The Clinical Aspects of Subarachnoid Hemorrhage

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Subarachnoid hemorrhage (SAH) is less frequent than ischemic stroke, but has a high public health relevance because it can affect young and middle-age adults, has considerable mortality and morbidity, it is treatable and preventable. Despite stable incidence, the mortality of SAH has decreased in the last two decades due to better neurosurgical techniques and neurocritical care and to advances in neuroendovascular treatment. Sudden headache is the cardinal feature. Rebleeding is the most imminent danger; a first aim is therefore occlusion of the aneurysms. Complications such as vasospasm / delayed cerebral ischemia, hydrocephalus, increased intracranial pressure, and seizures must be considered in the management of SAH. The authors reviewed the recent advances in the clinical aspects of SAH and grading system of the available evidence is included.

**Keywords:** Subarachnoid hemorrhage (SAH); Rebleeding; Vasospasm; Hydrocephalus; Grading system

Epidemiology

Most SAHs are caused by ruptured aneurysms including intracranial arterial dissections. Other causes include trauma, arteriovenous malformations/fistulae, vasculitides, amyloid angiopathy, bleeding diatheses, and illicit drug use (especially cocaine and amphetamines). The prevalence of intracranial saccular aneurysms by radiographic and autopsy series is 5 percent. Approximately 20 to 30 percent of patients have multiple aneurysms. Aneurysmal SAH occurs at an estimated rate of 3 to 25 per 100,000 population (2, 3). The mean age at onset is 55 years (4).

Clinical Manifestations

Rupture of an aneurysm releases blood directly into the subarachnoid space under arterial pressure. The blood spreads quickly within the subarachnoid space, rapidly increasing intracranial pressure. The bleeding usually lasts only a few seconds, but rebleeding is common and occurs more often within the first day. Consistent with the rapid spread of blood, the symptoms of SAH typically begin abruptly, occurring at night in 30 percent of cases. The premier symptom is a sudden, severe headache (97 percent of cases) classically described as the “worst headache of my life.” The
headache is lateralized in 30 percent of patients, predominantly to the side of the aneurysm. The onset of the headache may or may not be associated with a brief loss of consciousness, seizure, nausea, vomiting, or meningismus. Meningismus and often lower back pain may not develop until several hours after the bleed since it is caused by the breakdown of blood products within the cerebrospinal fluid (CSF), which lead to an aseptic meningitis (5).

Approximately 30 to 50 percent of patients have a minor hemorrhage or “warning leak,” manifested only by a sudden and severe headache (the sentinel headache) that precedes a major SAH by 6 to 20 days. A systematic literature review through September 2002 found that the incidence of sentinel headaches in aneurysmal SAH ranged from 10 to 43 percent (6).

Intracranial Arterial Dissections as Special Considerations of Aneurysmal SAH

Arterial dissection implies a tear in the wall of the artery leading to the intrusion of blood within the layers of an arterial wall. The important pathologic feature of intracranial arterial dissection is characterized by acute widespread disruption of the internal elastic lamina (Fig. 1) (7). Intracranial arterial dissection is mainly divided into two types: the ischemic type, which is manifest by ischemic symptoms and/or infarction of the carotid and vertebrobasilar circulation due to arterial narrowing and thromboembolism; and the hemorrhagic type, which presents as an SAH caused by rupture of an intradural dissecting aneurysm (Fig. 2) (7). Most dissections of the carotid and vertebral arteries heal spontaneously and especially, extracranial carotid and vertebral artery dissections generally carry a good prognosis. However, intracranial dissections are usually associated with severe neurological deficits or SAH and carry a poor prognosis because of a high rate of early rebleeding, so an urgent surgical intervention may be required in patients presenting with hemorrhage (7).

Complications

Subarachnoid hemorrhage (SAH) is associated with a high mortality rate (8). A systematic review found that the average case fatality rate for SAH was 51 percent (9). Approximately 10 percent of patients with aneurysmal SAH dies prior to reaching the hospital, 25 percent dies within 24 hours of SAH onset, and about 45 percent die within 30 days (10).

A number of additional complications commonly occur in patients who have suffered a SAH: rebleeding,
vasospasm and delayed cerebral ischemia, hydrocephalus, increased intracranial pressure and seizures.

