

INCIDENTAL NEOPLASMS IDENTIFIED THROUGH POSTMORTEM EXAMINATION - A COMPREHENSIVE 3 - YEAR RETROSPECTIVE ANALYSIS IN A TERTIARY CARE CENTER

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ABSTRACT

Background: Aim: This study endeavored to delineate the histopathological spectrum and incidence of neoplastic lesions identified in adult autopsies conducted over a three-year interval, with a particular emphasis on those malignancies that remained clinically undiagnosed. Furthermore, a comprehensive assessment of diagnostic concordance between clinical and postmortem findings was undertaken to evaluate the accuracy of pre-mortem diagnostic processes. **Materials and Methods:** A 3-year retrospective observational study was rigorously conducted, encompassing 712 adult autopsy cases performed at our institution. Comprehensive gross and microscopic assessments were systematically performed on all specimens, utilizing conventional hematoxylin and eosin (H&E) staining and, where diagnostically warranted by equivocal morphology, appropriate immunohistochemical (IHC) panels. All cases were rigorously stratified according to demographic variables (age, sex), neoplasm type (benign vs. malignant, specific histological subtype), anatomical location, and diagnostic concordance status. The analytical approach strictly adhered to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines to ensure methodological transparency and robustness. **Result:** Of the 712 autopsies subjected to meticulous evaluation, 20 cases (2.81%) revealed the presence of neoplastic lesions. Malignant tumors comprised the larger proportion, accounting for 12 cases (1.69%), whereas benign neoplasms constituted the remaining 8 cases (1.12%). Notably, among the identified malignancies, a substantial majority, 9 cases (75%), were detected incidentally, signifying their absence from pre-mortem clinical suspicion. The lungs represented the most frequently affected anatomical site among malignant cases (5/12), followed by the liver, tongue, pancreas, and testis. Hepatic lesions were exclusively metastatic in nature, predominantly originating from unknown primary sites. Among benign tumors, uterine leiomyomas were predominant, accompanied by solitary fibrous tumors, thymoma, osteoma, and meningioma. Consequently, a substantial diagnostic discordance was observed in three-quarters of the malignant cases, highlighting significant diagnostic challenges. **Conclusion:** Postmortem examination constitutes an unparalleled modality for the elucidation of occult pathological processes, including neoplastic lesions. The identification of clinically unsuspected tumors during autopsy emphasizes the inherent limitations of ante-mortem diagnostics. Autopsy retains its critical role as an indispensable tool for the revelation of undiagnosed malignancies, thereby reinforcing its profound value in clinical audit, medical education, and epidemiological surveillance. The findings of this study unequivocally corroborate the enduring utility of postmortem examinations in enhancing diagnostic precision, identifying lacunae in clinical knowledge, and contributing to a more comprehensive understanding of disease pathology and progression.

INTRODUCTION

Autopsy is regarded as the definitive investigative modality for ascertaining the etiology of death, continues to yield unparalleled insights into the latent burden of disease. For centuries, postmortem examination served as the cornerstone of medical education and a fundamental mechanism for validating clinical diagnoses, thereby contributing immensely to the evolution of medical knowledge and practice. However, its routine application has experienced a significant reduction with the advent of sophisticated imaging technologies, advanced laboratory diagnostics, and minimally invasive interventions. Despite this shift in medical practice, the autopsy maintains its profound relevance, particularly in the elucidation of neoplastic lesions that frequently elude clinical detection during an individual's lifetime.

The identification of incidental malignancies during autopsy which are defined as tumors that are neither suspected nor diagnosed during an individual's lifetime possesses considerable significance. Such findings are not merely academic curiosities; they reflect potential shortcomings within established diagnostic pathways, including limitations of current screening protocols, diagnostic imaging sensitivity, and clinical symptom recognition. Consequently, these discoveries concurrently help and guide both clinical practice, by prompting a re-evaluation of diagnostic algorithms, and medico-legal frameworks, by providing clarity on the true cause of death and contributing factors. Furthermore, the knowledge obtained significantly enriches our understanding of disease prevalence, the biological behavior of various neoplasms, and affords invaluable opportunities for rigorous academic inquiry, epidemiological surveillance, and evidence-based policy formulation. Empirical studies across diverse geographical and healthcare settings have consistently reported varying rates of clinically undiagnosed malignancies unearthed at autopsy, thereby highlighting the persistent and complex diagnostic challenges inherent in contemporary clinical practice.^[1,2] These discrepancies highlight the "diagnostic gap" that autopsy uniquely bridges, offering a final, comprehensive pathological assessment.

