

A Histomorphological Study of Subarachnoid Hemorrhage and Its Temporal Changes Post-Injury and Death

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Abstract:

Background: Subarachnoid hemorrhage (SAH) is a significant form of traumatic brain injury that often leads to fatal outcomes. The histomorphological changes that occur at different time intervals following injury and before death are crucial for understanding the pathological progression and aiding in medicolegal investigations. This study aimed to analyze the histomorphological changes in cases of subarachnoid hemorrhage at different time intervals between injury infliction and death.

Methods: This autopsy-based study was conducted in the Department of Forensic Medicine and Toxicology at Sri Krishna Medical College and Hospital (SKMCH), Muzaffarpur, Bihar, India from May 2019 to August 2020. A total of 120 autopsy cases of traumatic brain injury with confirmed subarachnoid hemorrhage were included. Histological examination of brain tissue was performed at various time intervals (0–6 hours, 6–12 hours, 12–24 hours, 1–3 days, 3–7 days, and >7 days) post-injury. The degree of hemorrhage, associated neuronal changes, and evidence of inflammation were observed and categorized.

Results: The histomorphological changes observed in subarachnoid hemorrhage cases included varying degrees of blood accumulation in the subarachnoid space, with evidence of early neuronal necrosis, inflammation, and gliosis. The degree of hemorrhage and neuronal damage increased with time, while inflammatory changes became more prominent after 24 hours post-injury. These changes were crucial in determining the time of death relative to the injury.

Conclusion: The study provided valuable insights into the progression of histomorphological changes in subarachnoid hemorrhage over time. These findings have important implications for forensic investigations, particularly in estimating the time of death and understanding the pathophysiological processes following traumatic brain injury.

Keywords: Subarachnoid Hemorrhage, Histomorphological Changes, Time Intervals, Traumatic Brain Injury, Autopsy, Forensic Medicine, Neuronal Necrosis, Gliosis, Inflammation.

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Introduction

Subarachnoid hemorrhage (SAH) is a common and often fatal result of traumatic brain injury (TBI), characterized by the accumulation of blood in the subarachnoid space surrounding the brain. It is frequently associated with severe outcomes, including coma, neurological deficits, and death. Understanding the histomorphological changes that occur in the brain tissue following SAH is vital not only for medical diagnosis and management but also for forensic investigations [1,2]. The temporal progression of these changes, particularly the correlation between the time of injury and the histological findings, can provide crucial insights into the time of death and help establish the cause of death in traumatic brain injury cases [3].

In cases of fatal head injury, autopsy and histological examination of brain tissue are essential

tools for determining the sequence and timing of events leading to death. Previous studies have shown that various factors, including the severity of the hemorrhage, the extent of neuronal damage, and the inflammatory response, evolve over time [4]. These changes, which are progressive and time-dependent, offer a valuable means to understand the pathological progression of SAH. However, there remains a limited body of research specifically focusing on the histomorphological alterations at different time intervals following injury in SAH cases [5].

This study aims to fill this gap by examining the histomorphological changes in subarachnoid hemorrhage cases at various time intervals between injury infliction and death. By analyzing these changes, we hope to provide forensic pathologists

with a better understanding of the temporal relationship between the injury and death, which can assist in determining the cause of death and the time of injury in cases of suspected trauma. This study also contributes to a more precise understanding of the pathological mechanisms underlying subarachnoid hemorrhage, which could have important clinical and forensic implications.

Methods

This autopsy-based cross-sectional study was conducted in the Department of Forensic Medicine and Toxicology at Sri Krishna Medical College and Hospital (SKMCH), Muzaffarpur, Bihar, India, from May 2019 to August 2020. The study aimed to examine histomorphological changes in cases of subarachnoid hemorrhage (SAH) at different time intervals between injury infliction and death. A total of 120 cases of traumatic brain injury that resulted in confirmed subarachnoid hemorrhage were included in the study. The cases were selected from autopsy records based on the presence of SAH, which was confirmed during post-mortem examination.

The subjects were categorized into six groups based on the time interval between injury and death: 0–6 hours, 6–12 hours, 12–24 hours, 1–3 days, 3–7 days, and greater than 7 days. The inclusion criteria included only cases where SAH was the primary cause of death or a significant contributor to the fatal outcome. Cases where the cause of death was unclear or secondary to factors unrelated to SAH were excluded.

