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REVIEW ARTICLE

Emergency Neurological Life Support: Subarachnoid Hemorrhage

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Abstract Subarachnoid hemorrhage (SAH) is a neurological emergency because it may lead to sudden neurological decline and death and, depending on the cause, has treatment options that can return a patient to normal. Because there are interventions that can be life-saving in the first hour of onset, SAH was chosen as an Emergency Neurological Life Support protocol.

Keywords Cerebral aneurysm · Hydrocephalus · Hunt Hess · Fisher group

Introduction

Subarachnoid hemorrhage (SAH) is a neurological emergency. Although trauma is the most common cause of blood in the subarachnoid space, this section will focus on non-traumatic SAH, of which the predominant cause is a ruptured intracranial aneurysm or arteriovenous malformation (AVM). At least half of the remainder of atraumatic SAH cases are caused by non-aneurysmal bleeding from a "perimesencephalic" SAH.

The American Heart Association (AHA)/American Stroke Association (ASA) updated guidelines for the evaluation and treatment of patients with SAH in 2012 [1], and the Neurocritical Care Society recently released SAH guidelines as well [2]. These guidelines discuss issues of diagnosis and management of SAH upon admission to the emergency department (ED) and provide an evidence-based review of SAH Management. Emergency Neurological Life Support (ENLS) is designed to address the initial management of SAH within the first hour and will focus on establishing the diagnosis followed by attention to several issues that may need intervention urgently before the patient is handed off to other treating physicians.

The ENLS algorithm for the initial management of SAH is shown in Fig. 1, and a list of things to accomplish in the first hour is listed in Table 1.

Clinical Features

The vast majority of patients with SAH experience abrupt onset of a severe headache, which may be associated with a brief loss of consciousness, vomiting, neck pain, or stiffness. In approximately 40–50 % of patients, mental status is normal, and there are no focal neurological deficits. Patients often describe this as the "worst headache of my life" or "like my head is exploding."

This headache is often referred to as a thunderclap headache, which has a differential diagnosis beyond SAH [3, 4]. The headache is almost always unique, as compared with prior headaches the patient may have had. Some of these patients will have meningismus, which is a physical exam finding to be distinguished from neck pain or stiffness that the patient may have by history. The remaining 50 % of patients have various neurological findings ranging from minor mental status changes to focal deficits associated with the headache, to coma.

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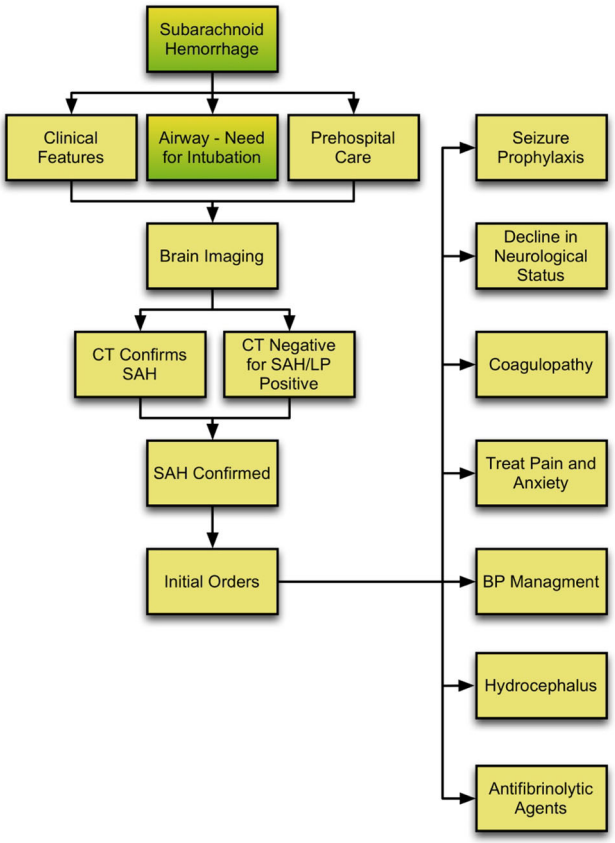

