Arterial dissection and cerebral venous thrombosis in sickle cell trait

Introduction

Although there is a well-established relationship between sickle cell disease and stroke (Prengler et al, 2002), there is a paucity of reports in the literature detailing any association between sickle cell trait and cerebrovascular disease. Extremely rare case reports suggest an association of sickle cell trait with cerebral venous thrombosis (Schenk, 1964; Feldenzer et al, 1987), none with arterial dissection. This article reports the unique case of an individual with documented sickle cell trait who suffered a carotid artery dissection initially, followed by an episode of cerebral venous thrombosis 10 years later.

Discussion

Sickle cell disease patients have an increased risk of cerebrovascular disease in the form of ischaemic or haemorrhagic stroke (Prengler et al, 2002). However, only scattered reports exist regarding the cerebrovascular complications of the sickle cell trait (Schenk, 1964; Feldenzer et al, 1987; Prengler et al, 2002).

The presentation of two distinct cerebrovascular syndromes in an individual under the age of 40 years is highly unusual, and the authors are unaware of any case reporting the occurrence of arterial dissection and cerebral venous thrombosis on separate occasions in the same individual, let alone with the presence of the sickle cell

Case Report

A 26-year-old African-American male with no significant past medical history first presented in 1994 to another hospital with sudden onset headache, right-sided weakness, and language expressive difficulties 3 days after mild and otherwise uneventful head trauma while playing football. Magnetic resonance imaging (MRI) of the head and neck demonstrated a large left middle cerebral artery territory infarct and a left internal carotid artery mass interpreted as a pseudoaneurysm suggestive of arterial dissection. Workup at that time included evaluation for protein C/S, antithrombin III, antinuclear antibody, lupus anticoagulant, the factor V Leiden mutation and erythrocyte sedimentation rate levels, all of which were negative or within normal limits. A transoesophageal echocardiogram did not show a thrombus or a patent foramen ovale. Haemoglobin electrophoresis, however, showed that the patient was a carrier of the sickle cell trait (haemoglobin A1 = 61%, haemoglobin A2 = 3%, haemoglobin S = 36%). He was discharged from the hospital on an antiplatelet agent.

He presented 10 years later to the authors' emergency room with 2 days of left frontal headache accompanied by nausea, vomiting and photophobia. Days before this headache there were no other precipitating factors such as illness, trauma or obvious dehydration. His general exam was unremarkable. Pertinent findings on neurological exam were non-fluent speech, mild right upper extremity distal weakness and brisk right-sided reflexes. All of these findings were unchanged from the prior stroke per previous medical records. An MRI of the brain done 2 days after symptom onset demonstrated the old left middle cerebral infarction without evidence of a new ischaemic or haemorrhagic lesion but with increased signal in the superior sagittal (*Figure 1*) and transverse sinuses. Computed tomography (CT) angiogram of the brain revealed enlargement and hyperdensity involving the superior sagittal, transverse and sigmoid sinuses consistent with widespread thrombosis. CT angiogram of the neck showed focal stenosis (about 40%) of the high cervical internal carotid artery, and a more proximal thrombosed pseudoaneurysm (*Figure 2*), all likely residual from his prior arterial dissection. New laboratory workup included the anticardiolipin antibody, beta-2-glycoprotein, factor VIII, activated protein C resistance, prothrombin 20210A mutation, homocysteine and alpha-1-antitrypsin, all of which were either negative or within normal limits. The patient was started on anticoagulation 3 days after symptom onset and within 1 week experienced complete resolution of his headache.

Figure 1. T1-weighted magnetic resonance imaging without contrast showing hypointensity in the region of the old left middle cerebral territory infarct and hyperintensity within the superior sagittal sinus (white arrow).

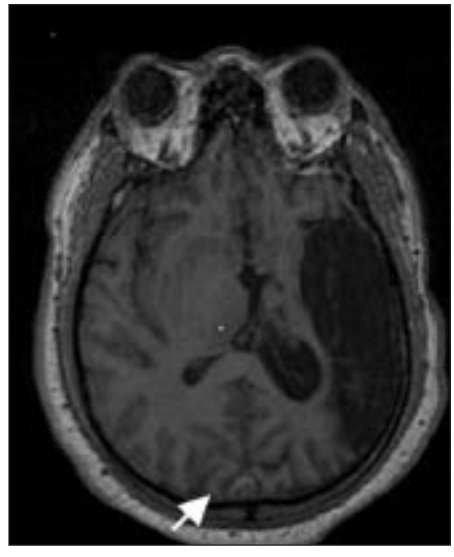
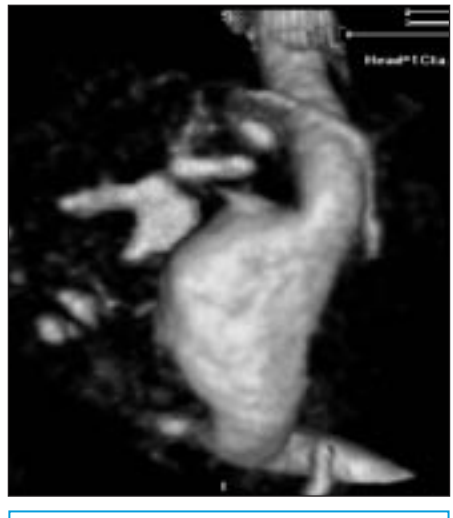


Figure 2. Computed tomography angiogram three-dimensional reconstruction of the left carotid pseudoaneurysm.



