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Original Article

Pathology Section

Histopathological Spectrum of Brain Autopsies: A Cross-sectional Study

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ABSTRACT

Introduction: Brain autopsy unveils diverse manifestations that enthrall the pathologists. These are often undiagnosed, sometimes misdiagnosed or may show progression during a person's lifetime. Due to paucity of literature on pathological spectrum of Central Nervous System (CNS) lesions on autopsy present study was conducted to broaden the horizon in this aspect.

Aim: To identify and document the histopathological findings incidentally detected in brain autopsies.

Materials and Methods: A retrospective cross-sectional study of medicolegal autopsies was performed in the conducted at the Department of Pathology, SCB Medical College and Hospital, Cuttack, Odisha, India for a period of one year from January 2024 to December 2024. A total of 103 CNS autopsy cases were documented. The histopathological findings in each case were noted. Age, gender, incidence, nature of lesions and histopathological findings were recorded in each case. Descriptive statistics was used for quantitative data described as frequency and percentage.

Results: This study consisted of a total of 103 cases. Among them, 81 cases (78.64%) of the lesions were non neoplastic while 22 cases (21.36%) were neoplastic. A total of 15 cases (14.56%) did not show any remarkable CNS pathology. Infection was the most common aetiology comprising of 35 cases (33.9%) followed by primary brain neoplasms 15 cases (14.56%). Traumatic causes 14 cases (13.6), degenerative causes including neurodegenerative diseases 12 cases (11.6%), secondaries in brain 7 cases (6.8%) and the vascular causes 5 cases (4.85%) summed up the spectrum of histopathological spectrum of CNS autopsies.

Conclusion: The incidental and interesting observations are essential for research and epidemiological studies. They have also diagnostic significance as they help to determine the natural evolution of diseases, treatment outcome and prognosis.

Keywords: Brain autopsy, Central nervous system, Medicolegal cases, Neoplasms

INTRODUCTION

"Autopsy" is derived from the Greek word autopsia, which means to "see for oneself" [1]. Medicolegal autopsies are performed to determine cause, time of death and identify the diseases which may or may not have contributed to death. Histopathological analysis is the gold standard in assessing the cause in cases of sudden death or when there is no previous history [2]. These findings not only help in studying naturally occurring lesions or treated cases but also call attention to uncommon, undiagnosed or misdiagnosed lesions which may have gone unnoticed antemortem. Moreover, they also aid in understanding the natural evolution of untreated diseases [3]. Incidental findings identified in histopathology are of great academic interest for both pathologists and the forensic experts. Besides, histopathology is an important tool for assessment of mortality statistics which are crucial for public health service planning [4]. Medicolegal autopsies of the brain, though routinely done, have not been widely documented according to review of literature. The pathologist encounters cases where the cause or a major contribution to the cause of death is due to damage to or disease of the Central Nervous System (CNS) [5]. There are various causes of death in CNS autopsy which could be due to traumatic, degenerative, infective or neoplastic causes. Histopathology aids in establishing concordance or discordance between antemortem and postmortem cause of deaths. The present study highlights the gamut of histopathological analyses and inferences in medicolegal brain autopsies in the study Institution.

Hence, the objectives of study were to study histopathological findings in CNS autopsy cases and to identify interesting incidental findings in the CNS autopsy cases.

MATERIALS AND METHODS

A retrospective cross-sectional study of medicolegal autopsies was performed in the conducted at the Department of Pathology, SCB Medical College and Hospital, Cuttack, Odisha, India for a period of one year from January 2024 to December 2024. The study was conducted after obtaining approval from the Institutional Ethics Committee (IEC No: 1735/24.07.2024). As this was a retrospective autopsy-based study, waiver of informed consent was granted.

Inclusion and Exclusion criteria: A total of 103 CNS autopsy cases were included in the study. Cases other than CNS autopsy, autolysed tissue and samples with incomplete requisition form were excluded.

