SUBARACNOID HEMORRHAGE
NON-TRAUMATIC

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December 23, 2009

General Information

Subarachnoid hemorrhage (SAH) affects approximately 30,000 individuals per year in the United States, with an annual incidence of 1 per 10,000. In most populations primary non-traumatic SAH accounts for 5 to 9% of all strokes. SAH as the result of aneurysms is about 10 to 11 per 100,000 populations in Western Countries, with somewhat higher frequencies in the United States and Finland and among the Asian countries, Japan. It is lower in New Zealand and the other Scandinavian countries.

Intracranial aneurysms are uncommon in children, being found in association with coarctation of the aorta or hypertension due to renal disease. In adults, intracranial aneurysms occur with a frequency of 2%, so that 2 to 3 million Americans have aneurysms. More than 90% of these aneurysms are small, less than 10 mm, and remain asymptomatic throughout the patient's life. The annual risk of rupture of an asymptomatic aneurysm is approximately 0.7%. Important risk factors for rupture are increasing size, prior SAH from a separate aneurysms, and basilar apex and posterior communicating artery location.

At all ages the presence of an aneurysm tends to parallel the height of the blood pressure. This is clearly demonstrated by the sudden change in sex ratio after the age of 50. Up until 50 the ratio of females to males with aneurysm is 3:2. Over 50 it rises to 10:1. This is believed to be due to the better long-term survival of females with significant hypertension, leading to the development of aneurysms in the 50 to 70 age group.

The annual incidence of aneurysmal subarachnoid hemorrhage increases linearly with age, from less than 1 per 100,000 before the age of 20 years to about 23 per 100,000 after the age of 60. The median age of onset of the first subarachnoid hemorrhage is 50 to 60 years. Women are affected more often than men.

The rate of rupture of saccular aneurysm is estimated at approximately 1 to 2% per year. Aneurysms in general increase in size with time. It appears the primary determining

factor as to whether an aneurysm will rupture is its size, with the critical size being 10 mm. Internal carotid artery aneurysms of less than 7 mm in diameter bleed at a rate of approximately 0.1% per year; compared to an annual rate of 8% for those greater than 25 mm in size. Other risk factors for aneurysm rupture in approximate order of importance include: cigarette smoking, aneurysm-related headache or cranial nerve compression, heavy alcohol use, cocaine, amphetamines and other sympathomimetic agent use, female gender, especially postmenopausal, multiple aneurysms and hypertension.

The prevalence of aneurysms increases with age and is higher in patients with atherosclerosis, a family history of intracranial aneurysms, or autosomal-dominant polycystic kidney disease (PCKD). Intrcranial aneurysms have also been associated with Ehlers-Danlos syndrome, Marfan syndrome, pseudoxanthoma elasticum, and coarctation of the aorta.

Ehlers-Danlos syndrome (EDS) is a group of inherited connective tissue disorders, caused by a defect in the synthesis of collagen, which is a protein in connective tissue. The collagen in tissue gives it pliability or if you will elasticity. Thus, collagen in skin, muscles, ligaments, blood vessels, and visceral organs plays a pivotal role in giving these structures elasticity. Consequently, abnormal collagen will adversely affect an organs elasticity, the severity of which will be determined by the individual mutation, which forms the foundation for the various types of EDS. The severity of EDS can vary from mild to life threatening. There is no cure, with supportive treatment being all that is available.

Marfan syndrome is a genetic disorder of connective tissue. It is caused by mutations in the FBNI gene on chromosome 15, which encodes a glycoprotein called fibrillin 1, which is a component of the extracellular matrix. Fibrillin 1 is essential for the proper formation of connective tissue, most especially the biogenesis and maintenance of elastic fibers. Elastin fibers are found throughout the body being especially prominent in the aorta, ligaments and the ciliary zonules of the eye; thus, these structures are most severely affected. One of the important functions of fibrillin 1 is that it binds to a transforming growth factor called TGFβ (transforming growth factory beta), which is a polypeptide. A peptide is a short polymer composed of α-amino acids. Polypeptides are composed of multiple peptide subunits.

When fibrillin 1 binds to TGFβ it keeps TGFβ from exerting its biological activity, one of which is to give rise to the release of proteases that slowly degrade the elastin fibers as well as other components of the extracellular matrix.

