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Spontaneous Subarachnoid Hemorrhage: updated clinical and therapeutic approach

Renato Serquiz e Pinheiro[1]; Yanny Cinara T. Ernesto[1]; Amália Cinthia Meneses Rêgo[1]; Lucidio Clebeson de Oliveira[2]; Luciana Cristina Borges Fernandes[2]; Dinalva Brito de Queiroz[1]; Fausto Pierdoná Guzen[1,2] and Irami Araújo-Filho[1].

[1]Post-graduation, Program in Biotechnology, School of Health, Potiguar University, Natal-RN, Brazil.

[2]Laboratory of Experimental Neurology, Department of biomedical sciences, Health Science Center, State University of Rio Grande do Norte, Mossoró-RN, Brazil.

*Corresponding author: Full Professor Dr. Fausto Pierdoná Guzen. Current Address: Laboratory of Experimental Neurology, Department of Biomedical Sciences, Health Science Center, State University of Rio Grande do Norte, Mossoró/RN, Brazil. E-mail address: **fauguzen@usp.br**

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Abstract

Despite advances in the treatment of subarachnoid hemorrhage, morbimortality rates remain elevated. Patients who have a sudden onset headache followed or not by altered consciousness, require a high degree of suspicion for the appropriate diagnosis in the emergency room. Those with lighter symptoms, presence of headache without other neurological alterations are the most susceptible to diagnostic error. All should be evaluated quickly, receiving specialized neurointensive care and ear-

ly treatment. The best results are usually obtained from the individualized discussion of each case, given the clash between surgical and endovascular treatment. Finally, it is safe to prevent, recognize and treat systemic delayed cerebral ischemia and vasospasm. The present study aimed to review and discuss, in a practical way, the approach of spontaneous subarachnoid hemorrhages.

Introduction

Subarachnoid hemorrhage (HSA) is a neurological emergency characterized by extravasation of blood to the space between the arachnoid and the pia mater, which may occur in a traumatic or spontaneous manner. Among the spontaneous, there is aneurysmatic HSA, in about 80% of the cases, and non-aneurysmatic, corresponding to 20% of the cases (Steiner *et al.*, 2013, Connolly et al., 2012).

Aneurysmatic HSA occurs in adults from 50 years of age; patients over 70 years of age have a more severe picture. The incidence is higher in women, about 1.2 times and varies by geographic region (Raya & Diringer, 2014).

In the United States, the incidence of HSA is between 10-15 people per 100,000 in habitants. Much lower rates are reported in China (2 cases/100,000), in South and Central America (4/100,000), while higher rates are reported in Finland and Japan(19-23/100,000) (Francoeur & Mayer, 2016).

The evolution of patients with HSA has high morbidity and mortality. The average lethality rate is approximately 51%, and about 10% of patients with HSA die before arriving at the hospital, 25% in the first 24h and about 45% within 30 days after HSA (Vivancos *et al.*, 2014).

The present study aimed to review and discuss, in a practical way, the clinical and therapeutic approach of spontaneous subarachnoid hemorrhages.

Methods

This is the literature review study, whose bibliographic research was carried out in PubMed, Scopus, Scielo, and Web of Scien-

ce. The descriptors used subarachnoid hemorrhage; intracranial subarachnoid hemorrhages; intracranial aneurysm, physiopathology, clinical decision rules, neurologic surgical procedure and interventional radiology. The inclusion criteria, were selected articles published in English, Spanish and Portuguese; Randomized Clinical Trials / Clinical Trials), Guidelines (Guideline), Systematic Reviews, Reviews, and Meta-Analysis. The selection of articles was made by listing those of greater relevance according to the proposed theme, both in the foreign and Brazilian literature, in a non-systematic way, addressing from its etiology to the definitive treatment.

Etiology

The rupture of intracranial saccular aneurysms is the leading cause of spontaneous HSA, about 80% of the cases (Bederson *et al*., 2009). These aneurysms occur mainly in arterial bifurcations near the polygon of Willis, as in the anterior communicating artery, a posterior communicating segment of the internal carotid artery and middle cerebral artery (Petridis *et al.*, 2017). They are called congenital aneurysms, but the term is inadequate because aneurysms are not found at birth. What is congenital is the defect in the arterial wall that provides the formation of the aneurysm by a failure in the middle layer of the arteries (Takeshita *et al.*, 2017).

