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Short report

Subcortical cerebral infarctions in sickle cell trait

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SUMMARY At necropsy, two patients with sickle cell trait and progressive motor and visual deficits, lethargy and coma showed infarctions of the deep cerebral white matter and brain stem. The findings in these patients and another reported in the literature suggest that subcortical infarctions may be more common in sickle cell trait than has been recognised and should be suspected in any patient with sickle cell trait who presents with an unusual neurological illness.

Although well documented, it is still not well recognised that sickle cell trait can rarely cause cerebral infarctions.[1-4] This report presents two other patients with sickle cell trait and cerebral subcortical infarctions.

Case reports

Patient 1. A 32 year old black woman with sickle cell trait had a transient right hemiparesis and slurred speech in April 1984. In August 1985, she presented with a 6 day history of weakness of both legs and blurred vision. Examination showed an alert, black woman who knew where she was but not the date, who Ronald Reagan was, how many nickels there were to a dollar or remember three items after 3 minutes. She said she was blind. Her optic discs were flat and her retina appeared normal. Her right pupil was 2 mm and her left 3 mm. Both reacted briskly to light, directly and consensually. Extraocular movements were intact. Pin prick sensation was diminished on the left side of her face and her left arm. Astereognosis and agraphesthesia were noted on her left hand. Position and vibratory sense could not be tested reliably. She had no weakness but tone was increased on her right limbs. Muscle stretch reflexes were hyperactive on the right and she had a Babinski sign intermittently on the left. She refused to do the finger to nose and heel to knee to shin tests. She could not stand by herself and would slump to the floor even when held by the examiner. Computed tomographic scan showed bilateral contrast enhancing lesions deep in her parietal lobes. Magnetic resonance scans showed increased T2 weighted signals in the white matter of both occipital and temporal lobes and internal capsule, splenium of the corpus callosum, deep white matter of the right parietal lobe, right side of the pons and white matter of both cerebellar hemispheres which were interpreted as consistent with ischaemic necrosis or multiple sclerosis. Cerebrospinal fluid (CSF) examination showed 16 lymphocytes/mm^3 and normal levels of protein and sugar. Smears and cultures for bacteria, fungi and acid fast bacilli were negative and viral antibody titres were within normal limits. Complete blood count, blood chemistries and electrolytes were normal. On her second day in the hospital she became withdrawn and immobile. She was treated with prednisone and acyclovir, lapsed into coma 2 days later and died of recurrent staphylococcal septicaemia in November 1986.

At necropsy she had bilateral pulmonary thromboembolism with sickled red blood cells, recent infarction of her right lung, bronchopneumonia and chronic pyelonephritis of her left kidney. The small blood vessels of her kidneys, spleen and other visceral organs showed sickled cells in the lumen but there was no thromboembolism, vasculitis or infarction. Neuropathologic examination revealed bilateral almost symmetrical old infarctions of the deep white matter of her parieto-occipital lobes and splenium of the corpus callosum (fig), frontal centrum semiovale, internal capsule and rostral corpus callosum. Microscopic examination showed organising and organised infarctions with sickled cells in nearby venules, capillaries and arterioles. The cerebral and cerebellar cortices and brain stem showed no infarctions. There were no demyelinating lesions.

Patient 2. A 29 year old black woman with sickle cell trait who as a child had pulmonary tuberculosis and kyphosis caused by a fall was hospitalised for headaches, diminished vision, numbness of the left side of her face, gums and arms, ringing of her ears, falling sideways to her left and diplopia of 5 days duration. Examination showed absent horizontal gaze to either side but there was slight medial movement of her left eye with near vision. Her pupils were small, equal and briskly reactive to light. Her visual fields and acuity were normal. She had a right peripheral facial weakness, 3/5 weakness of her left arm with athetoid posturing and clumsy finger to nose test and decreased pin prick and vibratory sensation of her left limbs. Her muscle stretch reflexes were symmetrically