Genetically we have a pair of FBN 1 genes. However, because Marfan's is inherited as a dominant trait, individuals who have inherited one affected FBN 1 gene from either parent will have Marfan's, which can be mild or severe.

Pseudoxanthoma elasticum (PXE) is a genetic disease that causes fragmentation and mineralization of elastic fibers in some tissues. The most common problem arises in the skin and eyes, and later in blood vessels in the form of premature atherosclerosis. 80% of cases have mutations in the ABCCG gene on the short arm of chromosome 16 (16p13.1).

85 to 90% of intracranial aneurysms are located in the anterior circulation, with the three most common sites being the junction of the posterior communicating and the internal carotid artery (approximately 40%), the anterior communicating artery complex (approximately 30%), and the middle cerebral artery at the first major branch point in the sylvian fissure (approximately 20%). Posterior circulation aneurysms most often occur at the apex of the basilar artery or at the junction of the vertebral and posteroinferior cerebellar artery. Saccular aneurysms of the distal cerebral arterial tree are rare. Nearly 20% have two or more aneurysms with many of those being "mirror" aneurysms on the same vessel, contralaterally.

Rupture of saccular aneurysms at the base of the brain account for approximately 80% (range 57 to 94%) of non-traumatic acute SAH.

Non-aneurysmal, non-traumatic causes for SAH are varied. Arteriovenous malformations are responsible for approximately 5 to 10% (range 5 to 28%). In 10 to 15% no cause is identified.

Arteriovenous malformations (AVMs) occur both within the cranial vault and the spinal canal. They involve vessels in the subarachnoid space extending into the brain parenchyma or may occur exclusively within the brain parenchyma. They are composed of greatly enlarged blood vessels separated by gliotic tissue, often with evidence of prior hemorrhage. Some of the vessels will appear as arteries with duplication and fragmentation of the internal elastic lamina, while others will show marked thickening or partial replacement of the media by hyalinized connective tissue. There are five main

types: AVMs, which are high flow and most often symptomatic; cavernous malformations; capillary telangiectasias; venous malformations, and mixed malformations. More than 90% of AVMs are asymptomatic. Bleeding may occur in patients of any age but is most likely to occur in patients younger than 40 years. They are occasionally familial, and in 7 to 10% of cases, AVMs coexist with saccular aneurysms. There are a small percentage of cases of SAH, which are due to hypertension and atherosclerotic cerebrovascular disease. Other non-aneurysmal causes of SAH are trauma, which will be addressed in the next article, idiopathic perimesencephalic SAH, intracranial arterial dissection, cocaine and amphetamine use, mycotic aneurysm, pseudoaneurysm, fusiform (Dolichoectatic) aneurysm, pituitary apoplexy, Moyamoya disease, CNS (central nervous system) vasculitis, sickle cell disease, coagulation disorders and primary or metastatic neoplasm.

In 10% of patients with non-traumatic SAH, acute SAH will be shown by CT to be confined to the perimesencephalic cisterns (pontine, superior and ambient cisterns), with the center of bleeding being adjacent to the midbrain and pons. In general patients with perimesencephalic SAH have a benign clinical course, often with a normal neurological examination. The source of the hemorrhage is believed to be venous. Rebleeding and symptomatic vasospasm or hydrocephalus virtually never occurs.

Mycotic aneurysms are caused by septic emboli, which are most often formed by bacterial endocarditis. They are usually only a few millimeters in size, and tend to occur on the distal branches of the middle cerebral artery. It has been reported they occur in up to 10% of patients with bacterial endocarditis. Mycotic aneurysmal rupture is fatal in 80%.

Septic emboli may also give rise to pyogenic segmental arteritis without aneurysm formation. These lesions may also rupture.

Pseudoaneurysm represents a dissection through a vessel wall, paralleling the lumen of the vessel. It is usually the result of trauma. The blood within the channel is contained either by a thin layer of adventitia of the vessel wall or by the surrounding tissues; a true aneurysm is not formed, hence the term pseudoaneurysm. Dissection through the adventitia can result in SAH.

Fusiform (Dolichoectatic aneurysms) tend to be tortuous circumferential vessel dilations, which usually involve the carotid, basilar, or vertebral arteries. Atherosclerosis most likely plays a role in their formation. These lesions seldom rupture.