1) Rebleeding

Most studies have found that the risk of rebleeding is highest in the first 24 hours after SAH (11), particularly within six hours of the initial hemorrhage. The risk of rebleeding in the first 24-hour ranges from 2.6 to 4 percent (11). Most rebleeding (73 percent) occurs within the first 72 hours of ictus (11). Factors that may be independent predictors of rebleeding include the Hunt-Hess grade on admission (11), maximal aneurysm diameter (11), and presence of a sentinel headache preceding SAH (12). The overall incidence of rebleeding after initial SAH in the modern era is uncertain. A prospective study from a tertiary care center involving 574 hospitalized patients admitted within 14 days of SAH found a rebleeding rate of 6.9 percent by three months (11). This rate may have been biased by over representation of high-risk aneurysms (e.g., large, anatomically complex, or located in the posterior circulation). Rebleeding is usually diagnosed on the basis of an acute deterioration of neurologic status accompanied by appearance of new hemorrhage on head CT scan. Only aneurysm treatment is effective for the prevention of rebleeding.

2) Vasospasm

Vasospasm causes symptomatic ischemia and infarction in approximately 20 to 30 percent of patients with aneurysmal SAH; it is the leading cause of death and disability after aneurysm rupture. Vasospasm typically begins no earlier than day three after hemorrhage, reaching a peak at days seven to eight. The onset of clinical vasospasm is characterized by a decline in neurologic status, including the onset of focal neurologic abnormalities. The severity of symptoms depends upon the artery affected and the degree of collateral circulation. Preliminary but accumulating data suggest that brain perfusion asymmetry demonstrated on CT perfusion (CTP) scanning in the acute stage of SAH may be a useful and highly sensitive method for predicting delayed cerebral ischemia, which is most cases is presumably due to vasospasm (13–15). However, the clinical utility of this method remains to be established.

Pathogenesis

The pathogenesis of delayed cerebral vasospasm involves an interaction between the metabolites of blood and the vasculature. Spasmogenic substances generated during the lysis of subarachnoid blood clots can cause endothelial damage and smooth muscle contraction (16). The vascular endothelium produces nitric oxide, which tonically dilates the cerebral vasculature; endothelial damage may interfere with nitric oxide production, leading to vasoconstriction and an impaired response to vasodilators (17). In addition, increased release of the potent vasoconstrictor endothelin may play a major role in the induction of cerebral vasospasm after SAH (16).

Risk Factors

The location of blood on computed tomography (CT) scan and its extent can help predict the likelihood of complicating cerebral vasospasm. In one series, severe vasospasm was correctly predicted and localized in 20 of 22 patients using the CT criteria of clots larger than 3 × 5 mm or layers of blood more than 1 mm thick. Radiologic grading scales including those of Fisher and Claassen are often used to predict the likelihood of vasospasm and cerebral ischemia. Other factors that may increase the risk of vasospasm include age less than 50 years and hyperglycemia (18, 19). Most but not all studies have found that poor clinical grade (e.g., Hunt-Hess grade 4 or 5, or Glasgow Coma Scale score < 14) is associated with an increased risk of vasospasm, and a longer duration of unconsciousness after SAH may also be a predictor (9). In contrast, the type of therapy chosen (surgical versus endovascular) does not appear to influence risk.

Early Vasospasm

Early vasospasm (EVSP) is arterial narrowing that is present at the time of or shortly after hospital admission; it is also called ultra early vasospasm, acute cerebral vasoconstriction, and acute arterial spasm (20). Although EVSP is rarely reported, a study that examined data from 3552 patients with aneurysmal SAH enrolled in clinical trials testing the drug tirilazad found that EVSP was present within 48 hours of admission in 339 patients (10 percent) (21). The following additional observations were made: EVSP was significantly more likely in patients with a poor neurologic grade on admission, intracerebral hematoma, larger aneurysm, thick SAH on CT scan, intraventricular hemorrhage, a history of previous SAH, and a history of hypertension. EVSP was not associated with delayed cerebral vasospasm, suggesting that the etiology of the two types of vasospasm is
different. EVSP was associated with cerebral infarction, neurologic worsening, and unfavorable outcome at three months, after adjustment for differences in admission characteristics.

Cerebral Infarction

Cerebral infarction is a frequent complication of SAH. Hypodense brain lesions on head CT have been noted in 40 to 60 percent of survivors at 3 to 12 months after SAH (4). In a case series of 143 patients with acute aneurysmal SAH admitted from 1998 to 2000 at a single center, cerebral infarction defined on CT scan was found in 56 patients (39 percent) (22). The time from SAH onset to the last CT scan during the acute hospital stay ranged from 5 to 32 days (mean 12 days). The two most common patterns of infarction in these 56 patients were: Single cortical infarcts, typically located near the site of the ruptured aneurysm, in 23 (40 percent). Multiple widespread infarcts, often involving bilateral and subcortical regions and frequently located distal to the ruptured aneurysm, in 28 (50 percent). The most common cause of infarction after SAH is assumed to be vasospasm. Other mechanisms of ischemia include occlusion (temporary or permanent) or damage to cerebral arteries during aneurysm surgery, thromboembolism related to turbulent or stagnant aneurysmal blood flow or clip application, and embolism unrelated to SAH.

