Bilateral Anterior Cerebral Artery Occlusion in an Alcohol Abuser with Sickle-Cell Trait

Thomas H. Swanson
John L. Zinkel
Patti L. Peterson

Follow this and additional works at: https://scholarlycommons.henryford.com/hfhmedjournal

Part of the Life Sciences Commons, Medical Specialties Commons, and the Public Health Commons

Recommended Citation
Available at: https://scholarlycommons.henryford.com/hfhmedjournal/vol35/iss1/14

This Article is brought to you for free and open access by Henry Ford Health System Scholarly Commons. It has been accepted for inclusion in Henry Ford Hospital Medical Journal by an authorized editor of Henry Ford Health System Scholarly Commons.
The contribution of ethanol ingestion to brain infarction is unclear, although many studies suggest that the two may be causally related. We report an unusual case of bilateral anterior cerebral artery occlusion in a young female ethanol abuser with sickle-cell trait whose platelets showed hyperaggregability during epinephrine and adenosine diphosphate-induced aggregation experiments. It is concluded that ethanol withdrawal and dehydration along with direct effects of ethanol on platelet aggregation may result in cerebral artery thrombosis. Sickling of red blood cells in the distal circulation also may be a compounding factor, but this is not proven. (Henry Ford Hosp Med J 1987;35:67-70)

Approximately 3% to 10% of all Americans are alcohol abusers, and about 25% of all hospital admissions are attributed to alcohol use (1). The effect of alcohol on the brain is well studied and includes diffuse cortical and cerebellar degeneration and localized degeneration of the hypothalamus, mamillary bodies, and hippocampus. An association with central pontine and corpus callosal degeneration also has been described (2). How and why these specific changes occur is still conjectural.

The contribution of alcohol to cerebral infarction is often overlooked. In one study of 23 patients under 40 years of age, 43% of the subjects with ischemic brain infarction were intoxicated within 24 hours preceding the onset of symptoms (3). A recent study concluded that stroke occurred more frequently in heavy alcohol users than in nonusers (4). How alcohol contributes to ischemic infarction is unclear, but its effects on platelet aggregation are probably significant.

Similarly, the contribution of hemoglobin A-S to vascular thrombosis and infarction in patients with sickle-cell trait (SCT) is unclear (5). Most authors feel that SCT is not life threatening; however, there are many reports of neurovascular complications in SCT patients, including increased frequency of complicated versus simple headaches in migraine sufferers (6), a case of superior longitudinal sinus thrombosis (7), and several cases of sudden death (8-10). Although no report has yet described an interaction between ethanol and hemoglobin A-S in promoting thrombotic infarction, SCT may compound ethanol-induced deranged platelet function and contribute to vascular stasis and thrombosis.

Case Report
A 38-year-old, right-handed, black woman presented with a history of hypertension, sickle-cell trait, and heavy alcohol abuse (about one-fifth of a gallon per day for many years). The night before admission, she had passed out from drinking alcohol. In the morning, she was unable to move her right leg and had some mild decreased strength in her right arm. Her only other complaint was a slight headache. She denied head trauma, nausea, vomiting, neck stiffness, seizures, or visual disturbances. Physical examination was remarkable for a blood pressure of 154/120 mm Hg and minimal arteriovenous nicking on fundoscopic examination. Cardiac evaluation was normal. Neurological examination revealed a flattened affect, slowness in following commands, and easy distractibility, all signs of akinetic mutism (abulia), in addition to one over five motor strength in the right lower extremity, four over five motor strength in the right upper extremity, and hypoesthesia to pinprick in the right lower extremity. Cranial nerve testing revealed no deficits.

Laboratory studies revealed normal electrolytes, BUN, creatinine, glucose, prothrombin time, partial thromboplastin time, hemoglobin, hematocrit, calcium, magnesium, phosphorus, ammonia, and erythrocyte sedimentation rate, and a platelet count of 240,000/μL. ECG was significant only for first-degree atrioventricular (AV) block. Twenty-four hour holter monitoring revealed normal sinus rhythm and first-degree AV block without associated high-grade conduction abnormalities. Echocardiogram of the heart failed to reveal pathology (notably absence of mural thrombus or left ventricular hypertrophy). A gallium scan of the heart was also normal. The bone marrow examination was unremarkable. Quantitative blood amino acid studies revealed modest elevations of aspartic acid, serine, glutamic acid, glycine, cysteine, tyrosine, phenylalanine, and ornithine, a nonspecific pattern.

Submitted for publication: November 17, 1986.
Accepted for publication: April 10, 1987.
*Formerly Department of Internal Medicine, Henry Ford Hospital, and Department of Physiology, Wayne State University School of Medicine. Currently Department of Neurology, Mayo Clinic, Rochester, MN.
†Department of Neurosurgery, Wayne State University School of Medicine, Detroit, MI.
‡Department of Neurology, Wayne State University School of Medicine, Detroit, MI.
Address correspondence to Dr. Swanson, Department of Neurology, Mayo Clinic, 200 SW 1st St, Rochester, MN 55905.
Fig 1—CT scan with intravenous contrast enhancement taken after the second stroke revealing bilateral, deep basal ganglionic, periventricular lucencies (present on admission CT scans, unchanged) and new bilateral frontoparietal lobe lucencies along the falx, with irregular areas of enhancement.

