



Original Article

Histopathological spectrum of outer and inner membranes in chronic subdural hematoma- A retrospective cross-sectional study from a tertiary care centre

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ABSTRACT

Background: Chronic subdural hematoma is a common neurosurgical condition, particularly in the elderly, characterized by the gradual accumulation of blood in the subdural space. Its pathogenesis involves recurrent microbleeding, inflammation, and neovascularization within encapsulating membranes. Histopathological evaluation of both the outer and inner membranes helps determine disease chronicity, activity, and potential for recurrence.

This study was done to analyze the histopathological spectrum of the outer and inner membranes in chronic subdural hematoma and classify them based on inflammatory activity, fibrosis, vascular proliferation, and hemorrhagic changes.

Materials and Methods: A retrospective observational study was conducted over one year in the Department of Pathology, Siddaganga Medical College and Research Institute. Outer and inner membrane samples obtained during burr-hole evacuation were examined histologically and classified into four types: Type I (non-inflammatory), Type II (inflammatory), Type III (hemorrhagic inflammatory), and Type IV (scar inflammatory). Data were analyzed using descriptive statistics, with categorical variables reported as frequencies and percentages.

Results: Among the 36 chronic subdural hemorrhage cases, the outer membrane most frequently exhibited an inflammatory pattern (Type II) in 48.4% of cases. The inner membrane predominantly showed hemorrhagic inflammatory (Type III) in 35.5%. Overall, most membranes displayed active inflammation and vascular proliferation, indicating ongoing membrane activity and potential risk for recurrence. Statistical analysis confirmed a significant difference in the distribution of membrane types between outer and inner membranes ($p < 0.05$).

Conclusions: This study shows that inflammatory and hemorrhagic inflammatory patterns are the predominant histopathological findings in both the outer and inner membranes of chronic subdural hematoma. Type II membranes were most frequently observed in the outer membrane, while Type III membranes predominated in the inner membrane.

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INTRODUCTION

Chronic subdural hematoma (CSDH) is one of the most frequently encountered neurosurgical conditions, particularly in elderly patients, characterized by the gradual accumulation of blood in the subdural space over weeks to months. It commonly arises following minor head trauma, leading to rupture of bridging veins and slow bleeding into the subdural space.¹ Due to its insidious onset, patients often present with non-specific symptoms such as headache, cognitive impairment, altered mental status, gait disturbances, and focal neurological deficits, making

early diagnosis and management crucial.² A key factor in the pathophysiology of CSDH is the formation of an outer membrane, which plays a significant role in hematoma persistence, expansion, and recurrence. Histopathological studies of outer and inner membranes have revealed essential cellular and vascular changes, including fibroblast proliferation, neovascularization, hemosiderin-laden macrophages, and chronic inflammatory infiltration.^{3,5} Fragile neocapillaries within the outer membrane are prone to microbleeding, contributing to cyclical hematoma growth,¹ while inflammatory mediators released by immune cells further promote angiogenesis and membrane thickening.²

Despite surgical evacuation being the standard treatment, recurrence rates of CSDH remain high, ranging from 10% to 30%, often necessitating repeat interventions.¹ Although several studies have examined radiological and clinical aspects, detailed histopathological characterization of both outer and inner membranes—particularly their inflammatory, vascular, and fibrotic changes—remains limited. Furthermore, data from tertiary care centers in the region are sparse, making it difficult to establish correlations between histopathological features and clinical outcomes, including recurrence risk.

A systematic analysis of the outer and inner membranes of CSDH can provide critical insights into the mechanisms driving hematoma persistence and recurrence. Understanding the spectrum of inflammation, fibrosis, and neovascularization may help identify patients at higher risk of recurrence and guide potential adjuvant therapies, such as pharmacological anti-inflammatory interventions or middle meningeal artery embolization, alongside surgical management.⁶

This study aims to fill the existing knowledge gap by evaluating the histopathological patterns of both membranes in surgically treated CSDH cases at a tertiary care center, thereby contributing to improved understanding, management strategies, and patient outcomes.