The non-aneurysmatic HSA represents about 15-20% of the HSA and is considered when the aneurysm is not identifiable, even after two or more angiographic studies (Vivancos *et al*., 2014, Müller & Müller, 2018). Other less common causes are arteriovenous malformations (AVM), cerebral artery dissection, intracranial neoplasms, Central NERVOUS System (CNS) vasculitis, coagulation disorders, sickle cell disease, among others (Connolly *et al*., 2012, Han *et al*., 2018).

Risk Factors

Non-modifiable

- Female sex;
- Family history of HSA and/

or cerebral aneurysm: at least one member of the first-degree family with an intracranial aneurysm or HSA and especially if ≥ two first--degree relatives are affected;

• Genetic syndromes: autosomal dominant polycystic kidney disease and Ehlers-Danlos syndrome type IV, among others (Rabinstein & Lanzino, 2018; Bederson *et al*., 2009).

Modifiable

• Arterial hypertension: independent risk for the development and rupture of intracranial aneurysms;

• Smoking: a risk factor common to other types of cerebrovascular accident (CVA); in HSA It is related to cerebral aneurysm formation;

• Alcoholism: it is believed that it contributes to the formation of an aneurysm due to hypertension since regular alcohol consumption is an independent cause of hypertension;

• Presence of unruptured cerebral aneurysm: particularly in symptomatic aneurysms, size >7mm and located in the posterior communicating segment of the internal carotid artery or the vertebrobasilar system (Francoeur & Mayer, 2016; Vivancos *et al*., 2014).

Clinical picture

Sudden onset headache, independent and severity/intensity, raise the clinical suspicion of subarachnoid hemorrhage (HSA) (Rabinstein & Lanzino, 2018). The patient complains of sudden headache and reaches maximum intensity (thunderous headache, described as the worst headache felt throughout the life), associated with nausea and/or vomiting, nuchal stiffness, photophobia, loss of consciousness or focal neurological deficits (including paralysis of the cranial nerves) (Yao *et al.,* 2017, Alotaibi *et al*., 2017).

Seizures can occur in up to 20% of cases in the first 24h. The phenomenon occurs during physical exertion or stress; however, the higher incidence of rupture aneurysmatic occurs while patient involved in their daily routines, in the absence of strenuous physical activity (Petridis *et al*., 2017,

Takeshita *et al*., 2017, Stehouwer *et al.*, 2018).

A warning headache preceding the ictus associated with HSA is reported by 10%-43% of patients; Usually, it is milder than that associated with a critical rupture (Steiner *et al*., 2013; Connolly *et al*., 2012, Gritti *et al*., 2018). They represent minor hemorrhages in the aneurysm wall, which can occur days to weeks before the ictus. These episodes are known as sentinel headache (Al--Mufti *et al.*, 2017).

Immediately after the clinical history and physical examination, the patient with HSA should be staged according to severity, in order to allow further clinical comparisons. To this end, the Hunt & Hess Scale (1968) is widely used (Table 1) (Steiner *et al*., 2013, Vivancos *et al*., 2014). Another way to evaluate HSA is through the gradation of HSA severity of the World Federation of Neurological Surgeons (WFNS) (Tables 1 and 2) (Bekelis *et al*., 2015, Francoeur & Mayer, 2016).

Table 1. Hunt Scale-Hess

Degree	Symptoms
0	Asymptomatic (no subarachnoid hemorrhage)
I	Asymptomatic or moderate headache, moderate stiffness of nape
II	Moderate to severe headache, neck stiffness, no neurological deficit (except cranial nerve palsy)
III	Somnolence, confusion or moderate focal neurological deficit
IV	Coma vigil, focal deficit, onset of stiffness decerebration, vegetative disturbances
V	Deep Coma, decerebration, dying

Sourse: STEINER *et al,* 2013.

Table 2. WFNS Scale for Subarachnoid Hemorrhages

Degree	Glasgow coma scale	Motor deficit
1	15	Absent
2	13-14	Absent
3	13-14	Present
4	7-12	Present or absent
5	3-6	Present or absent

Source: SINGER *et al*, 2017.

