ORIGINAL ARTICLE

Early Intraocular Complications of Subarachnoid Haemorrhage after Aneurysm Rupture

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ABSTRACT

The aim of this study was to identify factors predisposing for early intraocular complications of aneurysmal subarachnoid haemorrhage (SAH). The authors analysed 96 selected cases of aneurysmal SAH. Forty patients (42%) demonstrated abnormal fundus findings, including disc swelling (13.5%), retinal haemorrhages (23%), and vitreous haemorrhage (5%). The incidence of intraocular pathologies was significantly higher in patients who lost consciousness at the onset of SAH, were admitted with high scores of the Hunt-Hess and Fisher scales and low score of the Glasgow Coma Scale, as well as in those with arterial hypertension, more sizable aneurysm, and older.

Keywords: Optic disc swelling, retinal haemorrhages, subarachnoid haemorrhage, Terson syndrome

INTRODUCTION

The association of vitreous, subhyaloid (preretinal), or retinal haemorrhages with aneurysmal subarachnoid haemorrhage (SAH), was first described by Terson in 1900.¹ Since then, numerous studies have been published regarding the incidence, pathogenetic mechanism, and natural history of ocular haemorrhages associated with aneurysmal SAH.^{2–7} Intraocular haemorrhages of different types have been documented in 10–40% of individuals with SAH, but most of the relevant studies focused on the prognostic significance of Terson syndrome, a term exclusively reserved for subhyaloid and/or vitreous haemorrhage.^{8–12} In contrast, studies of comprehensive ocular fundus pathology in SAH survivors and especially of factors predisposing to their manifestation are sparse.^{8,13,14}

In this prospective study, we attempted to estimate the exact incidence of a whole spectrum of early intraocular complications in patients suffering from aneurysmal subarachnoid haemorrhage and to identify factors that are potentially associated with fundus findings in this group of patients.

MATERIALS AND METHODS

In our prospective study, all consecutive patients admitted to the Department of Neurosurgery of the Medical University of Białystok between 2011 and 2012 in whom aneurysmal SAH had been diagnosed were subjected to ophthalmological evaluation. Excluded from this consecutive series were patients who died before the ophthalmological examination. Also, two patients who received anticoagulants prior to SAH were not included in this study. The diagnosis of SAH has been established by computed tomography (CT). The extent of SAH (the amount of blood present in the subarachnoid space) was classified according to the Fisher scale (see Table A1) and its intraventricular components according to the Columbia scale (Table 1). Localisation and size of the ruptured aneurysm was confirmed using cerebral angiography within 12 hours from patient's admission to the department. The severity of SAH was classified according to the Hunt-Hess (H-H) scale (see Table A2) and Glasgow Coma Scale (GCS) upon admission. Patients were also subdivided into three groups depending on the symptoms present at the

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TABLE A1 The Fisher scale for grading SAH on admission CT scan.

Grade	CT scan
I	No blood visualised
II	A diffuse deposition or thin layer with all vertical layers of blood (interhaemispheric fissure, insular cistern, ambient cistern) less than 1 mm thick
III	Localised clots and/or vertical layers of blood 1 mm or greater in thickness
IV	Intracerebral or intraventricular clots with diffuse or no subarachnoid blood

TABLE 1 Clinical characteristics of the study group.

Grade	Criteria	Number of patients
0	No SAH or IVH	45
I	Minimal/thin SAH, no IVH in both lateral ventricles	22
II	Minimal/thin SAH, with IVH in both lateral ventricles	1
III	Thick SAH, no IVH in both lateral ventricles	22
IV	Thick SAH, with IVH in both lateral ventricles	6

SAH = subarachnoid haemorrhage; IVH = intraventricular haemorrhage.

TABLE A2 The Hunt-Hess scale for grading subarachnoid haemorrhage.

Grade	Description
I	Asymptomatic or minimal headache and slight nuchal rigidity
II	Moderate to severe headache, nuchal rigidity, no neurological deficit except cranial nerve palsy
III	Drowsy or confusion, minimal neurological deficit
IV	Stuporous, moderate to severe haemiparesis, possibly early decerebrate rigidity and vegetative disturbances
V	Deep coma, decerebrate rigidity, moribund appearance

onset of SAH (irrespective of symptoms presented on admission). In the first group, patients had only a sudden headache; in the second group—a headache, nausea, vomiting, and/or focal deficit with no loss of consciousness. The third group comprised patients who suffered from loss of consciousness at the onset of SAH, even if they were found conscious at admission/examination.

