Types and Etiologies of Strokes

An understanding of the types and etiologies of strokes is necessary to appropriately treat them.

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The enormous impact of stroke on society is devastating. It is the third leading cause of death, ranking only behind heart disease and cancer, and is the leading cause of disability in adults in the US.[1] There are approximately 750,000 new or recurrent strokes and 150,000 deaths from stroke reported every year, which result in approximately $40 billion in annual direct and indirect costs. The number of people affected by stroke is predicted to increase over the next decade due to the aging population. Stroke is divided into two major classifications: ischemic and hemorrhagic. Although the majority of stroke cases are ischemic, hemorrhagic strokes draw equal attention due to less favorable prognosis. Evaluation of stroke type and etiology plays a crucial role in acute management and prevention of recurrent strokes. In this article, we review the various etiologies of both stroke subtypes.

ISCHEMIC STROKE

Defined as an irreversible focal brain damage due to disrupted blood flow, ischemic stroke accounts for approximately 80% of all strokes. More common among men, the elderly population, as well as African American and Hispanic populations, it is relatively rare in children where its etiology is slightly different from that of the adult population. The etiology of ischemic strokes is divided into five categories.

Cardioembolic Stroke

Cardioembolic stroke accounts for 15% of all ischemic strokes.[2] However, its prevalence is much higher in younger patients. Almost 80% of emboli lodge in the anterior circulation, with the middle cerebral artery distribution being the most common receiver. Its embolus is usually larger than those arising from the proximal arteries.[3] The most common characteristic in patients with cardioembolic stroke is the sudden onset of neurologic symptoms that are maximal at onset without warning signs. Another pattern quite characteristic of brain embolism has been called the "spectacular shrinking deficit," which is described as sudden, complete or nearly complete clearing of the neurologic deficit.[4] Nonvalvular atrial fibrillation remains the most common cause of cardiac emboli, afflicting 0.4% of the population, and its incidence increases with age. Several large studies, such as the Framingham study, demonstrated the high risk of atrial fibrillation for ischemic stroke.[5] Table 1 summarizes all the potential cardiac causes of embolism.

TABLE 1. POTENTIAL CARDIAC CAUSES OF EMBOLISM

- Atrial fibrillation
- Atrial flutter
- Sick sinus syndrome
- Congestive heart failure
- Akinetic region
- Mitral valve stenosis
- Myocardial infarction within 6 months
- Valve surgery
- Atrial myxoma
- Ventricular aneurysm
- Aortic arch atherosclerosis
- Infective endocarditis
- Patent foramen ovale through paradoxical emboli
- Marantic endocarditis

TABLE 2. CAUSES OF LARGE ARTERY DISEASE

- Atherosclerosis
- Arterial dissection
- Fibromuscular dysplasia
- Moya Moya disease
- Accelerated atypical atherosclerosis by radiation therapy
- Arterial invasion by head and neck cancer
- Syphilis
- Takayasu disease
- Migraine

TABLE 3. CAUSES OF SMALL VESSEL DISEASE

- Arteriosclerosis from chronic hypertension
- Amyloid angiopathy
- Vasculitis
- Chronic meningitis
- Neurocysticercosis
- Neuroboreliosis
- Drug abuse, particularly cocaine
- Acquired immunodeficiency syndrome
- Rare genetic condition such as CADASIL

Large Artery Disease

Large artery disease includes both extracranial and intracranial vessel diseases. The mechanism by which it causes a stroke is either through thrombosis with artery-to-artery embolism or through thrombosis with *in situ* occlusion. The most common cause of large artery disease is atherosclerosis, which is often associated with peripheral and cardiovascular diseases. The various causes of large artery disease are listed in Table 2.

Small Vessel Disease

Small vessel disease accounts for approximately 19% of all ischemic strokes and results in small deep infarcts in which its manifestation includes the following five lacunar syndromes described by Fisher:[6,7] pure motor hemiparesis (the most common lacunar syndrome), pure sensory stroke, dysarthria-clumsy hand syndrome, ataxic hemiparesis, and isolated motor/sensory stroke. The most common cause of small vessel disease is arteriosclerosis from chronic hypertension. Rashid et al[8] conducted a systematic review and meta regression of completed, randomized controlled trials on the use of antihypertensive agents for secondary stroke prevention. The results of the study showed that the use of antihypertensive agents significantly reduces the recurrent stroke events. Moreover, vascular prevention was associated positively with the magnitude by which blood pressure was reduced. A complete list of the different causes of small vessel disease is compiled in Table 3.

Undetermined Etiology

Despite a complete evaluation, the etiology of ischemic stroke remains unknown in about 30% of patients.[2]

Hypercoagulable State

Hypercoagulable state accounts for only 4% of all ischemic strokes[9] and is usually preceded by a history of venous thrombosis. Evaluating for hypercoagulable state should be considered in patients who are young, have a family history of thrombosis, have a history of deep vein thrombosis, or have recurrent unexplained strokes. The various hematologic disorders that lead to hypercoagulable state are listed in Table 4.