Fig. 1 ENLS subarachnoid hemorrhage protocol

Table 1 Subarachnoid hemorrhage checklist for the first hour

Checklist
☐ Brain imaging
☐ Labs: PT, PTT, CBC, platelets, electrolytes, creatinine, troponin, toxicology screen
☐ 12 lead ECG
☐ Blood pressure goal established
☐ Address hydrocephalus

Although the classic presentation of SAH includes onset of headache with exertion or a Valsalva maneuver, this finding (headache developing with exertion) actually occurs in a minority of patients, some of whom develop symptoms during sleep [5]. Some patients with abnormalities in mental status may not be able to give a cogent history of the headache onset. Others may report that the headache did not begin suddenly. A favorable response of the pain to any type of analgesic, including a triptan, should not be used as definitive evidence of a benign etiology [6, 7].

Historic studies suggest that 12–25 % of patients with SAH are misdiagnosed [8] and that approximately 5 % of ED patients with SAH presenting with headache are misdiagnosed on their first visit [9]. Well-appearing patients with normal neurological exams may be mistaken to have migraine or "sinus headache" [3, 8]. In one study, the most common reason for misdiagnosis was failure to perform a computed tomographic (CT) scan [10]. Not surprisingly, patients with smaller hemorrhages and normal mental status are more often misdiagnosed, and their outcomes are worse than had they been correctly diagnosed [3, 8, 10].

Some SAH patients present with specific symptoms or combinations of symptoms that suggest another diagnosis [3, 8]. These include the following:

- Isolated neck pain (cervical strain or degenerative arthritis)
- Fever and headache (viral syndrome or viral meningitis)
- Prominent nausea and vomiting (gastroenteritis—note the absence of diarrhea and vertigo)
- Elevated blood pressure (BP) or electrocardiographic abnormalities (hypertensive encephalopathy or acute coronary syndrome).

In other situations, a particular physical examination finding, such as a third nerve palsy or a retinal hemorrhage, may suggest the diagnosis of SAH. All patients with a new, severe headache, and with a new abnormality in their neurological exam should be investigated further.

Among neurologically intact patients, physicians should strongly consider investigating patients with abrupt onset or a severe, unique headache for that patient, especially if the patient exhibits or describes worrisome associated symptoms. A large study (2131 patients presenting to an emergency department with acute headache, of whom 132 [6.2 %] had SAH) found that all patients were correctly identified if they had one or more of the following 6 clinical characteristics: (1) age $\geq$ 40 years, (2) neck pain or stiffness by history, (3) limited neck flexion on physical examination, (4) witnessed loss of consciousness, (5) onset during exertion, and (6) "thunderclap" onset. Unfortunately the specificity was only 15 % [11].

Prehospital Care

For patients presenting with isolated headache who are neurologically intact, there are no specific prehospital interventions, apart from consideration of analgesics. For patients presenting with headache who are neurologically altered, pre-notification to the ED and check of a finger stick glucose are important steps. Patients who are severely altered or comatose or are vomiting repeatedly may need to have their airways controlled by tracheal intubation in the field. Prehospital providers should be prepared to use suction to facilitate visualization during direct larygoscopy. Transfer to the nearest stroke center will likely expedite care, especially if the center is comprehensive.

Diagnosis

Brain Imaging

The first step in the diagnosis of SAH in the ED is non-contrast brain CT [1, 3, 8]. The CT in patients with aneurysmal SAH will show blood (appears white) in the subarachnoid space, typically in the basal cisterns around the circle of Willis, major fissures, and occasionally isolated intraventricular location. Subarachnoid blood that is present high along the convexity is often due to non-aneurysmal causes, most commonly with head trauma. Less common causes include AVMs, cerebral amyloid angiopathy, vasculitis, reversible cerebral vasoconstriction syndrome, and other toxic and inflammatory vasculopathies [12].