Initial computed tomography (CT) scans of the head obtained with and without contrast enhancement revealed very small lucencies in the left and right deep basal ganglionic paraventricular areas, but were otherwise normal. The serum VDRL, FTA, antinuclear antibody, rheumatoid factor, and lupus erythematosus cell preparation all were negative. Cerebrospinal fluid (CSF) obtained via lumbar puncture was otherwise normal. The serum VDRL, FTA, antinuclear antibody, rheumatoid factor, and lupus erythematosus cell preparation all were negative. Cerebrospinal fluid (CSF) obtained via lumbar puncture was otherwise normal.

The patient was treated with clonidine and furosemide to maintain a diastolic pressure under 110 mm Hg. She maintained admission neurological status throughout the first two days. On the third hospital day the patient developed tachycardia, diaphoresis, and tremulousness, with a blood pressure of 200/110 mm Hg, and pulse of 110 beats/min. Her blood pressure remained elevated despite treatment with clonidine, but at 4 PM it dropped to 90/60 mm Hg. Thirty minutes later, the patient's neurological status deteriorated. She became lethargic, disoriented, and globally dysphasic, was unable to move her lower extremities, and exhibited bilateral Hoffmann's signs and extensor plantar responses. In addition, decorticate posturing could be elicited upon painful stimulation. Repeat lumbar puncture revealed a pressure of 210 cm water, but was otherwise normal. Serum electrolytes remained normal, but the platelet count rose to 500,000/μL. EEG studies revealed evidence of a grade II bifrontotemporal dysrhythmia and a generalized grade I dysrhythmia. Auditory-evoked potentials were normal. Repeat CT scanning revealed new lucencies in the frontoparietal lobes bilaterally, paralleling the falx, with irregular areas of enhancement, in addition to the basal ganglial hypodense areas present on previous CT scans (Fig 1). Four vessel arteriography disclosed occlusion of both anterior cerebral arteries, without other large vessel involvement (Fig 2). Standardized platelet aggregation studies, performed in an outside laboratory, were consistent with a hyperaggregable state at this time. Repeat platelet studies ten days later demonstrated a return to normal control aggregation status.

After the patient was treated with a course of steroids to quell potential brain edema and fluid status was carefully maintained, further neurological deterioration halted. Except for a urinary tract infection, the patient's subsequent hospital course was uneventful, and she eventually was transferred to a rehabilitation unit where she regained use of her upper extremities and the ability to speak.

Comment

Determining the cause of cerebral infarction in young individuals without atheromatous vessel disease is difficult. In a study of 101 young adult stroke victims, Tengborn et al found that 60% of the patients had no predisposing risk factors to stroke (11). Hart and Miller list a lengthy differential diagnosis of cerebral infarction in young adults and suggest that a highly systematic approach be used to sort through the many diagnostic possibilities (12).

In our patient, all possible causes of both thrombotic and embolic stroke were investigated, based on a similar differential diagnostic scheme as described by Hart and Miller (12). Although the patient was hypertensive and thus at greater risk for atherosclerotic vessel disease, no vessel disease was noted on arteriography (Fig 2). In addition, evidence of extensive end-organ damage from hypertension was lacking: the serum creatinine was normal, minimal retinal changes were present, and no left ventricular hypertrophy was evident by ECG or echocardiography. Although CT scans of the brain showed evidence of hypertensive "lacunar"-type ischemic damage, this could not sufficiently account for the clinical course of our patient, and it is felt that the findings on CT scan represent chronic changes, since they were present on the initial scan and did not change with subsequent scans. Also, studies have shown that up to 80% of stroke victims manifest an increased systemic blood pressure in response to an increased intracranial pressure caused by stroke (in this case 210 cm water) to maintain cerebral perfusion (13). It is just as likely that our patient's hypertension was the result, as opposed to the cause, of her stroke. The nature of the initial stroke, having occurred during sleep, suggested a thrombotic episode, as did the onset of the second infarct. That this patient's strokes were caused by anterior cerebral artery involvement is supported by the clinical findings, the CT scans obtained after the second event, and the arteriogram findings.

The anterior cerebral artery consists of two portions: the precommunal (A1) portion connecting the internal carotid artery to the anterior communicating artery, and the postcommunal (A2) portion arising from the junction of the A1 segment and the anterior communicating artery. These two segments supply the anterior four-fifths of the medial portion of the orbital surface of the frontal lobe, the frontal pole, part of the superior medial border of the cortex (A2), and the anterior limb and genu of the internal capsule, anterior perforate substance, amygdala, anterior hypothalamus, and the anteromedial aspect of the head of the caudate nucleus (A1) (14). Our patient presented with paralysis of the right leg, suggesting involvement of the motor area supplied...
by the anterior cerebral artery, and weakness in the right arm, indicating involvement of either the arm area of the cortex or fibers descending from the corona radiata, both areas supplied by the anterior cerebral artery (15). The hypoesthesia of the right leg indicates involvement of the sensory area of the foot and leg (15). Abulia, a common component of anterior cerebral artery stroke syndromes, could represent cingulate gyrus, medial parietal, or temporal lobe involvement, although the anatomical correlates of this condition are less well characterized (15).

