Cerebrovascular complications of sickle cell disease are well known, while cases associated with sickle cell trait are rare. Only 2 cases of superior sagittal sinus (SSS) thrombosis and sickle cell trait, confirmed by hemoglobin electrophoresis, have been reported in the English literature. In both cases, SSS thrombosis followed a recently administered general anesthetic. To our knowledge, this is the first case of sickle cell trait complicated by SSS thrombosis in which another precipitating cause could not be identified.

Report of a Case

A previously healthy, 17-year-old right-handed black female was admitted to a local hospital with a diagnosis of pseudotumor cerebri. She had an 8-week history of intermittent blurred and double vision and a diagnosis of pseudotumor cerebri. Cranial computed tomography, initially normal, subsequently revealed multiple hemorrhagic infarctions. Suspected superior sagittal sinus thrombosis was confirmed by cerebral angiography. Superior sagittal sinus thrombosis associated with sickle cell trait is exceedingly rare, and the accompanying increased intracranial pressure may require aggressive management. 

CT with and without i.v. contrast material was repeated and was normal. A lumbar puncture revealed an opening pressure of > 55 cm. The patient was treated with 8 mg q 6 h. dexamethasone, 35 mg b.i.d. furosemide, and 250 mg q 6 h. acetazolamide. Initial cerebrospinal fluid (CSF) analysis showed glucose, 60 mg% (serum, 87); protein, 13 mg%; 1 white blood cell/mm³; 7 red blood cells/mm³; no organisms on Gram stain; and no growth on bacterial cultures. She underwent daily lumbar punctures (cultures negative) with a normal opening CSF pressure on the fourth day. The patient remained alert, but with persistent headache despite low CSF pressure. On the sixth day, she became increasingly lethargic with worsening headache. Within 24 hours, she was deeply comatose with a left hemiparesis. CT without i.v. contrast material (Figure 2) showed peripheral hemorrhagic lesions suggesting dural venous sinus thrombosis. SSS thrombosis was confirmed by cerebral angiography (Figure 3). The patient was started on i.v. antibiotics and heparin (1,000 U/hr) and transferred to the University of Michigan for further treatment.

Our initial examination revealed normal vital signs in a comatose patient with papilledema, anisocoric pupils (left > right) reactive to light, a right sixth cranial nerve palsy, left central seventh cranial nerve palsy, and a left hemiparesis. She responded to deep painful stimuli only. Because of hemorrhages on recent CT (Figure 2), heparin was discontinued. Laboratory values revealed hematocrit, 43.7; white cell count, 26,000 with a left-shifted differential; platelets, 338,000; prothrombin time, 12.2 seconds; thrombin clotting time, 17.9 seconds (normal, 8.0–10.0 seconds); and fibrinogen, 302 mg% (normal, 150–350 mg%). Hemoglobin electrophoresis confirmed 38.5% S, 57.9% A, and 3.6% A₂. Antithrombin III level and platelets were normal, and a pregnancy test was negative.

The patient was given anticonvulsant prophylaxis (100 mg t.i.d. phenytoin), 0.25 gm/kg q. 2 h. mannitol, and was continued on dexamethasone. Transfusion with packed red cells reduced the hemoglobin S content to 24.1%. A ventriculostomy was placed after the partial thromboplastin time had returned to normal. CSF opening pressure was > 50 cm. Ventricul-
Before hospital admission. Computed tomography (CT) with i.v. contrast material. This normal study was obtained during outpatient treatment for pseudotumor cerebri (see text). The prominent enhancement in the region of the straight sinus was not visualized on the noncontrast CT.

Lar drainage was set at 20 cm, and she was intubated and hyperventilated to $\text{PCO}_2 = 25 \text{ mm Hg}$. Hypertension (maximum, 170/108 mm Hg) was vigorously controlled with methyl dopa, sodium nitroprusside, and hydralazine.

Three days after transfer, severe intracranial pressure (ICP) spikes ($>60 \text{ cm}$) occurred despite hyperventilation, osmotic diuresis, ventricular drainage, sedation with morphine sulfate, and neuromuscular blockade with pancuronium bromide. Pentobarbital coma was induced, and a burst-suppression pattern was demonstrated on EEG. ICP spikes ($>60 \text{ cm}$) continued for several days, and pentobarbital was discontinued after 4 days. CT showed no significant change in the left hemispheric hemorrhagic venous infarcts. Continuous ventricular CSF drainage (400–470 ml/day) with intermittent mannitol controlled ICP below 30 cm. Neurologic improvement occurred gradually with spontaneous eye opening and movement of the right side. The patient tolerated extubation, and on the eighteenth day of hospitalization a lumbar–peritoneal shunt was placed after removal of the ventriculostomy. High lumbar CSF pressure was noted intraoperatively.

Sixth hospital day. Computed tomography (CT) with no i.v. contrast material. Multiple left cerebral hemispheric hemorrhagic venous infarctions. These are most marked in the temporal and parietal lobes.
The patient showed dramatic, progressive improvement beginning on the second postoperative day and was following commands on the fourth day. She was transferred to the Physical Medicine and Rehabilitation Service and was speaking 2 weeks later. There was a residual left hemiparesis and cognitive deficits including verbal apraxia and impairment of immediate recall and recent memory. Cortical blindness resolved to 20/50 acuity bilaterally with a dense left homonymous hemianopsia and severe bilateral visual field constriction. These deficits were progressively improving at the time of her discharge, 5 months after admission.