Complementary exams

The Non-contrast-enhanced Cranial Computerized Tomography (NCCT) is the diagnostic pillar of the HSA since the blood in the subarachnoid space is detectable in approximately 90% of cases when this exam is performed in the range of 24h after bleeding. Has Sensitivity higher in the first 6-12h after the HSA (about 100%) and declines progressively over time (Lawton & Vates, 2017).

In the case of a strong cli-

nical suspicion of HSA, despite imaging exams, such as CT and/or Resonance of the negative encephalic brain (MRI), lumbar puncture is the next diagnostic step (Yao *et al*., 2017, Stehouwer *et al*., 2018). The distinction between cerebrospinal fluid (CSF) due to HSA or puncture accident with the needle may be severe, however, the persistence of elevated erythrocytes count in consecutive collection tubes (CSF remains well bleeding throughout the collection) and immediate centrifugation of the CSF with the presence of xanthochromia (rose/yellow supernatant resulting from the degradation of hemoglobin, indicates the blood present in the CSF there are at least 2h) classic HSA findings (Xie *et al*., 2017).

Once the diagnosis of HSA has been confirmed, the etiology of hemorrhage should be elucidated by angiographic studies. Of the available exams, then Angiography Digital Subtraction (ADS) has the resolution to detect intracranial aneurysms and define its anatomical characteristics, being, therefore, the gold standard exam (Stehouwer *et al*., 2018, Al-Mufti *et al*., 2017, Pasarikovski *et al*., 2017). However, currently the angiothomography, as a non-invasive test, is the first examination performed as an alternative to conventional cerebral angiography, although it does not identify small aneurysms (<3mm) reliably (Hayman *et al.*, 2017).

Treatment

In the same way as intraparenchymal hemorrhage (HIP), patients with HSA should be admitted to an intensive care unit for hemodynamic and neurological monitoring constants (Hayman *et al*., 2017).

Airway stabilization, respiration, and circulation (ABC) are essential, and the need for orotracheal intubation should be evaluated (Lawton & Vates, 2017, Xie *et al*., 2017, Zhou *et al*., 2017).

It is recommended complete rest, potent analgesia, prophylactic therapy for gastrointestinal ulcers and intravenous administration of fluids in order to maintain hemodynamic stability and healthy electrolytic balance (Müller & Müller, 2018).

Regarding the prophylaxis of venous thromboembolism, pneumatic compression socks are used associated with trobotic prophylaxis with low molecular weight heparin after aneurysm treatment (Steiner *et al*., 2013, Connolly *et al.*, 2012).

Other physiological disturbances, such as hyperthermia, hyperglycemia (glycemia >180mg/dL) and anemia (Hb<10 mg/dL), which are common in HSA and are related to poor prognosis, should be addressed (Zhao & Wei, 2017).

Blood pressure

Blood pressure (BP), usually elevated, should be controlled sparingly because usually, these patients need to maintain stable cerebral blood flow. While elevated BP contributes to increasing the likelihood of rebleeding, its reduction at normal levels contributes to the occurrence of vasospasm (Hayman *et al*., 2017, Zhou *et al*., 2017, Macdonald & Schweizer, 2017).

Thus, the maintenance of systolic blood pressure lower than 160mmHg is recommended to reduce the risk of rebleeding, according to the guidelines of the American Stroke Association. When blood pressure control is necessary, other medications are preferable, such as Nicardipine, Labetalol and Nitroprussiate of Sodium (Gritti *et al*., 2018, Al-Mufti *et al.,* 2017).

Aneurysm

Treatment

The main objective of the treatment of aneurysmatic HSA is the occlusion of the ruptured aneurysm, that is, to close the source of bleeding avoiding a new hemorrhage. Therefore, it should be treated early, as soon as possible (Mistry *et al.*, 2016).

Two main treatment options are available: microsurgical clipping and the endovascular approach (Bederson *et al*., 2009). The choice between the methods depends on the patient's clinical picture, anatomical characteristics, location of the aneurysm and the experience of the surgical team2. In cases in which both therapeuti-

cs can treat the aneurysm, embolization is the treatment of choice. (Class I, level of evidence B) (Yao *et al.*, 2017).

