**Stroke in neurofibromatosis Type 2**

*Commentary on the manuscript by Lascelles et al*

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The paper by Lascelles in this issue1 adds three cases of stroke in children with neurofibromatosis type 2 (NF-2) to three previously reported. Ischaemic stroke is therefore part of the Wishart NF-2 phenotype presenting in childhood with multiple intracranial and spinal tumours as well as rapid loss of hearing and cranial nerve palsies related to schwannomas of cranial nerves III to VIII. Interestingly, hemiplegia was reported in nearly 25% of patients presenting aged <20 years in the Japanese NF-2 registry.2 One of the cases from the literature reported by Lascelles1 underscores the difficulty in distinguishing focal ischaemia from tumour. In addition, stroke may present before the characteristic vestibular schwannomas can be diagnosed clinically or radiologically. The association between cerebral infarction and NF-2 has probably been missed previously; ocular and skin signs of NF-22 should be looked for in posterior fossa stroke.

These cases further our understanding of stroke pathophysiology in those with NF-2 gene variants or deletions leading to reduced production of Merlin, a tumour suppression protein. The involvement of the Ras signalling pathway, important in in NF-1 and Noonan syndrome, is not currently clear for NF-2. When vascular imaging includes the neck vessels, children with NF-1 may have carotid and vertebrobasilar disease as well as moyamoya.3 Two of the patients reported by Lascelles et al have left internal carotid disease, but moyamoya has not so far been reported in NF-2. Focal cerebral blood flow (CBF) abnormalities occur in NF-1, particularly in the posterior circulation,4 but any relationship with arteriopathy is not clear and in NF-2 the focus so far has been imaging CBF in the tumours. It is possible that focal hypoxia-ischemia or modifying genes, such as RNF213, play a role in whether or not compensating vascular changes, including moyamoya collaterals, develop in a wide variety of conditions predisposing to steno-occlusive arteriopathy, including NF-2. This would be easier to study in NF-1 which is 10 times more common.  
  
All the infarcts reported1 are in the posterior circulation, but the available arterial imaging of the vertebrobasilar system is normal. As only one case had conventional angiography soon after the acute stroke, it is possible that dissection or small vessel pathology small vessels was missed. Alternatively, the infarcts could be venous, generally considered rare in the posterior fossa because of the collateralisation, although there are few data in NF-2. There is no evidence of venous sinus thrombosis (VST) or haemorrhage,1 but this pathology may also reverse quickly. Fever, anaemia and dehydration1 are triggers for VST, which has been reported after surgery for vestibular schwannoma in adults.5 Rapid progression of hearing loss as well as cerebellar and brain stem infarction could be secondary to lateral sinus and/or internal jugular vein thrombosis. Even in the absence of VST, in a young brain in which the cerebrovascular system is also developing, the growth of schwanommas in a small posterior fossa might lead to compression or stretching of the basilar, internal jugular, superior petrosal or small perforating veins, eventually compromising the circulation. Interestingly, tortuosity of the ocular veins has been reported in NF-1.

Now that these cases have been recognised, it is clinically important that the vascular pathology is understood, particularly as surgical or medical treatment may increase stroke risk. As part of MRI surveillance of children with NF-2, and studies in acute stroke, as well as population-based studies it is worth including venography, susceptibility weighted imaging of venular density, CBF and angiography of the neck and aorta as well as the circle of Willis. Dehydration and iron deficiency anaemia should be avoided. This should improve outcomes for individuals as well as furthering our understanding.

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