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Original Article

Pathology Section

Diagnostic Yield of Post-mortem Needle Biopsies and their Spectrum: Experience from a Tertiary Care Hospital

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ABSTRACT

Introduction: Conventional autopsy provides important information regarding cause of death, clinico-pathological correlation and is a paramount source of learning. Developing countries have low acceptance rates, denial and limited accessibility for conventional autopsy. Needle autopsy has come up as an alternative to conventional autopsy.

Aim: Aim of the study was to analyse postmortem needle biopsies to gauge their utility in lending postmortem diagnosis as well as study its spectrum.

Materials and Methods: This was a retrospective study and includes 334 patients. Different organs sampled were liver, lung, kidney, spleen, brain, heart, testis, lip and nose. Clinical data and histopathology slides were retrieved and reviewed by three pathologists.

Results: A total of 428 biopsies were received from 334 patients. Forty five (10.5%) biopsies from different organs were non representative. A definite diagnosis was offered in 304 biopsies with an overall diagnostic yield of 79.4%. Liver and kidney biopsies had the maximum diagnostic yield of 89.2% and 69.2%, respectively and most diagnostic category encountered were multiacinar necrosis and fungal infection respectively.

Major disagreement (Class 1 and Class 2) between clinical diagnosis and needle autopsy diagnosis was found to be in 21/334 cases (6.3%), where patient would potentially have survived if the clinical diagnosis had been correct.

Conclusion: Diagnostic dilemma is a wistful part of medical science. Postmortem needle biopsy has an important role in diagnosis making, improvising the quality of academics and patient care. Level of information and diagnostic yields are high with liver and kidney.

Keywords: Autopsy, Histopathology, Postmortem needle biopsy

INTRODUCTION

The cases which are difficult to diagnose or do not reach a definite diagnosis during life may be helped by conventional autopsy for reaching to a reasonable conclusion and can serve as a gold standard. This will provide necessary information regarding the cause of death, clinicopathological correlation and is a paramount source of learning. In developing countries like India an open autopsy is practiced in a very limited number of places.

Post-Mortem needle biopsy / Needle Autopsy can overcome many barriers that limit the use of conventional autopsies and have come up with several edges over known shortcomings of conventional autopsy [1]. Needle autopsy is a common modality in most of the academic institutes, and the supremacy is further attained; as it is fast, minimally invasive, inexpensive and more acceptable to patient's relatives [2-4]. It has been used in various settings and for multiple speculations including increased acceptability, simplicity and decreased risk of disease transmission when compared to complete autopsies [5, 6]. This can also enable the safe collection of diagnostic material and successfully procure tissue for further pathological and molecular review [7].

The aim of this study was to review the spectrum of post-mortem needle biopsies in a tertiary care referral hospital where conventional autopsy is not practiced and find out the diagnostic accuracy of post-mortem needle autopsies in lending a diagnosis or cause of death.

MATERIALS AND METHODS

All retrospective cases of post-mortem needle biopsies received between January 2010 and December 2015 in the Department of Pathology, SGPIMS, Lucknow, India were included in the study. Biopsies were unguided and performed per-cutaneously with 16G Tru-Cut needle by clinicians. Samples were fixed in 10% formalin; sent to pathology department and processed as for routine histopathology specimens. Single or multiple biopsies from different organs were done, included liver, lung, kidney, spleen, brain, heart, testis, lip and nose; as a different protocol by various departments. Histopathology is a gold standard in many conditions. In post-mortem scenario, needle autopsy or conventional autopsy with clinicopathological correlation is the only way to reach diagnosis and cause of death. Review of all the histopathology slides by three histopathologists (NN, RM, and NiK) specialised in this field has been done along with clinico-radiological correlation. In this study, post-mortem biopsy was performed for diffuse pathologies. So biopsy from a single site is also considered as diagnostic.

