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CSF Picture In Aneurysmal Subarachnoid Hemorrhage

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Abstract

Objectives: The current study aims to observe the effect of the disease pathology on the CSF picture at admission and how the individual CSF determinants affect the patient outcome.
Materials and Methods: A retrospective review of the levels of CSF glucose, protein, white blood cell count and culture in 661 cases of aneurysmal subarachnoid hemorrhage was done from the records of Thomas Jefferson University Hospital. Parameters were analyzed by student's *t* test, $p < 0.05$ is taken as significant.
Results: Higher CSF glucose as well as CSF protein at admission worsened the chances of a good outcome, although CSF glucose < 40mg/dl and CSF protein < 15mg/dl at admission were associated with higher mortality. CSF white blood cell count of 3-5 /ml was associated with the best outcome, also culture negative cases had a better prognosis.
Conclusions: All the CSF parameters studied gave the best prognostic results in their median values. More elaborate and prospective studies may be considered to give us a clearer picture.

Key words:

Aneurysmal subarachnoid hemorrhage, cerebrospinal fluid, protein, glucose, white blood cell, extended Glasgow outcome score.

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Introduction

Intracranial aneurysms (IA) affect 2 to 5% of the entire population [1], with ruptured IAs comprise of 1% of all IAs [2]. Ruptured aneurysms classically cause subarachnoid hemorrhage (SAH), but may cause intraventricular hemorrhage and subdural blood [3]. About 65% of patients die of the first SAH and a further 20 to 25% experience complications [4]. The complications that occur are mostly neurological viz. vasospasm or rebleeding [5] but they might be non neurological too such as pulmonary edema [6], cardiac arrhythmias [7], electrolyte disturbances [8] and hematologic abnormalities [9, 10].

Although there has been considerable amount of research on aneurysmal subarachnoid hemorrhage (aSAH) patients; the effect of the basic cerebrospinal fluid (CSF) analysis, which are routinely performed in such patients at even the most remote centers, is seldom studied. We have measured the effect of the disease process on the CSF picture and determined the effect of each of these basic CSF indicators on the patient outcome.

Materials and Methods

Records of aSAH patients admitted in Thomas Jefferson University Hospital, Philadelphia, USA from March 2006 to January 2010 were obtained from their billing codes and retrospectively reviewed. The diagnosis of subarachnoid hemorrhage was established on the basis of conventional CT or CT/MR angiography. Patients with preexisting systemic infections and patients admitted > 72 hours after the onset of SAH were excluded from the study. Patients who were not subjected to a detailed CSF analysis at admission were also excluded. 661 patients met the criteria; their age, sex, levels of CSF glucose, protein, white blood cell (wbc) count and reports of CSF culture in chocolate agar media at admission as well as their prognosis on 15 day follow up based on extended Glasgow outcome score (GOS-E) were documented. All biochemical tests were done in Thomas Jefferson Hospital general laboratory. GOS-E score ≥ 5 was taken as good prognosis. GOS-E was further

dichotomized at 1 and 2-8 for death and survival respectively. Table I shows how the GOS-E scores were divided. Approval for the collection and review of data was obtained from the Institutional Review Board (Control Number 10D.79) at the Thomas Jefferson University.

Statistical Analysis

All data were analyzed using JMP 7.0.2, SAS Institute, Cary, NC. Data "outliers" were identified for each parameter from box-and-whisker plots. Then, a two-tailed independent Student's *t* test was performed for each parameter (both including and excluding the outliers) to assess the statistical significance of the observed difference between the mean values for good and bad outcome. *P* values and 95% confidence intervals from the *t* test were calculated and reported, *p* value <0.05 is taken as significant. Kruskal-Wallis nonparametric tests were used when appropriate.

Results

Among the 661 aSAH patients, 398 (60.21%) were females. The mean age of the patients at admission was 54.7± 9.8 years, females being about 3.6 years younger than males (p=0.53). Table 2 depicts baseline characteristics of the patients that were included in this analysis. 15 days after occurrence of the SAH, 229 (34.64%) patients had poor outcome scores, i.e. GOS-E ≤ 4, among them 93 (14.07%) had died.

Table 1: The Extended Glasgow Outcome Scale (GOS-E) And the way it was dichotomized

GOS-E Score	Categories	Division of Good and Bad Prognosis	Division of Death and Survival
1	Dead		
2	Vegetative State	Bad	
3	Lower Severe Disability	Prognosis	Death
4	Upper Severe Disability		
5	Lower Moderate Disability		
6	Upper Moderate Disability	Good Prognosis	
7	Lower Good Recovery		Survival
8	Upper Good Recovery		

Kruskal-Wallis (non-parametric) comparisons across outcomes came significant for CSF glucose and protein levels as well as CSF wbc count and CSF culture result (p < 0.001). While higher level of CSF glucose and protein levels as well as CSF wbc count were associated with poor outcome; CSF glucose < 40mg/dl, CSF protein < 15mg/dl and CSF wbc count < 3/ml also had terrible effects on patient prognosis (p<0.001).