The mean interval between the onset of SAH and initial ophthalmological examination was 3.5 ± 3 days. The examination of both eyes was conducted by the same experienced ophthalmologist (I.O.) within 24 hours from admission. Moreover, some patients were reexamined after the procedure of aneurysm obliteration, but these findings were not included in present analysis in order to not obscure the main

TABLE 2 Clinical characteristics of the study group.

Characteristic	Number of patients
Mean age in years $\pm$ SD	48.1 $\pm$ 13.1
Gender: M/F	31/65 (32.3%/67.7%)
Gender ratio (M:F)	1:2.1
Glasgow Coma Scale	
14–15	83
9–13	10
≤ 8	3
Hunt-Hess scale	
I	67
II	18
III	8
IV	3
V	0
Fisher scale	
I	45
II	23
III	15
IV	13
Size of aneurysm	
<12 mm	80
≥ 12 mm	16
Site of aneurysm	
Anterior communicating artery	33 (34.4%)
Internal carotid artery	26 (27.1%)
Middle cerebral artery	29 (30.2%)
Basilar/vertebral artery	8 (8.3%)
History of hypertension	42 (43.7%)
History of diabetes	7 (7.3%)
Smoking	27 (28.1%)

SD = standard deviation; M/F = male/female.

message of our study, i.e. assessment of ocular complications after spontaneous aneurysmal SAH rather than cumulative rate of complications associated with both SAH and neurosurgical intervention.

The ophthalmological examination was performed using direct and/or indirect ophthalmoscopy after pharmacological pupil dilation. Fundus changes were classified as optic disc swelling, retinal haemorrhages or subhyaloid/vitreous haemorrhage. Visual acuity and other functional tests could not be obtained due to the fact that patients ought to stay in bed till aneurysm obliteration, and a significant part of them exhibited reduced consciousness.

Finally, the study group included 96 patients, 31 men (32.3%) and 65 women (67.7%). The median age of the patients was 50 years (range: 19–75 years, mean: 48.1 ± 13.1 years). Clinical characteristics of the study group at the time of admission are shown in Table 2.

The incidence of fundoscopic findings was documented and stratified according to gender, age, symptoms at onset of SAH, clinical status at admission (as graded in GCS and HH scales), severity of SAH (Fisher scale), the features of ruptured aneurysm (its size and localisation), and history of hypertension, diabetes, and smoking.

The protocol of the study was approved by the university institutional review board (according to the

guidelines of the Helsinki Declaration), and all patients gave written informed consent for the use of their clinical material in this publication.

Statistical Analyses

Normal distribution of continuous variables was verified with the Kolmogorov-Smirnov test, and their statistical characteristics were presented as arithmetic means and their standard deviations (SD) or medians and interquartile ranges (IQR). Depending on the type of distribution, the Student *t* test and analysis of variance (ANOVA) or the Mann-Whitney *U* test and the Kruskal-Wallis test were used for intergroup comparisons. The distributions of qualitative and discrete variables were compared with the Pearson's chi-squared test or the Fisher's exact test. The variables that differed significantly or showed a trend ($p < 0.1$) to differ between the studied subgroups were tested in univariate logistic regression models as potential risk factors of ocular fundus lesions. Variables that proved significant on the univariate analysis or remained at a threshold of statistical significance ($p < 0.1$) were included in the multivariate model of logistic regression. In the case of continuous variables that proved independent risk factors on multivariate analysis, a cutoff value distinguishing between patients with/without the fundus lesions was established on the basis of ROC (receiver operating characteristic) analysis. The following characteristics of ROC curve were determined: positive predictive value (PPV), negative predictive value (NPV), and the area under ROC curve (AUC) together with its 95% confidence interval (95% CI). All calculations were carried out with Statistica 10 (StatSoft, Tulsa, OK, USA) package, with the level of significance set at $p \leq 0.05$.