Study Procedure

Whole brain specimens were received in 10% neutral buffered formalin. After adequate fixation, systematic gross examination was performed and representative sections were sampled. All sections were stained with Haematoxylin and Eosin (H&E). Special stains, including Periodic Acid–Schiff (PAS), Ziehl–Neelsen (ZN), and Giemsa, were employed wherever indicated. The histopathologic findings in each case were studied and the data was meticulously recorded. The following variables were recorded: age, gender, type and distribution of lesions, histopathological diagnosis, and nature of lesions (neoplastic or non neoplastic). Lesions were categorised into infective, traumatic, vascular, degenerative, neoplastic, and normal groups.

STATISTICAL ANALYSIS

Data were analysed using descriptive statistics. Categorical variables were expressed as frequency (n) and percentage (%). All percentages were calculated using the total sample size (N=103) as the denominator.

RESULTS

The present study included 103 CNS cases of the medicolegal autopsies conducted from January 2024 to December 2024. The histopathological findings displayed a wide spectrum of lesions [Table/Fig-1]. No abnormality was detected in 15 cases (14.56%). Bacterial abscess was the commonest CNS lesion on autopsy comprising of 12 cases (11.65%).

Lesions	Cases n (%)
Bacterial abscess	12 (11.65)
Neurodegenerative disease	7 (6.8)
Encephalomalacia	5 (4.85)
Diffuse axonal injury	8 (7.77)
Subdural Haemorrhage	6 (5.82)
Tuberculosis	7 (6.8)
Rabies	7 (6.8)
Fungal abscess	2 (1.94)
Cerebral malaria	7 (6.8)
Cavernous angioma	5 (4.85)
High grade glioma	5 (4.85)
CNS lymphoma	2 (1.94)
Meningioma	5 (4.85)
Schwannoma	2 (1.94)
Pituitary adenoma	1 (0.97)
Metastasis	7 (6.8)
Normal (NAD)	15 (14.56)
Total	103 (100.0)

[Table/Fig-1]: Spectrum of lesions in CNS autopsy.
NAD: No abnormality detected

The cerebrum was involved in 78 cases and 20 cases involved the cerebellum while in five cases both were involved. Most common age group affected was 61-80 years comprising of 62 cases (60.19%). [Table/Fig-2]. There was a male predominance with 63 cases (61.20%) with male: female ratio being 1.59:1 [Table/Fig-3]. Non neoplastic lesions were more common, accounting for 81 cases (78.64%) shown in [Table/Fig-4].

Age group (in years)	n (%)
0-20	06 (5.82)
21-40	08 (7.77)
41-60	24 (23.3)
61-80	62 (60.19)
>80	03 (2.91)
Total	103 (100)

[Table/Fig-2]: Age distribution of cases.

Gender	n (%)
Male	63 (61.20)
Female	40 (38.80)

[Table/Fig-3]: Gender distribution of cases.

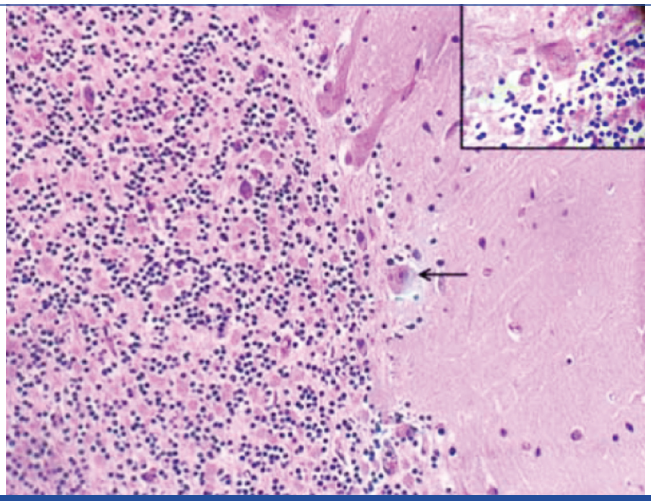
Category	n (%)
Non neoplastic lesions	81 (78.64)
Neoplastic lesions	22 (21.36)
Total	103 (100.0)

[Table/Fig-4]: Broad categorisation of CNS lesions.