A further classification of ischemic stroke can be performed based on the site of occlusion and the presence or absence of collateral supply. The Qureshi classification scheme (Table 5) has been used to stratify patients with ischemic stroke based on the previously mentioned criteria and has been validated in previous studies.[10,11]

HEMORRHAGIC STROKE

Hemorrhagic stroke is defined as an irreversible focal brain damage due to a ruptured intracranial blood vessel. It accounts for approximately 20% of all strokes. Hemorrhagic strokes are further subdivided into intraparenchymal and subarachnoid hemorrhage.

Intraparenchymal Hemorrhage

Intraparenchymal hemorrhage is more common than the subarachnoid hemorrhage.[12] Most patients present with focal neurologic deficit frequently associated with headache. Clinical presentation and neurologic examination are not adequate to differentiate hemorrhagic stroke from ischemic stroke. The use of imaging modalities such as CT is necessary to differentiate between the two.

TABLE 4. DISORDERS ASSOCIATED WITH HYPERCOAGULABLE STATE

- Mutation in factor V (factor V Leiden)
- Prothrombin mutation
- Dysfibrinogenemia
- Antiphospholipid antibodies
- Homocystinuria and homocystenemia
- Sickle cell disease
- Increased platelet reactivity
- Heparin-induced thrombosis
- Increased blood viscosity
- Mucin-secreting carcinoma

TABLE 5. CLASSIFICATION OF ACUTE ARTERIAL OCCLUSIONS IN PATIENTS WITH ISCHEMIC STROKE ACCORDING TO THE QURESHI GRADING SCHEME

Grade 0	No occlusion		
Grade 1	MCA occlusion (M3 segment)	ACA occlusion (A2 or distal segment)	One BA/VA branch occlusion
Grade 2	MCA occlusion (M2 segment)	ACA occlusion (A1 and A2 segments)	Two BA/VA branch occlusions
Grade 3	MCA occlusion (M1 segment)		
3A	Lenticulostriate arteries spared and/or leptomeningeal collaterals visualized		
3B	No sparing of lenticulostriate arteries nor leptomeningeal collaterals visualized		
Grade 4	ICA occlusion (Collaterals present)	BA occlusion (Partial filling direct or via collaterals)	
4A	Collaterals fill MCA	Anterograde filling*	
4B	Collaterals fill ACA only	Retrograde filling*	
Grade 5	ICA occlusion (No collaterals)	BA occlusion (Complete)	

Abbreviations: ACA, anterior cerebral artery; BA, basilar artery; ICA, internal carotid artery; MCA, middle cerebral artery; VA, vertebral artery.

**The predominant pattern of filling.*

Prognosis depends on the size of hemorrhage, extension to the ventricles, age of the patient, and the level of consciousness at presentation. The most common cause of hemorrhagic stroke is hypertension. The most common regions of the brain that are affected by hypertensive hemorrhage are the putamen, thalamus, pons, cerebellum, and lobar white matter. Treatment of elevated blood pressure in acute intraparenchymal hemorrhage is still controversial. However, a recent pilot multicenter study showed the safety and potential efficacy of treating elevated blood pressure in patients with hemorrhagic stroke.[13]

A 3-year, multicenter, open-labeled, nonrandomized phase I pilot trial has been proposed.[13] The primary objective of the study is to determine the tolerability and safety of three escalating levels of antihypertensive treatment goals for acute hypertension in subjects with supratenorial intracerebral hemorrhage.

Less common causes include trauma, arteriovenous malformation, amyloid angiopathy, bleeding diathesis (eg, anticoagulants), drugs (eg, cocaine), vasculitis, and cerebral venous thrombosis.

Subarachnoid Hemorrhage

Ruptured intracranial aneurysms are responsible for 80% of subarachnoid hemorrhage, which usually presents with an abrupt severe headache. Saccular aneurysms are also called *berry aneurysms* because their morphology resemble a berry (out pouch). They mostly originate from the anterior circle of Willis and are associated with several conditions such as polycystic kidney disease, Marfan syndrome, fibromuscular dysplasia, Ehlers-Danlos syndrome, and coarctation of the aorta. They are often complicated with vasospasm that results in ischemic stroke. Morbidity and mortality is high, and early rebleeding is common. Other less common causes include trauma and ruptured arteriovenous malformation.

SUMMARY

Stroke is the third leading cause of death ranked behind heart disease and cancer. Moreover, stroke is the leading cause of disability among adults. The two classifications of stroke are hemorrhagic and ischemic, with ischemic constituting approximately 80% of cases. Cardioembolic, larger vessel diseases, smaller vessel diseases, and hypercoagulable state constitute approximately 70% of the ischemic stroke. The etiology of the remaining 30% of ischemic stroke is unknown. Hemorrhagic stroke is further divided into intraparenchymal and subarachnoid hemorrhages. An understanding of the type and underly-

ing etiology of stroke is important in guiding appropriate treatment. ■

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