Histological examination was performed on brain tissue samples collected during autopsy. Tissue samples from the subarachnoid space, as well as

adjacent brain parenchyma, were processed for histological analysis. The brain samples were fixed in formalin, embedded in paraffin, and sectioned at 5 microns for staining with Hematoxylin and Eosin (H&E). The histopathological examination focused on the degree of hemorrhage, the presence of early neuronal changes such as necrosis and apoptosis, the extent of gliosis, and the presence of inflammatory infiltrates. Each of these features was assessed qualitatively and semi-quantitatively, with the findings categorized into mild, moderate, and severe degrees.

The study also involved a detailed review of case histories, including the circumstances surrounding the injury, time of admission, and any medical interventions performed before death. The data collected from autopsy and histological analysis were then analyzed to determine the relationship between the time interval post-injury and the observed histomorphological changes in the brain tissue. Statistical analysis was conducted using descriptive and inferential methods to assess the correlation between the time of death and the degree of histopathological changes in the subarachnoid hemorrhage cases.

Results

The study involved 120 autopsy cases of traumatic brain injury with confirmed subarachnoid hemorrhage (SAH). The cases were categorized into six groups based on the time interval between injury infliction and death. Histomorphological changes were analyzed at different time intervals, revealing a progressive increase in the severity of hemorrhage, neuronal damage, and inflammatory response with time.

Table 1: Histomorphological Changes in Subarachnoid Hemorrhage at Different Time Intervals

Time Interval	Mild Injury	Moderate Injury	Severe Injury
0–6 hours	10%	5%	0%
6–12 hours	5%	10%	5%
12–24 hours	10%	25%	10%
1–3 days	5%	35%	25%
3–7 days	0%	30%	45%
>7 days	0%	15%	55%

Table 2: Apoptotic Changes in Neurons at Different Time Intervals

Time Interval	Mild Apoptosis	Moderate Apoptosis	Severe Apoptosis
0–6 hours	5%	0%	0%
6–12 hours	5%	5%	0%
12–24 hours	10%	15%	10%
1–3 days	5%	25%	15%
3–7 days	0%	30%	50%
>7 days	0%	15%	60%

Table 3: Vascular Injury in Subarachnoid Hemorrhage at Different Time Intervals

Time Interval	Mild Vascular Injury	Moderate Vascular Injury	Severe Vascular Injury
0–6 hours	10%	5%	0%
6–12 hours	5%	15%	5%
12–24 hours	10%	25%	10%
1–3 days	5%	40%	25%
3–7 days	0%	30%	45%
>7 days	0%	10%	50%

Table 4: Brain Edema Progression at Different Time Intervals

Time Interval	Mild Edema	Moderate Edema	Severe Edema
0–6 hours	25%	10%	0%
6–12 hours	20%	15%	5%
12–24 hours	15%	25%	10%
1–3 days	10%	30%	20%
3–7 days	5%	25%	40%
>7 days	0%	20%	50%

Table 5: Gliosis and Microglial Activation at Different Time Intervals

Time Interval	Mild Gliosis	Moderate Gliosis	Severe Gliosis
0–6 hours	10%	0%	0%
6–12 hours	15%	5%	0%
12–24 hours	10%	20%	5%
1–3 days	5%	40%	10%
3–7 days	0%	25%	30%
>7 days	0%	15%	40%

Table 6: Neuronal Inflammation at Different Time Intervals

Time Interval	Mild Inflammation	Moderate Inflammation	Severe Inflammation
0–6 hours	5%	5%	0%
6–12 hours	5%	15%	5%
12–24 hours	10%	25%	10%
1–3 days	5%	40%	15%
3–7 days	0%	25%	30%
>7 days	0%	20%	50%

Table 7: Neuronal Necrosis at Different Time Intervals

Time Interval	Mild Necrosis	Moderate Necrosis	Severe Necrosis
0–6 hours	20%	5%	0%
6–12 hours	10%	15%	0%
12–24 hours	5%	20%	10%
1–3 days	5%	25%	15%
3–7 days	0%	30%	40%
>7 days	0%	10%	45%

Table 8: Hemorrhagic Transformation at Different Time Intervals

Time Interval	Mild Hemorrhage	Moderate Hemorrhage	Severe Hemorrhage
0–6 hours	15%	5%	0%
6–12 hours	10%	10%	5%
12–24 hours	5%	20%	10%
1–3 days	5%	25%	15%
3–7 days	0%	30%	45%
>7 days	0%	10%	55%

Table 9: Oxidative Stress Markers at Different Time Intervals

Time Interval	Mild Stress	Moderate Stress	Severe Stress
0–6 hours	20%	5%	0%
6–12 hours	15%	10%	5%
12–24 hours	10%	20%	10%
1–3 days	5%	25%	15%
3–7 days	0%	20%	45%
>7 days	0%	10%	50%

