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## Original Research Article

## Analysis of undiagnosed neoplasms identified at post-mortem: A descriptive study

Zini Chaurasia<sup>1,\*</sup>, Swapnil Agarwal<sup>1</sup>, Renu Gupta<sup>1</sup>, Cheta Singh<sup>1</sup>,  
Dishant Kumar Malik<sup>1</sup>Dept. of Pathology, Dr. Baba Saheb Ambedkar Medical college and Hospital, New Delhi, India

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## ABSTRACT

**Introduction:** Autopsy which is also known as post-mortem examination has been derived from the greek term “autopsia” meaning “to see for one self”. Autopsies performed by the forensic medicine specialists are followed by histopathological examination of various concerned organs for underlying cause of death. histopathological examination of various organs thus always present an interesting plethora of unsuspected findings. These findings could have been present ante mortem with symptoms or completely asymptomatic. The undetectable lesions could have contributed to the death of the person. There fore the alertness and inquisitiveness of a pathologist while examining the autopsy cases can contribute significantly towards the subject of pathology and also serve as a learning process for the clinician to establish clinicopathological correlations.

**Aims:** This study has been conducted with the following aims & objectives in mind: To analyse the neoplastic lesions detected incidentally on histopathology and correlate with the symptoms if any present ante mortem. Settings and design: this is a retrospective, descriptive study done in the department of pathology, dr. bsa hospital, delhi.

**Methods and Material:** A retrospective study of medicolegal autopsies for five years was undertaken in a tertiary care centre to analyse the tumors incidentally detected on histopathological examination. Autopsy records of 663 cases were reviewed and cases where a histopathological diagnosis of tumor was given were included in our study. Gross and histopathologic findings were noted and the salient features were studied. Clinical data of these cases were noted in detail from the forensic post mortem records and tabulated.

**Results:** This study includes 12 cases of tumor out of 663 cases. Most common benign tumor was leiomyoma and most common malignant tumor was adenocarcinoma. An interesting case of hodgkins lymphoma in spleen and liver was also documented. A single case of meningioma, squamous cell carcinoma metastasis to heart and astrocytic tumor were noted.

**Conclusions:** This study highlights the various undetected tumors both benign and malignant. This study also gives a perspective to correlate ante mortem findings with post mortem findings to the clinician and pathologist.

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## 1. Introduction

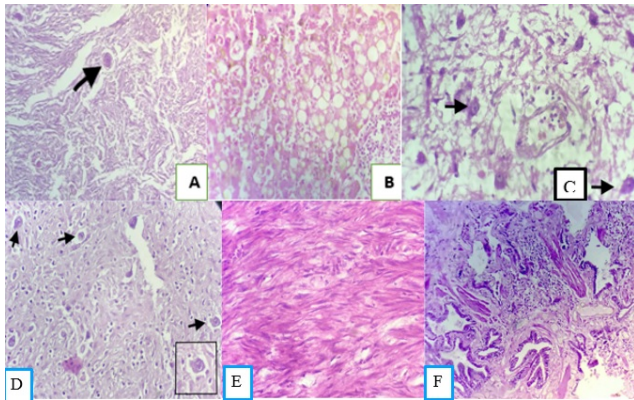
Autopsy which is also known as post-mortem examination has been derived from the greek term “autopsia” meaning “to see for one self”. Autopsies are conducted for mainly

two purposes. It is either medical/clinical and medico legal. Many a times both of these overlap. Clinical autopsy, is done to diagnose the disease which has caused the mortality. Clinical autopsy also helps the pathologist in studying the natural course of disease and hence is carried out despite the cause of death having been established ante mortem.

\* Corresponding author.

E-mail address: [1989.zini@gmail.com](mailto:1989.zini@gmail.com) (Z. Chaurasia).

This greatly contributes to the knowledge of existing disease course and also helps in teaching of the post graduate students. medico-legal (ml) autopsies are performed with multiple aims of providing answers to questions about the identity, cause of death, time of death, circumstances of death, etc, for helping the law enforcing agencies to solve a crime.<sup>1</sup> Autopsies performed by the forensic medicine specialists are followed by histopathological examination of various involved organs. histopathological examination of various organs thus always present an interesting plethora of unsuspected findings. These findings could have been symptomatic or asymptomatic. These undetectable lesions could have contributed to the death of the person. Therefore, the alertness and inquisitiveness of a pathologist while examining the autopsy cases can contribute significantly towards the subject of pathology and also serve as learning clinicopathological correlations for the clinician.