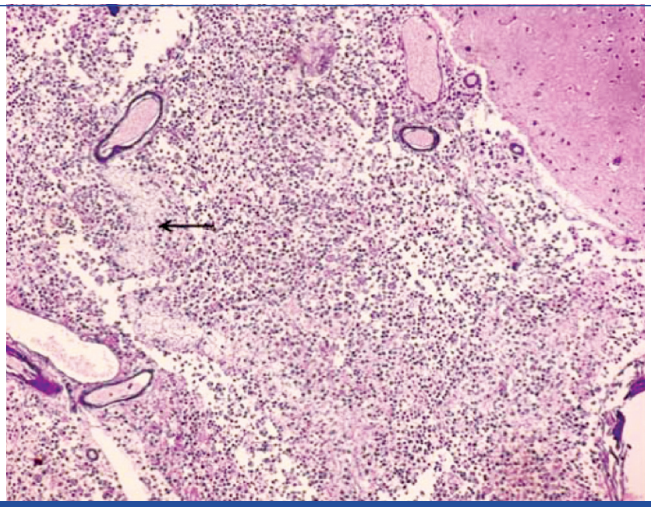
The pattern of lesions is summarised in [Table/Fig-5]. Among the non neoplastic causes, infections were most common 35 (34%), with bacterial abscess being the predominant cause 12 (11.6%). Interestingly, there were seven cases each of viral encephalitis due to rabies, TB and cerebral malaria. In rabies encephalitis, there were sharply delineated, round or oval eosinophilic intracytoplasmic inclusions called Negri bodies [Table/Fig-6]. Cerebral malaria is a parasitic infection and Mycobacterium tuberculosis identified histopathologically by presence caseating granulomas. Brain abscesses with fungal hyphal forms along with foamy macrophages and acute and chronic inflammatory cells [Table/Fig-7], constituted only two cases. Cerebral malaria on histopathology exhibited presence of haemozoin pigment in macrophages and red cells which occluded the dilated sinusoids. One of the cases of cerebral malaria apparently had sickle cell disease demonstrating sickled red cells in blood vessels.

Pattern of lesions	n (%)
Infective	35 (33.9)
Neoplastic	22 (21.4)
No abnormality detected	15 (14.6)
Degenerative	12 (11.6)
Traumatic	14 (13.6)
Vascular	05 (4.8)
Total	103 (100)

[Table/Fig-5]: Pattern of lesions.



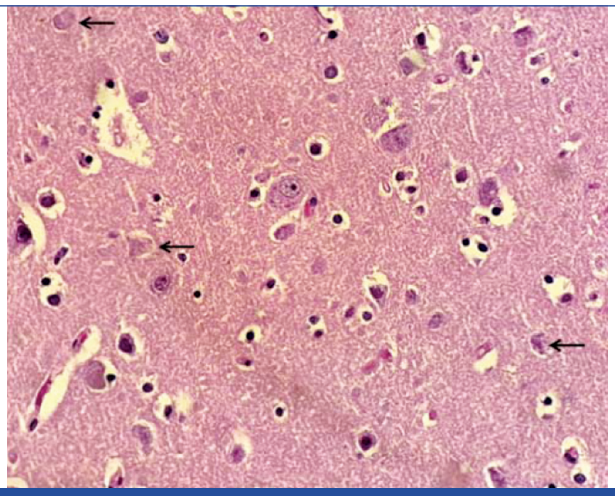
[Table/Fig-6]: Rabies revealing Negri bodies in cerebellar Purkinje cells (H&E, 100x); inset- cell at arrow.



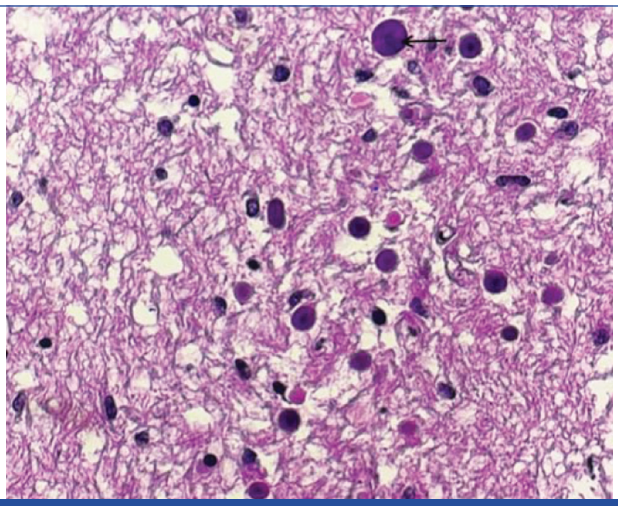
[Table/Fig-7]: Fungal abscess with hyphal forms (arrow) and inflammatory cells in brain parenchyma (H&E, 100x).