MATERIALS AND METHODS

This was a cross-sectional study conducted over a period of one year in the Department of Pathology, Siddaganga Medical College and Research Institute, a tertiary care level.

All patients diagnosed with CSDH and admitted under the Department of Neurosurgery during the study period, irrespective of age and sex, were included in the study. Patients with acute subdural hematoma and those with chronic subdural hematoma who were managed conservatively without surgical intervention were excluded from the analysis.

A retrospective sampling technique was adopted. Medical records and histopathology reports of patients who underwent burr-hole evacuation for CSDH were retrieved and reviewed. Only cases with complete clinical, radiological, operative, and histopathological data were included.

Relevant data, including demographic details, clinical presentation, radiological findings, and operative notes, were collected from hospital archives. During surgery, both outer and inner membrane samples of the subdural hematoma cavity were obtained and sent for histopathological evaluation. The specimens were fixed in 10% buffered formalin, routinely processed, and stained with hematoxylin and eosin. Microscopic features were examined and classified according to membrane type, and findings were correlated with available clinical data.

Histopathological findings of both outer and inner membranes of chronic subdural hematomas were classified into four types based on the degree of maturity and intensity of the inflammatory response, vascular proliferation, and hemorrhagic changes.

Type I (Non-inflammatory membrane):

These membranes showed immature fibroblasts and collagen fibers with very sparse inflammatory cell infiltration and minimal neovascularization, indicating an early stage of membrane formation.

Type II (Inflammatory membrane):

Characterized by a single layer of immature connective tissue, this type exhibited marked inflammatory cell infiltration and dense vascularization throughout the membrane, suggestive of an active inflammatory process.

Type III (Hemorrhagic inflammatory membrane):

These membranes showed a multilayered structure with two to three layers. The dural side demonstrated capillaries with large lumina, while the hematoma side revealed numerous thin-walled neovessels and dense inflammatory cell infiltration. Intervening fibrocollagenous layers were often present. Frequent areas of hemorrhage within the membrane were observed, reflecting ongoing bleeding and organization.

Type IV (Scar inflammatory membrane):

This type displayed features of chronic inflammation with mature fibrocollagenous tissue, neovascularization, and areas of old and recent hemorrhage, indicative of a healing or organizing stage.

Data were entered and analyzed using SPSS version 26.0. Categorical variables were expressed as frequencies and percentages. Continuous variables such as age were presented as mean $\pm$ standard deviation. The Chi-square test was used to assess associations between categorical variables. A p-value <0.05 was considered statistically significant.

Missing data were handled by excluding cases with incomplete clinical or histopathological information from the final analysis to maintain data integrity. Subgroup analyses were planned to evaluate correlations of histopathological patterns with recurrence, age groups ($<60/ \geq 60$ years), and hematoma laterality (unilateral/bilateral).

Institutional Ethical Committee approval was obtained before commencement of the study. Confidentiality of patient identity and data was maintained throughout the study.

RESULTS

This retrospective study included a total of 36 patients diagnosed with CSDH who underwent burr hole evacuation during the study period. The age of presentation ranged from 36 to 87 years, with a median age of approximately 66 years. There was a male predominance with 25 males (69.4%) and 11 females (30.6%). (Table 1)

Table 1: Distribution of patients with CSDH according to age

Age group (years)	Number of patients (n = 36)	Percentage (%)
30-39	1	2.8
40-49	3	8.3
50-59	6	16.7
60-69	10	27.8
70-79	9	25.0
80-89	7	19.4
Total	36	100

In the present study, headache was the most common presenting symptom, observed in about 63.9% of patients. Altered sensorium was noted in 30.6%, followed by vomiting in 25% and vertigo or giddiness in 8.3% of cases. Less frequent complaints included blurring of vision (2.8%), urinary or fecal incontinence (11.1%), and hemiparesis (27.8%). Paraparesis and quadriparesis were seen in 2.8% of patients each. Papilledema was present in 5.6%, third and sixth cranial nerve palsy, and seventh nerve palsy in 2.8% of patients.