**Fig. 1:** Figure 1 A: H&E 40X, Meningioma Tumor present in sheet like growth pattern with syncytial (meningothelial) cells, at places showing whorling pattern. Arrow pointing towards the psammoma body. Figure 1B: H&E 40X, Steatohepatitis Multiple hepatocytes showing ballooning and necrosis along with foci of inflammatory cells. At places mallory denk bodies also seen. Figure 1C: H&E 40X Astrocytic tumor Tumor present in sheets with increased cellularity, nuclear atypia. Several arrows showing the astrocytic nuclei with a distinct nucleolus. Figure 1D: H&E 40X Hodgkins lymphoma, Spleen Infiltration by numerous large cells with single to multiple nuclei and a prominent nucleoli the size of small lymphocyte, lymphocytes and plasma cells. Inset showing characteristic Reed Sternberg cells seen. Figure 1E: H&E 40X Leiomyoma Fascicles of smooth muscle cells with eosinophilic cytoplasm and bland cigar shaped blunt ended nuclei. Figure 1F: H&E 10X Adenocarcinoma, Lung Tumor showing patterns of lepidic growth and also solid growth areas of glandular growth with tumor cells showing atypia along with inflammation.

## 2. Aims & Objectives

This study has been conducted with the following aims & objectives in mind:

- To analyse the neoplastic lesions detected incidentally on histopathology and correlate with the symptoms if any present ante mortem.

## 3. Materials and Methods

A retrospective, descriptive study of medicolegal autopsies of five years duration from january 2016 to december 2020 was undertaken in a tertiary care centre to determine incidental neoplastic lesions related or unrelated to the cause of death. In view of the medicolegal nature and legal bonding as per law, no ethical clearance for conducting this retrospective study were required. Autopsy records of 663 cases were reviewed and cases where a histopathological diagnosis of tumor was given were included in our study. The organs sent for routine autopsy in our institution comprise predominantly of heart, liver, spleen, kidneys, brain, lungs and pancreas. Representative bits from the concerned organs were processed in a routine manner. All sections were stained with haematoxylin and eosin (h & e) stain and special stains were used, as and when required. Gross and histopathologic findings were noted and the salient features were studied. Clinical data of these cases were noted in detail from the forensic post mortem records and tabulated (Table 1).

## 4. Results

The present study consists of 12 cases out of 663 cases sent for histopathological examination in the department of pathology, Dr. BSA hospital & medical college. All the cases where a diagnosis of tumor was made has been included in the study. The cases where the tissue were autolysed and where a diagnosis of tumor was not made has not been included in the study. Table 1 displays the alleged cause of death, spectrum of neoplasm and other significant lesions found on histopathological examination of these autopsies. Only two of these cases were diagnosed of neoplasm ante mortem but their status of metastasis was unknown. In both cases metastatic deposits were established only on post mortem histopathological examination. Out of total 12 cases, 10 were females and only two males. The majority of pateints were between age group 26-45 years of age 7/12(58.3%). Most common benign lesion was found to be leiomyoma (5/12) and malignant lesion was adenocarcinoma (4/12). One case had both a leiomyoma and adenocarcinoma. Rest one case each of meningioma, hodgkins lymphoma, squamous cell carcinoma and astrocytic tumor were detected.

One case was reported as meningioma which was previously undiagnosed (case no.1). The patient was a 45years female, who was operated for cholelithiasis, died due to post operative complications on the same day and body sent for medico legal autopsy. Autopsy revealed a 3.5cms solid lesion occupying the posterior cranial fossa