**Discussion**

Sickle cell disease (homozygous sickle cell anemia) is a well-recognized risk factor for the development of cerebrovascular thrombosis. The prevalence of cerebrovascular complications may be as high as 17%. However, like most other hemoglobinopathies, the heterozygous form, sickle cell trait, is relatively asymptomatic. Portnoy and Herion reported a stroke incidence of 1.7% in 227 patients with sickle cell trait compared with a 1.8% occurrence of stroke in the black control group with normal hemoglobin. Nevertheless, the surgical and obstetric risks of sudden death related to hypoxia or vascular stasis are greater than normal in individuals with sickle cell trait. Sudden death related to hypoxemia and acidosis has been described with sickle cell trait at high altitude. McCormick, in an autopsy series of 120 patients with sickle cell trait, demonstrated massive intravascular sickling or visceral infarcts (including 2 cerebral infarcts) in 33%. Sickle cell trait was thought to be a major factor in the death of 12.5% of these patients. In another series of 175 patients with sickle cell trait, 11 had neurologic symptoms, but no infarcts were demonstrated.

There are 13 previously reported cases of cerebrovascular complications associated with sickle cell trait, including 2 cases of SSS thrombosis. A sickling crisis associated with the recent administration of gen-
eral anesthesia and/or a perioperative hypoxic event was the proposed etiology in both cases of Schenk and Dalal. In our case, there was no known precipitating event or other risk factor.

When erythrocytes containing hemoglobin S are exposed to low oxygen tension, tactoids or polymerized fibers of abnormal hemoglobin are formed, resulting in gel formation and abnormal sickle-shaped cells. This structural change is accompanied by a marked increase in blood viscosity contributing to stasis. Cerebrovascular thrombosis was traditionally thought to involve small vessel occlusion secondary to stasis in capillaries, precapillary arterioles. However, Stockman et al reported partial or complete occlusion of large cerebral vessels by angiography in 6 of 7 patients and concluded that neurologic deficits in sickle cell disease cannot be attributed solely to multiple small vessel occlusions. Large vessel occlusion has been postulated to result from vascular wall ischemia resulting in proliferation of the intima and media. Occlusion of the vasa vasorum by sickled cells is the proposed mechanism of ischemia. Postmortem pathologic changes in large cerebral arteries of patients with sickle cell disease have not been demonstrated consistently. Dural sinuses thrombosis is less common than occlusion of large or small cerebral arteries. The pathogenesis of sinus thrombosis most likely involves stasis caused by increased blood viscosity during hypoxic episodes.

Neurologic complications are often devastating and progressive in sickle cell disease, and recurrent infarctions are not uncommon. Because an effective antisyckling agent has not been developed, acute and prophylactic transfusion regimens have been employed to reduce the number and percent of circulating hemoglobin S-containing erythrocytes. The maximum hemoglobin S concentration tolerated in patients without risk of cerebrovascular thrombosis is unknown. Several studies have demonstrated that cessation of short-term transfusion was associated with recurrent infarctions, even in cases with <20% hemoglobin S. Transfusions of sufficient volume and frequency to suppress endogenous erythropoiesis are recommended. Our patient presented with 38.5% hemoglobin S and received 2 transfusions of packed erythrocytes during the acute illness. To our knowledge, this is the first reported case of sickle cell trait with stroke to undergo transfusion therapy.

In sickle cell trait the hemoglobin S concentration may vary from 25 to 45%. In vitro studies suggest that the risk of sickling in sickle cell trait with high hemoglobin S approaches that in sickle cell disease. In our case and the only 3 reported cases of sickle cell trait with stroke and hemoglobin quantification, hemoglobin S values were >36%.

SSS thrombosis has been associated with multiple clinical entities including oral contraceptives, pregnancy, puerperium, dehydration, congestive heart failure, hemolytic anemia, sickle cell disease, cerebral arterial occlusions, trauma, neoplasm, and others. The definitive diagnosis is made by cerebral angiography. The clinical presentation and ICP dynamics of SSS thrombosis and pseudotumor cerebri are so similar that some workers consider dural venous sinus thrombosis as the significant pathogenetic mechanism for pseudotumor cerebri. Ray and Dunbar demonstrated SSS thrombosis as the cause of pseudotumor cerebri using sinus venography and surgical exploration in 1 case. Bresnan et al were able to show venous sinus occlusion by angiography in 10 of 12 children with pseudotumor cerebri. It is possible that the occurrence of pseudotumor cerebri in this patient with sickle cell trait was fortuitous. However, the patient was initially diagnosed with pseudotumor cerebri while, in fact, she was developing progressive SSS thrombosis. We feel that the patient’s hemoglobinopathy contributed to the SSS thrombosis.

In this case of SSS thrombosis, the associated increased ICP required aggressive treatment. Elevated ICP may be exacerbated by the mass effect of accompanying hemorrhagic venous infarcts or by surrounding edema. We employed hyperventilation, osmotic diuresis, steroids, ventricular drainage, sedation, and barbiturate coma to limit persistently elevated ICP.

Anticoagulant therapy has been utilized since 1942 for the treatment of dural sinus thrombosis. It is recommended by some investigators to prevent further thrombosis, while others consider it contraindicated because of the added risk of intracranial hemorrhage. We considered the use of heparin contraindicated in our patient with multiple hemorrhagic infarctions. Tissue plasminogen activator, recently employed in the treatment of acute coronary thrombosis, may find application in the therapy of dural sinus thrombosis.

In conclusion: Hemoglobin electrophoresis should be carried out in young black patients with unexplained neurologic symptoms or signs. Sickle cell trait in addition to sickle cell disease represents an increased risk of cerebrovascular thrombosis especially with an elevated level of hemoglobin S (≥36%). Dural venous sinus thrombosis should be considered in patients with sickle cell disease or trait who are being treated for pseudotumor cerebri. Increased ICP associated with dural sinus thrombosis may require aggressive management.

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