Moyamoya disease in an inherited disease, in which certain arteries in the brain are constricted. This gives rise to inhibition of blood flow, but also, because of the inhibition it enhances thrombosis (blood clot) formation. Although, a collateral circulation develops around the areas of blockage, the vessels, which form these collaterals, are small, weak, and prone to hemorrhage, aneurysm formation and thrombosis. The disease primarily affects the internal carotid artery often with extension into the middle and anterior cerebral arteries.

SAH may be the result of an intracerebral hemorrhage, which has dissected through the cortex into the subarachnoid space. It can also be the result of intraventricular hemorrhage, which has entered the basal cisterns following which it enters the subarachnoid space.

The rupture of the aneurysm typically occurs at the fundus, being frequently associated with an acute rise in blood pressure. The relationship between rupture of an aneurysm and blood pressure is underscored by the fact it occurs more frequently in the morning, than at night due to the diurnal variations in blood pressure with much higher transient pressure peaks during the hours in which most are waking-up. This variation in blood pressure is greater in the older age group as well as hypertensive individuals, which is due to the decrease in compliance of their vascular walls.

Clinical Presentation

About 20 to 50% of patients with acute SAH have experienced warning symptoms the preceding 1 to 3 weeks before the definitive aneurysmal rupture. These are generally due to the local effects of aneurysmal expansion such as localized head pain, cranial nerve palsies or visual defects or to ‘warning leaks’ from the aneurysm such as generalized headache lasting hours to days, nausea and neck pain.

The headaches are often referred to as “thunderclap headaches” which develop in seconds, reaching maximum intensity in minutes, and can last hours to days. The headache is often described as “the worst headache of my life.” Although the headache is typically generalized, it can be in any location including focal. The focal pain may be

due to the site of aneurysmal rupture, as an example, periorbital pain due to an ophthalmic artery aneurysm. Common associated symptoms include loss of consciousness, nausea and vomiting, back or leg pain, and photophobia (this is a symptom of excessive sensitivity to light manifested by experience of discomfort or pain to the eyes due to light exposure). In those who lose consciousness, tonic posturing may occur. Most aneurysmal ruptures occur during periods of physical stress, however, they can rupture anytime, including during sleep.

Initial misdiagnosis of SAH occurs in approximately 15% of patients, and those with the mildest symptoms are at the greatest risk for being misdiagnosed. As an example, the headache experienced may be mild, easily relieved by non-narcotic analgesics or may resolve spontaneously. Such headaches are often diagnosed as tension-type or sinus-related and on occasion a migraine. Even when frank hemorrhage has occurred, the similarity of the resulting 'thunderclap headache' to a migraine is striking. What can be of help is that in the headaches associated with SAH there is often the simultaneous onset of vertigo and vomiting. In the migraine headache, vertigo and vomiting often precede the headache by 30 minutes or more, or occur as a later feature in the course of the headache, rather than simultaneously. To further compound the problem, photophobia and neck stiffness may occur in a severe migraine. Also, headache, acute nausea, vomiting and neck stiffness occur in both SAH and meningitis. Some of the literature suggests neck stiffness associated with Kernig sign is a hallmark of SAH. Kernig sign is considered positive when the leg is fully bent in the hip and knee and the knee is subsequently extended leading to discomfort. Unfortunately, neck stiffness and Kernig sign is also positive in meningitis. To put this in proper perspective, the triad of nuchal rigidity (neck stiffness), photophobia and headache is referred to as meningism, which is a sign of irritation to the meninges; irritation to the meninges can occur as the result of SAH, meningitis (inflammation of the meninges) and other diseases.

There is another sign that is frequently mentioned as a clinical sign of menigism and that is Brudzinski's neck sign. A positive Brudzinski sign is the appearance of involuntary lifting of the legs in meningeal irritation when lifting the patient's head.

Other possible foundations for misdiagnosis of SAH are: vomiting, if associated with a fever is often diagnosed as a viral syndrome, viral meningitis, influenza, as

gastroenteritis; prominent neck pain can be diagnosed as cervical sprain or arthritis; blood within the subdural space of the spinal canal causing irritation of the lumbar theca diagnosed as sciatical; those who are confuse, agitated, or restless, who cannot give a cogent history can be given a psychiatric diagnosis; approximately 90% of patients with acute SAH have acute cardiac arrhythmias which give rise to ECG patterns indicating acute myocardial ischemia or infarction, thus indicating a cardiac abnormality, and glycosuria (excretion of glucose in the urine), which suggest elevated blood glucose due to untreated diabetes. Such misdiagnoses often lead to delayed treatment after rebleeding or neurologic deterioration has occurred, resulting in increased morbidity and mortality.