A total of 14 patients (13.6%) harboured traumatic injury to the brain which made up the second highest category in non neoplastic causes. Of these, eight cases showed diffuse axonal injury displaying multiple axonal spheroids [Table/Fig-8] while six patients presented with subdural haemorrhage. Axonal spheroids are singular swellings known as axonal bulb formed on completely disconnected axons. Degenerative changes represented the third highest group 12

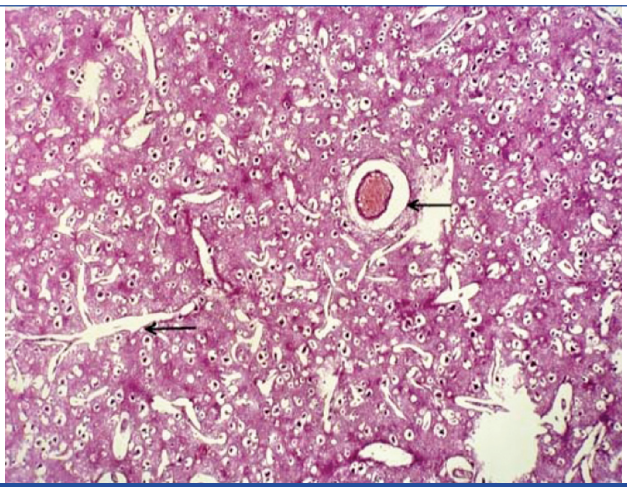
(11.6%). There were seven intriguing cases of neurodegenerative diseases, five being Parkinson's disease, which show cased abnormal spherical cytoplasmic Lewy bodies with few neuronal cells with melanin pigmentation [Table/Fig-9]. Lewy bodies are intracytoplasmic inclusions with a granular and fibrillar core and a surrounding halo. Two patients of Alzheimer's disease revealed extracellular diffuse amyloid plaques and intracellular neurofibrillary tangles within the neuronal cytoplasm in histopathology. Five other cases could have been due to either traumatic, infective, hypoxic, toxic or metabolic causes leading to encephalomalacia [Table/Fig-10].



[Table/Fig-8]: Diffuse axonal injury displaying multiple axonal spheroids (H&E, 200x).



[Table/Fig-9]: Intraneuronal inclusions called Lewy bodies illustrated in Parkinsonism (H&E, 200x).

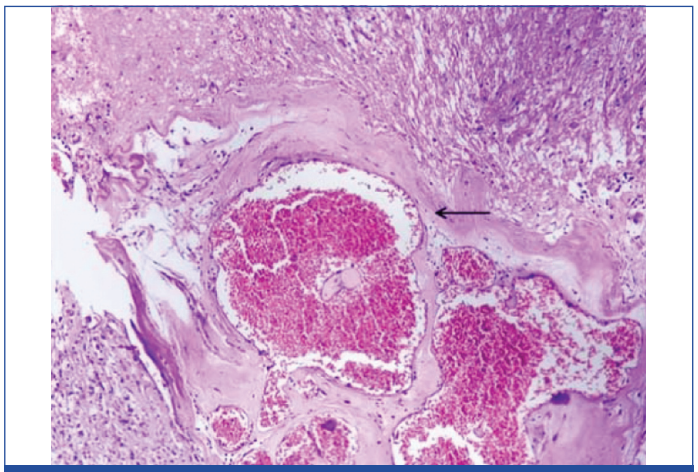


[Table/Fig-10]: Encephalomalacia with liquefactive necrosis of brain, dilated sinusoids and congested blood vessels (H&E, 100x).