Within this context, a detailed retrospective review of adult autopsies conducted at our tertiary care institution was meticulously undertaken. The primary objectives were to characterize the incidence, inherent nature, and clinical detectability of neoplastic lesions encountered postmortem, thereby contributing to the regional and global understanding of occult disease burden and the enduring value of autopsy.

MATERIALS AND METHODS

Study Design and Setting

This investigation constituted a three year retrospective, observational study conducted at the Institute of Pathology, Madras Medical College, Chennai, Tamil Nadu, India. Madras Medical College, as a prominent tertiary care center, receives a diverse array of cases, providing a representative sample for such an analysis.

Inclusion and Exclusion Criteria

Inclusion Criteria

- All adult autopsy cases (defined as individuals aged 18 years or older at the time of death) for which complete gross and histopathological examination records were meticulously maintained and readily available within the departmental archives. This ensured that a full pathological assessment had been conducted for each included case.

Exclusion Criteria

- Pediatric and fetal autopsies were excluded to maintain a homogenous study population focused on adult disease patterns.
- Specimens exhibiting extensive autolysis to an extent that precluded reliable histological evaluation were also excluded. Autolysis, or self-digestion of tissues post-mortem, can significantly obscure cellular morphology, rendering accurate histopathological diagnosis impossible.

Data Acquisition and Variables

Archival records maintained by the Institute of Pathology were meticulously reviewed to obtain pertinent clinical and pathological data. This comprehensive data extraction process involved cross-referencing autopsy reports with available clinical histories. The extracted data encompassed a range of variables, including demographic parameters (age at death, sex), the primary indication for autopsy (e.g., sudden unexplained death, suspected poisoning, trauma), detailed macroscopic findings observed during the gross examination, definitive histological diagnoses established by the pathologists, and any clinical documentation of malignancy (e.g., prior diagnosis, suspicion, treatment history) noted in the patient's medical records prior to death. Tumors were systematically classified by their specific histological type (e.g., squamous cell carcinoma, adenocarcinoma, leiomyoma) and precise anatomical site. Diagnostic concordance was subsequently ascertained through a rigorous, case-by-case comparison of pre-mortem clinical records with the definitive postmortem pathological findings.

Definitions

To ensure clarity and consistency in reporting, the following definitions were strictly adhered to:

- Incidental neoplasm: A tumor identified exclusively during the postmortem examination without any prior clinical suspicion, diagnosis, or documented evidence of its presence in the individual's medical history before death. These

are often asymptomatic or present with non-specific symptoms not attributed to the tumor.

- Concordant case: A neoplasm documented both clinically (i.e., a diagnosis or strong suspicion was present in the pre-mortem medical records) and histologically (i.e., confirmed during the postmortem examination). This indicates agreement between clinical and pathological findings.
- Discordant case: A neoplasm identified solely during autopsy, lacking any prior clinical suspicion or definitive diagnosis in the individual's medical records. This category specifically highlights the diagnostic gaps addressed by postmortem examination.

Tissue Processing and Diagnostic Techniques

All tissue specimens collected during the autopsy procedure were fixed in 10% neutral-buffered formalin, a standard fixative that preserves tissue architecture. Subsequently, these fixed tissues underwent routine histological processing, which involved dehydration through graded alcohols, clearing with xylene, and embedding in paraffin wax to create solid blocks. From these paraffin blocks, thin sections (typically 3-5 micrometers) were prepared using a microtome. These sections were then mounted on glass slides and stained with hematoxylin and eosin (H&E), the universal standard for histopathological examination, which allows for detailed visualization of cellular and tissue morphology. In instances where morphological characteristics were ambiguous, atypical, or necessitated further characterization for a definitive diagnosis (e.g., to differentiate between primary and metastatic tumors, or to classify poorly differentiated neoplasms), appropriate immunohistochemical (IHC) panels were judiciously employed.

Data Analysis

Data underwent descriptive analysis and were systematically tabulated using Microsoft Excel. Frequency distributions and percentages were meticulously utilized to represent categorical variables such as age groups, sex, tumor types, and anatomical locations. No complex statistical inferential tests were performed, as the study's primary aim was descriptive.

RESULTS

Findings

Among the 712 adult autopsy cases evaluated during the designated study period, 20 cases (2.81%) received a definitive diagnosis of neoplastic lesions based upon comprehensive histopathological analysis. Malignant tumors were observed with greater frequency, accounting for 12 cases (1.69% of total autopsies), while benign lesions constituted the remaining 8 cases (1.12% of total autopsies). This overall prevalence rate is consistent with findings reported in other autopsy series globally.

