Chapter 52
STROKE AND RELATED DISORDERS

Stroke (a poorly descriptive term for acute brain injury of vascular origin) is the third leading cause of death in the United States and is responsible for approximately one-fourth of all deaths in the adult population. Considering these credentials, stroke should occupy a top position in the hierarchy of life-threatening conditions. However, stroke has traditionally received little attention from critical care specialists. This has changed in recent years. The current view of acute cerebral infarction emphasizes the similarities to acute myocardial infarction and stresses the value of approaching a *brain attack* with the same aggressive measures used in the approach to a heart attack (1,2).

DEFINITIONS

The clinical disorders described in this chapter are cerebrovascular disorders. The following are some definitions and classifications for these disorders proposed by the National Institute of Neurologic Disorders and Stroke (3).

STROKE

Stroke is a clinical condition with all the following features (3,4):

1. An **acute** neurologic disorder

2. Produced by **nontraumatic** injury in the central nervous system that is vascular in origin

3. Accompanied by **focal** rather than global neurologic dysfunction

4. Persists for **longer than 24 hours** or results in death within the first 24 hours

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Classifications

Stroke can be classified as ischemic or hemorrhagic based on the type of pathologic injury. Approximately 80% of strokes are ischemic and 15% are hemorrhagic (10% caused by intracerebral hemorrhage, and 5% caused by subarachnoid hemorrhage) (5). Ischemic strokes can be further classified as thrombotic or embolic in origin. Thrombotic strokes originate in the same fashion as described for acute myocardial infarction (MI) (see Chapter 19). Embolic strokes account for 20% of ischemic strokes (6). Most emboli originate from thrombi in the left atrium (from atrial fibrillation) and left ventricle (from acute MI), but occasionally they can arise from deep vein thrombosis in the legs that embolized through a patent foramen ovale (7).

Stroke can also be classified according to the rapidity of neurologic recovery. A minor

stroke, also called a *reversible ischemic neurologic deficit* (RIND), is characterized by complete recovery of neurologic function within 3 weeks after the acute event (3). A major stroke is characterized by neurologic deficits that persist for longer than 3 weeks after the event.

TRANSIENT ISCHEMIC ATTACK

A transient ischemic attack (TIA) is an episode of focal loss of brain function (as a result of ischemia) that lasts less than 24 hours (3). The major distinction between TIA and stroke is the underlying pathology; i.e., ischemia in TIA versus infarction or hemorrhage in stroke. This, in turn, determines the duration of the neurologic deficits: less than 24 hours in TIA and longer than 24 hours in stroke.

BEDSIDE EVALUATION

The patient with a suspected stroke will have new-onset focal neurologic deficits that are not traumatic in origin. If the deficits have been present for less than 24 hours, it is often impossible to distinguish TIA from stroke. The following features of the clinical presentation can be useful in the evaluation of suspected stroke (8). These features are included in Table 52.1.

TABLE 52.1. THE BEDSIDE EVALUATION OF SUSPECTED STROKE

Seizures

Generalized convulsive seizures and convulsive status epilepticus are uncommon in TIA and stroke. Seizures develop in approximately 10% of cases of stroke (4). They usually appear in the first 24 hours and are focal rather than generalized in most cases.

Fever

Fever is uncommon in TIA but can be present in approximately 50% of patients with stroke (9).

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In most cases of fever associated with stroke, the fever is due to a process other than the stroke (e.g., infection or thromboembolism).

Consciousness

The reticular activating system in the brainstem is responsible for arousal or wakefulness (consciousness). Because most cases of stroke are the result of *cerebral* infarction, loss of consciousness is not a common finding in uncomplicated stroke (1,4). When focal neurologic deficits are accompanied by coma, the most likely diagnoses are intracerebral hemorrhage, massive cerebral infarction with cerebral edema, brainstem infarction, or seizures (nonconvulsive seizures or postictal state).

Aphasia

The left cerebral hemisphere is the dominant hemisphere for speech in 90% of subjects. Damage involving the left cerebral hemisphere produces a condition known as aphasia, which is defined as a disturbance in the comprehension and formulation of language (10). Patients with aphasia can have difficulty understanding verbal remarks (receptive aphasia), difficulty in verbal expression (expressive aphasia), or both (global aphasia). Most patients with aphasia will have a cerebral infarction in the distribution of the left middle cerebral artery (10). Other causes of aphasia are tumors, head injury, and Alzheimer's dementia.