Factors in favor of open surgical intervention (microsurgery) are: younger age, presence of HIP (>50mL of volume) and specific factors of the aneurysm: localization in the middle cerebral artery and distal arterial segments, neck full aneurysmatic, arterial branches coming directly from the aneurysmal sac or other unfavorable vascular and aneurysmatic configurations for embolization (Figure 1) (Bekelis *et al.*, 2015).

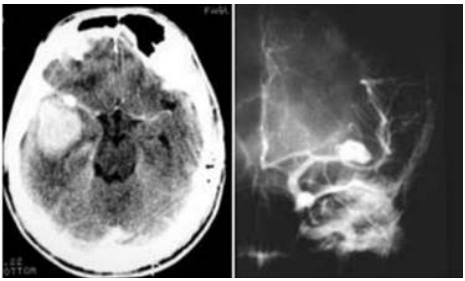

Figure 1. CT scan performed after intravenous contrast injection showing left temporal hematoma and dilatation (aneurysm) in the left middle cerebral artery. Carotid angiography confirming the presence of an aneurysm in the left middle cerebral artery. Source: SINGER et al, 2017.

Favorable factors of endovascular intervention: age ≥70 years, HIP not present, severe neurological condition and specific factors of the aneurysm such as localization in the posterior circulation (upper artery aneurysms basilar), small aneurysmal neck and unilobar form (Figure 2 and 3) (Petridis *et al.*, 2017, Takeshita *et al*., 2017).

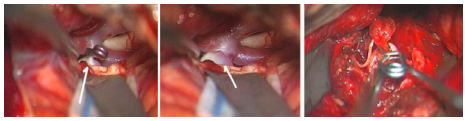

Figure 2. Microsurgical clip of basilar artery top aneurysm.Source: Petridis *et al*, 2017.

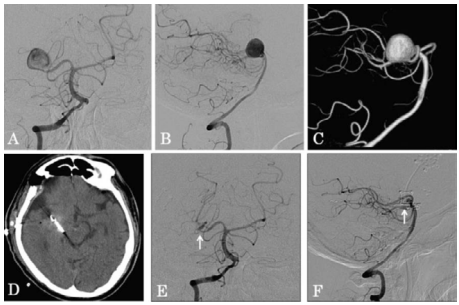

Figure 3. Preoperative digital subtraction angiography (DSA) showing a large saccular aneurysm arising from the P2 segment of the rightposterior cerebral artery ((a) anteroposterior view, (b) lateral view, (c) three-dimensional DSA). Posto-

perative computed tomography showing no ischemic or hemorrhagic lesions (d). Postoperative DSA showing complete obliteration of the aneurysm with slight dilatation of the parent vessel (arrow in (e), (f)).

Complications

Recurrence

In general, rebleeding causes much more severe clinical manifestations than the initial bleeding and is associated with very high mortality. Its prevention is obtained by reducing the map and treatment of the aneurysm (surgical clipping or endovascular embolization), which justifies the earliest possible therapeutic approach (Zhao & Wei, 2017, Mapa *et al.,* 2016).

Although antifibrinolytic agents such as aminocaproic acid and tranexamic acid have not been approved for the prevention of aneurysm rebleeding by the Food and Drug Administration (FDA), in the United States, the guidelines of the American Stroke Association (2012) affirm that when the definitive treatment of the aneurysm is delayed, and there are no other contraindications, the short-term therapy (<72h) with these drugs is recommended to reduce the risk of early rebleeding (Mapa *et al*., 2016, Zhao *et al*., 2017).

Vasospasm

It is a significant cause of clinical worsening, determining in about 40% of the cases worsening headache, lowering the level of consciousness and focal neurological signs, sometimes in different topography of the ruptured aneurysm. It manifests mainly between the 4th and 14th days after the HSA and may occur late (third week) (Francoeur & Mayer, 2016, Bederson *et al*., 2009). Transcranial Doppler is a useful tool to detect and monitor its occurrence, since it may show increased blood flow velocity in the great arteries, indicating vasospasm (Serrone *et al.*, 2015).

