Short report

Large cerebral vessel disease in sickle cell anaemia

L. BOROS, C. THOMAS, AND W. J. WEINER

From Michael Reese Hospital and Medical Center, Chicago, Illinois, USA

SYNOPSIS  An 18 year old male with documented sickle cell disease was admitted to the hospital for the final time in coma. Cerebral angiography revealed multiple stenotic lesions of the large cerebral vessels. The pathology of this large vessel involvement is demonstrated and the potential contribution of large as opposed to small cerebral vessel disease in the neurological manifestations of sickle cell anaemia is discussed.

The association between sickle cell anaemia and acute neurological deficits was first recorded in 1923 with a report of convulsions, rigidity, and hemiplegia in a 5 year old boy with sickle cell disease (Sydenstriker et al., 1923). Since that time, numerous attempts have been made to define the relationship between vascular insults in the central nervous system and sickle cell anaemia. The pathogenesis is believed to involve in vivo sickling as the initial insult. This leads to increased blood viscosity, stasis, hypoxia, thrombosis, and infarction causing damage in the lung, liver, spleen, eye, and other organs (Armaly, 1974; Bromberg, 1974; Konotey-Shuler, 1974). The widespread concept of small vessel intracerebral disease to explain acute neurological deficits in young patients with sickle cell anaemia (Arena, 1939; Diggs and VanderBuegg, 1954; Baird et al., 1964) has been challenged by the angiographic demonstration of large vessel occlusions in this syndrome (Stockman et al., 1972). The identification of patients whose neurological symptomatology can be attributed to large as opposed to small vessel disease may have therapeutic implications since there is some evidence that the large vessel lesions may be reversible (Russell et al., 1974a,b).

CASE REPORT

This was the final hospital admission for an 18 year old male with homozygous haemoglobin S disease. Between age 8 and 13 years he experienced four separate episodes of acute left hemispheral dysfunc-

1 Address for correspondence: Dr William J. Weiner, Division of Neurology, Michael Reese Hospital and Medical Center, 2929 South Ellis Avenue, Chicago, Illinois 60616, USA.

(Accepted 19 August 1976.)
Large cerebral vessel disease in sickle cell anaemia

arterial changes extended into the proximal portions of the middle and anterior cerebral arteries. The basilar artery was patent with no significant changes on microscopy.

**DISCUSSION**

Acute central nervous system abnormalities are a significant and common complication in sickle cell disease. In fact, neurological involvement is exceeded only by painful crisis and cardiomegaly as the most common clinical findings in this syndrome (Greer and Schotland, 1962; Portnoy and Herion, 1972).

Neuropathological changes in patients with sickle cell anaemia can take many different forms including small vessel occlusion (Seeler, 1972), massive intracranial haemorrhage (Baird et al., 1964; Adeloye et al., 1970), large vessel occlusion (Greer and Schotland, 1962), subarachnoid, subdural, or epidural haemorrhage (Hughes et al., 1940), leptomeningitis, encephalomalacia (Bridges, 1939), and ruptured aneurysm (Cheatham and Brackett, 1965). In spite of the early recognition of these complications, little has been written to define the aetiology of central nervous system abnormalities in sickle cell anaemia. In 1964 Baird et al. summarised earlier work suggesting that small vessel occlusion by sickled erythrocytes caused infarction and haemorrhage. It was suggested that this process, which involved the capillaries and pre-capillary arterioles, caused the central nervous system symptoms. Stockman et al. (1972) highlighted a new dimension by demonstrating angiographic occlusion of large cerebral vessels in six patients with sickle cell

bands and fibroblasts. No capillary spaces were identified and there was no recanalisation within the proliferating fibrous tissues. Endothelial cells could not be identified. The right internal carotid artery was partially occluded by an identical process. The end-

**FIG. 1** Left carotid angiogram demonstrating complete occlusion of internal carotid artery distal to opthalmic artery.