Weakness

The hallmark of ischemia or hemorrhagic injury involving the cerebral hemispheres is weakness in the contralateral limbs. Limb weakness is present if the patient is unable to hold the arm in 90 degrees of abduction for 10 seconds or unable to hold the leg 30 degrees above

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the horizontal plane for 5 seconds (11). The presence of a hemiparesis supports the diagnosis of TIA or stroke. However, hemiparesis has also been described in metabolic encephalopathy caused by renal failure (12) and sepsis (13).

DIAGNOSTIC EVALUATION

The diagnostic evaluation of suspected stroke has traditionally proceeded at a slow pace. However, as mentioned in the introduction to this chapter, the current view of ischemic stroke stresses the similarities with acute MI, and the need to approach acute stroke with the same alacrity used in the approach to acute MI. According to the U.S. National Stroke Association, the evaluation of suspected stroke should be completed within 6 hours after the onset of symptoms (14). Or stated more succinctly, *time is brain* (15).

ROUTINE STUDIES

The evaluation of suspected stroke should include blood chemistries to search for hypoglycemia, hyponatremia, hypernatremia, and renal failure. Additional routine studies should include an INR if the patient is being treated with coumadin, an electrocardiogram if atrial fibrillation is suspected, and a chest x-ray if the patient has fever.

COMPUTED TOMOGRAPHY

Computed tomography (CT) of the brain can identify ischemic infarction and hemorrhage and can distinguish between the two (16). The sensitivity of CT scans is 70% for cerebral infarction (17) and over 90% for intracerebral hemorrhage (1). However, the sensitivity of CT scans is influenced by the time passed from the onset of stroke to the time the scans are performed.

Timing

The influence of timing on the diagnostic yield from CT scans is illustrated in Figure 52.1.

For cerebral infarctions, the diagnostic yield from CT scans is 50% lower if the scans are performed within 24 hours after the infarction (16). Therefore, an unrevealing CT scan performed within 24 hours after the onset of suspected stroke does not rule out the possibility of cerebral infarction.

Figure 52.1. The influence of timing on the yield from CT scans. Both CT scans are from the same patient with suspected stroke. The scan on the left was obtained within 24 hours after the onset of symptoms and is unrevealing. The scan on the right was obtained 3 days later and shows a large hypodense area (infarction) with mass effect in the left cerebral hemisphere. (Reproduced with permission from Reference 16.)

Indications

Two major benefits are derived from CT scans in suspected stroke. First, CT scans can distinguish infarction from hemorrhage, which is

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important for selecting the appropriate therapy. Second, CT scans will identify the occasional case of suspected stroke caused by a space-occupying lesion (tumor or abscess). For these reasons, CT scans are recommended as a routine diagnostic procedure in patients with suspected stroke (1).

Cost

As may be expected, CT scans are costly. At Presbyterian Medical Center (University of Pennsylvania), the charge to the patient for an unenhanced CT scan of the head is **$1342** (charge for the fiscal year 1996).

MAGNETIC RESONANCE IMAGING

Magnetic resonance imaging (MRI) has a higher diagnostic yield than CT scans for bland infarctions (particularly those involving the cerebellum and brainstem) (18). The value of MRI in suspected stroke

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is illustrated by the case in Figure 52.2. The MRI scan in this figure is from a previously healthy 39-year-old woman who experienced acute onset of right arm and leg weakness. The initial CT scan was unrevealing, but the MRI scan reveals multiple (hyperdense) infarctions along the course of the left middle cerebral artery (whereas infarctions are hypodense on CT scans, they are hyperdense on MRI scans). This prompted a cerebral angiogram, which revealed probable vasculitis as a cause of the cerebral infarction.

Figure 52.2. A T$_2$-weighted MRI scan from a 39-year-old woman with acute onset of right-sided weakness and a normal CT scan. The arrows point to hyperdense areas of infarction along the distribution of the left middle cerebral artery. (Case history and MRI scan courtesy of Dr. Sami Khella, M.D.)

Indications

MRI is reserved for the occasional case of suspected stroke in which CT scans are unrevealing. However, because of the expense of MRI

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(see below), it should be reserved for cases in which the results of MRI will lead to improved therapy and a better chance for recovery.

Contraindications

Because MRI uses magnetic pulses, it is contraindicated in patients with implanted pacemakers, cerebral aneurysm clips, intraocular metal, and cochlear implants (18). Other metal implants and vena cava filters are relative contraindications to MRI (18).