In order to avoid this complication, all patients should receive Nimodipine 60mg every 4 hours orally or nasoenteral tube for 21 days, and euvolemia should be maintained with 0.9% saline solu-

tion, under continuous monitoring (Hayman *et al*., 2017, Chen *et al*., 2017).

Vasospasm treatment included hypervolemia, hemodilution, and pharmacologically induced arterial hypertension (Raya & Diringer, 2014). This approach, called "Triple H" therapy, was instituted to elevate the mean arterial pressure and thus cerebral perfusion. However, new recommendations address the maintenance of euvolemia due to the lower risk of volume overload, pulmonary or cerebral edema (Zhao *et al.*, 2017, Lin, Kuo & Wu, 2014).

Hydrocephalus

It can occur acutely, subacute or late. It is related to the amount of blood in the subarachnoid space and the difficulty of transit and reabsorption of the CSF (Alotaibi *et al*., 2017).

In about one-third of patients, hydrocephalus is asymptomatic, and half of the patients with initial hydrocephalus improve spontaneously within 24 hours (Macdonald & Schweizer, 2017). Therefore, it is recommended to initiate External Ventricular Drainage (SVD) in cases of deterioration in the level of consciousness, an increase in ICP, and in patients who do not improve hydrocephalus in 24 hours, despite the high risk of ventriculitis/meningitis associated DVE (Rabinstein & Lanzino, 2018, Yao *et al*., 2017).

Approximately one-half to two-thirds of patients with acute hydrocephalus develop chronic hydrocephalus, requiring ventricular-peritoneal or ventricular-atrial shunt posteriorly (Zhao *et al*., 2017).

Hyponatremia

Hyponatremia after subarachnoid hemorrhage is relatively common and mediated by the hypothalamic lesion. Water retention is due to increased secretion of antidiuretic hormone (ADH), which may result from inadequate ADH, secretion syndrome (SIADH) or volume depletion induced by salt-wasting brain syndrome (Mapa *et al.*, 2016, Lin, Kuo & Wu, 2014). Although the treatment of asymptomatic hyponatremia in SIADH consists of water restric-

tion, fluid restriction is not desirable in patients with HSA, since it raises the risk of ischemic injury related to vasospasm (Gritti *et al*., 2018, Lawton & Vates, 2017).

Hyponatremia should be treated with isotonic saline or hypertonic saline solution, if severe natriuresis – Na+<133 mEq/L or reduction of 6mEq/L in 48h (Steiner *et al*., 2013, Vivancos *et al*., 2014, Xie *et al*., 2017).

The salt-losing brain syndrome is less common than SIADH and is characterized by volume depletion. It is usually treated with infusions of isotonic saline solution to restore euvolemia and suppress the release of ADH (Raya & Diringer, 2014, Al-Mufti *et al*., 2017, Serrone *et al*., 2015).

Prognosis

The severity of the initial clinical presentation, assessed by the Hunt and Hess scale or the WFNS scale for HSA, is the most important prognostic indicator in the HSA. In addition to the diagnostic value, the cranial TCSC assists in the prognostic evaluation (Takeshita *et al*., 2017, Gritti *et al*., 2018). The patients with a higher amount of blood in the cerebral cisterns are more likely to develop vasospasm. The gradation of this bleeding is validated by the Fisher scale (Table 3) (Lawton & Vates, 2017).

Table 3. Fisher Scale

Degree	Computed tomography (CT)
I	Absence of Blood
II	Vertical layers of diffuse and thin blood (<1mm thick)
III	Vertical layers of blood >1mm thick
IV	Intraparenchymal or intraventricular haemorrhage with or without diffuse SAH

Source: Fisher *et al*, 1980.

Other predictive factors of poor prognosis include rebleeding of the aneurysm, advanced age, preexisting severe comorbidity, diffuse cerebral edema in the computed tomography of the skull, intraventricular and Intraparenchymal hemorrhages, symptomatic vasospasm, late cerebral infarction (especially if multiple), hyperglycemia, hyperthermia, anemia and systemic complications, such as pneumonia and sepsis (Macdonald & Schweizer, 2017, Mistry *et al*., 2016, Zhao *et al*., 2017, Kuo & Wu, 2014).

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