Long-Term Follow-Up of Anterior Pituitary Deficiency after Aneurysmal Subarachnoid Hemorrhage: Prospective Cohort

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Objective: The aim of this study was to evaluate the prevalence of hypopituitarism in the acute stage after aneurysmal subarachnoid hemorrhage (SAH) as well at the chronic stage, at least 1 year after bleeding, to assess its implications and correlation with clinical features of the studied population. *Patients and Methods:* This was a prospective cohort study that evaluated patients admitted between December 2009 and May 2011 with a diagnosis of SAH secondary to cerebral aneurysm rupture. Clinical and endocrine assessment was performed during the acute stage after hospital admission and before treatment at a mean of 7.5 days (SD ± 3.8) following SAH, and also at the follow-up visit at a mean of 25.5 months (range: 12-55 months) after the bleeding. *Results:* Out of the 119 patients initially assessed, 92 were enrolled for acute stage, 82 underwent hormonal levels analysis, and 68 (82.9%) were followed up in both acute and chronic phases. The mean age and median age were lower among patients with dysfunction in the acute phase compared to those without dysfunction ($P < .05$). The prevalence of dysfunction in the acute phase was higher among patients with hydrocephalus on admission computed tomography (57.9%) than among those without it ($P < .05$). At chronic phase, there was an association between dysfunction and Hunt & Hess scale score greater than 2 ($P < .05$). *Conclusions:* We believe that there is not enough literature evidence to incorporate routine endocrinological evaluation for patient victims of SAH, but we should always keep this differential diagnosis in mind when conducting long-term assessments of this population. **Key Words:** Subarachnoid hemorrhage—intracranial aneurysms—pituitary anterior lobe—hypopituitarism.

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Introduction

Despite the progress in the clinical and surgical management observed in recent decades, spontaneous subarachnoid hemorrhage (SAH) remains a disease with very high morbidity and mortality rates. Victims of this disease frequently present with impairments that resemble those of patients with pituitary insufficiency. Nonspecific symptoms that occur frequently and can provoke important limitations include fatigue, headaches, mood swings, depression, cognitive impairment, and reduced independence in daily activities, which may be related to hypopituitarism.[1-4]

Some evidence of the relationship between pituitary dysfunction and SAH has been reported in the literature, often with contradictory data. Studies suggest that these endocrine disorders might be caused by different physiopathological conditions. The main causes reported are as follows: compression of the hypothalamus–pituitary complex by the aneurysm; SAH itself due to perfusion alterations, toxins from extravasated blood, ischemia due to vasospasm, increased intracranial pressure, and hydrocephalus; or even injury during the surgical procedure.[4,5] Also cited as an important factor for pituitary dysfunction is the fact that most aneurysms are anatomically close to the hypothalamus and pituitary.

The long discussion on increased morbidity and mortality in patients with hypopituitarism following SAH can be more pertinent if discussion is applied not only to acute phase but also to chronic phase of pituitary dysfunction. Determining the prevalence of hypopituitarism in patients with SAH is fundamental because this would permit the study of more effective measures to improve the quality of life of patients with this serious disease.[2,4,6,7] The aim of this study was to evaluate the prevalence of hypopituitarism in the acute stage after SAH as well as at the chronic stage, at least 1 year after bleeding, to assess its implications and correlation with clinical features of the studied population.

Methods

Patient Selection Criteria

This was a prospective cohort study that evaluated patients admitted to the Neurosurgical Service of Santa Casa Hospital at Belo Horizonte between December 2009 and May 2011 with a diagnosis of SAH secondary to cerebral aneurysm rupture, which was confirmed by computed tomography (CT) scan and digital subtraction cerebral angiography. We already had published our initial acute stage results.[8]

The inclusion criteria were as follows: SAH secondary to ruptured aneurysm, an absence of endocrine changes prior to hormone data collection (performed within the first 15 days after SAH), and patients aged more than 18 years. The exclusion criteria were as follows: patients aged less than 18 years, more than 15 days since the ictus of SAH, those with prior endocrine dysfunction, those who refused endocrine tests, patients whose data were not collected properly, and those who had recent or prolonged use of corticosteroids. In eligible patients, endocrine function was evaluated in the acute stage after SAH and at follow-up after 12 months.

This study was performed with approval from the Ethics Research Committee of Santa Casa Hospital and registered in *Plataforma Brasil*. Written informed consent was obtained from the patients or by the person responsible for them.

Acute Stage

After admission, patients received clinical support in neurosurgical intensive care unit, and the decision for treatment modality between microsurgery or embolization occurred after discussion of the neurosurgical team.

Clinical evaluation was performed at admission using the Glasgow Coma Scale (GCS) and the World Federation of Neurosurgical Societies (WFNS) scale. SAH severity was graded clinically using the Hunt & Hess (HH) scale and radiologically using the Fisher scale. The presence of hydrocephalus was recorded using admission CT.

Endocrine Function Testing

Blood samples for hormonal assessment were collected at admission after the patient had fasted for at least 8 hours, when this practice would not compromise the surgical decision. The endocrine assessment was performed during the acute stage after hospital admission and before treatment at a mean of 7.5 days (SD ± 3.8) following SAH, and also at the follow-up visit at a mean of 25.5 months (range: 12-55 months) after the bleeding.

We used commercially available kits to determine hormone levels. Morning cortisol, morning adrenocorticotropic hormone (ACTH), growth hormone (GH), insulin growth factor (IGF-1), thyroid-stimulating hormone (TSH), free thyroxine (fT4), total triiodothyronine (T3), follicle-stimulating hormone (FSH), luteinizing hormone (LH), estradiol (for women), testosterone (for men), and prolactin were measured using chemiluminescence or immunoassay methods. The reference values were appropriate for patient's age and sex in accordance with the manufacturer's recommendations. The hormonal levels obtained, together with the respective methods and reference values, are presented in Table 1. The following criteria were used to diagnose hormonal disturbances[3,9,10]:

- ACTH deficiency was diagnosed based on low cortisol associated with low or inappropriately normal ACTH.
- GH deficiency was diagnosed based on low IGF-1.
- TSH deficiency was defined as decreased fT4 in the presence of inadequately low basal TSH.