In the present study, detailed histopathological evaluation of the outer and inner membranes of CSDH revealed distinct patterns of organization and inflammation. The outer membrane most frequently demonstrated the inflammatory Type II pattern, which was observed in 48.4% of cases. The hemorrhagic inflammatory type (Type III) was the second most common, seen in 29% of cases, and showed foci of recent and old hemorrhage admixed with inflammatory infiltrates. The non-inflammatory type (Type I) accounted for 12.9%, showing thin fibroblastic layers with minimal inflammation, while the scar inflammatory type (Type IV) was the least frequent, observed in 9.7% of cases, characterized by dense hyalinized collagen with minimal vascularity and few inflammatory cells.

In contrast, the inner membrane predominantly exhibited the hemorrhagic inflammatory type (Type III) pattern in 35.5% of cases, suggesting its active role in recurrent bleeding and hematoma persistence. This was followed by the inflammatory type (Type II) in 32.3% and the

non-inflammatory type (Type I) in 25.8% of cases. The scar inflammatory type (Type IV) was the least common, observed in 6.4%, representing a relatively late, fibrotic phase of membrane maturation. These findings suggest that while the outer membrane is largely inflammatory and vascular in nature, the inner membrane often reflects hemorrhagic and reactive changes contributing to the chronicity of the lesion. (Table 2)

Table 2: Histopathological Types of Outer and Inner Membranes in CSDH

Histopathological Type	Outer Membrane n (%)	Inner Membrane n (%)
Type I – Non-inflammatory	5(12.9)	9(25.8)
Type II – Inflammatory	17(48.4)	12(32.3)
Type III – Hemorrhagic inflammatory	10(29)	13(35.5)
Type IV – Scar inflammatory	4(9.7)	2(6.4)
Total	36	36

Histopathological evaluation of both the outer and inner membranes in CSDH provides valuable insight into the disease process, its stage of evolution, and potential prognosis. The outer membrane generally reflects the site of active inflammation and neovascular proliferation.

Overall, the combined assessment of both membranes helps in understanding the chronicity, activity, and biological behavior of the hematoma, and provides useful information for clinicopathological correlation and prognosis. (fig.1-4)

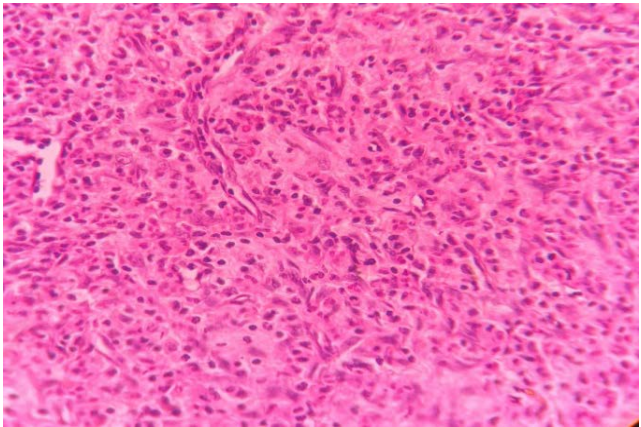


Figure 1: Photomicrograph showing Type I non-inflammatory membrane (HE stain, x400)

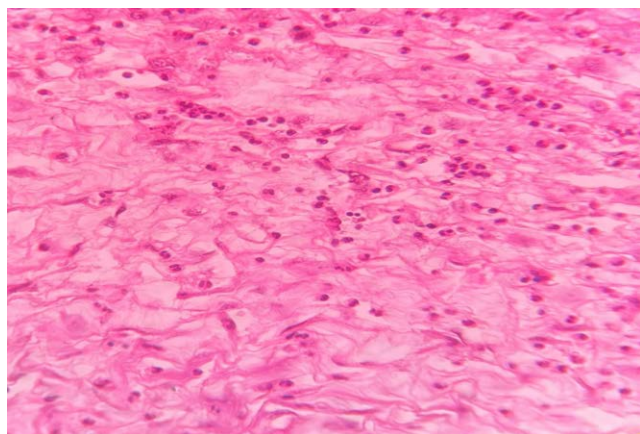


Figure 2: Photomicrograph showing Type II inflammatory membrane (HE stain, x400)