Dr Doris Cardenas *is Resident Physician and* **Dr Bruce Ovbiagele** *is Assistant Professor and Attending Physician in the Department of Neurology, UCLA Medical Center, UCLA School of Medicine, Los Angeles, CA 90095, United States*

Correspondence to: Dr B Ovbiagele

trait. This case adds to the very small yet prevailing body of evidence indicating an increased risk for cerebral venous thrombosis among persons with the sickle cell trait.

Previous reports have suggested that an increased risk of cerebral venous thrombosis occurs as a result of the direct effects of intravascular sickling from oxygen desaturation, and some of the cerebral venous thrombosis cases occurred in the setting of general anaesthesia (Schenk, 1964; Feldenzer et al, 1987). Although this patient did have mild head trauma before his presentation of an arterial dissection, one may also consider the possibility of an inherent predisposition to this because of his sickle cell trait.

Interestingly, pathological studies indicate that medial hypertrophy and intimal hyperplasia or fibrosis can be found in the vasculature of young sickle cell trait patients (Haque et al, 2002), and arterial tortuosity on MRI has been shown to be significantly more common in sickle cell trait patients compared to the normal population (Steen et al, 2003). Further case series are needed in order to examine this possibility.

Conclusions

This case suggests that the relatively inexpensive haemoglobin electrophoresis test may be an important diagnostic test to evaluate the presence of the sickle cell trait in black patients with arterial dissection or cerebral venous thrombosis, who have no other obvious mechanistic explanation for these events. BJHM

Feldenzer J, Bueche MJ, Venes JL, Gebarski SS (1987) Superior sagittal sinus thrombosis with infarction in sickle cell trait. *Stroke* **18:** 656–60

Haque A, Gokhale S, Rampy BA, Adegboyega P, Duarte A, Saldana MJ (2002) Pulmonary hypertension in sickle cell hemoglobinopathy: A clinicopathologic study of 20 cases. *Hum Pathol* **33:** 1037–43

Prengler M, Pavlakis SG, Prohovnik I, Adams RJ (2002) Sickle cell disease: The neurological complications. *Ann Neurol* **51:** 543–52

Schenk E (1964) Sickle cell trait and superior longitudinal sinus thrombosis. *Ann Intern Med* **60:** 465–70

Steen R, Hankins GM, Xiong X, Wang WC, Beil K, Langston JW, Helton KJ (2003) Prospective brain imaging evaluation of children with sickle cell trait: Initial observations. *Radiology* **228:** 208–15

Unlucky 13: diluting the evidence

On 23 May, 13 doctors and scientists went public in asking NHS trusts not to spend money on unproven complementary therapies. I don't know what had been on the programme earlier, but I turned on Radio 4's 'PM' to hear the presenter reading out an e-mail from a listener whose allergies had been cured by homoeopathy. Since taking the potions, the listener had not needed to visit the doctor's surgery again. So much for doctors and scientists.

The 13 were responding pre-emptively to a speech Prince Charles was making to the World Health Organisation later that day. I think their response was a mistake. No doubt, even if they had ignored him, the *Daily Mail* would have lauded the Prince's well-worn pleas to take good notice of the thousands of years old tradition of smearing cow dung on the umbilical stump. As it was, all they ensured was that the media gave the speech full coverage, which reverberated for weeks as the two polarized communities weighed in by e-mail and letter, column and counter-column.

The argument has gone nowhere for decades and continues to go nowhere, but while conventional medicine had advanced mightily – with occasional slip-ups – complementary therapies are still stuck with explanations thought up by imaginative people who did not know how the body worked at all. When randomized controlled trials suggest a complementary therapy works for a condition, the complementarists claim it as evidence that all their therapies work; when meta-analyses suggest a therapy does not work, the complementarists say that controlled trials and meta-analysis cannot be applied to therapies that have to take into account the whole patient.

The argument has no chance of being won until people realise the weakness of anecdote as proof, and until the BBC stop letting Mrs C from Epping provide evidence that neutralizes meta-analysis. It will not do to say, as I saw quoted many times, 'We have so much anecdotal evidence'. So much anecdotal evidence is just that: no more than anecdote, until it is put into a proper body of knowledge, with allowance for biases and all the problems that underlie and undermine even the best constructed medical research.

The media can't even get the facts of homoeopathy – such as they are – correct. Homoeopathy works in dilutions, but the newspaper that described a medicine that had been diluted 99 times was wrong by a large number of magnitudes: each time the original substance is diluted it is diluted by 99 times, and these further dilutions take place many times. The higher the dilution, the greater is the strength.

If you want more details, look up homoeopathy at http://www.quackwatch.org/index.html. From there, I learned that 'to expect to get even one molecule of the "medicinal" substance allegedly present in 30X pills, it would be necessary to take some two billion of them, which would total about a thousand tons of lactose plus whatever impurities the lactose contained.' I simply cannot understand how anyone with even a basic understanding of modern physics and chemistry can possibly think that these preparations have any specific effect.

Which makes it not just a shame but tragic that it seems science is too expensive to teach in today's schools and universities. BJHM

Dr Neville Goodman *is Consultant Anaesthetist at Southmead Hospital, Bristol*