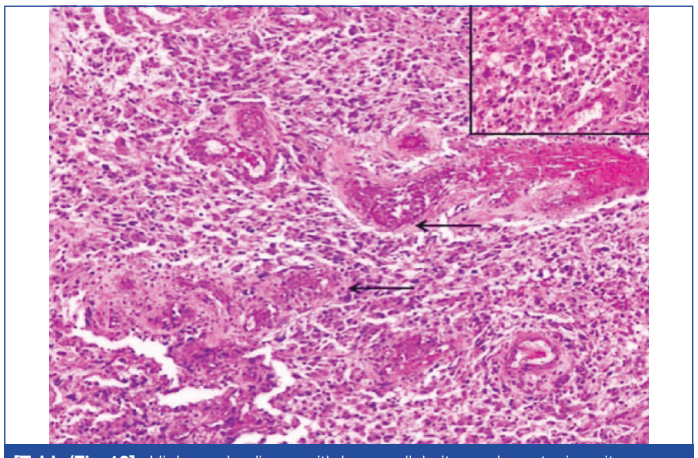
Neoplasms comprised of 22 cases with 15 cases (14.56%) being primary neoplasms of the central nervous system and seven cases (6.79%) being metastatic tumours [Table/Fig-11]. There were five cases (4.8%) of cavernous angioma which is a vascular malformation with presence of dilated thin walled vascular channels with a single endothelial lining, separated by fibrous septa. Some of them demonstrated hyalinised vessels [Table/Fig-12]. One of the cases typically had thrombosed vessels along with atheromatous plaque formation. Five patients had high-grade glioma [Table/Fig-13] and two had primary CNS lymphoma. Rest of the primary neoplasms included five cases of meningioma, and two of schwannoma. A case with metastatic mucinous adenocarcinomatous deposits in brain illustrated mucinous pools with tumour cells in glandular pattern, small clusters, discretely [Table/Fig-14] and had a circumferential ulceroproliferative growth in the colon. Neither relevant history regarding a primary neoplasm nor the consent for Immunohistochemistry (IHC) for the secondaries in brain could be obtained in this as this was a medicolegal case.

Type of neoplasm	n (%)
Primary CNS tumour	15 (14.56)
Secondary (metastatic) tumour	7 (6.79)
Total	22 (21.35)

[Table/Fig-11]: Types of neoplasms.



[Table/Fig-12]: Cavernous angioma in brain demonstrating large dilated blood vessels (arrow) separated by fibrous septae (H&E, 100x).

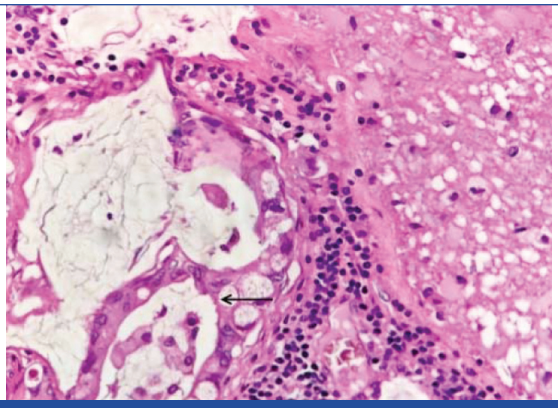


[Table/Fig-13]: High-grade glioma with hypercellularity, nuclear atypia, mitoses and microvascular proliferation (arrows) (H&E, 100x) (inset: nuclear atypia).

DISCUSSION

The present study systematically entails all the findings in our histopathology department in one year. It shows a gamut of lesions, although authors could not rule out a cause of death due to CNS involvement in the cases showing unremarkable histology. Causes like sudden unexplained death in epilepsy may not show any pathological findings as noted in study by Zhang X et al., [6].

The cerebrum was most commonly involved. Since not many studies have compiled brain autopsy cases exclusively, according



[Table/Fig-14]: Metastatic mucinous adenocarcinomatous deposits in brain parenchyma with extracellular mucin pools and tumour cells in glandular pattern (arrow) (H&E, 200x).

to literature reviewed, comparison study is challenging. These study findings were similar to another autopsy study by Hugar BS et al., on sudden neurological deaths where most of the cases belonged to the ≥60 years age group [7]. The number of cases increased with age and had a male preponderance. It is consistent with increased chances of subarachnoid haemorrhage or stroke in the elderly caused by any of the CNS lesions. The three cases above 80 years presented with neurodegenerative diseases. A study by Kovac GG et al., reported that even non-Alzheimer neurodegenerative pathologies were more frequent in the elderly [8].

