syringomyelia and had the typical features of dropped head syndrome.

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The patient gave consent for reproduction of the photograph.

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Vitamin B-12, serum folate, and cognitive change between 11 and 79 years

A recent Cochrane review reported that although vitamin B-12 deficiency is known to be associated with cognitive impairment in old age, benefits of supplementation on mental ability are unclear.[1] The situation is similar to that for blood pressure, in which hypertension is associated with neuropsychological deficits in adulthood but cognitive outcomes of lowering blood pressure in randomised controlled trials are equivocal. We found that for blood pressure, the limited effect of intervention is partly explained by the relation between childhood IQ and adult blood pressure—children with higher IQs had lower mid-life blood pressures.[2] As approximately 50% of the variance in adult IQ is explained by childhood IQ, studies failing to account for ''pre-morbid'' mental ability are likely to overestimate the association between adult IQ and blood pressure. Previously we reported significant relations between various tests of mental ability in old age and vitamin B-12 and folic acid concentrations in the blood.[3] We now describe the association between vitamin B-12 and serum folate and lifetime change in mental ability using the same cognitive test at age 11 and age 79.

As reported more fully elsewhere,[4] the 1932 Scottish Mental Survey (SMS1932) measured the mental ability of almost all (n = 87 498) children born in 1921 and attending Scottish schools on 1 June 1932 with a validated test of IQ, the Moray House test (MHT). With local ethics approval, 550 survivors of the SMS1932 were recruited in Lothian, Scotland by a variety of means. They underwent a health assessment, including blood sampling for vitamin B-12 and folate, and the MHT was re-administered.[4] In all, 483 participants were matched to age 11 MHT scores from the SMS1932, and an age-in-days-adjusted IQ score was calculated. As previously, we included only participants with mini-mental state examination scores greater than 23 and no history of dementia, to exclude pathological cognitive decline as far as possible.[4] None of the participants had a history of head trauma or ongoing CNS affecting disease. The resultant sample comprised 470 participants (194 men, 276 women).

Mean (SD) serum vitamin B-12 was 390 (161) ng/l (n = 422) and mean serum folate was 337 (155) μg/l (n = 391). Pearson correlation coefficients with age 11 IQ were: $r = 0.04$ ($p = 0.42$) for B-12 and $r = 0.13$ ($p = 0.010$) for folate; and with age 79 IQ, $r = 0.12$ ($p = 0.018$) for B-12 and $r = 0.12$ ($p = 0.016$) for folate. Linear regression of age 79 IQ controlling for age 11 IQ confirmed a significant effect on age 79 IQ for B-12 ($\beta = 0.092$, $p = 0.016$, R^2 improvement = 0.008) but not for folate ($\beta = 0.038$, $p = 0.33$). Only two participants had folate levels below the normal range (<5 μg/l) and omitting these did not affect correlation coefficients with age 11 and age 79 IQ scores. Twenty five participants had vitamin B-12 levels below the normal range (<200 ng/l) and there was a stronger correlation with age 79 IQ in this group ($r = 0.57$, $p<0.001$) than in those well within the normal range ⩾250 ng/l ($r = 0.10$, $p = 0.031$). The difference between these two correlation coefficients was significant ($p = 0.016$). After adjusting for all variables known to be associated with lifetime change in IQ (sex, *APOE* ε4 status, cigarette smoking, statin use, and number of drugs prescribed),[4] vitamin B-12 remained a significant contributor ($\beta = 0.095$, $p = 0.011$). Together, these variables explained 4.5% of total variance in age 79 IQ scores after adjusting for IQ at age 11. The number of units of alcohol consumed per week was also positively correlated with age 79 IQ score (Spearman $\rho = 0.10$, $p = 0.026$), but was no longer significantly associated ($\beta = -0.01$, $p = 0.73$) once age 11 IQ and vitamin B-12 were adjusted for.

COMMENT

Both vitamin B-12 and folate correlate with IQ in old age in a non-demented population. Lower serum B-12 at age 79 is associated with cognitive decline between age 11 and age 79. By contrast, serum folate at age 79 correlates with age 11 IQ, and controlling for this reduces the correlation with IQ in old age to almost zero. Hence, in this sample the relation between serum folate and old age mental ability can be fully explained by its correlation with IQ scores on the same test given 68 years previously. This is a similar situation to that with blood pressure.[2] This further emphasises the importance of interpreting associations between cognition and other variables in older people in the context of ''pre-morbid'' mental ability. The effect size of vitamin B-12 is smaller than those found with more domain specific cognitive tests,[3] contributing less than 1% of total variance in age 79 IQ. It is unlikely to be clinically apparent. However, the effect was more significant in the small subsample with laboratory defined deficiency.