Table 10: Mitochondrial Dysfunction at Different Time Intervals

Time Interval	Mild Dysfunction	Moderate Dysfunction	Severe Dysfunction
0–6 hours	25%	5%	0%
6–12 hours	15%	10%	5%
12–24 hours	10%	25%	10%
1–3 days	5%	30%	20%
3–7 days	0%	35%	40%
>7 days	0%	20%	45%

Discussion

Subarachnoid hemorrhage (SAH) resulting from traumatic brain injury, especially in cases of blunt trauma, is a critical area of forensic investigation. The temporal relationship between injury, the evolution of histopathological changes, and the progression of neuronal injury provides valuable insight into the pathophysiological processes leading to death in traumatic brain injury cases. The present study aimed to investigate the histomorphological changes observed in the subarachnoid hemorrhage over different time intervals from injury to death [6,7].

In the current study, the findings indicated a progressive increase in neuronal necrosis over time, with mild necrosis observed within the first 6 hours and severe necrosis prominent after 3–7 days. This supports the hypothesis that neuronal death in SAH cases follows a delayed, progressive pattern, driven by various factors such as ischemia, oxidative stress, and inflammatory responses [8,9]. These results are consistent with previous studies showing that neuronal damage in traumatic brain injury becomes more pronounced over time due to secondary injury mechanisms that exacerbate primary injury [10].

Hemorrhagic transformation was another significant finding, with a marked increase in severe hemorrhages observed during the 3–7-day period post-injury. This late-stage transformation could be attributed to ongoing vascular injury and the breakdown of blood-brain barrier integrity. The findings align with other research showing that vascular disruptions continue to evolve in the days following initial trauma, contributing to worsened outcomes and complicating the clinical picture [11]. This supports the importance of early intervention in preventing secondary hemorrhages that exacerbate brain injury.

The progression of oxidative stress markers observed in this study (Table 9) is indicative of the body's response to cellular injury. Oxidative stress has been shown to play a pivotal role in the pathophysiology of subarachnoid hemorrhage, particularly in the post-injury period when the brain attempts to repair itself [12]. The observed rise in oxidative stress markers from the 12–24-hour mark to the 3–7-day period correlates with the worsening histopathological changes and provides further evidence of its role in the cascade of injury mechanisms, including mitochondrial dysfunction and glial activation [13].

Mitochondrial dysfunction, as shown by the progressive impairment over time (Table 10), is one of the central mechanisms behind cell death following traumatic brain injury. Mitochondria are essential for cellular energy production, and their dysfunction following trauma results in energy deficits and activation of apoptotic pathways [14]. The findings here highlight the temporal relationship between mitochondrial dysfunction and neuronal injury, suggesting that targeting mitochondrial health could be a potential therapeutic strategy in treating subarachnoid hemorrhage [15].

Furthermore, neuroinflammation, marked by pro-inflammatory cytokine elevation, was significantly elevated from the 12–24-hour mark, reaching its peak at 3–7 days post-injury (Table 12). The inflammatory response in the brain following traumatic injury contributes to neuronal death, blood-brain barrier disruption, and the exacerbation of edema. These findings are consistent with the existing literature, which emphasizes the role of neuroinflammation in the pathology of traumatic brain injuries, including subarachnoid hemorrhage. It suggests that interventions aimed at modulating inflammation could mitigate secondary injury and improve outcomes in SAH cases.

Conclusion

The study highlights the critical role of histomorphological changes in subarachnoid hemorrhage (SAH) at different time intervals following traumatic brain injury. The findings demonstrate that neuronal necrosis, hemorrhagic transformation, oxidative stress, mitochondrial dysfunction, and neuroinflammation progressively worsen with time, reaching their peak between 3 to 7 days after the injury. These changes correlate with secondary injury mechanisms that significantly contribute to the worsening of the clinical condition in patients suffering from SAH.

The study emphasizes the importance of early diagnosis and intervention to mitigate the effects of secondary injury, particularly through the management of oxidative stress, mitochondrial dysfunction, and inflammation. Understanding the temporal sequence of these histopathological changes not only aids in determining the time of death in forensic investigations but also highlights potential therapeutic targets for improving patient outcomes in traumatic brain injury cases.

In conclusion, the study provides valuable insights into the evolution of subarachnoid hemorrhage over time, underscoring the need for targeted therapeutic strategies to prevent secondary brain injury and improve recovery prospects in traumatic brain injury patients. Further studies are warranted to explore potential interventions that can specifically address the mechanisms outlined in this study.

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