Negative CT scans can occur in several settings. The two most important are bleeds too small to be detectable and bleeds that have occurred hours to days before the CT scan (CT is more sensitive soon after the bleed). The first factor is self-evident. The second, timing bias, is due to the normal circulation of cerebrospinal fluid (CSF). Other possibilities include incorrect interpretation (CT is actually positive), patients whose hematocrits are $\leq$30 % (blood is isodense with brain), and technical factors (poor CT quality) [3, 8].

Again, CT sensitivity drops over time [7]. Studies relying on older CT technology suggest that CT sensitivity is approximately 90 % on the day of the hemorrhage, falls to 60–85 % on day 5, and is approximately 50 % at 1 week. Modern scanners are likely more sensitive; however, in one recent study using multi-detector scans, CT sensitivity in SAH patients with a normal mental status was still only 91 % [13].

The normal volume of CSF present in the body (150 ml) turns over three times daily. This circulation accounts for the drop-off in CT sensitivity. One recent study suggests that CT was 100 % sensitive within 3 days of the headache onset [14]. However, nearly 60 % of patients in this referral to a neurosurgical center had SAH, so this was not a typical ED population in which one would expect an incidence of SAH between 8 and 12 % [3].

Multiple studies now suggest that a technically adequate scan, done on a modern generation CT scanner done within 6 hours of onset of headache (and not just isolated neck pain) and interpreted by an attending level radiologist (or other individual skilled in diagnosing SAH by CT scan) has a sensitivity that approaches 100 % [15–17]. Physicians may consider not doing a lumbar puncture if all of these characteristics above are met. Because this step has not yet been incorporated into clinical guidelines, physicians should consider an informed discussion with the patient about this.

CT Confirms SAH

Although there are rare occasions in which CT is falsely positive, patients whose CT shows SAH should be assumed to have SAH and managed accordingly [2, 3].

CT Negative for SAH/LP Positive

Based on current evidence, patients under evaluation for SAH whose CT scans are negative, equivocal, or non-diagnostic should undergo lumbar puncture (LP) with the possible exception of patients meeting the CT criteria in the previous paragraph [1, 3, 8]. As with CT, CSF results are also time-dependent. Large amounts of red blood cells (generally in the thousands) are initially present but rapidly diminish with time (due to the circulatory cycle discussed in the Brain Imaging section above).

Xanthochromia—the yellowish discoloration of CSF that results from in vivo degradation of hemoglobin into bilirubin (as well as oxyhemoglobin and methemoglobin)—begins to develop and is nearly universally present by 12 h after the onset of the bleed [3]. It can be measured by visual inspection of the centrifuged CSF or by spectrophotometry.

Although some recommend that spectrophotometry be used as a more sensitive method to detect xanthochromia, this method leads to a high proportion of false positives [18]. Further, nearly all hospital clinical laboratories in North America use visual inspection following sample centrifusion to assess xanthochromia [19]. Finally, CSF deemed “clear” by visual inspection is very unlikely to be compatible with SAH [20]; however, this visual inspection should be performed in a conical-base test tube (typically supplied in the LP kit) and not in a capillary tube. The tube of fluid should be compared with water against a white background in neutral lighting.

Measuring the opening pressure is recommended, and it will be elevated in approximately 2/3 of SAH cases [21]. The presence of elevated opening pressure may also help to distinguish traumatic taps from true SAH [22]. The best indicator is absence of xanthochromia.

Alternative Diagnostic Pathways

Other diagnostic pathways have been suggested, including an LP-first strategy based on mathematical modeling that indicated improved resource management and a higher rate of LP (it should be noted that this method has not been clinically tested in the CT era) [23]. Another model includes the use of magnetic resonance imaging (MRI), which is quite sensitive for blood, including SAH, and is superior to CT in terms of timing the bleed. However, due

to greater availability, lower cost, and greater experience with its interpretation, CT remains the recommended first test [1, 3]. If MRI is used as the initial imaging test, an LP is still necessary if the MRI is negative [1].

More recently, primary CT followed by CT angiography (CTA) has been suggested as a possible diagnostic pathway [24, 25]. Among other issues, however, the CT (if negative) followed by CTA will primarily diagnose an aneurysm as opposed to diagnosing a bleed. There are many downstream implications of this technique that clinicians should consider [26].