Symptoms and signs of un-ruptured intracranial aneurysm are typically due to compression of adjacent neural structures or thromboembolism. Generally such aneurysms are large often greater than 2.5 cm (giant aneurysm). Aneurysms of the posterior communicating artery frequently compress the oculomotor nerve giving rise to dilatation of the pupil on the same side (ipsilateral); compression aneurysms of the intracavernous segment of the internal carotid artery may damage the third, fourth, fifth, or sixth cranial nerve; a rupture of this portion of the internal carotid can give rise to the formation of a carotid cavernous fistula. Large aneurysms can also compress the cortex or brainstem, giving rise to focal neurological signs or symptoms. Thrombosis within the aneurysmal sac occasionally sends emboli to the distal territory of the artery, giving rise to transient ischemic attacks or ischemic infarction. These aneurysms in of themselves, without evidence of rupture, can cause sudden severe headaches, but no signs of nuchal rigidity, thrombosis or meningeal irritation. These symptoms often dissipate with clipping of the un-ruptured aneurysm.

Before continuing there are two terms which need to be clarified, meningism and meningismus. Meningism describes the triad of nuchal rigidity, photophobia and headache due to irritation of the meninges seen in meningitis, subarachnoid hemorrhages and various other diseases. Meningismus is the term used when the above triad of symptoms occurs but there is no evidence of meningitis or SAH. Thus, large aneurysms, with no evidence of rupture, can produce meningismus.

Diagnostic Studies

The immediate diagnostic test of choice is the CT scan. This will reveal blood in the subarachnoid space, on occasion the aneurysm, blood in the cisterns and within the ventricular system. The CT may also show focal intraparenchymal or subdural hemorrhage, ventricular enlargement, a large thrombosed aneurysm, or infarction due to vasospasm.

The reported sensitivity of CT scans for SAH is 90 to 95% within 24 hours, 80% at 3 days and 50% at 1 week. Consequently, a normal CT scan never rules out SAH; a lumbar puncture should always be performed in patients who you suspect have a SAH, but have a normal CT.

Although CT and MRI can be used to detect an aneurysm, cerebral angiography is the definitive diagnostic procedure for detecting intracranial aneurysms as well as defining their anatomy.

Complications of SAH

The most important cause for morbidity and mortality following SAH is **vasospasm** of the cerebral arteries with its consequent cerebral ischemia and infarction. The cause of this vasospasm is believed the result of an increase in potassium within the CSF due to lysis of the RBC (red blood cells) within the subarachnoid space. Other inflammatory mediators, which also play a role in the genesis of vasospasm are prostaglandins, leukotrienes and those released by platelets, lack of inhibition of nitric oxide synthetase and dysfunction of ion channels in the vessels and brain manifested by increased endothelial pinocytosis and channel formation, opening of interendothelial tight junctions, and endothelial detachment and destruction, as well as intraluminal platelet adhesion and aggregation onto the damaged endothelium within a few hours after subarachnoid hemorrhage. The resulting continuous contraction of vascular smooth muscle may be due to the released vasoconstrictive agents such as oxyhemoglobin, hydroperoxides, endothelin-1, thromboxane A2, catecholamines and serotonin. Inhibition of vasodilating agents such as prostacyclin, endothelium-derived relaxing factor or NO, or an imbalance between the vasoconstrictive and vasodilating agents such as prostacyclin and thromboxane A2 or NO and endothelin may also play a role.

What needs to be understood is that although progressive arterial narrowing occurs in approximately 70% of those with SAH, only 15 to 35% show delayed ischemic effects. The delayed cerebral ischemic effects begin typically between 3 and 5 days after the hemorrhage, reaching it maximum at 5 to 14 days and gradually resolve over 2 to 4 weeks. Thus, if there is evidence of a neurological deficit before 3 days it is not the result of vasospasm. Neurologic deficit due to vasospasm has its peak frequency between 5 and 7 days.

There are two features, which when seen on CT scan, raise a red flag for the possibility of significant vasospasm with neurological sequelae, presence of thick cisternal blood and large amounts of blood in the ventricles. A clinical feature, which is a strong predictor of impending vasospasm, is the length of time of initial unconsciousness. Symptomatic vasospasm usually involves a decrease in the level of consciousness, hemiparesis or both.