RESULTS

Intraocular pathologies were found in 40 patients with aneurysmal SAH (41.7%). In 13 of them (13.5% of the whole group and 32.5% of patients with intraocular pathologies), the only finding was swollen, blurred optic disc. Other 22 patients (22.9% of the whole group and 55% of patients with intraocular pathologies) had flame-shaped or blot-shaped retinal haemorrhages, which accompanied disc swelling in 10 cases (Figure 1). The remaining five patients, constituting 5.2% of the whole study group and 12.5% of patients with intraocular pathologies, had haemorrhage within the vitreous cavity and/or in the subhyaloid space (Terson syndrome). In all patients with optic disc swelling and retinal haemorrhages, both eyes were affected. Among five patients with Terson syndrome, bilateral haemorrhages were found

FIGURE 1 Retinal haemorrhage and optic disc swelling after subarachnoid haemorrhage.

in one person and unilateral haemorrhages in the remaining four individuals.

The occurrence of fundus changes was significantly higher in patients who lost consciousness at the onset of SAH ($p < 0.01$), were graded as II and III on the Hunt-Hess scale ($p < 0.01$ and $p < 0.05$, respectively), scored $\geq$ III on the Fisher scale ($p < 0.01$), and suffered from arterial hypertension ($p < 0.05$). Mean age of patients with intraocular pathologies amounted to 52.7 ± 11.9 years, and was significantly older than in the case of individuals without pathologies (45.6 ± 11.5 years; $p < 0.01$). Also the aneurysm size was significantly greater in patients with intraocular pathologies (median: 9 mm, IQR: 7–12 mm) than among those in whom no fundus changes were found (median: 8 mm, IQR: 6–9.5 mm; $p < 0.05$).

The intraocular findings were less common among patients who experienced solely headache at the onset of SAH ($p < 0.01$), whose GCS on admission was 15, and in persons with Hunt-Hess and Fisher scores equal to I ($p < 0.001$). It is of note that 60% of patients who harboured intraocular pathologies after SAH underwent loss of consciousness, but only 7.5% of them remained unconscious (IV grade in H-H scale) on admission. All five patients with Terson syndrome had an episode of loss of consciousness, whereas all of them were scored II or III on the H-H scale on admission.

Univariate logistic regression model revealed factors predisposing the patients with aneurysmal SAH to ocular fundus changes. They are listed in Table 3, in descending order of their potential influence. It is of note that the severity of SAH, represented by first four variables with the highest odds ratios, appeared the most powerful predictor of ocular changes. Arterial hypertension, older age, and the size of aneurysm turned out to be weaker predictors of SAH-related ocular changes. Among the analysed factors, the size of aneurysm appeared an independent risk factor on multivariate model of logistic regression. The 12 mm

TABLE 3 Potential predictors of intraocular changes at the onset of SAH identified on univariate logistic regression analysis (in descending order of power).

Variable	Univariate model		
	OR	95% CI	<i>p</i>
Fisher scale III/IV at admission	13.8	4.5–42.6	0.000
Hunt-Hess scale $\geq$ II at admission	11.3	3.7–34.7	0.000
GCS score $\leq$ 14 at admission	7.5	2.3–24.4	0.001
Loss of consciousness at the onset of SAH	5.5	2.2–13.7	0.001
History of hypertension	2.6	1.1–6.1	0.023
Greater size of aneurysm	1.2	1.0–1.3	0.017
Older age	1.1	1.0–1.1	0.007

OR = odds ratio; CI = confidence interval.

size of aneurysm performed best on ROC analysis as a threshold value for cutting off the occurrence of fundus changes. PPV and NPV associated with this size of aneurysm amounted to 0.45 and 0.67, respectively.

DISCUSSION

Our study has demonstrated that in this selected population, more than 40% of patients with aneurysmal SAH have abnormal fundus findings. The most frequent changes were retinal haemorrhages ($n=22$) and disc swelling ($n=23$). Disc swelling was the only finding in 13 patients from the latter group, and was accompanied by retinal haemorrhages and in the remaining 10 individuals. Terson syndrome was documented in five patients.

