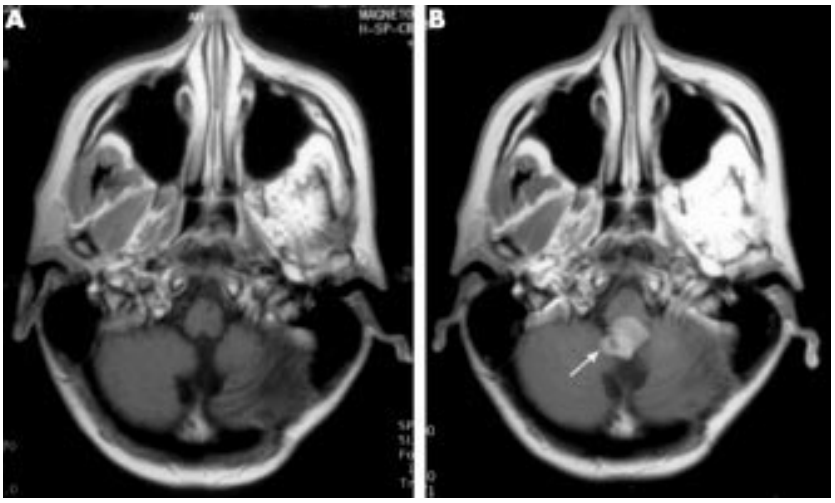

Figure 1 (A) Axial T1 weighted magnetic resonance imaging (MRI) (without contrast), eight months before discovery of a cervicomedullary lesion, showing no evidence of tumour. (B) Axial T1 weighted MRI (without contrast) at presentation showing a large tumour at the level of the foramen magnum.

nerve palsy. A further MR scan was obtained and this revealed a 20 mm diameter tumour behind the brain stem, which was extending through the foramen magnum to the posterior arch of C1 (fig 1B).

The tumour was removed using a posterior approach. Macroscopically it originated from the posterior surface of the brain stem and was remote from any peripheral nerve. Histology showed tumour composed exclusively of compact spindle cells arranged in short bundles and with focal nuclear palisading. It was more cellular than previously and showed moderate nuclear polymorphism and slightly more frequent mitotic figures than the previous specimens. There was a large central area of necrosis and it was diffusely positive for S100. The appearance was that of a cellular schwannoma. The proliferative index was measured (two years later) using MIB1 (Ki67) antibody and counting automatically using the Kontron 3000 system. The result, counting 1000 nuclei, was 22%.

In early 2000, the patient underwent genetic testing which revealed no alterations in the NF2 gene.

In March 2000 she presented again with neck pain and headaches. An MR scan showed recurrence of the tumour at the foramen magnum. This was resected, and the histology indicated recurrences of the cellular schwannoma. Her postoperative recovery was complicated by a breakdown of her wound, following which she developed pseudomonas meningitis. This led to the development of hydrocephalus, which required external ventricular drainage. An MR scan two months after the operation showed several lesions in the mid-thoracic spinal cord, which were suggestive of metastases. There was also dural thickening at the level of S2 downwards. These findings suggested extensive meningeal spread of the disease. She died soon afterwards from aspiration pneumonia.

In this patient, the cervicomedullary schwannoma arose from the pia of the brainstem, and was well away from the lower cranial or upper cervical nerves. These intraparenchymal schwannomas are generally indolent in nature and present in a variety of ways. Younger patients tend to present with a longer duration of illness (often seizures or headaches), whereas older patients tend to have a more rapid clinical course, with marked neurological deficits.[3] Comparison between the two MR scans (fig 1A and B) shows that the cellular schwannoma had grown to 20 mm diameter in eight months (that is, a growth rate of 30 mm a year). This is faster than in any previously published report.

However, it is possible that the cervicomedullary tumour was a metastasis from the previous trigeminal schwannoma. This cervicomedullary tumour was originally considered to be benign on the basis of the histological findings, but was later found to have a proliferation index of 22%—surprisingly high considering the relative sparsity of identifiable mitotic figures.[4] As our patient developed spinal lesions that were suggestive of metastases (unfortunately these were not sectioned at necropsy), the possibility that the original foramen magnum tumour was a metastasis from the previous trigeminal schwannoma is more likely. The difficulty in determining whether or not these lesions are malignant has important implications for the surgeon when considering how aggressive to be with treatment.