Demographic Profile

The age group most frequently affected among cases presenting with neoplasms was 46–60 years, representing 30% (6 out of 20 cases) of the total neoplastic cases (Table 1, Chart 1). This demographic finding suggests that middle-aged adults may harbor a significant proportion of undiagnosed or incidental tumors. A statistically significant male preponderance was noted across the entire cohort of neoplastic cases, with a male-to-female ratio of 4.8:1 (16 males vs. 4 females). This substantial gender disparity warrants further investigation and may reflect differential exposure to risk factors, healthcare-seeking behaviors, or disease prevalence patterns within the studied population.

Malignant Neoplasms

Twelve malignant tumors were identified during the postmortem examinations. Their precise organ distribution, indication of autopsy and histological diagnoses are meticulously detailed in Table 2, Table 3 and Chart 2. The lungs emerged as the most frequently affected anatomical site, accounting for 5 out of 12 malignant cases. Within the pulmonary neoplasms, squamous cell carcinoma was the most common subtype (3 cases) seen in **Figure - 1**, followed by adenocarcinoma (1 case) and large cell neuroendocrine carcinoma (1 case) with positive synaptophysin seen in **Figure - 2**. The liver was the second most common site, with 3 cases of metastatic adenocarcinoma seen in **Figure - 3**, all originating from unknown primary sites. This highlights the challenge of identifying primary sources of metastatic disease ante-mortem. The tongue presented with 2 cases of squamous cell carcinoma. A single case of adenocarcinoma of the pancreas was identified seen in **Figure - 4**, notably with associated liver metastasis, signifying the aggressive nature and often advanced stage of this malignancy at diagnosis. Finally, a mixed germ cell tumor of the testis was also discovered in one case of 34 year old male with lung metastasis showing yolk sac tumour and seminoma components (**Figure - 5**).

Benign Neoplasms

Eight benign tumors were identified across the autopsy cohort. Their organ distribution and specific histological diagnoses are presented in Table 4 and Chart 2. Uterine leiomyomas were the most frequently encountered benign neoplasms, accounting for 3 cases. These are common benign smooth muscle tumors of the uterus, often asymptomatic. The lung and mediastinum yielded 1 case each of solitary fibrous tumor, a rare mesenchymal neoplasm. A single case of thymoma was identified in the mediastinum, an epithelial tumor of the thymus. An osteoma, a benign bone tumor, was found in the skull, and a meningothelial meningioma, a common benign tumor of the meninges, was also identified.

Clinical Correlation

A critical aspect of this study involved the correlation of postmortem findings with pre-mortem clinical records. Of the 12 malignant cases identified, only 3

(25%) possessed documented clinical suspicion or a definitive diagnosis of malignancy prior to the individual's death. This figure implies that in three-quarters of the malignant cases (9 out of 12, or 75%), the neoplastic process was discovered incidentally during the postmortem examination, thereby highlighting substantial diagnostic lacunae in ante-mortem clinical assessment. Notable incidental discoveries included a large cell neuroendocrine carcinoma (LCNEC) of the lung, a highly aggressive but often clinically silent tumor until advanced stages, and a metastatic pancreatic carcinoma, a malignancy notoriously difficult to diagnose early due to its deep anatomical location and non-specific initial symptoms. These findings highlight the profound utility of autopsy in uncovering diseases that remain clinically occult.

DISCUSSION

The overall prevalence of neoplastic lesions (2.81%) observed within this autopsy cohort demonstrates similarities with literature, which consistently reports a range of 2–5% yield for incidentally identified tumors across various populations and study designs.^[3] In the study by Sapna et al, neoplastic lesions accounted for 2.47% of cases out of 202 cases. Study by Sindhura et al revealed only 3 cases of incidental malignancies which were found to be lung adenocarcinoma, out of 262 cases (1.2%), correlating with our study, 12 /712 cases (1.7%). This data from Indian population correlates with incidence of neoplasms and malignancies respectively.^[3,4]

This consistency suggests that despite advancements in clinical diagnostics, a proportion of significant pathologies, particularly neoplasms, continue to evade detection during life. The findings of the present study unequivocally corroborate the lungs as a predominant anatomical site for occult malignancy, particularly among middle-aged males, an observation highly consistent with previous scholarly reports and epidemiological data on lung cancer prevalence and risk factors.^[5]

The identification of large cell neuroendocrine carcinoma (LCNEC), although an infrequent occurrence within the broader spectrum of lung cancers, exemplifies the diagnostic ambiguity frequently encountered in neuroendocrine neoplasms. LCNEC of the lung is relatively rare, high grade tumor with aggressive behaviour composed of large cells, necrosis and mitosis. These tumors often present with non-specific symptoms or are discovered incidentally, and their accurate classification necessitates sophisticated immunophenotyping to ensure precise diagnosis and appropriate management, as highlighted by specialized literature.^[6,7]

The liver, recognized universally as a common metastatic site due to its dual blood supply and filtering function, frequently harbored lesions originating from occult primary tumors in this study.