Another significant complication of SAH is **rebleeding.** The greatest risk for rebleeding is within the first 24 hours after the initial rupture (4%), and remains elevated (approximately 1 to 2%/day) for the next 4 weeks. The cumulative risk for rebleeding in untreated patients after the initial bleed is approximately 15% at 7 days, 20 to 25% at 2 weeks, 30% at 1 month, and 40 to 50% at 6 months. After the first 6 months the risk of rebleeding is between 2 and 4% per year until the 10-year mark after which the risk approaches an un-ruptured aneurysm. The prognosis of patients who rebleed is dismal, with approximately 50% dying immediately and another 30% dying from subsequent complications.

The underlying pathogenesis for rebleeding is hypertension, vascular shear stress and endogenous fibrinolysis of the clot.

Another complication is **acute hydrocephalus**, which occurs in 15 to 20% of those with acute SAH. It appears the determinate factor is the volume of subarachnoid hemorrhage and intraventricular blood. Clinical manifestations of mild hydrocephalus are lethargy, psychomotor slowing, impaired short-term memory, limitation of upward gaze, sixth cranial nerve palsies, and lower extremity hyperreflexia. In severe cases there is substantive increase in intracranial pressure manifested by stupor, coma, and show progressive brainstem herniation due to continued CSF production, unless the patient is shunted.

Delayed hydrocephalus may develop in from 3 to 21 days after acute SAH manifesting itself by failure to fully recover with symptoms of dementia, gait disturbance, and urinary incontinence. Approximately 20% of all survivors of acute SAH require ventriculoperitoneal shunting.

General cerebral edema is seen in approximately 8% of those patients with acute SAH who receive CT scan on admission to the hospital. It subsequently develops in another 12%. One of the strong predictors of impending global brain edema is unconsciousness at ictus (ictus refers to a sudden attack, whether that be stroke, intracranial hemorrhage, etc.) and an increasing Hunt-Hess grade.

The Hunt-Hess Grade Scale is utilized to access the clinical presentation of aneurysmal SAH. It consists of 5 grades. Grade I (asymptomatic or mild headache) and Grade II (moderate to severe headache, or oculomotor palsy) has a relatively good prognosis. Grade III (confused, drowsy, or mild focal signs) has an intermediate prognosis and Grade IV (stupor-localizes to pain) and Grade V (coma-posturing or no motor response to pain) have a poor prognosis.

Delayed global edema was predicted by aneurysm size greater than 10 mm, loss of consciousness at ictus, use of vasopressors and increasing Hunt-Hess grade. 37% of the patients who developed global edema were dead or severely disabled at 3 months. It appears global edema is an independent risk factor for mortality and poor outcome following acute SAH. Loss of consciousness, which may reflect ictal cerebral circulatory arrest, is a risk factor for seeing global edema on admission to the hospital, and vasopressor-induced hypertension is associated with the development of delayed global edema.

Seizures are another complication, which occur in 5 to 10% of SAH patients with another 10% developing during the first year. Seizure development after SAH is related to focal pathology: large subarachnoid clots; subdural hematoma; or cerebral infarction.

Fluid and electrolyte disturbances also occur as a complication of SAH. Hyponatremia occurs in 5 to 30% of patients after SAH. This development is related to inappropriate secretion of antidiuretic hormone (SIADH) and free-water retention. This development is often exacerbated by excessive natriuresis that occurs after SAH, which is referred to as ‘cerebral salt-wasting.’ This is related to elevations of atrial natriuretic factor and the

glomerular filtration rate, which is secondary to elevations in atrial natriuretic factor/peptide.

Cerebral salt-wasting syndrome manifest itself through hyponatremia and dehydration in response to traumatic and non-traumatic injury to the brain. An example of the latter would be acute SAH secondary to rupture of an aneurysm. The resulting RBC within the subarachnoid space can give rise to activation of the sympathetic nervous system through the release of catecholamines as well as the release of vasoconstrictive agents such as endothelin via inflammatory mediators, thus ultimately causing the release of ANP and the development of the 'cerebral salt-wasting syndrome.'