Cost

At Presbyterian Medical Center (University of Pennsylvania), the patient charge for an MRI of the brain is **$1761** (for fiscal year 1996).

OTHER DIAGNOSTIC TESTS

The following tests are appropriate for the indications cited.

1. **Lumbar puncture** is not indicated in most patients with suspected stroke. It can be useful in the occasional case when a CT scan reveals equivocal evidence of subarachnoid hemorrhage or when an abscess is in close proximity to the subarachnoid space.

2. **Echocardiography** is indicated when stroke is associated with atrial fibrillation, acute MI, or left-sided endocarditis. It may also be indicated in stroke of undetermined etiology to identify a patent foramen ovale (and possible paradoxical cerebral embolism).

3. **Electroencephalography** is indicated in cases in which seizures are suspected as the cause of the neurologic deficits.

EARLY MANAGEMENT

The following discussion refers to the management in the first 24 hours after acute stroke.

HYPERTENSION

Hypertension is common in the early period after acute stroke, but antihypertensive therapy is not advised as a routine practice for two reasons. First, cerebral autoregulation may be lost in the region of the brain that is damaged, and thus acute lowering of the blood pressure could enhance the extent of injury. This is verified by a clinical study showing that acute lowering of blood pressure in hypertensive stroke victims is often accompanied by worsening of the neurologic deficits (19). This is applied to patients with severe hypertension (diastolic blood pressure above 120 mm Hg) as well. The second reason to avoid

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antihypertensive therapy is the tendency for the hypertension to resolve spontaneously in the days following an acute stroke (20).

The Stroke Council of the American Heart Association recommends antihypertensive treatment when the systolic pressure is above 220 mm Hg or when the mean blood pressure is above 130 mm Hg (1). However, this recommendation lacks experimental validation. If antihypertensive therapy is used, the goal must be *gradual* rather than prompt reduction of blood pressure. Both **nitroglycerin and nitroprusside should be avoided** because these cerebral vasodilators can increase intracranial pressure (1). Nicardipine (a calcium channel blocker that preserves cerebral blood flow) or angiotensin-converting enzyme inhibitors (which have little effect on cerebral vessels) may be the most appropriate agents for lowering blood pressure in acute stroke.

ANTICOAGULATION

Approximately 20% of patients with acute ischemic stroke develop progressive neurologic deficits over the ensuring 4 days (21,22). Therapeutic anticoagulation with heparin has been the traditional practice for patients with progressive ischemic stroke (22). Although early studies showed a possible benefit from this practice, these studies were not well designed. More recent studies reveal **little or no benefit from full anticoagulation in progressive ischemic stroke** (22).

THROMBOLYTIC THERAPY

Considering the similarities between acute thrombotic infarction of the brain and acute (thrombotic) MI and the success with thrombolytic therapy in acute MI (see Chapter 19), it follows that thrombolytic therapy should be evaluated in acute ischemic stroke. The studies of thrombolytic therapy in ischemic stroke have not been encouraging. However, in the most recent study, which was sponsored by the National Institute of Neurologic Disorders and Stroke (NINDS) (23), patients given tissue plasminogen activator (0.9 mg/kg over 1 hour) within 3 hours after the onset of ischemic stroke showed significantly fewer neurologic deficits 3 months later. (The clinical course in the early period after acute ischemic stroke was not favorably influenced by thrombolytic therapy in this study.)

Based on the NINDS study just described, **the Food and Drug Administration has approved the use of tissue plasminogen activator in the first 3 hours after the onset of acute ischemic stroke** (24). However, because a CT scan must be obtained to rule out

hemorrhage before thrombolytic therapy is started, this means that patients with ischemic stroke must seek treatment in the emergency department *and* have a CT scan completed within 3 hours to be candidates for thrombolytic therapy. In light of these strict requirements, it is unlikely

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that thrombolytic therapy will become a common treatment modality in acute ischemic stroke.

INCREASED INTRACRANIAL PRESSURE

Increased intracranial pressure can be the result of intracerebral hemorrhage or massive infarction with cerebral edema. In either case, it carries a poor prognosis. Several measures are used to lower intracranial pressure following head injury (25). However, many of these are aimed at reducing cerebral blood flow, which can aggravate an ischemic stroke. The use of selected methods to lower intracranial pressure in acute ischemic stroke can be summarized as follows:

1. Intracranial pressure monitoring is of unproven value for managing intracranial hypertension in ischemic stroke (1) and is not recommended as a routine measure.