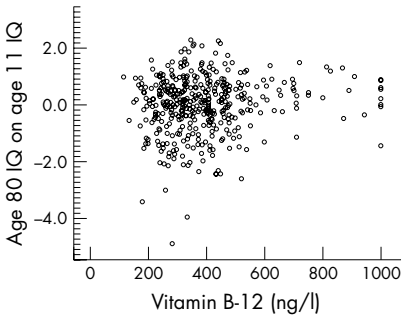

Figure 1 Vitamin B-12 levels and standardised residuals of age 79 IQ regressed on age 11 IQ in a surviving cohort of the Scottish Mental Survey 1932 (n = 422).

Inspection of the relation between vitamin B-12 and the standardised residual score of age 79 IQ regressed on age 11 IQ (fig 1) suggests that the overall correlation is accounted for by a subgroup that is cognitively vulnerable to vitamin B-12 deficiency. Moreover, this vulnerability occurs at levels within the normal laboratory range. An IQ decline of >1 SD occurred in seven of 18 participants (39%) with a serum vitamin B-12 of <200 ng/l, 19 of 84 (23%) with levels of 200–299 ng/l, 21 of 103 (20%) with levels of 300–399 ng/l, and 21 of 149 (14%) with levels of >399 ng/l. Further work is required to confirm this and ascertain what makes these individuals vulnerable. One explanation is that this is a group having ''metabolically significant'' vitamin B-12 deficiency within the normal range with raised homocysteine or methylmalonic acid levels.[5] This may help target B-12 therapy, but at present identifying this group remains challenging. Our data suggest that in a non-demented, relatively healthy population, serum folate concentrations were not related to IQ in old age after controlling for childhood mental ability. However, only two participants in our sample had folate values below the normal range, so other studies are needed to assess the cognitive effects of folate deficiency and treatment with folic acid.

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Stent assisted endovascular thrombolysis of internal carotid artery dissection

Spontaneous dissection of the extracranial internal carotid artery (ICA) is a major cause of stroke with severe residual handicap in young adults.[1] Recently, stent supported angioplasty has been used to treat intimal dissection in case of neurological symptoms while on anticoagulation or as an alternative to the traditionally accepted use of anticoagulation.[2 3] We report a case of internal carotid artery dissection causing hemiplegia successfully treated with emergent endovascular stenting followed by intra-arterial thrombolysis.

Case report

A 44 year old right handed man was admitted to the emergency room after an acute episode of left side weakness, which resolved within three hours. The patient had been well until the onset of symptoms. There was no history of trauma, strenuous exercise, hypertension, or other medical problems. In the week prior to admission, he reported intermittent headaches and right sided neck pain after four days of diving. A cranial computed tomography (CT) scan was normal. Diffusion weighted imaging (DWI) of the brain performed six hours after the onset of symptoms while the patient was asymptomatic showed no evidence of infarction. T2-weighted magnetic resonance images and fat suppressed images showed a semilunar hypersignal of a mural haematoma in the infrapetrous segment of the right ICA suggestive of a dissection. Low molecular weight heparin treatment (enoxaparin sodium 1 mg/kg subcutaneously every 12 hours) was started to obtain true anticoagulation.

Three hours later, the patient had sudden left sided hemiplegia, hypaesthesia, hemianopia, and hemineglect. The National Institutes of Health Stroke Scale (NIHSS) score was 12. Transcranial Doppler ultrasound did not show any flow signal from the middle cerebral artery (MCA) pointing to an acute occlusion. Because of the likely poor chance of revascularisation with intravenous thrombolytic therapy, emergent endovascular revascularisation followed by intra-arterial thrombolysis was planned. Angiography (fig 1A) performed within three hours and 30 minutes of onset of the new symptoms showed the typical narrowed aspect of the ICA with no opacification of the intracranial arteries. Right hemispheric circulation was analysed on the left carotid angiogram: the right anterior cerebral artery (ACA) filled via anterior communicating artery, and the distal branches of the right MCA was filled via pial collaterals from the right ACA. The right M1 and A1 segments were completely occluded. Proximal ICA recanalisation was achieved by implantation of two tandem self-expandable stents (Carotid Wall stent, Boston Scientific Inc, Natick, MA), covering the suprabulbar cervical portion of the ICA (fig 1B). Subsequent intracranial angiography showed a fresh thrombus in the right carotid siphon and confirmed the occlusion of the MCA. Intra-arterial tissue plasminogen activator (tPA) was infused directly into the thrombus four hours after the onset of the new symptoms (40 mg total). There was good proximal recanalisation with residual filling defects in some branches of the MCA (fig 1C) and immediate clinical improvement. The patient received a 5000 U heparin bolus during the procedure and then continuous 500 U/h infusion for 24 hours. Heparin therapy was then replaced by clopidogrel and aspirin, both 75 mg daily. On day 2, MRI showed brain infarct in the deep MCA territories with asymptomatic haemorrhagic transformation. The carotid artery and the MCA were fully patent at ultrasound examination with no evidence of restenosis. There were no periprocedural complications and the patient's symptoms improved gradually after the procedure. On day 7, he was discharged on aspirin and clopidogrel with no residual symptoms.