The level of glucose in the CSF had an odds ratio of 1.087 (95% confidence interval, 1.078-1.096) for a poor outcome with per 1 mg/dl increase and had an odds ratio of 1.048 (95% confidence interval, 1.041-1.055) for death per 1mg/dl rise; but although there were only 8 patients with CSF glucose< 40mg/dl at admission, all of them had a bad prognosis. The CSF protein level had an odds ratio of 1.93 (95% confidence interval, 1.84-2.1) for a poor outcome with per 1 mg/dl increase and had an odds ratio of 1.55 (95% confidence interval, 1.37-1.73) for death per 1mg/dl rise; however CSF protein level < 15 mg/dl was associated with 77.1% mortality. 78.97% of patients had CSF wbc count > 5/ml, among them 15.9% died (p=0.031) and 37.93% had a poor outcome (p < 0.001); while 1.66% had CSF wbc count < 3/ml and 9.09% of them died (p=0.03) and 54.55% had a poor outcome (p < 0.001). Patients with CSF wbc count between 3-5 had the best outcome; with 80.47% showing a good prognosis (p < 0.001) and with a mortality rate of only 7.03% (p < 0.001). Patients with negative CSF cultures at admission fared better: with 68.69% having a good prognosis (p < 0.001) and only 10.98% mortality (p < 0.001), compared to 25.49% good prognosis and 50.98% mortality in CSF culture positive patients.

Table 2: Baseline Characteristics of the 661 patients

CHARACTERISTIC	Mean Value
Over All Age	54.7±9.8
Age of Males in Years	56.9±8.5
Age of Females in Years	53.25±11
Percentage of patients with a high csf white blood cell count at admission	78.97%
Percentage of patients with a positive csf culture at admission	0.08%
Mean csf protein level at admission	88.6 mg/dl
Mean CSF protein level at admission for those having a good outcome	68.7 mg/dl
Mean CSF protein level at admission for those having a poor outcome	99.1 mg/dl
Mean csf glucose level at admission	86.8 mg/dl
Mean Csf glucose level at admission for those having a good outcome	64.9 mg/dl
Mean Csf glucose level at admission for those having a poor outcome	128.11 mg/dl

Discussion

Subarachnoid hemorrhage resulting from the rupture of intracranial aneurysms is a virtual catastrophe; the annual incidence being estimated to be nine per 100, 000 [11]. In recent times there has been several studies [12, 13] regarding the role of complex biochemical markers of brain damage: such as S100B protein, neuron-specific enolase (NSE), glial fibrillary acidic protein (GFAP), apolipoprotein E (ApoE), tumor necrosis factor (TNF)-α, soluble tumor necrosis factor receptor I (sTNFR-I), and interleukins (IL) and markers of oxidative stress, such as malondialdehyde (MDA) in aSAH patients. But the role of basic CSF parameters like

CSF protein and glucose level and CSF leukocyte count or culture, which are routinely monitored in all aSAH patients; is frequently ignored.

In this study it is observed that higher levels of both CSF protein are associated with poor prognosis and very low values are associated with greater mortality. Although there have never been any study in the past considering CSF protein levels in aSAH patients, the higher CSF protein levels may be an indirect evidence of the process of ongoing vasospasm but there should be elaborate studies on the molecular level to justify the reason behind poor prognosis with both higher and lower CSF protein levels.

Previous studies considering CSF glucose levels have either shown that there exists no relation between CSF glucose and the patient prognosis [14]; or have reported low CSF glucose levels in acute cases due to hyperglycolysis in the brain [15]. Low CSF glucose has been also accounted for severe metabolic distress as evidenced by increased levels of glutamate, glycerol and lactate: pyruvate ratio in microdialysate [16]. This study illustrated poor prognosis with high CSF glucose, which may have resulted from a rise in serum glucose, and increased mortality with CSF glucose < 40mg/dl.

CSF leukocyte count of > 5/ml as well as < 3/ml was found to be associated with poor prognosis as well as higher mortality. While higher CSF leukocyte count leading to poor prognosis may be explained on the basis of the fact that CSF neutrophils directly and via myeloperoxidase and NADPH oxidase, are known to be associated with the development of vasospasm post subarachnoid hemorrhage [17]; the role of lower leukocyte count in prognosis needs to be studied more ornately. Although there is dearth of studies regarding CSF cultures in aSAH patients; the poor prognosis with culture positive cases can be easily understood due to the effect of the superadded infection.

Although the study has an enormous sample size and only SAH cases admitted within 72 hours of onset are well deliberated, the study still has a few flaws. Firstly it is a retrospective analysis providing only the findings with no hint regarding the reason behind those findings. Secondly the follow up period for the patients is 15 days, hence long term outcomes of the patients has not been assessed. Then with regards to CSF culture, only a chocolate agar culture was considered for all the patients; where a detailed microbiological analysis of culture positive cases could have revealed which organisms were associated with inferior prognosis. Also the radiological comparison of the quantum of hemorrhage in the patients and its effect on the respective CSF parameters were not analyzed.

Conclusion

The study shows that all of the basic CSF parameters which are routinely studied in aSAH patients even at the most remote centers, gave the best prognostic results in their median values. Hence monitoring their values can provide a good track of the patients' prognosis and may be a ground breaking discovery in the management of such patients. More intricate studies regarding these aspects, preferably on the molecular level, may be conducted to understand the pathologic processes beneath to offer a clearer picture.

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