2. Elevating the head of the bed to 30 degrees will reduce intracranial pressure by promoting venous return from the head (25), and this measure is recommended for all patients with intracranial hypertension (1).

3. Endotracheal suctioning can increase intracranial pressure, even when hypoxemia is prevented by a preceding period of 100% oxygen inhalation (26). Therefore, endotracheal suctioning should be reduced in frequency and duration (if possible) in patients with intracranial hypertension (26).

4. Hyperventilation to induce hypocapnia and reduce cerebral blood flow does not improve outcome in patients with a head injury (25). This lack of documented benefit, together with the risk of exaggerated ischemia during hyperventilation, makes hyperventilation an undesirable intervention is ischemic stroke.

5. High-dosage corticosteroids do not improve outcome in ischemic stroke with cerebral edema and can increase the risk of infection (1). Therefore, steroids should be avoided in all cases of intracranial hypertension.

6. Mannitol lowers intracranial pressure by drawing water out of cerebral tissues (27). Although of unproven value, mannitol can be given in cases of severe or progressive cerebral edema from acute stroke. The dose is 0.25 to 0.5 g/kg IV over 20 minutes. Hypertonic fluids like mannitol can increase the permeability of the blood-brain barrier (25), which favors the entry of mannitol into cerebral tissues. Because of this risk, mannitol should not be given in repeated doses to control intracranial pressure (25).

SUBARACHNOID HEMORRHAGE

Subarachnoid hemorrhage (SAH) is usually the result of aneurysmal rupture or bleeding from an arteriovenous malformation. Predisposing factors for SAH include cocaine abuse and bleeding disorders (28).

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Although classified as a type of stroke (5), SAH can differ from the other types of stroke in both presentation and management.

CLINICAL PRESENTATION

The hallmark of the clinical presentation of SAH is headache. The full-blown syndrome may be preceded by a severe but self-limited headache called a sentinel headache (29), which is presumably the result of aneurysmal dilation or a small hemorrhagic leak. The headache of SAH is usually abrupt in onset, persistent and progressive, and worse with exertion. Severe headache that is worse with exertion is more characteristic of SAH than the myriad other causes of headache (29). Although the headache of SAH tends to be centered at the base of the skull or in the cervical region, this feature is not specific for SAH. Other manifestations, such as nausea and vomiting, mental status changes, and stiff neck, may or may not be present.

DIAGNOSTIC EVALUATION

As mentioned earlier, CT scans of the head (unenhanced) have a 90% sensitivity for the detection of hemorrhage, including subarachnoid hemorrhage, and thus are the initial diagnostic test of choice for suspected SAH. However, CT scans can miss SAH in the posterior fossa (where the brainstem and cerebellum are located). The image in Figure 52.3 is an MRI scan from a 30-year-old woman with severe and persistent headache who had a normal CT scan of the head. The MRI scan shows a hyperdense area (indicated by the arrows) just ventral to the pons, which represents a SAH. Thus, even though CT scans have a high sensitivity for SAH, a negative CT scan does not eliminate the possibility for SAH.

Figure 52.3. An MRI scan from a 30-year-old woman with severe, persistent headache and a normal CT scan of the head. Note the arrows pointing to a hyperdense area ventral to the brainstem. This represents a prepontine subarachnoid hemorrhage. Lumbar puncture confirmed the presence of blood in the subarachnoid space. (Case history and MRI scan courtesy of Dr. Sami Khella, M.D.)

MANAGEMENT

The morbidity and mortality in SAH is related to two processes: recurrence of the hemorrhage and cerebral vasospasm.

Recurrent SAH

In most cases of SAH, the bleeding has subsided at the time of diagnosis. To prevent a recurrence of the SAH, cerebral angiography is performed to identify the responsible vascular abnormality for surgical correction. However, angiography is usually delayed until

the patient is awake and clinically recovered.

Cerebral Vasospasm

The neurologic deficits in SAH are caused by vasospasm of cerebral vessels with resultant cerebral ischemia. The vasospasm is produced

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by blood in the subarachnoid space, although the exact mechanism is unclear. This vascular response is attenuated by nimodipine, a calcium channel blocker that has a preferential vasodilating effect on cerebral vessels. Nimodipine in a dosage of 0.35 mg/kg orally every 4 hours has proven effective in reducing vasospasm (30) and improving neurologic function (31) in patients with SAH. As a result, this agent is used routinely in SAH.

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