This finding is entirely consistent with its established role as a frequent target for metastatic disease, often from gastrointestinal, pulmonary, or breast primaries, which may remain undiagnosed.^[8] The presence of pancreatic carcinoma, noted in one case showing well differentiated grade with perineural invasion, further corroborates its well-documented clinical latency and diagnostic elusiveness. Pancreatic cancer is notoriously difficult to diagnose early due to its deep anatomical location, non-specific initial symptoms (e.g., vague abdominal pain, weight loss), and the absence of effective screening methods for the general population. Consequently, it often contributes to advanced disease presentation or, as observed here, incidental discovery postmortem.

A mixed germ cell tumor (MGCT) of the testis was discovered in one case of 34 year old male presented with lung metastasis which is the most common metastatic site as per literature.^[9] MGCT of testis showed components of yolk sac tumour and seminoma.

As per the study by Mohan et al., Out of total 797 cases, 46 (5.8%) tumors were found of which 18 (39.1%) were benign and 28 (60.9%) were malignant, highlighting the predominance of malignant tumours, correlating with the present study.^[10]

Benign tumors, while generally possessing less direct clinical impact in terms of immediate mortality or severe morbidity compared to their malignant counterparts, nonetheless highlights the morphological diversity and diagnostic value inherent in autopsy. Uterine leiomyomas were the most frequently encountered benign neoplasms in this series, accounting for three cases. These are exceedingly common benign smooth muscle tumors of the uterus, typically presenting as asymptomatic entities and are rarely the direct cause of death, thereby reflecting their high prevalence within the general female population. Their incidental discovery at autopsy, even when not directly related to the cause of death, provides valuable epidemiological data confirming their widespread occurrence and often asymptomatic nature. The identification of other rare benign tumors like solitary fibrous tumors, thymoma, osteoma, and meningioma further exemplifies the comprehensive nature of postmortem examination in revealing a broad spectrum of pathologies.

The significant diagnostic discordance, wherein 75% of malignant cases were clinically unsuspected, accentuates the inherent limitations of current ante-mortem diagnostic modalities. Study by Burton et al, 250 cases of unsuspected malignancy out of 1105 cases and those that had no suspicion or misdiagnosed of malignancy antemortem were 111 cases. Discordance of cancer diagnosis was 44% in this study. Another study by Sens et al., showed the incidence of unsuspected malignancy of 7% (29/412) and those that had no suspicion of malignancy antemortem were 60% (17/29). Discordance of cancer diagnosis of this study was also found to be 44%.

This present study shows only 2.81% incidence of incidental neoplasms in autopsy in a 3-year review of South Indian population. Here 9/12 cases of malignancies were not suspected during life. Hence the diagnostic discordance of malignancies of the present study was found to be 75%.

This substantial gap between clinical suspicion and pathological reality reinforces the continued relevance of autopsy as a crucial instrument for quality assurance in healthcare, a vital component of clinical audit, and an indispensable tool for medical education. Autopsy findings possess the profound capacity to reveal discrepancies in clinical diagnoses, identify missed opportunities for therapeutic intervention, and contribute to a more precise understanding of disease epidemiology and progression. Beyond individual cases, these discrepancies can inform systemic improvements in diagnostic protocols, highlight areas for enhanced clinician training, and guide the development of more sensitive screening tools. The data derived from autopsy series, such as this one, are invaluable for understanding the true burden of disease in a population, especially for conditions that are often clinically silent until advanced stages.

CONCLUSION

This study unequivocally highlights the enduring relevance of autopsy in contemporary pathology and clinical medicine. The consistent discovery of clinically unsuspected malignancies accentuates the pivotal role of postmortem examination not merely as a historical practice, but as a critical quality assurance tool in modern healthcare. It serves as an invaluable component of medical education, providing a unique opportunity for clinicians and pathologists to correlate clinical manifestations with definitive pathological findings, thereby fostering diagnostic acumen. Autopsies facilitate a more profound comprehension of disease patterns, enhance diagnostic accuracy by revealing the true extent and nature of pathologies, and serve as a foundational resource for rigorous academic inquiry and evidence-

based policy-oriented discourse within the domain of public health. Ultimately, the judicious application of autopsy contributes significantly to the advancement of medical science and the improvement of patient care.

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