Another possibility is that our patient may have had NF2 or schwannomatosis. Tumours in both of these conditions behave differently from solitary cases, with faster growth rates and a more fulminant clinical course.[5] In our patient, genetic studies showed no alteration in the NF2 gene (although these are only 60–70% sensitive). Also, she had a trigeminal rather than a vestibular schwannoma. These two factors suggest that NF2 is less likely but not impossible. Schwannomatosis is characterised by multiple non-vestibular schwannomas, in the absence of meningiomas, intraspinal ependymomas, and other clinical signs of NF2.[5] Although this is consistent with our case, the aggressive behaviour of the tumour, as well as the histological findings (in particular, a lack of Verocay bodies, which are common in schwannomatosis[5]), suggest that this diagnosis was unlikely.

In summary, our unusual case of a cellular schwannoma of the posterior fossa underlines the difficulty in determining the exact nature of these lesions, both histologically and clinically. Despite benign histological appearances, this posterior fossa tumour behaved as a malignant peripheral nerve sheath tumour (MPNST). This is the first time that growth rate has been reported for this particular type of tumour.

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Multiple cerebral aneurysms and the Diamond-Blackfan syndrome

A 17 month old girl presented with pallor, lethargy, and tiredness. She had an uncomplicated birth and no delays in attaining her developmental milestones. There was no family history of either neurological, haematological, or connective tissue disorders. There was no preterm exposure to noxious substances. On examination physical features were within normal limits. She was noted to have a squint in the left eye but no other craniofacial or musculoskeletal abnormalities. Investigations revealed a macrocytic anaemia (Hb 3.9 g/dl, MCV 105 fl) and on haemoglobin electrophoresis there was a raised level of HbF. Bone marrow examination showed erythroblast hypoplasia only. Erythrocyte adenosine deaminase (ADA) levels were moderately raised and a diagnosis of Diamond-Blackfan anaemia was made.

Three months after presentation there was no change in red cell indices, and treatment with high dose prednisolone (2 mg/kg) was begun. There was marked symptomatic improvement within four weeks, without the need for blood transfusion. Maintenance prednisolone (1 mg/kg) was discontinued at the age of four years, by which stage her Hb had normalised while the MCV remained raised (100 fl). There were no relapses following cessation of steroids.

At the age of nine years, she suffered recurrent small pneumothoraces. By the age of 16 she had become a heavy smoker and presented with a sudden onset of frontal headache with signs of meningism, but no other abnormalities. Cranial computed tomography showed diffuse subarachnoid haemorrhage in the right perimesencephalic region extending into the right Sylvian fissure, as well as early hydrocephalus. Subsequent cerebral angiography revealed multiple aneurysms: a right internal carotid artery aneurysm, a left middle cerebral artery aneurysm, a left posterior communicating artery aneurysm, and a small right middle cerebral artery aneurysm (fig 1A).