SAH Confirmed

Once SAH is confirmed by any means (CT, LP, or other), several management steps must be addressed. In addition to the specific steps below, the patient should be placed on bed rest with cardiac monitoring, and a 12-lead electrocardiogram should be obtained. If not already done, blood should be sent to the laboratory for a complete blood count as well as coagulation tests (PT, PTT, INR, platelets), electrolytes, renal function, and troponin.

Definitive therapy is the obliteration of the aneurysm, either by clipping or endovascular coiling; both of these isolate the aneurysm from the general circulation and should be carried out as soon as feasible [1]. Several studies have shown that patient outcomes are improved when they are treated at high-volume centers defined as those that treat >35 cases per year [1, 27, 28]. Low-volume centers should strongly consider transfer of the patient to a high-volume center as soon as feasible. Ideally, pre-arranged transfer agreements should be in place.

Initial Orders

Once the diagnosis of SAH is made and the patient is stabilized, the physician should speak to a cerebrovascular specialist. The Communication section below includes the checklist of communications that should be discussed in this conversation (Table 2).

In addition to the standard communication about a patient, the conversation should include airway status, the clinical status of the patient (often measured using the Hunt and Hess or the World Federation of Neurological Surgeons scores), results of brain imaging and/or CSF analysis, and presence or absence of hydrocephalus. The discussion should also include goals of BP control, review of administered medications for pain and anxiety, and treatments to prevent rebleeding, seizure prophylaxis, as well as which clinician will take responsibility for vascular imaging. Since vasospasm typically happens days later, the role of acute (first hour) administration of nimodipine is unclear and will require placement of a feeding tube in patients who cannot swallow. Placing a feeding tube can lead to retching or combativeness and may increase the risk re-rupture of the aneurysm so likely should be delayed until decision is made about aneurysm treatment.

Table 2 Subarachnoid hemorrhage communication regarding assessment and referral

Communication
☐ Airway status
☐ Clinical presentation (level of consciousness, motor exam, pupils)
☐ WFNS and Hunt–Hess Grade
☐ Imaging/LP results
☐ Coagulopathy present?
☐ Hydrocephalus present?
☐ Medications given (dose and time administered), including sedatives, analgesics, seizure prophylaxis, anti-hypertensives, and nimodipine
☐ Coordination of other vascular imaging

Airway: Need for Intubation

The determination to place an endotracheal intubation follows standard factors: ability of the patient to control his or her airway; hyperventilation or hypoxia resistant to supplemental oxygen; or anticipated clinical decompensation over time, especially if a transfer to another facility is involved (see the Airway, Ventilation, and Sedation protocol).

Seizure Prophylaxis

Fewer than 20 % of SAH patients have seizures, but when they occur, they can result in aneurysm re-rupture and increased intracranial pressure (ICP). Actual seizures should be treated with anticonvulsants, but prophylactic anticonvulsants are optional. Also, in patients with altered mental status, non-convulsive status epilepticus may be present, which can only be diagnosed by continuous electroencephalography (EEG).

Both the AHA and NCS guidelines [1, 2] suggest consideration of anticonvulsants in the immediate post-hemorrhage period [1], while other experts recommend against this practice [29]. A very short course (<7 days) of prophylactic anticonvulsants may be recommended in the period following diagnosis and before definitive aneurysm treatment. As phenytoin may lead to worse long-term cognitive outcomes, use of a different agent, such as levetiracetam, could be considered.

Decline in Neurological Status

Some patients with SAH will experience an early deterioration in neurological status. It is important in these

patients to consider the full differential diagnosis, since the causes, and thus treatments, will vary.

Reassessment of the vital signs and telemetry monitor is critical. New hypotension will decrease cerebral perfusion pressure. New hypoxia may result from neurogenic pulmonary edema. Arrhythmias may also lead to hypotension. Cardiovascular collapse could be the result of increasing hydrocephalus and or brain herniation (Cushing's response) or, infrequently, neurocardiogenic shock from Takasubu's syndrome or respiratory failure from neurogenic pulmonary edema. Physical examination may show further evidence of herniation or a new seizure requiring treatment.