**Table 1:** Clinical, histopathological findings of autopsy cases

Case no.	Age/gender	Alleged cause of death	Primary tumor	Tumor morphology on histopathology	If symptoms present ante mortem	Other significant findings
1	45/f	Allegedly died due to post operative complications during hospital stay	Brain	Meningioma	Cholecystitis symptoms	Brain-edema, liver-steatohepatitis, spleen/lung-congestion, kidney-tubular necrosis.
2	17/m	Allegedly brought dead to hospital	Brain	Astrocytic tumor	no	Tumor present in right side of brain extending upto left side, and temporal lobe. cerebrum showing edema
3	24/f	Allegedly brought dead to hospital	liver, spleen	Hodgkins lymphoma	no	Focal sclerosis-kidney, interstitial fibrosis and alveolar macrophages seen-lungs
4	35/f	Allegedly brought dead to hospital	uterus	Leiomyoma	no	Uterus- a single 3cms leiomyoma, brain-edema, lungs-hemorrhage, kidney-congestion, large blood vessel-ante mortem clot
5	39/f	Allegedly died during hospital stay for dengue treatment	uterus	leiomyoma	no	Uterus - a single fibroid measuring 2cms, fatty change liver,chronic cervicitis
6	42/f	Allegedly died due to cardiopulmonary arrest During treatment for complaints of dub	uterus	leiomyoma	yes	Uterus- three leiomyomas measuring 3.5,3,2cms, brain-edema, lungs-congestio
7	38/f	Allegedly brought dead to hospital	uterus	leiomyoma	no	Kidney-patchy tubular necrosis, fallopian tube - paratubal cyst
8	73/f	Allegedly brought dead to hospital	lung	Adenocarcinoma	no	3 leiomyomas measuring 10,8,7cms. heart- thrombus identified in right ventricle
9	40/f	Allegedly brought dead to hospital	lung	Adenocarcinoma	no	Congestion liver, focal sclerosis-kidney, congestion-spleen
10	72/f	Allegedly died during hospital stay during treatment	large intestine	Adenocarcinoma	no	Brain-edema, liver-steatohepatitis, kidney/spleen-congestion
11	32/f	Diagnosed case of gall bladder carcinoma, died during course of treatment .	Gall bladder	Mucin secreting adeno ca,leiomyoma	Primary diagnosed,metastasis unknown	Fatty change liver, focal sclerosis-kidney, congestion-lungs
12	18/m	Diagnosed case of scc, oral cavity, died during course of treatment.	primary- oral cavity	Squamous cell carcinoma	Already diagnosed primary, matastasis unknown	Metastatic deposits in liver, spleen. lung showing features suggestive of tuberculosis, single 1cm submucosal leiomyoma

originating from falx cerebelli. Sections from the solid lesion showed tumor comprising of spindle cells present in sheets and whorling pattern. Cells in the sheets were oval with round to oval nuclei with finely stippled chromatin and a small nucleoli resembling meningothelial cells. psammoma bodies were also seen. Findings were suggestive of meningioma (Figure 1 A). Surrounding sections from brain showed edema. liver showed features suggestive of steatohepatitis, (Figure 1 B) whereas kidney showed large areas of tubular necrosis. Spleen & lung showed congestion.

A single case of astrocytic tumor (case no.2) was reported. The patient was a 17year old boy, who had a history of one episode of headache, vomiting and was allegedly brought dead to the hospital. Only brain tissue was sent for histopathological examination. Autopsy revealed a cavity with a solid mass measuring 10x4x4cms in right cerebral hemispheres, accompanied by necrosis around the internal capsule and presence of blood clots. The left hemisphere was edematous and congested. Gross examination of right hemisphere measuring 14x12x7 cms, weighing 500 grams revealed a solid cystic mass measuring 6.5x6x2 cms in the temporal lobe adjacent to capsule. Sections from mass revealed a tumor with increased cellularity, nuclear atypia and minimal mitotic activity. Significant microcyst formation was also identified. The astrocytic nuclei was oval to elongated, had vesicular chromatin and few had a distinct nucleolus. Focal calcifications were also identified. Findings were suggestive of an astrocytic tumor ( Figure 1 C). The left hemisphere revealed only pin point hemorrhages, congestion and edema.

A case of unsuspected hodgkin's lymphoma in liver and spleen was identified (case no.3). This was a case of 24 years female who was a known hiv+ and follow up case of pulmonary tuberculosis, and was admitted following complaints of vomiting and weakness and died during the course of treatment. Autopsy revealed both the lungs firmly adherent to the internal wall at places. on cut section markedly congested, fibrosed areas were seen. Pus pockets were also seen. Grossly liver and spleen were enlarged. Liver had granular consistency on cut section. Spleen had multiple nodules and on cut section was granular in consistency. Sections from liver and spleen showed infiltration by plasma cells, lymphocytes, eosinophils and numerous large cells. These large cells had multiple nuclei, few had a single nuclei with multiple nuclear lobes, each with a large inclusion nucleolus about the size of small lymphocytes characteristic of reed sternberg cell(Figure 1 D). Sections from kidney showed focal glomerular sclerosis. Lungs had areas of interstitial fibrosis and chronic inflammatory infiltrate.