3) Hydrocephalus

Hydrocephalus (acute and chronic) is a common complication of SAH. In one large series, hydrocephalus was documented by CT scan in 15 percent of patients, 40 percent of whom was symptomatic. Factors associated with an increased risk for hydrocephalus included intraventricular hemorrhage, posterior circulation aneurysms, treatment with antifibrinolytic agents, and a low Glasgow score on presentation. The incidence was also increased in patients with hyponatremia or a history of hypertension. Older age is an additional risk factor. Spontaneous improvement occurs in one-half of patients with acute hydrocephalus and impaired consciousness, usually within 24 hours. In the remainder, acute hydrocephalus is associated with increased morbidity and mortality secondary to rebleeding and cerebral infarction (23).

4) Increased intracranial pressure

Patients with SAH may develop increased intracranial pressure (ICP) due to a number of factors, including increased cerebrospinal fluid outflow resistance, acute hydrocephalus, hemorrhage volume, reactive hyperemia after hemorrhage, vasoparalysis, and distal cerebral arteriolar vasodilation (24, 25). In a series of 234 patients with SAH who had ICP monitoring, increased ICP occurred during the hospital stay in 54 percent, including 49 percent of those considered to have a good clinical grade.

5) Seizures

Seizures at the onset of SAH appear to be an independent risk factor for late seizures and a predictor of poor outcome (26). One study of 247 patients with SAH found that 7 percent developed new-onset epilepsy (defined as two or more unprovoked seizures after hospital discharge), and these patients had poor functional recovery and quality of life. Associated cerebral infarction and subdural hematoma predicted epilepsy, suggesting that epilepsy in this setting is due to focal rather than diffuse brain injury. The incidence of late epilepsy (more than two weeks after surgery) after surgical management of SAH is unclear. Multiple studies have cited an incidence of up to 25 percent. However, the true incidence now may be lower, given advances in surgical management that have occurred since these studies took place. Patients with a poor grade SAH appear to have a higher incidence of late epilepsy (27).

Overview of the More Commonly Used Clinical and Radiologic Grading Scales for SAH

An ideal SAH grading scale would provide the following capabilities (28): 1) Guide management decisions that are influenced by the severity of SAH. 2) Provide prognosis for clinicians, patients, and family members. 3) Assist practitioners in their ability to compare individual patients and groups of similar patients regarding studies that examine the impact of new treatments. 4) Enable practitioners to detect and quantify changes in disease severity while following an individual patient. While a number of SAH grading scales have been proposed, none meets all these requirements or is universally accepted (28). Furthermore, there is a paucity of validation studies, and no prospective controlled comparison studies have been performed.

A number of SAH grading scales have been proposed - Glasgow Coma Scale, Hunt and Hess, World Neurointervention 4, August 2009
Federation of Neurological Surgeons (WFNS), Claassen, Ogilvy and Carter grading system. Among these grading scales, Glasgow Coma Scale (GCS), Hunt and Hess grading system, Fisher, and Claassen grade are briefly discussed here.

Glasgow Coma Scale

The Glasgow Coma Scale (GCS) was devised in the early 1970s. The GCS is not a true SAH grading scale, but is rather a standardized method for evaluating the level of consciousness in a number of neurologic conditions including SAH. The GCS assigns points based on three parameters of neurologic function: eye opening, best verbal response, best motor response. In a prospective series of 765 patients with SAH, a higher GCS correlated with better outcome after aneurysm occlusion (29). However, a significant difference in outcome was observed only between patients with GCS scores of 15 and 14, while no significant differences were found between the remaining adjacent GCS scores.

Hunt and Hess Grading System

The grading system proposed by Hunt and Hess in 1968 is one of the most widely used (30). The scale was intended as an index of surgical risk. The initial clinical grade correlates with the severity of hemorrhage. The grade is advanced one level for the presence of serious systemic disease (hypertension, diabetes, severe arteriosclerosis, chronic pulmonary disease) or vasospasm on angiography. A subsequent modification proposed by Hunt and Kosnik added a Grade 0 for unruptured aneurysms and a Grade 1a for a fixed neurologic deficit without other signs of SAH. A systematic review of SAH grading scales found conflicting data regarding the utility of the Hunt and Hess scale for prognosis (28). In a study assessing a series of 185 patients with SAH, the Hunt and Hess score correlated more strongly with outcome at six months than the GCS or World Federation of Neurological Surgeons Scale. However, individual grades for all three scales demonstrated suboptimal sensitivity, specificity, and predictive value. In addition, nearly half of the patients with poor scale grades on admission had a good outcome. Furthermore, it is unclear if there are significant differences in outcome for adjacent Hunt and Hess grades. Some studies evaluating Hunt and Hess grades found significant differences in outcome for some adjacent grades and not others (31). A study of 230 patients with SAH found a significant difference in outcome for compressed but not adjacent Hunt and Hess grades; patients with grades 1 to 3 had better outcomes compared with those with grades 4 and 5. Another study of 405 patients with SAH found no significant difference for the risk of poor outcome or death between patients with Hunt and Hess grades 0 to 2. Furthermore, the risk was significantly different only when comparing patients with Hunt and Hess grade 3 to those with grade 0.