A repeat CT scan is also necessary, as it may show herniation, ultra-early rebleeding, development of or increase in hydrocephalus, or, rarely, development of an intraparenchymal or subdural hematoma.

Coagulopathy

Coagulopathy should be treated (see the algorithms in the ENLS Pharmacology protocol for more details). Patients taking warfarin with an international normalized ration (INR) >1.4 should be treated with some combination of fresh frozen plasma, intravenous (IV) vitamin K, and prothrombin complex concentrates, depending upon many different factors. Low platelet count below 50,000 can be treated with platelet transfusions. See the ENLS Pharmacology manuscript regarding reversal of Factor Xa and thrombin inhibitors.

There are no specific management guidelines to address patients with SAH taking antiplatelet agents, such as aspirin, clopidogrel, or prasugrel. These agents can potentially increase the risk and severity of aneurysm re-rupture. Moreover, profound platelet inhibition with clopidogrel has been associated with significant procedural-related complications. Reversal with platelet transfusions and other hemostatic agents should be considered as risk versus benefit for the individual patient in consultation with local experts in coagulopathy management.

Treat Pain and Anxiety

In addition to a primary motive of achieving the patient's comfort, treatment of pain, vomiting, and anxiety are clinically important. Judicious amounts of short-acting IV analgesics, such as fentanyl, should be used to help the patient avoid straining, Valsalva, and stress. Treating vomiting with anti-emetics may also be helpful. If there is a significant component of anxiety, small intermittent doses of IV lorazepam may help. All of these steps may also help to control elevated BP if BP elevation is related to pain and/or anxiety. Over-medication, which could mask subtle mental status changes, should be avoided. Additionally, administration of rescue narcotic antidotes in the setting of over sedation risks causing marked agitation and aneurysm re-rupture.

BP Management

AHA/ASA and Neurocritical Care Society guidelines [1, 2] acknowledge the lack of quality data about BP control in SAH patients and suggest only that BP should be monitored and controlled to "balance the risk of stroke, hypertension-associated rebleeding, and maintenance of the cerebral perfusion pressure" [1]. That said, retrospective data suggest a higher rate of rebleeding with systolic BPs above 160 mmHg.

Current guidelines suggest treating extreme hypertension in patients with an unsecured ruptured aneurysm. Modest hypertension (mean arterial pressure, or MAP, <110) does not require treatment. Pre-morbid BPs should be considered and used to inform the risks and benefits of treatment. Experts in the field use antihypertensive medications that are short acting, easily-titratable, and can be administered as a continuous infusion to reduce the systolic pressure to below 160 mmHg, or the MAP $<$ 110, keeping in mind the principles mentioned above. Nicardipine is commonly used for this purpose, and nitroprusside and nitroglycerine should be avoided because these agents may raise ICP.

Hydrocephalus

The clinician should carefully evaluate the CT scan for hydrocephalus, which occurs in up to 30 % of SAH patients in the first 3 days. This may be asymptomatic but is more often seen in severely affected patients. If the hydrocephalus is symptomatic, it can be treated with an external ventricular drain, although some data suggest this may be associated with rebleeding [1]. Additionally, comatose patients with hydrocephalus may have elevated ICP, so placement of a drain (external ventricular drain or lumbar drain) will not only reduce ICP by allowing draining of CSF, but it will also provide a means to monitor ICP throughout the hospitalization. Refer to the ENLS protocol on ICP management for further information.

Antifibrinolytic Agents

Prevention of rebleeding prior to definitive aneurysm treatment is an important strategy. In the past, when surgical treatment was delayed for weeks, pre-operative antifibrinolytic treatment was standard. Currently, early definitive treatment of the aneurysm is generally recommended [1]. Thus, there has been an increased interest in early, short-term antifibrinolytic treatment with either Epsilon

Aminocaproic acid or tranexamic acid in situations where surgical options are not readily available. One study of immediate use of tranexamic acid to SAH patients, most of whom were treated within 24 h, demonstrated an 80 % reduction in rebleeding before the definitive treatment [2, 30]. Since this area is controversial it should be discussed with the consultant, as the drug is not without risks. Because of the procoagulant properties, and the already higher risk of pulmonary embolism and deep venous thrombosis during SAH, there is concern that these side effects may exceed benefits of preventing aneurysm re-rupture. On the other hand, aneurysm re-rupture is often fatal, and since most re-ruptures happen with the first 12–24 h of the initial hemorrhage, use of these procoagulant drugs for a few days until the aneurysm is secured may be a good strategy.