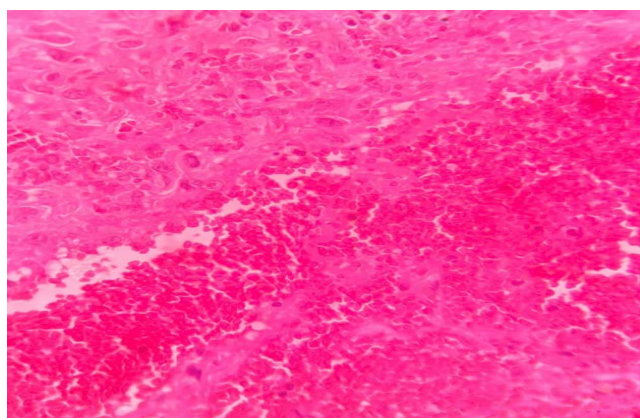


Figure 3: Photomicrograph showing Type III hemorrhagic inflammatory membrane (HE stain, x400)

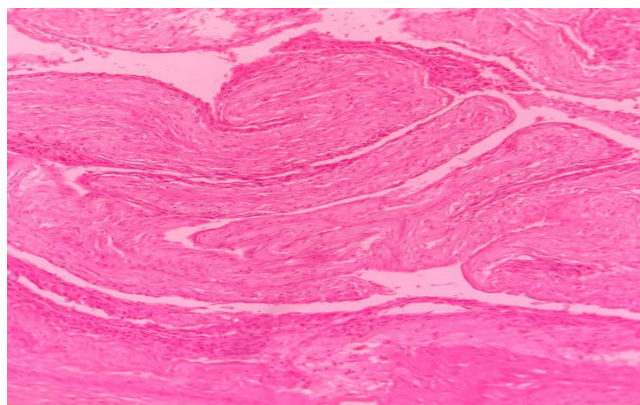


Figure 4: Photomicrograph showing Type IV scar inflammatory membrane (HE stain, x400). Statistical analysis demonstrated that the distribution of outer and inner membrane types was not uniform. Associations between membrane types and clinical parameters—including age groups, hematoma laterality and recurrence with p -values <0.05 indicating statistical significance.

DISCUSSION

CSDH is a frequently encountered neurosurgical condition, especially among the elderly, characterized by recurrent or persistent bleeding into the subdural space. The evolution of CSDH reflects a dynamic interplay between hemorrhage, inflammation, fibrinolysis, and neovascularization within the

encapsulating membranes. Histopathological examination of the outer and inner membranes offers valuable insight into disease activity, chronicity, and potential for recurrence.¹⁻³

In the present study, histopathological evaluation of both outer and inner membranes revealed a predominance of Type II (inflammatory) and Type III (hemorrhagic inflammatory) patterns.

The Type I (non-inflammatory) membranes correspond to the earliest stage of organization, comprising immature fibroblasts and scant vascular proliferation.³⁻⁷ In contrast, Type II (inflammatory) membranes show dense fibrocollagenous tissue with neovascularization and inflammatory cell infiltration—hallmarks of active exudation and ongoing hematoma expansion.^{1,7,8} Type III (hemorrhagic inflammatory) membranes display mixed features with fresh and old hemorrhage, thin-walled neovessels, and hemosiderin-laden macrophages, suggestive of repeated microbleeding from fragile capillaries.^{9,14} Type IV (scar inflammatory) membranes represent late or resolving stages with hyalinization and minimal inflammation.^{3,24} These patterns are consistent with the classification proposed by Bokka and Trivedi et al.³ and with the morphological observations of Nagahori et al.⁷ and Park et al.^{4,24} who demonstrated that inflammatory and hemorrhagic membranes dominate in most cases, while purely fibrotic membranes are less frequent. The predominance of these active forms emphasizes that CSDH is a self-perpetuating lesion rather than a static collection, maintained by recurrent microhemorrhages and local inflammatory processes.^{12,14}