The global dysphasia noted during the second stroke does not typically accompany anterior cerebral artery stroke, occurring mostly in middle cerebral artery strokes, and thus presented problems in clinical diagnosis. Although atypical aphasia syndromes involving both the anterior limb of the internal capsule and corona radiata fibers en route to the genu (areas supplied by the anterior cerebral artery) have been described (16), raising the possibility that bilateral anterior cerebral artery occlusion could precipitate aphasia, there are too few reported cases to ascribe this to our patient's dysphasia. A reasonable explanation for our patient's dysphasia, which may also explain the transient decorticate posturing noted, is that a diffuse hypercoagulable state transiently existed which affected multiple small vessels diffusely throughout the brain, resulting in reversible ischemia to the speech areas and to brain stem areas rostral to the red nucleus.

Since no evidence suggesting another etiology was found, and since symptoms of alcohol withdrawal (tachycardia, diaphoresis, and tremulousness) were present on the morning of the second stroke, we hypothesized that ethanol ingestion contributed in some way to this patient's infarct. A review of the literature on this subject revealed evidence that alcohol intoxication predisposes to both arterial and venous thrombosis and cerebral infarction (3,17). Many mechanisms are responsible for this predisposition. An increase in hematocrit and blood viscosity (3), ethanol-induced sludging of blood (3), disturbed platelet function (17), and reduced erythrocyte flexibility (3) all are described effects attributable to alcohol ingestion. It also has been shown that cerebral blood flow is reduced and autoregulation of the cerebral vasculature impaired during acute intoxication in monkeys and dogs (18). In light of these reports, it is worthy of note that our patient's platelets exhibited hyperaggregability during epinephrine and adenosine diphosphate induced aggregation experiments, a property known to cause transient ischemic attacks (19).

Alcohol withdrawal symptoms begin to appear about three days following cessation of ingestion. This corresponds well to the time our patient's condition deteriorated. It is intriguing to speculate that a sympathetic outpouring secondary to ethanol withdrawal might contribute to, or cause, thrombosis via epinephrine-induced platelet aggregation. This also would help explain the tachycardia and diaphoresis noted on the third day of

Fig 2 (right)—Cerebral arteriograms via right intracarotid injection, early, late, and lateral views, demonstrating failure of contrast to fill either anterior cerebral arteries on the early film (A) and retrograde filling of both anterior cerebral arteries on the late film (B).
the patient's hospitalization. However, further studies must be undertaken to substantiate this observation.

The aforementioned hemodynamic factors would be expected to most affect circulatory beds farthest removed from the heart, because our patient's anterior cerebral arteries, the distal-most aspect of the cerebral circulation, became thrombosed, altered blood rheology is more likely than other more common etiologies such as atheromatous disease, which tends to occur more proximally, or embolic phenomena, which usually cause unilateral occlusion.

The role of hemoglobin A-S in this patient's condition is unclear. Controversy exists regarding the role of hemoglobin A-S in disease, the occurrence of hematuria and renal and splenic infarction being more commonly accepted complications. Many reports have associated neurovascular disease with the presence of hemoglobin A-S. Sicking of red blood cells occurs by reduction of S hemoglobin, which can be caused by hypoxemia, acidity, dehydration, and the presence of reducing agents. Lactate and NAD both are potent, endogenous reducing agents and increase in tissues during alcohol intoxication. Lactate also causes local tissue acidosis. These factors may interact to cause sickling in the intoxicated patient, as has been suggested by Diggs (20).

In view of our patient's platelet aggregation status, coupled with the chronology of neurological deterioration related to alcohol ingestion, we concluded that the anterior cerebral artery occlusion was secondary to an alcohol-induced derangement of hemodynamic and rheologic parameters. This may have been compounded by sickling of red blood cells secondary to both the metabolic effects of alcohol and the local hypoxemia created by increased viscosity and hemodynamic sludging, but proof of this requires further studies on SCT blood.

The pathophysiology of hypercoagulability is complex, and interpretation of studies used to document hypercoagulability is controversial. Since the presence of lupus-type inhibitors and levels of protein C, protein S, and antithrombin III were not determined, their affect on coagulation and thus their contribution to this patient's stroke is unknown. It may be useful to assess such parameters in patients with alcohol-related thrombotic strokes.

Of final note in the clinical course of this patient is that her blood pressure decreased to 90/60 mm Hg on the third day following the initial stroke, predictably the chronology of return to normal cerebral blood flow autoregulation following stroke according to Gill et al (13). This drop in blood pressure may have contributed to the second stroke, and as such, overaggressive treatment of blood pressure following stroke should be avoided. Furthermore, hypertension based solely on presenting blood pressure should be used reluctantly to label stroke causation, since it may be the result rather than the cause of cerebral infarction.

References