Discussion

Ischaemic stroke in patients with ICA dissection mainly results from thromboembolic, or, less frequently, haemodynamic mechanisms.[4] Formation of a false channel in the vessel wall or endothelial damage may favour formation of a local thrombus, which becomes less adherent and prone to embolise distally.[1] Although no general agreement exists on the best management of extracranial carotid artery dissection, and because of the threat of an embolic complication, anticoagulation with heparin followed by oral warfarin is used in most institutions.[5] In case of an embolic complication in a patient with known carotid artery dissection revealed by local signs or a transient ischaemic attack, as in our patient, no recommendation exists about emergent therapy. Some reports suggest that intravenous thrombolysis might be safe and effective when given within three hours of onset of stroke without worsening the arterial wall tearing.[6] However, in case of severe stenosis, near occlusion, or even occlusion of the ICA, regardless of the cause, intravenous or intra-arterial thrombolysis has had a poor recanalisation rate, less than 15%.[7]

Endovascular stenting in patients with carotid artery dissection has been successfully used in either selected cases with haemodynamically significant stenosis or when anticoagulation failed to prevent embolic stroke.[2 3] It permitted resolution of the stenosis with immediate recanalisation of the artery. After the procedure, there was no need for anticoagulation and the patient was treated with antiplatelet agents. Our patient had acute hemiplegia with MCA occlusion despite adequate medical therapy. Intravenous thrombolysis given within three hours of onset of symptoms might be an alternative treatment,[8] but it would have likely not been effective since ICA near occlusion would have been left in place; systemic thrombolysis was contraindicated because of the anticoagulation therapy.

We chose a new approach combining endovascular stenting and intra-arterial thrombolysis. Mechanical reopening of occluded large vessels is currently being explored only in carefully selected cases of acute stroke management to minimise the risk of haemorrhagic complications. By taking advantage of the immediate recanalisation of completely occluded vessels it permits delivery of thrombolytic agents directly in the clot, maximising the chance of total distal recanalisation.

Although so far no clinical trial has documented the efficacy of emergent revascularisation in the setting of acute stroke, accumulated anecdotal data show that endovascular mechanical revascularisation is likely to become an important alternative therapeutic approach in properly selected stroke patients. A potential disadvantage of mechanical reopening is the production of embolic debris.[9] With stent deploying in dissected carotid artery, there is a theoretical risk of the intramural clot contained within the dissected segment breaking into the cerebral circulation leading to embolisation distally. In our case, the MCA emboli were demonstrated prior to stenting using transcranial Doppler ultrasound. Another alternative to intra-arterial thrombolysis could be the use of mechanical thrombectomy devices to remove the clot from the carotid siphon and MCA.

This case report is to our knowledge the first example of the potential use of stenting followed by intra-arterial thrombolysis to treat and cure symptomatic carotid artery dissection. However, no conclusions can be drawn about the safety of endovascular approach in this clinical setting. Further evaluation is needed to address its risk–benefit ratio.

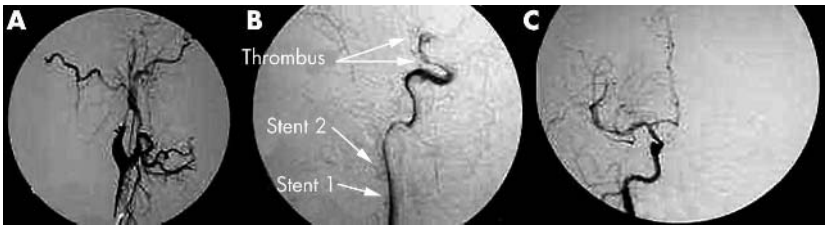

Figure 1 (A) Baseline right common carotid artery (CCA) angiogram shows near occlusion distal to the origin of the infrapetrous segment of the right internal carotid artery (ICA). (B) Post stenting right ICA angiogram demonstrates complete resolution of the ICA occlusion and shows the thrombus in the carotid siphon and in the MCA. (C) Right ICA angiogram after 40 mg of intra-arterial tissue plasminogen activator, recanalisation of the carotid siphon and of the M1 and M2 segment of the MCA and partial recanalisation of some branches of the MCA.

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