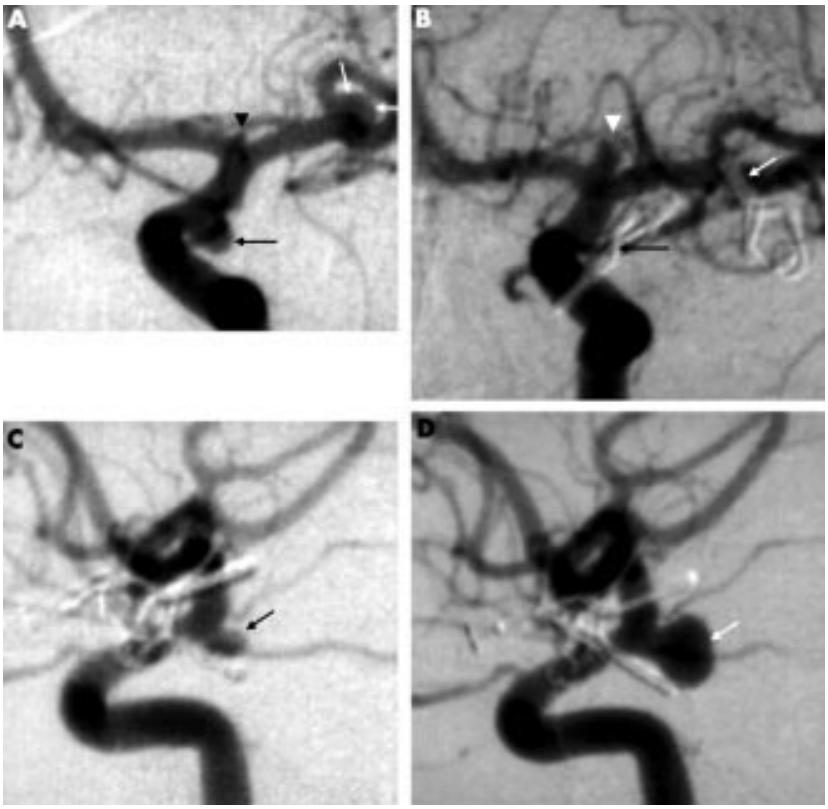

Figure 1 (A) Frontal digital subtraction cerebral angiography following selective injection into the left internal carotid artery showing a left posterior communicating artery region aneurysm (black arrow). A left middle cerebral artery aneurysm is also seen (white arrows), as well as a suggestion of a terminal left internal carotid artery aneurysm (arrowhead). (B) Surveillance digital subtraction cerebral angiography in a frontal projection at two years showing the left posterior communicating artery region aneurysm clip (black arrow), the left middle cerebral artery artery aneurysm clip (white arrow), and growth of the terminal left internal carotid artery aneurisms (white arrowhead). (C) A lateral projection showing residual filling of the left posterior communicating artery region aneurysm at two years (white arrow). (D) Further surveillance cerebral angiography in a lateral projection demonstrating significant growth of the left posterior communicating artery region aneurysm (white arrow).

In view of the distribution of blood products, the right internal carotid aneurysm was thought to have ruptured, and three days after admission it was successfully clipped. Surgical appearances were of very thin walled aneurysms, unlike the usual appearance of degenerate aneurysms. Four weeks later, both the left middle cerebral and the left posterior communicating artery aneurysms were occluded in a similar fashion, again without complication. Twenty two months after the subarachnoid haemorrhage, a terminal left internal carotid artery aneurysm was clearly demonstrated on surveillance angiography (fig 1B). With hindsight this probably started as an infundibulum of the terminal left internal carotid artery (fig 1A). At this stage a conservative course was adopted. However, repeat angiography 12 months later showed enlargement of the clipped left posterior communicating artery aneurysm (fig 1C). Two years later, surveillance angiography demonstrated a significant increase in the size of the left posterior communicating artery artery aneurysm (fig 1D) and she subsequently underwent a further clipping of this aneurysm. During the surveillance period, follow up by a specialist geneticist excluded other predisposing conditions, including autosomal dominant polycystic kidney disease and Ehlers-Danlos syndrome type IV.

Comment

We report a previously undescribed case of rapidly growing multiple cerebral aneurysms in a young woman diagnosed as having Diamond-Blackfan anaemia. We offer a possible explanation for the aetiology of cerebral aneurysms in this condition and consider the presence of coexisting conditions such as type III Ehlers-Danlos syndrome.

Diamond-Blackfan anaemia results from a maturation abnormality in the bone marrow erythroid series, and is usually associated with other anomalies including craniofacial dysmorphism and musculoskeletal defects, particularly abnormalities of the thumb.[1]

Genetic advances in the last few years have linked the Diamond-Blackfan (DBA) phenotype to a locus on chromosome 19 in approximately 25% of familial and sporadic cases of Diamond-Blackfan anaemia.[2] The gene encodes a ribosomal protein (RPS19) which is ubiquitously expressed in both haematopoetic and non-haematopoetic tissues,[3] though its precise role is not known.

The incidence of Diamond-Blackfan anaemia is low, and the finding of multiple cerebral aneurysms in a young non-predisposed person is also rare. Diamond-Blackfan anaemia is not known to predispose to either aneurysm formation or connective tissue disease. Thus the finding of multiple cerebral aneurysms in a patient with this condition is likely to represent an incidental but novel finding. However, if subtle vascular abnormalities are an inherent feature of Diamond-Blackfan anaemia, the possibility is raised that the development of the cerebral aneurysms in this patient may have been accelerated by steroid treatment. As this is the first reported case of cerebral aneurysms in a patient with Diamond-Blackfan anaemia, this seems unlikely as there are many patients with this disease in whom prolonged courses of high dose steroids have not resulted in intracranial vascular anomalies. Similarly, although superficial vascular fragility is a recognised manifestation of steroid treatment, there are no reports of ruptured cerebral aneurysms in association with prolonged high dose steroids.

It has been suggested that mutations in the ribosomal protein encoding gene (RPS19) on chromosome 19, occurring at critical points in embryonal development, may account for features of this syndrome.[4]

Whatever the aetiology of the aneurysms, their management continues to be based on the clinical and angiographic findings following subarachnoid haemorrhage, and in favourable cases occlusion of the aneurysm is indicated. Management of unruptured incidental aneurysms remains difficult. Current scientific evidence suggests that the risk of spontaneous rupture of incidental cerebral aneurysms is less than 0.05% a year, and following a subarachnoid haemorrhage it increases to approximately 0.5% a year. This is independent of underlying predisposing conditions, but is influenced by the size and location of the aneurysm.[5] In addition, very little is known about the factors that affect the rate of growth of cerebral aneurysms in patients with predisposing conditions, and it is unproven whether incidental aneurysms progress to spontaneous rupture. In the case we describe, we have adopted a pessimistic view because of the operative appearances and an apparently rapid rate of aneurysm growth.

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