Oral Nimodipine

The use of oral (or per nasogastric tube) nimodipine has been shown in multiple randomized trials to improve overall outcomes of SAH patients presumably by limiting delayed cerebral ischemia [31]. However, because these are given orally, and many acute SAH patients cannot swallow, and vasospasm is not an immediate concern, the implementation of oral nimodipine is not listed as a priority in the first hour. The effect of nimodipine is not mediated by amelioration of angiographically documented vasospasm; rather, nimodipine works via a presumed cellular neuroprotective mechanism.

Pediatric Considerations

Ruptured aneurysms are rare in children, and more commonly occur in adolescence than early childhood. Pediatric aneurysms differ from adult aneurysms in etiology, location, morphology, and natural history, which have implications for their management. Dissecting and fusiform aneurysms are relatively more common than in adults, who tend to harbor mostly saccular aneurysms. Co-morbidities are more common—there may be associated sickle cell anemia, Moyamoya disease, co-arctation of the aorta, Marfan's syndrome, and Ehlers–Danlos syndrome. Infective aneurysms, mostly from congenital or rheumatic cardiac anomalies, also are more common in children and tend to favor peripheral vessels. AVMs as a cause for SAH are proportionally more common than in adults; there may also be an underlying condition such as hereditary hemorrhagic telangiectasia.

The presenting history may not be as suggestive as in adults, depending on the age of the child and the origin of the bleed. Because SAH is uncommon in children, the diagnosis often is not suspected at first presentation, which has implication for early diagnosis and management. Although CT is usually the first-line emergency investigation, consideration should be given to limiting CT scan dosage for children where appropriate. If available and the patient is stable, MRI/MRA is more sensitive for diagnosis and limits CT radiation to the developing brain.

As with adults, for a suspected SAH and negative imaging a LP is appropriate. It is worth stating again that imaging in this scenario must precede LP because the diagnosis is easily missed. SAH in children is much less common in children than meningitis, for which LPs are performed often without imaging. However, raised ICP can cause neck stiffness that mimics meningismus. Raised ICP, especially in the posterior fossa, may cause descent of the cerebellar tonsils and/or vermis through the foramen magnum. Because of the narrowed space in the foramen, flexion of the neck causes compression of the lower brainstem against the anterior rim of the foramen, which may cause acute cardiorespiratory arrest.

Conventional angiography in young children is difficult because of their small femoral vessels and the limited amount of contrast that may be given. Therefore, if diagnostic angiography is required after CTA/MRA, it may be worth preparing for endovascular treatment in the same sitting if the need for it can be anticipated.

Because SAH is much less common in children, the imperative to treat at a specialist or high volume center is arguably even stronger than in adults. Pediatric neurosurgeons and/or neurologists are preferred as treating clinicians. However, definitive treatment sometimes needs clinicians with endovascular skills, who tend to be neurosurgeons or neuroradiologists in adult services.

BP must be treated by balancing the risk of cerebral hypoperfusion (increased by ICP and possible vasospasm) and the risk of rebleeding. Vasospasm does occur but is less common than in adults. In absence of specific information about cerebral perfusion or ICP, aiming for BP as close to normal for age is reasonable to start.

Nimodipine has been used in childhood SAH but its role still needs clarification. If it is used, consideration should be given to adjusting the dosage and hypotension must be avoided. If Transcranial Doppler is used to monitor cerebral blood flow velocities, consideration must be given to age-related physiological changes in normal values.

Healthcare Provider Communication

When communicating to an accepting or referring physician about this patient, consider including the key elements listed in Table 2.

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