A detailed study by Kok EH et al., revealed that though common above 80 years, Lewy body accumulation starts in middle age and may not present with known neurological symptoms [9]. The importance of knowing the age at which such pathologies develop necessitates the effectiveness of treatments.

Non neoplastic diseases contributed to 64% of the cases in concordance with Hugar BS et al., where tumours comprised only 6.9% of cases [7]. In a study by MacRae CB et al., which examined the diagnostic yield of postmortem brain autopsy following premortem biopsy, the concordance between both was the least in non neoplastic diseases [10]. This suggested that postmortem biopsies demonstrate specific diagnostic histological features like microorganisms, accumulation of protein aggregates and abnormal blood vessels. They could have been missed premortem following a non-diagnostic premortem biopsy. Infections constituted a larger part of the cases as it is a tertiary Institution and patients may have visited late. This finding was dissimilar to Hugar BS et al., where subarachnoid haemorrhage was the most common non neoplastic cause of sudden neurological death [7].

Cerebral malaria and tuberculosis though still quite common, show a decreasing trend due to government programs. Rabies shows an alarming trend and is a fatal disease [11]. Traumatic causes like subdural haemorrhage and diffuse axonal injury comprised the second bulk of neurological autopsies in keeping with the increasing number of road traffic accidents. Subarachnoid haemorrhage followed by stroke was the most common types of sudden neurological death in another study. The higher incidence could be attributed to them being very common in the elderly and in the males with hypertension, smoking and diabetes.

All the neurodegenerative diseases occurred in the older ages. Due to lack of an evolutionary need, the ubiquitin-proteasome pathway, which repairs and clears neurodegeneration-related proteins, cannot cope in the elderly [8]. Histological examination of autopsied brain tissue along with clinical evaluation remains the gold standard for diagnosing neurodegenerative diseases [12]. Knowledge of the prodromal phase helps determine at which age the pathologies develop in the brain [9]. If therapies emerge prior to biomarker validation, cerebral biopsies may become important for diagnosis [12,13]. Postmortem biopsies in encephalomalacia help in determining a specific etiology apart from diagnosis. Vascular malformations like cavernous angioma may present with haemorrhage or stroke. CNS neoplasms presenting with clinical signs and symptoms are often detected and diagnosed premortem. However, multiple factors may cause a sampling error and result in non diagnostic biopsies. Moreover, there may be tumour progression also in many cases [10]. Primary CNS neoplasms were more common than metastatic in present study. Intracranial tumours account for 8% of non traumatic brain haemorrhage and in about 50%, it may be the very first manifestation [7]. Tissue from high grade gliomas has tremendous utility in studying treatment effect, both for therapy and in investigating oncocytic viruses [10]. Brain is a common site for metastasis. There was only one case of metastatic mucinous adenocarcinoma in present study with history of a primary lung adenocarcinoma. Detailed history and histopathological study of postmortem biopsies, is invaluable in detection and evaluation of the cause of death, aiding to the statistics of true cancer incidence [14,15].

Limitation(s)

Only limited number of cases was retrieved from the hospital records. Few case details were either missing or incomplete leading to exclusion of those cases hence reducing sample size. History is unknown in many cases and consent for ancillary studies could not be obtained.

CONCLUSION(S)

The present study is one of the handful accounts documenting the varied central nervous system lesions in autopsies. Improved CNS imaging modalities, testing for cerebrospinal fluid or blood biomarkers and neurosurgical techniques has made possible accurate diagnosis and treatment of neurological diseases. Yet, the spectrum of routine, incidental and interesting findings presents us the void to be filled in. Brain autopsies help to understand the disease process and are imperative for research and academic purposes, to assess treatment outcomes and assist in epidemiological studies. However, only medicolegal autopsies cannot provide insight into the true prevalence of diseases. Moreover, variations in postmortem interval and time of fixation can influence the IHC results. It hence necessitates the importance of a brain autopsy in any patient with a neurological illness or an unexplained cause of death. A brain bank was proposed in a study to alleviate the burden of neurological diseases. Ultimately, such studies benefit the improvements in diagnostic modalities and therapeutic outcomes in the living.

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