A single (case no.12) known case of squamous cell carcinoma, oral cavity with mental retardation was also included in our study. The patient was a 18 years old male. He died during the course of treatment while being operated

for the carcinoma. On autopsy, post surgical therapeutic wound with excision over facial skin, underlying tissues, oral mucosa and upper half of mandible on right side was recorded. histopathological examination of myocardium demonstrated infiltration by nests of malignant squamous cells. Sections from lungs also had nests of malignant squamous cells along with pulmonary edema and interstitial inflammation. Another neck mass also showed moderately differentiated scc. Leiomyoma was identified in five cases (case no 4,5,6,7and 11). Two cases (case no4 and 7) had ante mortem clots in great vessels, and leiomyomas were completely incidental. Two cases (case no 4,5) had small submucosal fibroids measuring 2,3 cms respectively. Rest of the two cases (case no 6,7) had three fibroids. Case no 6 was a 42years female, admitted with complaints of dysfunctional uterine bleeding and died due to cardiopulmonary arrest. On histopathology three leiomyomas measuring 3.5,3,2 cms in size were seen. Case no. 7, a 38years old female had a tubular clot in right ventricle on autopsy. histopathological revealed three fibroids measuring 10x9x4, 9x8x4, 8x7x4cms in size. The leiomyomas were grey white to grey brown, globular on gross appearance. On cut section they were grey white and showing a whorling pattern. This was much appreciated in the large leiomyomas. Microscopic examination showed a tumor comprising of spindle cells arranged in whorling pattern(Figure 1 E). Few of them also showed focal areas of hyalinisation. Fifth case (case no. 11) of leiomyoma has been described below.

Four cases of adenocarcinoma (case no 8,9,10 and 11) were noted out of which one was known case of adenocarcinoma gall bladder (case no.11). Rest three were undiagnosed ante mortem, two of which were present in lung and one in large intestine. Case no.8 was a 73years old female was allegedly brought dead to hospital following unconsciousness. Autopsy revealed that both lungs were pale and had multiple pus pockets. Histopathology revealed focal areas of necrosis in both lungs and areas of atypical adenomatous hyperplasia. These glands were also seen infiltrating into adjacent interstitium, suggestive of adenocarcinoma of lung. Kidney showed congestion and focal glomerulus sclerosis. Fourth case (case no 9) was a 40years old female who was allegedly brought dead to hospital following complaints of chest pain. Autopsy revealed both the lungs to be firmly adherent to the thoracic cavity at places and weighed 444grams and 328grams on right and left side respectively. On cut section congestion was seen. Microscopic sections from lungs showed interstitial fibrosis. The fibrotic areas were infiltrated by small to large sized glands lined by cuboidal to columnar epithelium with mild degree of atypia, loss of polarity and nuclear stratification suggestive of adenocarcinoma. Liver showed faetures suggestive of staetohepatitis. Sections from kidney and spleen showed congestion. Case no.10 was a 72years old female who was

admitted in hospital and died six days after her admission. Autopsy revealed mucosal ulcerations at few places in large intestine. On microscopy multiple sections from large intestine showed infiltration by closely packed atypical glands lined by cells exhibiting moderate degree of nuclear pleomorphism and dysplasia suggestive of adenocarcinoma (Figure 1 F). Fatty change was observed in liver and kidney showed mild chronic inflammatory infiltrate and focal glomerular sclerosis and tubular necrosis. Case no 11, 32years old female was undergoing treatment for mucin secreting adenocarcinoma of gall bladder and allegedly died during the course of treatment. Autopsy findings revealed enlarged liver weighing 1850gms and an irregular mass was adhered to it. Spleen was also slightly enlarged, weighed 234gms and adhered to the liver. Uterus had a small submucosal mass measuring 1.5x1x1cms. Grossly liver with the adhered part measured 10x6x3 cms. Multiple sections from them revealed fatty change and infiltration of liver and spleen by mucin secreting malignant cells suggestive of adenocarcinoma. On microscopic examination of uterine submucosal mass, it showed characteristic features of a leiomyoma.

## 5. Discussion

Giovanni morgagni (1682-1771), celebrated as father of anatomical pathology conducted 700 postmortems and co-related the findings with their clinical details, thus introducing the concept of clinicopathological correlation (cpc). He thus helped in establishing a coherent sequence of cause, symptoms, lesions with their outcomes.<sup>2</sup>