**FIG. 2** Cross-section of left internal carotid artery. Note marked endarteritic process nearly totally occluding vessel lumen (H and E, ×25).
This controversy, vasorum of suggested damage vessels, sized possible severe, necropsy venous with proliferation diminished to fic therapy large cell disease. The abnormalities. instances saw transient and the of the pathology. et al., 1972, of endothelial was narrowed vessel was acute neurological disorders. Only incomplete descriptions are available (Bridges, 1939; Hughes et al., 1940; Wertham et al., 1942). In 1939 Bridges et al. described the pathological changes seen in a child with medium-sized cerebral vessel occlusions. There was endothelial proliferation, fibroblastic reaction, hyalinisation and occasional loss or fragmentation of the internal elastic lamina. They postulated that the process leading to occlusion was endarterial intimal proliferation and not thrombosis. The following year, Hughes et al. (1940) confirmed the pathological findings and described fresh and organizing thrombi in the narrowed vessel lumen. Significantly, they also saw instances of thrombosis without associated vessel wall abnormalities. They concluded that the arterial wall changes were secondary to chronic stasis and diminished blood volume leading to capillary and venous thrombosis. Stockman et al. (1972), without necropsy data, postulated yet a third process. They suggested that sickled erythrocytes occlude the vasa vasorum of large blood vessels causing ischaemic damage and leading to progressive intimal and medial proliferation with eventual obliteration of the lumen. This controversy, as it applies to large and medium sized vessels, is unresolved.

In the patient presented here, the stenotic lesions demonstrated on the arteriogram correspond to the severe, fibrotic endarteritic changes. We were unable to demonstrate a thrombotic process or to identify the vasa vasorum. It seems reasonable to suggest that the transient and permanent neurological deficits were caused by episodic occlusion of cerebral vessels. The primary pathological process could be intraluminal with damage to the endothelium produced by either the sludging sickled cells or by flow abnormalities. On the other hand, destruction of the vasa vasorum could also have led to the same final picture of fibrotic obliteration.

An important question remains as to whether the aetiology of the multiple cerebral vessel occlusions affects the choice of therapy. Indeed, response to specific therapy may distinguish patients with sickle cell disease from those with large vessel occlusion due to other or no known causes (Suzuki and Takaku, 1969; Solomon et al., 1970). Russell et al. (1974a,b) have preliminarily reported that, in children with sickle cell disease who had angiographically demonstrated stenotic large vessel lesions, chronic transfusion therapy could reverse the vascular pathology. In children who were not transfused there was progression of vascular disease in follow-up angiography. It is possible that transfusion therapy may offer new hope for patients with sickle cell disease and large cerebral vessel occlusion.

REFERENCES


The November 1976 Issue

THE NOVEMBER 1976 ISSUE CONTAINS THE FOLLOWING PAPERS

Brain function in epilepsy: midbrain, medullary, and cerebellar interaction with the rostral forebrain R. G. Heath .................. page 1037

Epilepsy after two different neurosurgical approaches to the treatment of ruptured intracranial aneurysm R. J. Cabral, T. T. King, and D. F. Scott ................................ page 1052

Space representation in unilateral spatial neglect F. Chedru ................................ page 1057

Aphasic disorder in patients with closed head injury H. S. Levin, R. G. Grossman, and P. J. Kelly ..................................... page 1062


Serum globulin changes in patients with cranio-cerebral trauma L. Auer and W. Petek page 1076

Lactate dehydrogenase and aspartate transaminase of the cerebrospinal fluid in patients with brain tumours, congenital hydrocephalus, and brain abscess S. R. Dharker, R. S. Dharker, and B. D. Chaurasia ................. page 1081

Neuromyotonia: an unusual presentation of intrathoracic malignancy J. C. Walsh... page 1086

Dysautonomia in Parkinsonism: a clinicopathological study A. H. Rajput and B. Rozdilsky... page 1092

Bromocriptine in Parkinsonism: long-term treatment, dose response, and comparison with levodopa J. D. Parkes, A. G. Debono, and C. D. Marsden ......................... page 1101

Cyclic compression of the intracranial optic nerve: patterns of visual failure and recovery L. Frisen, J. Sjostrand, K. Norkell, and S. Lindgren .......... page 1109

Weakness associated with the pathological presence of lipid in skeletal muscle: a detailed study of a patient with carnitine deficiency H. Isaacs, J. J. A. Heffron, Margaret Badenhorst, and Avonnie Pickering...Page 1114


Occurrence of familial spastic paraplegia in only one of monozygous twins I. Bone, R. H. Johnson, and M. A. Ferguson-Smith ... page 1129

Short report: Arterial spasm and recovery from subarachnoid haemorrhage J. T. E. Richardson page 1134

Book reviews ...................... page 1137

Letters ......................... page 1143

Copies are still available and may be obtained from the PUBLISHING MANAGER, BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE, LONDON, WC1H 9JR, price £2.00, including postage