneurysm, Horner’s syndrome is usually caused by aneurysms of the carotid cavernous artery compressing the sympathetic nerve on its course through the cavernous sinus. Rarely, giant basilar bifurcation aneurysms or large mid-basilar aneurysms may compress the midbrain and pons causing neuro-ophthalmological signs including sixth nerve palsies, horizontal gaze paresis, skew deviation, internuclear ophthalmoplegia, lid retraction, and nystagmus typically in association with long tract brain stem signs such as hemiparesis or alterations in consciousness. Symptoms may also accrue from thrombus in a midbasilar aneurysm obstructing flow resulting in local pontine ischaemia. Thromboembolic disease may also result in widespread posterior circulation ischaemia, the top of the basilar syndrome, causing abnormalities of convergence and vertical gaze, skew deviation, visual field defects, visual hallucinations, amnesia, and delirium.

The patient we describe had both head pain and features of parasympathetic activation and sympathetic impairment that we consider to be secondary to the aneurysm. We consider that her ptosis was secondary to sympathetic dysfunction rather than from third nerve compression because of the lack of diplopia and pupillary dilatation that would be typical of third nerve palsy. She did not show miosis that would be typical of sympathetic dysfunction but this would be in keeping with primary trigeminal autonomic cephalgia that do not always have a full house of local autonomic features: lacrimation is the commonest feature reported in cluster headache (80%) followed by conjunctival injection (64%) with miosis being apparent in less than 10%. However, we cannot rule out the possibility that there may have been subtle pupillary changes that may be missed without pharmacological pupillary testing. It is difficult to know the exact cause of her blurring of vision, but it is likely to be due to a combination of lacrimation and subclinical pupillary change. The aneurysm was adjacent to the midbrain but we do not attribute her neuro-ophthalmological symptoms to compression of the brain stem or ischaemia because she did not have involvement of other cranial nerves or long tracts that would be expected to be affected in a midbrain lesion. Similarly, ischaemic changes were not apparent on the patient’s MRI. We also consider that her headache was secondary to the aneurysm. Although the basilar artery only has sensory innervation from C2, the head pain that she described occurred in the distribution of the first division of the ipsilateral trigeminal nerve (supraorbital) as well as that supplied by C2 (occipital), again emphasising the cross talk between the trigeminal and cervical sensory systems in the trigeminocephalic complex.

Basilar artery aneurysms represent only 3%-5% of all intracranial aneurysms but are the most common aneurysms in the posterior fossa. Treatment of basilar aneurysms by angiographic embolisation with electrolytically detachable coils achieves a high success rate in suitable patients. However, periodic angiographic follow up after coil embolisation is recommended to identify aneurysm recurrence and those patients with a high risk of late rebleeding.

The patient reported here had a basilar artery aneurysm causing headache combined with symptoms indicating autonomic dysfunction, features usually associated with stimulation of trigeminally innervated structures. This may be considered a secondary trigeminal autonomic cephalgia. Basilar aneurysms have not previously been reported to be associated with such features, but neuronal connections exist within the caudal brain stem that could mediate such an effect. We cannot pretend to know, given the probably ubiquitous nature of the trigeminal-autonomic connections, why this particular lesion caused their activation when similar lesions do not necessarily cause this clinical picture. The patient’s presentation, however, provides a useful human confirmation of experimental animal studies that illustrate the physiology of the trigeminal-autonomic reflex.

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