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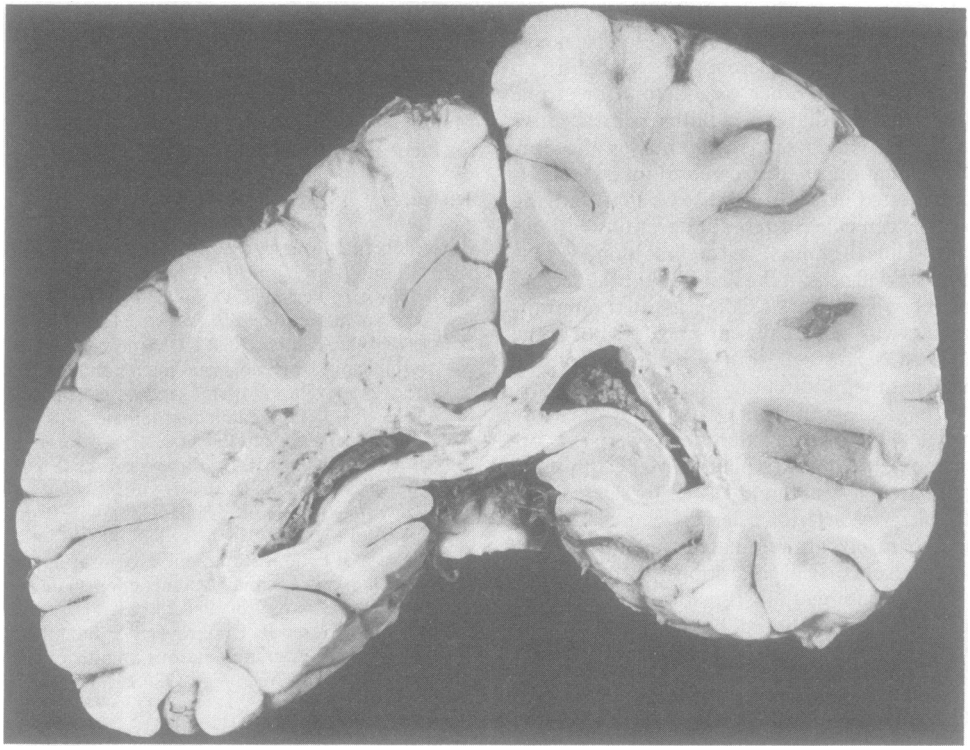

Fig *Bilateral infarctions of parieto-occipital white matter, optic radiation and splenium of the corpus callosum of patient 1.*

normoactive. She had no Babinski sign. Her mental status examination was normal. Complete blood count was normal. Radiographs of her chest and thoracic spine showed kyphosis with fusion of several vertebral bodies. On her second day in the hospital, she lost her upward gaze and the position sense of her left hand. CSF examination showed clear colourless fluid, 350 white blood cells/mm^3, 30% of which were polymorphonuclear leukocytes, protein 118 mg/dl and glucose 28 mg/dl (blood sugar 87 mg/dl). Smears and cultures for bacteria and acid fast bacilli were negative. She was treated with isoniazid, ethambutol, streptomycin and dexamethasone. Twelve days later, she became stuporous and developed a left hemiparesis with hyperactive muscle stretch reflexes. She would open her eyes but did not blink to visual threats. Her right pupil was bigger than her left and both were sluggishly reactive to light. Her eyes were fixed on forward gaze and she was unable to move them on command. Head turning elicited only slight conjugate downward deviation of her eyes but cold caloric tests failed to elicit any movements. She was unable to move her tongue and her gag reflex was absent. CSF examination showed five lymphocytes, protein 103 mg/dl and sugar 101 mg/dl. She died of bronchopneumonia two and a half months later.

Necropsy examination of her lungs showed only pleural adhesions of both apices. There were no scars or granulomas. No sickled cells, thrombosis, vasculitis or infarctions were found in her visceral organs. Instead, there was acute bronchopneumonia with mucus plugs of both main stem bronchi. Her brain showed an irregular, collapsed, rusty brown discoloured infarction in the floor of the fourth ventricle of the caudal third of the pons destroying the medial longitudinal fasciculus and parabducens and abuducens nuclei and impinging on the genu of the right facial nerve. There were irregular, tan, granular shrunken infarctions of her right internal capsule and subthalamus, deep white matter of both frontal and occipital lobes and optic radiation. Also, the cortex of her left parietal lobe in the borderzone supplied by the anterior, middle and posterior cerebral arteries showed laminar necrosis. Microscopic examination confirmed the organised and organising infarctions noted on gross examination. There was no leptomeningitis, leptomeningeal fibrosis or sickled cells in her cerebral blood vessels.

Discussion

Although it is well known that patients with sickle cell trait can develop infarctions from low oxygen concentration or acidosis due to infection, anaesthesia, congestive heart failure or flying in an airplane,[5] cerebral infarction was not suspected in my patients

because they were not exposed to these risks before or at the onset of their neurological illnesses. Absence of arteriosclerosis, arteriolosclerosis or vasculitis, a source of embolism or other risk factors for stroke such as hypertension, diabetes mellitus, contraceptive pills or smoking leaves sickle cell trait as the only plausible explanation of their cerebral infarctions. It has been suggested in sickle cell disease that sludging of sickled cells can cause cerebral infarctions without thrombosis.[6] Thus the finding of cerebral blood vessels occluded by sickled cells in the first but not the second patient merely affirms that sickling is often intermittent in patients with sickle cell trait[5] and does not argue for or against sickle cell trait as a cause of the infarction. That their infarctions and those of another patient with sickle cell trait who died of acute haemorrhagic white matter infarctions[4] were subcortical is curious but can be explained by occlusion or sludging of parenchymal blood vessels by sickled cells similar to the way arteriolosclerosis causes lacunar infarctions or rarely granulomatous angiitis causes predominantly subcortical infarctions.[7] Because they may be more common than previously recognised, subcortical infarctions should be suspected in any patient with sickle cell trait who presents with an unusual neurological illness.

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