SHORT REPORT

New onset migraine with a brain stem cavernous angioma

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A case of new onset migraine is described following a pontine bleed from a cavernous angioma.

There is increasing evidence that migraine is primarily a brain disorder, probably involving subcortical sensory modulating areas with a secondary neurovascular response.¹ It is also well recognised from experimental work that activity in nociceptive pathways is modulated by structures in the brain stem.² Cavernous angiomas are reported to occur in 0.1–0.5% of the general population, with about 10–30% of these involving the brain stem or cerebellum.³

We describe a case of new onset migraine in a patient who had a pontine bleed from a cavernous angioma.

CASE REPORT

A 22 year old woman presented in June 2000 with symptoms of ataxia, dysarthria, dysphagia, and left facial numbness that

had developed over two weeks. She was admitted to hospital and went on to develop a sudden onset severe, generalised headache. On examination she was found to have horizontal nystagmus on left gaze, hyperreflexia of right upper and lower limbs, an extensor plantar response on the right, and right ankle clonus. Her gait was markedly ataxic.

The headache persisted for two weeks. Magnetic resonance imaging of the brain showed a bleed from a left pontine cavernous haemangioma as well as a Dandy–Walker variant malformation (fig 1).

Following this episode her neurological symptoms improved but she was left with episodes of severe head pain three to four times a month. She describes attacks that start as a left sided retro-orbital and occipital sharp pain, eventually becoming bilateral, and associated with photophobia and worsening of pain on movement. The headache is also associated with transient ataxia and paraesthesiae in the right hand, as well as fuzziness of vision. These symptoms last less than an hour and occur during the headache. The headaches last 24 to 48 hours. Stress was the only trigger she had noted. Before June 2000 there was no history of headaches.

Figure 1 Panels A & B: Magnetic resonance imaging showing left pontine cavernous angioma and Dandy–Walker malformation.

In her past medical history she underwent cranial irradiation and had intrathecal methotrexate for acute lymphoblastic leukaemia in 1987; full remission was achieved. She is a non-smoker and does not drink alcohol. There is a family history of migraine affecting her father, and her uncle had a Dandy–Walker malformation.

Her drug treatment was paracetamol (acetaminophen), tramadol, or morphine for her severe headaches. She was on the oral contraceptive pill.

On examination there were no abnormal neurological findings.

DISCUSSION

This patient provides further evidence for a role of the brain stem in the pathophysiology of migraine. The patient describes symptoms that fulfil the International Headache Society (IHS) criteria for migraine with aura³ following on from an episode during which she sustained a haemorrhage from a previously undiagnosed left pontine cavernous angioma. Before that event she had no history of headaches.

Functional evidence of a role for the brain stem in migraine has been provided by positron emission tomography (PET) studies showing increases in regional blood flow that persist after the headache is relieved.^{5,6} Areas activated are slightly contralateral to the side of pain and include the dorsal midbrain and dorsolateral pontine tegmentum. These areas have not been found to be active in other primary headache disorders, such as cluster headache⁷ and short lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT),⁸ nor in experimentally induced facial pain.⁹ Structural evidence of brain stem involvement in primary headache is provided by observations of excess iron deposition in the periaqueductal grey matter (PAG) in both episodic and chronic migraine,¹⁰ although no grey or white matter changes could be seen using the sensitive automated method of voxel based morphometry.¹¹

It is of interest that her headaches always start on the left side and then may become bilateral. These findings are consistent with those observed in a seminal observation of headache after implantation of stimulating electrodes into the PAG of 15 patients with no previous headache history.¹² All 15 developed migrainous headaches. Although most of these had bilateral implants, two had left sided implants and those patients developed left sided headache. In contrast, however, the PET findings⁹ and a report of a bleed into a brain stem cavernous angioma¹³ both documented headache contralateral to the area of abnormality. The question of ipsilateral versus contralateral pain with regard to brain stem involvement in migraine remains unresolved.