The histopathological examination of autopsy cases reveal some histopathological findings which were either asymptomatic or unnoticed when the person was alive. Its these findings that interest not only the pathologist, forensic scientist but also the treating clinician of the patient. the findings which the pathologist and forensic scientist reveals makes the clinician wonder, “what if these lesions were diagnosed ante mortem”, “would the clinician treat the pateint differently which would have altered the prognosis of the pateint”. It’s the learning through different cases and histopathological findings from autopsy that answer such queries. The incidental neoplasms which were asymptomatic may or may not be related to the underlying cause of death.<sup>3</sup> it becomes even more important to study such cases where there has been sudden death and no probable cause of death was suspected by the clinician. The clinicopathological corelation in cases of unsuspected findings of autopsies thus contributes to the dynamic learning for the students of medicine, pathology, forensic medicine but also for the treating physicians and teachers. We therefore present few intersting cases in our study which were missed ante mortem and give us scope of learning. Few studies have given the incidence of unsuspected neoplasia as 7% by sens et al.<sup>4</sup> and 9% for malignant neoplams by burton

et al.<sup>3</sup> In our study we found 12 cases of neoplasia out of 663 cases of autopsy that constitute 1.8%. The discrepancy of incidence between our study and that of burton et al. and sens et al. might be because of the fact that not all hospital cases are subjected to medico legal autopsy unless there is a suspicion of unnatural death. Also, many a times consent from the family regarding postmortem examination is not given.

In our study we found hodgkins lymphoma in liver and spleen, which is a rare finding.<sup>5-8</sup> Primary hl of spleen and liver is even rarer. Most patients have concomitant involment of mesentric and splenic lymph nodes. F. gaudia et al. reported incidence of hodgkins lymphoma at extra nodal sites like liver (8%) and kidney (3%).<sup>5</sup> Our patient was hiv+, which is a known risk factor for the development of lymphomas. since, the lymphoma was undocumented, and we found it on autopsy, at a rare site, it significantly contributes to the pool of cases detected incidentally. since it was found at both liver and spleen, most probably this was a case of disseminated hl.

Another interesting case we found was of squamous carcinoma metastasis to heart. Primary tumors of heart are very rare in contrast to metastasis. Metastasis from lung, breast and lymphomas make the majority of cases. Due to silent nature of cardiac mets, the diagosis is often missed and diagnosed incidentally on autopsy. In our case, the primary was diagnosed in oral cavity. The spread of matstasis of squamous carcinoma from head and neck region to heart is rare and the mechanism is poorly understood. Thus presented as a surprising and interesting finding for academic purposes in our case study. Both the cns tumors in our study were undiagnosed and could have been the reason for the mortality of the pateint. A single case of meningioma was seen in our study. Meningioma is one of the most common primary brain tumors comprising of 37.6% of cns tumors. incidental meningiomas detected on autopsy comprise about 2-3% of pateints.<sup>9</sup> according to who, astrocytic tumors have high incidence amongst cns tumors.<sup>10</sup> The absence of symptoms ante mortem can easily lead to non diagnosis of this otherwise good prognosis tumor. The morbidity and mortality can be reduced when diagnosed timely. We observed two cases incidental cases of adenocarcinoma lung on autopsy, their incidence being around 2.08% on autopsy.<sup>11</sup> Adenocarcinoma is the most common histologic subtype of lung cancer in men and women.<sup>12</sup>

Leiomyoma of the uterus was found to be the most common benign tumor observed in our study. In living also, leiomyoma is the most common benign tumor found in females of reproductive age group.<sup>13</sup> in our study also, all the females were in reproductive age group. Though three cases had small sized fibroids that can be missed antemortem, but case no 9 had large fibroids which must have caused symptoms, which were ignored ante mortem

for reasons unknown. Large fibroids are known to cause significant morbidity and mortality,<sup>14</sup> therefore warranting attention from both patient and clinician.

## 6. Limitation

The number of cases in present study are very few, hence a longer duration study would contribute more number of cases. No IHC was performed on the tumors, due to cost factor.

## 7. Suggestion

Considering the morbidity and mortality associated with tumors, more autopsy studies need to be conducted and more literature to be made available so as to enhance learning for both clinician and histopathologist.

## 8. Conclusion

This study contributes to the fact that incidental findings on autopsy are invaluable to the clinician and pathologist. Also the neoplasm detected add to the true cancer incidence statistics. Hence, it's always a good learning exercise for both the clinician and pathologist to go back to the ante mortem findings and correlate them in the light of new incidental histopathological findings on autopsy.

## 9. Source of Funding

None.

## 10. Conflict of Interest

None.

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## Author biography

**Zini Chaurasia**, Senior Resident  <https://orcid.org/0000-0002-5804-735X>

**Swapnil Agarwal**, Medical Officer

**Renu Gupta**, Specialist

**Cheta Singh**, Senior Resident

**Dishant Kumar Malik**, Senior Resident

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