

An evaluation of neuroendocrine dysfunction following acute aneurysmal subarachnoid hemorrhage: A prospective study

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ABSTRACT

Objective: The aim was to investigate the incidence and pattern of neuroendocrine changes in cases of acute aneurysmal subarachnoid hemorrhage (SAH).

Materials and Methods: Endocrine assessment was performed in 100 consecutive cases of acute aneurysmal SAH presenting within 7 days of ictus. The gonadotropic, somatotrophic, thyrotrophic, and corticotrophic axes were evaluated for their possible dysfunction.

Results: A total of 100 cases (38 males, 62 females; age range - 17-76 years; mean age - 43.6 years) of acute SAH were studied. The aneurysms were located in the anterior circulation ($n = 95$) and posterior circulation ($n = 5$). The most common hormone deficiency was of growth hormone ($n = 67$), followed by gonadotrophin ($n = 50$), corticotrophin ($n = 49$) and thyrotrophin ($n = 35$). Hyperprolactinemia was noted in 10 cases. One-pituitary hormone axis deficiency was noted in 26 cases while 67 cases had two or more pituitary hormone axes dysfunction. A total of 93 cases had hormonal dysfunction in one or more pituitary hormone axes, and seven cases had no hormonal dysfunction.

Conclusions: Endocrine dysfunction occurs in 93% cases of acute SAH and multiple pituitary hormone axes dysfunction occurs in 67% cases. It is suggested that hormonal evaluation should be considered as part of management of acute SAH.

Key words: Aneurysmal subarachnoid hemorrhage, endocrine dysfunction, hormone

Introduction

Endocrine dysfunction is an infrequent consideration in the management of aneurysmal subarachnoid hemorrhage (SAH).^[1-3] Studies showing that aneurysmal SAH might be associated with neuroendocrine dysfunction come mainly from case reports or small series of patients.^[4-7,9-14] Systematic studies investigating this issue are limited in number and have yielded

conflicting results. Moreover, no study has been done in cases of acute SAH, and all the previous studies have been performed after at least 12 months following SAH.^[4-14] The objectives of this study are to investigate the incidence, pattern, and the magnitude of neuroendocrine changes in cases of acute aneurysmal SAH.

Materials and Methods

This prospective study included all consecutive cases of aneurysmal SAH admitted in the Department of Neurosurgery of our Institute from September 2008 to April 2009. Patients

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with ictus of SAH more than 7 days, those on drugs affecting the hypothalamic–pituitary function and those having a preexisting pituitary disorder were excluded. Informed consent was obtained from all patients. Data regarding age, sex, clinical severity of SAH on admission by the Hunt and Hess grading system, aneurysm location and treatment modality (surgery or embolization) were noted. Endocrine evaluation was done next day after admission in the morning between 8:00 and 9:00 am and included the measurement of the following hormones: Cortisol, free thyroxine, thyroid-stimulating hormone, prolactin, growth hormone (GH), insulin-like growth factor 1 (IGF-1), and luteinizing hormone (LH), follicle stimulating hormone and testosterone in case of males and estrogen in the case of females.

Results

A total of 121 consecutive cases of aneurysmal SAH were admitted in the Department of Neurosurgery of our Institute from September 2008 to April 2009. Twenty-one cases were excluded due to ictus more than 7 days and/or preexisting endocrinopathy. Thus, total 100 cases were considered for the study. Their detailed clinical and endocrine evaluation was performed. There were 38 males and 62 females with age range from 17 to 76 years (mean age - 43.6 years). The aneurysms were located in the anterior circulation ($n = 95$; middle cerebral artery - 15, anterior communicating artery - 49, posterior communicating artery - 16, internal carotid artery - 9, anterior choroidal artery - 1, distal anterior cerebral artery - 5) and posterior circulation ($n = 5$; basilar artery - 4, posterior cerebral artery - 1). The most common hormone deficiency was of GH ($n = 67$) followed by gonadotrophin ($n = 50$), corticotrophin ($n = 49$) and thyrotrophin ($n = 35$). Hyperprolactinemia was noted in 10 cases [Table 1]. One-pituitary hormone axis dysfunction was noted in 26 cases while 67 cases (31, 27, 7 and 2 cases had two, three, four and five pituitary hormone axes dysfunction respectively) had two or more pituitary hormone axes dysfunction. A total of 93 cases had hormonal dysfunction in one or more pituitary hormone axes, and seven cases had no hormonal dysfunction [Table 2].