The incidence of intraocular pathologies found in our group of patients falls into the 20–50% range reported in the literature.^{2–4,6,13–16} The rate of intraocular pathologies documented in our material corresponds to the upper limit of the range reported in the literature. It is noteworthy that the true incidence of intraocular pathologies in general population of aneurysmal SAH survivors can be even higher, as our analysis did not include the patients hospitalised at other wards, who could not be transferred to neurosurgical department due to their poor clinical condition. Therefore, the prevalence of intraocular complications in this subpopulation, especially vitreous haemorrhages, was likely higher than hereby reported. It must be noted, however, that only some of the authors studied the comprehensive spectrum of intraocular pathologies. Most of them restricted their interest to intraocular haemorrhages, specifically to bleeding of Terson type, and often ignored optic disc swelling. Entezari *et al.*¹³ extensively studied a full array of ocular findings in spontaneous SAH, demonstrating fundoscopic abnormalities in as many as 50.5% of patients; the list of abnormalities included disc swelling (42%),

retinal haemorrhages (25%), and vitreous/subhyaloid haemorrhages (4.5%).

It is of note that Terson syndrome, which is often referred to as the “flagship” of ocular manifestations of aneurysmal SAH, was seen only in five patients, i.e. in 5.2% of our group, whereas other authors reported its incidence as 3–27%.^{2–9,11,12,14} Such significant discrepancy can be in part explained by the fact that the term “Terson haemorrhage”, which was originally used for vitreous haemorrhage, has been extended onto other types of ocular haemorrhages in some contributions.^{3,10} On the other hand, the presence of Terson syndrome is well known to correlate with the severity of SAH.^{2–5,7,8,10} Our group included only three patients in Hunt-Hess grade $>$ III, whereas according to the authors who reported higher incidence of Terson syndrome, patients in grades IV and V corresponded to 12%, 17%, or 18% of the studied groups.^{5,8,11}

Although our findings confirmed high incidence of blood infusion to different intraocular compartments after aneurysmal SAH, the exact way by which blood enters the eye remains unclear. Several potential mechanisms were proposed.^{3,8,17,18} According to the most widely accepted hypothesis, the bleeding results from a sudden increase in pressure within the retinal venous system, occurring secondarily to rapid elevation of intracranial pressure (ICP) at the onset of SAH. High pressure propagates from the skull to the retinal veins alongside the subarachnoid space of the optic nerve sheaths. Also, general venous return from the orbit to the cavernous sinus is hindered, which results in rupture of the retinal veins and intraocular bleeding. Other authors hypothesised that the SAH-related increase in ICP is reflected by a rapid effusion of cerebrospinal fluid to the subarachnoid space within the optic nerve sheath. Dilated retrobulbar portion of the nerve sheath could compress both the retinochoroidal anastomoses and the central retinal vein, with resultant obstruction thereof. The acute decrease in venous drainage from the retina would result in stasis and vein rupture. According to some more historical theories, due to elevated ICP, blood from SAH located in the vicinity of the optic nerve can penetrate the porous region of the sclera (lamina cribrosa) and appear in the eye globe.

Among the factors identified as predictors of the ocular consequences of SAH, four were related to the severity of SAH: scores on the Fisher, H-H, and Glasgow Coma scales, and loss of consciousness at onset of SAH (Table 3). Yet, severity of SAH itself appears to be not a straightforward notion because several biological factors can contribute to the final clinical effect of the haemorrhage, including the appearance of post-haemorrhagic ocular pathologies. Whereas the first three factors are conventionally admitted as a measure of SAH severity, the role of initial loss of consciousness (irrespective of

consciousness state on admission) remains to be discussed. Frizzell et al.² first pointed out that “coma-producing” haemorrhage can be a sensitive indicator for screening of patients with retinal haemorrhages. In his group of 99 patients with aneurysmal SAH, all individuals with Terson syndrome and 89% of those with other ocular haemorrhages had history of transient (or prolonged) coma. A similar conclusion was presented by Kuhn et al.¹⁹ as to the Terson syndrome. Ness et al.⁴ also noticed that some patients who were in relatively low grade in the H-H and Fisher classifications on admission, had developed intraocular haemorrhages; this finding suggests a need to search for other reasons of intraocular SAH manifestations.