The outer membrane plays a crucial role in the persistence and progression of CSDH. It originates from the dural border cell layer and demonstrates intense vascular proliferation driven by cytokines and angiogenic mediators such as VEGF, IL-6, and TNF- α .^{10,28} Newly formed capillaries in this membrane are structurally immature and leaky, predisposing to repeated hemorrhages and hematoma enlargement.^{9,25} Choi et al.^{10,26} recently highlighted the importance of neovascularization originating from the dural side, whereas Ryu et al.⁹ and Kim et al.²⁵ demonstrated that outer membrane vascular density strongly correlates with the risk of recurrence after burr-hole evacuation. In contrast, the inner membrane, which forms at the interface between the hematoma and the arachnoid, is relatively less vascular and less inflammatory.^{1,7} It is thought to serve as a boundary limiting further exudation into the subdural cavity. However, persistent inflammation or rebleeding can transform an initially thin fibroblastic layer into an inflamed, hemorrhagic, or even fibrotic form, reflecting various stages of disease activity.^{8,23}

Several studies have demonstrated an association between membrane histology and CT findings. Park et al.²⁴ and Gandhoke et al.¹ noted that hyperdense or mixed-density hematomas correspond to inflammatory and hemorrhagic membrane types, whereas hypodense hematomas are often associated with fibrotic, less vascular membranes. Similarly, Potdar et al.² and Nomura et al.²³ observed that highly

vascularized outer membranes correlated with greater recurrence and need for repeat intervention. In our cohort, patients with hemorrhagic and inflammatory membranes often exhibited thicker hematomas and heterogeneous CT densities, supporting this clinico-radiological concordance.

Understanding membrane histopathology has therapeutic relevance. Anti-inflammatory agents and angiogenesis inhibitors have been explored to stabilize the outer membrane and reduce recurrence.^{11,14,22} Middle meningeal artery embolization (MMAE) has emerged as a promising adjunct treatment targeting the vascular supply to the outer membrane, thereby reducing neovascular permeability and microbleeding.^{15,26} Our findings—demonstrating active inflammation and hemorrhage in most membranes—further support the rationale for such targeted vascular interventions.

While non-inflammatory (Type I) and scar inflammatory (Type IV) membranes represent early and late stages respectively, the dominance of Types II and III in both outer and inner membranes in our study mirrors previous reports.^{3,8,25} Ryu et al.⁹ reported 70% of cases showing inflammatory or hemorrhagic patterns, similar to our combined 77.4%.

This consistency across studies reinforces the concept of CSDH as a chronic, angiogenesis- driven inflammatory process rather than a passive clot.

The study was retrospective, single-centered and lack of long-term follow-up data on recurrence which may limit external validity. The relatively small sample size constrains generalizability to broader populations. Potential confounders, including use of anticoagulant or antiplatelet therapy, comorbidities, and variable chronicity of hematomas, were not controlled for, which could influence membrane histopathology and clinical outcomes.

Nonetheless, the inclusion of both outer and inner membranes in histopathological evaluation provides a more comprehensive understanding of disease evolution than most previous studies that examined only the outer membrane.

CONCLUSIONS

The present study demonstrates that inflammatory and hemorrhagic inflammatory patterns constitute the predominant histopathological findings in both the outer and inner membranes of chronic subdural hematoma. Type II membranes were most commonly observed in the outer membrane, whereas Type III membranes predominated in the inner membrane. These findings outline the histopathological spectrum of membrane changes in chronic subdural hematoma and fulfill the objective of characterizing membrane pathology in the study population.

Conflict of interest: None.

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