Fisher Grade

The Fisher scale was devised in 1980 as an index of vasospasm risk (but not clinical outcome) based upon the hemorrhage pattern seen on initial head CT scan (32). The Fisher scale was validated in a small prospective series of 41 patients with SAH (33). The interobserver variability for the Fisher scale indicates excellent agreement between observers (34). The Fisher scale has also been incorporated into other SAH grading systems.

Claassen Grade

Like the Fisher scale, the Claassen grading system proposed in 2001 is an index of the risk of delayed cerebral ischemia due to vasospasm after SAH (35). It does not address clinical outcome. Unlike the Fisher scale, the Claassen scale takes into account the separate and additive risk of SAH and intraventricular hemorrhage (IVH). Ten cisterns or fissures are evaluated for blood with the Claassen scale. These include the frontal interhemispheric fissure, the quadrigeminal cistern, the bilateral suprasellar and ambient cisterns, and the bilateral basal sylvian and lateral sylvian fissures. The scale is graded as follows: grade 0: No SAH or IVH, grade 1: Minimal SAH and no IVH, grade 2: Minimal SAH with bilateral IVH, grade 3: Thick SAH (completely filling one or more cistern or fissure) without bilateral IVH, grade 4: Thick SAH (completely filling one or more cistern or fissure) with bilateral IVH. The Claassen scale was derived from analysis of data from 276 patients with SAH who had a head CT scan within 72 hours of onset (35). The best predictors of delayed cerebral ischemia due to vasospasm were thick SAH completely filling any cistern or fissure (odds ratio [OR] 2.3, 95% CI 1.5–9.5) and bilateral IVH (OR 4.1, 95% CI 1.7–9.8).
While a number of subarachnoid hemorrhage (SAH) grading scales have been proposed, there are few validation studies of these scales and no prospective controlled comparison studies (28). Furthermore, the available data concerning SAH grading scales are limited and often conflicting. As a result, none of the existing scales is universally accepted or clearly established. Thus, the use of any particular SAH grading scale is largely a matter of individual or institutional preference.

Summary & Conclusion

SAH is less frequent than ischemic stroke, but it is responsible for 25% of all fatalities related to stroke. A number of additional complications commonly occur in patients who have suffered a SAH. The recent advances in the clinical aspects of SAH and grading of the available evidence have been reviewed on this manuscript.

The patients with SAH should be referred urgently to a hospital providing expert cerebral aneurysm treatment, including neurosurgical, endovascular and neurointensive care management.

References

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뇌지주막하 출혈의 임상적 측면

박 훈, 박관용, 황선철, 김범태

뇌지주막하 출혈은 허혈성 뇌졸중보다는 드물게 발생하나, 주로 청장년층에 발생하고, 이환율과 사망률이 높으며, 치료 및 예방이 가능한 점에서 공중보건과의 연관성이 크다고 할 수 있다. 꾸준한 발생율에도 불구하고, 신경외과 수술 기법, 신경계 중환자 치료 및 뇌혈관내치료의 발전에 힘입어 뇌동맥류 출혈의 사망률은 지난 20여년에 걸쳐 감소해 오고 있다. 감각연관 두통이 뇌지주막하 출혈의 중요한 특징이다. 뇌동맥류의 재출혈이 가장 긴급한 문제이며, 치료의 일차적 목적은 뇌동맥류의 폐쇄이다. 뇌지주막하 출혈의 치료에 있어서 뇌혈관내치료 / 지연성 뇌혈관 폐쇄 / 수두증, 뇌압상승, 경련과 같은 합병증을 반드시 고려하여야 한다. 저자들은 뇌지주막하 출혈의 임상적 측면을 재검토하고, 근거를 바탕으로 한 뇌지주막하 출혈의 분류 체계에 대해 제시하고자 한다.

**Key Words**: Subarachnoid hemorrhage (SAH); Rebleeding; Vasospasm; Hydrocephalus; Grading system

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