In view of the evidence mentioned above we distinguished three groups of patients based on their status of consciousness at the onset of SAH (irrespective of the status on ophthalmological examination). We found that the occurrence of fundus changes was significantly higher in patients who lost consciousness at the onset of SAH, and the intraocular changes were less common among individuals who experienced only headache at the onset of the haemorrhage. Furthermore, as many as 60% of patients who harboured intraocular pathologies after SAH underwent loss of consciousness, but only 7.5% of them remained unconscious (IV grade on the H-H scale) on admission. Furthermore, it should be emphasised that all five patients with Terson syndrome had an episode of loss of consciousness, whereas all of them were on admission scored on II or III on the Hunt-Hess scale (i.e. were conscious). All the above findings point to the initial loss of consciousness as a potential prognostic factor of intraocular complications of aneurysmal SAH.

Such a notion seems reasonable considering the known pathology of SAH. A history of loss of consciousness implies that cerebral perfusion pressure (defined as mean arterial pressure minus intracranial pressure) was severely reduced for a period of time. Because the mean arterial pressure remains stable or even increases during the trauma, loss of consciousness must be associated with significant elevation of intracranial pressure. In turn, it is known that an increase in pressure within the subarachnoid space of the optic nerve sheath can obstruct the central retinal vein and axons of the optic nerve, leading to intraocular haemorrhages and swelling with elevation of the optic disc.

There is no consensus as to the role of other factors potentially predisposing SAH survivors to intraocular complications. Entezari et al.,¹³ who examined the problem in question in a setup similar to our study (i.e. screened a whole array of intraocular pathologies and not only Terson syndrome), found a significantly higher occurrence of retinal haemorrhage (and fundus findings) in patients with aneurysm of the anterior

communicating artery (ACoA). No influence of gender, age, and number of aneurysms was confirmed by these authors. Fahmy¹⁴ also reported that the ACoA aneurysms are associated with the appearance of Terson syndrome more often than other aneurysms. In contrast, Fountas et al.⁸ did not find any significant association between gender, the location and size of the aneurysm and the occurrence of Terson syndrome. Also, He et al.⁹ did not reveal significant differences in the localisation of ruptured aneurysm in patients with Terson syndrome.

None of the authors mentioned above studied extensively the role of other factors potentially influencing ophthalmological status of patients with SAH. We revealed that patients with fundus pathologies more frequently had history of arterial hypertension, were older, and more often had sizable aneurysm when compared with those with no intraocular abnormalities. In turn, gender, smoking habit, and history of diabetes were not found in our study to play a role in the development of SAH-related intraocular complications.

Our study has several potential limitations. As to the influence of different factors on the appearance of SAH-related intraocular pathologies, it must be emphasised that we considered the presence of retinal and vitreous haemorrhages and disc swelling taken as a single dependent variable. This decision resulted from the insufficient number of cases with each of these three pathologies. Consequently, we cannot conclude on the relation between the studied risk factors and vitreous haemorrhages, retinal haemorrhages, or optic disc swelling. Specifically, our study cannot contribute significantly to the long-lasting and relatively abundant research and discussion around the incidence and pathogenesis of Terson type vitreous haemorrhage. Among 96 patients with SAH, we identified only 5 with Terson syndrome. This can result from the relatively low prevalence of patients in IV grade in the studied group, as well as from the lack of patients in V grade of H-H scale. Such distribution of H-H scale grades reflects the policy of our neurosurgical department to postpone surgical/intravascular intervention in patients with persistent coma and moribund.

CONCLUSIONS

As many as 42% of patients with aneurysmal SAH had abnormal fundus findings in the acute post-haemorrhagic phase. Isolated disc swelling was documented in 13.5% of this group, retinal haemorrhages with or without disc swelling in 23%, and vitreous haemorrhage (Terson syndrome) in 5%. The risk factors for intraocular consequences included the severity of SAH, loss of consciousness at the stroke,

more sizable aneurysm, older age, and arterial hypertension.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

Note: Figure 1 of this article is available in colour online at www.informahealthcare.com/oph.

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