Animal studies support a role for the brain stem, specifically the PAG, in inhibition of trigeminovascular specific nociception traffic. Stimulation of the ventrolateral PAG produces inhibition of nociceptive signals,¹⁴ while blockade of P/Q type voltage gated calcium channels, known to be involved in familial hemiplegic migraine,¹⁵ is pronociceptive.¹⁶ In a study examining the modulatory effects of the PAG on trigeminal activation, 74% of the cells received contralateral inhibitory PAG input and 41% ipsilateral.¹⁴ Moreover, both contralateral and ipsilateral projections from PAG to spinal neurones are well documented.¹⁷ These findings could help to explain an initial unilateral headache developing into a bilateral headache, as in this case.

The patient's past medical history is relevant in that she underwent cranial irradiation for acute lymphoblastic leukaemia at the age of 8. Cavernous angiomas have previously been reported after CNS irradiation for childhood malignancies, and a causal link has been suggested.^{18,19} We are not aware of any association between Dandy–Walker malformations and cranial irradiation. The Dandy–Walker malformation is a congenital abnormality of the posterior fossa involving dilatation of the

fourth ventricle and dysgenesis of the cerebellar vermis. In 1914 Dandy and Blackfan described the case of a 13 month old infant with the triad of posterior fossa cyst, hydrocephalus, and hypoplasia of the cerebellar vermis.²⁰ Dandy went on to publish a larger number of cases,²¹ later augmented by Taggart and Walker, who presented a review of three cases involving congenital atresia of the foramina of Magendie and Luschka.²² Headache in association with the Dandy–Walker malformation has not been described in detail. One review of 40 cases cited headache as a feature in six, although it was not clear whether this was in association with hydrocephalus, which is a common complication of the malformation.²³ The headache in our patient fulfilled the International Headache Society criteria for migraine with aura. It is of interest that her uncle had a Dandy–Walker malformation, as familial cases are uncommon.

In summary, this is a case of new onset migraine starting after a haemorrhage from a pontine cavernous angioma. The site of the pain is ipsilateral to the lesion. This case provides further evidence for the involvement of the brain stem in the initiation of migraine and adds to the debate over the lateralisation of the lesion.

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NEUROLOGICAL PICTURE.....

Faces of the giant panda and her cub: MRI correlates of Wilson's disease

A 26 year old man with cirrhosis and subacute cognitive decline was admitted with a decrease in his activities of daily living. Hyperpigmentation of his lower extremities, asterixis, and Kayser-Fleischer rings were observed. Neurologic examination revealed psychomotor retardation, upper extremity weakness, hypertonia, a left upper extremity tremor, and extensor plantar responses. Serum ceruloplasmin and urine copper studies confirmed the diagnosis of Wilson's disease. He subsequently developed stereotypical episodes of fever, diaphoresis, tonic decorticate posturing, and autonomic instability followed by somnolence. Infectious investigation and serial EEG were unrevealing. Progressive neurological decline ensued, despite D-penicillamine, trientine, and

zinc sulphate, leading to akimetic mutism and rigidity with profound autonomic dysfunction.

Serial MRI revealed symmetric bilateral areas of T2-hyperintensity involving subcortical white matter, basal ganglia, external capsules, thalami, midbrain, and pons. Progressive involvement of the midbrain demonstrated the characteristic MRI evolution of the "face of the giant panda" (Figure 1, A, C, and E).¹ Contemporaneous evolution of dorsal pontine signal abnormalities (Figure 1, B, D, and F) resembled the face of a cub, with eyes formed from the central tegmental tracts. Encircling signal abnormality was possibly because of involvement of the superior cerebellar peduncles, pedunculopontine tegmental nuclei, rubrospinal tracts, or lateral lemnisci.² Selective vulnerability

and progressive involvement of midbrain and dorsal pontine structures may be chronicled on MRI by the faces of the giant panda and her cub, respectively.

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Figure 1 Serial T2-weighted MRI of Wilson's disease over a six month period illustrating evolution of the characteristic "face of the giant panda" in the midbrain (A, C, and E) and face of her cub in the dorsal pons (B, D, and F).