Atrial natriuretic peptide (ANP) is a potent vasodilator secreted by cardiac myocytes located in the atrium of the heart. It is released in response to atrial stretch and a variety of other signals induced by hypervolemia, exercise or caloric restriction; thus ANP is secreted in response to: atrial distention, stretching of the vessel walls, sympathetic stimulation of β-adrenoceptors, raised sodium concentration (hypernatremia), angiotensin-II and endothelin, which is a potent vasoconstrictor. ANP acts to reduce the water, sodium and adipose loads on the circulatory system, thus reducing blood pressure. The resulting hyponatremia and intravascular volume contraction increases the risk of cerebral ischemia, most especially if it occurs in the presence of severe vasospasm. To decrease the likelihood of these complications the patients should be given large volumes of isotonic crystalloid.

The ability of acute SAH to give rise to an increase in catecholamines levels and thus sympathetic tone, can also lead to **neurogenic cardiac dysfunction, neurogenic pulmonary edema, or both.** The most abundant catecholamines are epinephrine, norepinephrine and dopamine. Norepinephrine and dopamine serve as neuromodulators in the CNS and also act as hormones in the blood. These catecholamines give rise to an increase in heart rate, blood pressure, blood glucose levels, and an enhanced activity of the sympathetic nervous system. Such an increase in catecholamines accounts for the transient ECG abnormalities seen in 50 to 80% of SAH patients as well as inducing the 'cerebral salt-wasting syndrome' in some patients as discussed above. In some patients with a high Hunt-Hess grade you may see cardiac enzyme release and a reversible form of neurogenic "stunned myocardium" manifested by hypotension and reduction in cardiac

output, which in turn leads to impaired cerebral perfusion, which is occurring in a patient with increased ICP and or vasospasm.

Neurogenic pulmonary edema is characterized by increased permeability of the pulmonary vasculature, which may occur in isolation or in combination with neurogenic injury.

Treatment of Aneurysmal SAH

Surgical clip application is considered the definitive treatment for most aneurysms. The ideal operative window is somewhat controversial. In the first 7 days coexistent spasm my complicate surgery and lead to infarction, but with the most frequent rebleeds occurring between days 7 and 10, delay beyond 7 days may subject the patient to the compound risk of a fatal outcome from a second bleed.

In the 1980s, neurosurgeons began to desert the practice of delaying surgery for several weeks following aneurysmal rupture, in favor of early clip application within the first 48 to 72 hours. However, this early clip application is associated with a 5 to 10% risk of major morbidity and mortality. In comparison, the risk of major morbidity or mortality from clip application of an un-ruptured aneurysm is 2 to 5%. The risk is greatest when the aneurysm is large or when it is located on the basilar artery.

There is another treatment for aneurysm, which is referred to as “coiled embolization,” which became available in the 1990s. This involves endovascular packing of aneurysms with soft, thrombogenic detachable platinum coils. This method is primarily used to obliterate small-necked aneurysms. For wide-necked and complex aneurysms a different technique is used, which involves placing a flexible stent in the parent vessel that has given rise to the aneurysm, and then passing platinum coils through the stent into the aneurysm. This method prevents the coils from migrating out of the wider neck of the aneurysm.

Overall, coil embolization has a complication rate of approximately 9%. Endovascular coil insertion is slightly safer than surgical clip application. In one study, at the end of one year, 23.7% of patients with coils were dead or dependent, compared to 30.6% of those treated with clip application.

The disadvantage of endovascular therapy is the potential for rebleeding after several years, due to coil compaction and aneurysm regrowth at the residual neck.

Morbidity

Survivors of SAH are primarily disabled by cognitive impairment manifested by long-term problems in memory, concentration, psychomotor speed, visuospatial skills, or executive function.

Executive function constitutes a collection of brain processes, which are responsible for planning, cognitive flexibility, abstract thinking, rule acquisition, initiating appropriate actions and inhibiting inappropriate actions, and selecting relevant sensory information. Depression and anxiety are also quite common. What these disturbances do is affect the persons work capabilities, relationships and quality of life.

Mortality

Helpern and Rabson evaluated 2,030 cases of sudden and unexpected death and found SAH in 5% and were involved in 26% of the cases in which the cause of death involved CNS pathology.

Deaths caused by rupture of saccular aneurysms constitute 16 to 24% of all patients dying from cerebrovascular disease. Approximately 12% die before receiving medical treatment with another 20% dying after admission to the hospital