Discussion

Evidence that aneurysmal SAH might be associated with neuroendocrine dysfunction comes mainly from case reports or small series of patients.^[4-7,9-14] Systematic studies investigating this issue are limited in number and have yielded conflicting results. In 1975, Osterman investigated 50 patients, 3.5 months after SAH. The hypothalamic–pituitary–adrenal axis was assessed by the circadian rhythm of plasma 11-hydroxycorticosteroids and the metyrapone test. Thyroid and gonadal function were evaluated clinically and by the corresponding baseline hormones. The author found that endocrine abnormalities were rare; 6% of the patients had an abnormal circadian rhythm in cortisol, 11% had a

pathological metyrapone test, 2% had mild thyroid function abnormalities, whereas hypogonadism was not present.^[12] Kreitschmann-Andermahr investigated 21 patients between 14 and 43 months after SAH. Pituitary function was investigated by a combined thyrotropin-releasing hormone–LH-releasing hormone arginine test and the insulin tolerance test. This study showed that 43% of the patients screened showed isolated or combined endocrine abnormalities; these included adrenocorticotrophic hormone (ACTH) ($n = 4$) or GH deficiency ($n = 3$) and ACTH plus GH impairment ($n = 2$).^[7] Brandt studied 10 cases, 1-year after SAH by routine laboratory investigation and by dynamic tests. A significant number of patients (50%) had some degree of diminished pituitary capacity. Abnormalities consisted of isolated or combined gonadotroph and somatotroph deficiencies, whereas adrenal and thyroid functions were preserved in all cases.^[2] Dimopoulou analyzed 30 patients between 12 and 24 months after SAH and concluded that endocrine abnormalities are common in survivors of SAH, affecting 47% of the patients screened. The most common alteration in this series was a diminished secretion of GH, as reflected by the finding of low IGF-1 levels in a substantial proportion of our patients. Table 3 summarizes these studies. Although a dynamic assessment of GH reserve

Table 1: Details of cases with various hormonal disturbances

Parameters	Number of cases	Percentage
ACTH deficiency	49	49
TSH deficiency	35	35
Hyperprolactinoma	10	10
GH deficiency	67	67
GTH deficiency	50	50

ACTH – Adrenocorticotrophic hormone; TSH – Thyroid-stimulating hormone; GH – Growth hormone; GTH – Gonadotropin hormone

Table 2: Number of pituitary axes involvement

Number of pituitary axes dysfunction	Number of cases	Percentages
One	26	26
Two	31	31
Three	27	27
Four	7	7
Five	2	2
None	7	7

Table 3: Summary of the reported series of endocrine dysfunction in SAH

Authors	Number of cases	Months after SAH	Endocrine dysfunction (%)
Osterman ^[13]	50	3-5	8
Kreitschmann-Andermahr <i>et al.</i> ^[7]	21	14-43	45
Brandt <i>et al.</i> ^[2]	10	12	50
Dimopoulou <i>et al.</i> ^[4]	30	12-24	67

SAH – Subarachnoid hemorrhage

is usually recommended for assessing somatotroph function, there is now good evidence that low-IGF-1 concentrations represent a good marker of GH deficiency. Hypogonadism was the second most common deficiency observed in this study. The adequacy of cortisol was assessed by dynamic testing. For this purpose, the low-dose (1 µg) ACTH stimulation test was used.^[7] This test correlates closely with the insulin-induced hypoglycemia test,^[7] the generally agreed reference standard for the evaluation of the hypothalamic–pituitary–adrenal axis, and seems to be superior to the high-dose ACTH test in detecting subtle defects of adrenal reserve. Although a diminished cortisol response was observed in only three patients, this finding is of paramount importance because unrecognized cortisol deficiency may have serious consequences if the patient has to cope with a stressful situation. Finally, the thyroid abnormalities observed in the study demonstrated a pattern compatible with subtle primary thyroid failure.^[4]

In our study, the most common hormone deficiency encountered was of GH ($n = 67$) followed by gonadotrophin ($n = 50$), corticotrophin ($n = 49$) and thyrotrophin ($n = 35$). Hyperprolactinemia was noted in 10 cases. One-pituitary hormone axis dysfunction was noted in 26 cases while 67 cases had two or more pituitary hormone axes dysfunction. A total of 93 cases had hormonal dysfunction in one or more pituitary hormone axes, and seven cases had no hormonal dysfunction.

Conclusions

Endocrine dysfunction occurs in 93% cases of acute SAH, and multiple pituitary hormone axes dysfunction occurs in 67% cases. The most common endocrine dysfunction is GH dysfunction occurring in 67% of cases and the least common is hyperprolactinemia occurring in 10% of cases. It is suggested that hormonal evaluation should be considered as part of the management of acute SAH.

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Conflicts of interest

There are no conflicts of interest.

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