RESULTS

A total of 428 biopsies were received from 334 patients; out of which single organ biopsies were from 270 cases (81.4%), and multiple organ biopsies were from 64 cases (18.6%). One hundred sixty-three cases (48.8%) were of pediatric age group (age range <1 to 18 years) out of which 11 children (2.5%) were less than one year of age. The overall mean and median age was 27 years and 20 years (range -9 months to 80 years) with a male to female ratio of 1.6:1 (206 males, 128 females). Forty-five (10.5%) biopsies from different organs were non-representative. Rest of the 383 (89.5%) biopsies were evaluated, with a sampling accuracy rate of nearly 90%. A definite diagnosis was offered in 304 biopsies with an overall diagnostic yield of 79.4%. In 79 (20.6%) biopsies, a morphological description was provided as the biopsies showed mostly normal morphology of the parent tissue. The details of the anatomic site with a total number of biopsies performed and diagnostic accuracy are given in [Table/Fig-1].

In the present study, liver and kidney biopsies had the maximum overall diagnostic yield after excluding non-representative biopsies of 89.2% and 69.2%, respectively. Diagnostic accuracy in infants

were also found to be high in liver (86.4%) and kidney (71.8%). Abdominal mass and stomach had one biopsy each which were diagnostic. Lung (50%), spleen (54.5%) and brain (42.8%) had a diagnostic yield of around 50%.

Site	Total no. of bx	Diagnostc biopsy	Normal morphology	Non-representative	Diagnostic yield
Liver	284 (66.3%)	248	30	6	89.20%
Lung	55 (12.8%)	19	19	17	50%
Kidney	39 (9.1%)	18	8	13	69.2
Brain	20 (4.6%)	6	8	6	42.8%
Spleen	13 (3%)	6	5	2	54.5%
Bone marrow	3 (0.7%)	1	1	1	50%
Muscle	2 (0.5%)	1	1	0	50%
Abdominal mass	1 (0.2%)	1	0	0	100%
Colon	2 (0.5%)	0	2	0	0
Heart	1 (0.2%)	0	1	0	0
Lip	2 (0.5%)	0	2	0	0
Skin	4 (0.9%)	2	2	0	50%
Stomach	2 (0.5%)	2	0	0	100%

[Table/Fig-1]: Details of anatomic sites with total number of biopsies performed and diagnostic yield.

Most common diagnoses encountered in liver was of multiacinar necrosis, in the kidney it was a fungal infection and thrombotic microangiopathy and in the lung was that of alveolar hemorrhage. The diagnostic spectrum of post-mortem liver, kidney and lung biopsies was tabulated in [Table/Fig-2-4] respectively.

The sampling adequacy was high for single organ biopsy (95.5%) with 12 of 270 cases being inadequate than multiple organ biopsy (84.2%) where 25 of 158 cases were insufficient. Provisional clinical diagnosis was provided by clinicians and disparity with pathological diagnosis was also ascertained. Goldman L et al., classified discrepancies into four categories [8].

Class 1: a discrepant diagnosis with a potential impact on survival

Class 2: a major discrepant diagnosis but with equivocal or no impact on survival

Class 3: a minor discrepant diagnosis that could have been diagnosed before death

Class 4: a discrepant minor diagnosis that could not have been made before death

In our study, major disagreement (Class 1 and Class 2) between clinical diagnosis and needle autopsy diagnosis was found to be in 21/334 cases (6.3%), where the patient would potentially have survived if the clinical diagnosis had been made antemortem [Table/Fig-5,6].

DISCUSSION

Post-Mortem needle biopsy/needle Autopsy has been used in various settings and for many speculations including increased acceptability, simplicity and decreased risk of disease transmission when compared to complete autopsies [2-4].

Twenty-year study (1948-1968) of 394 post-mortem cases, evaluated by Wellmann K et al., with 357 multiple site biopsies and 37 limited organ biopsy showed high inadequacy rates of 22.8%. The success rate was high for liver (92%) followed by the kidney (34%) [2]. Celiloglu OS et al., found much higher inadequacy rates of 36.3%; in 247 neonatal post-mortem needle biopsies; from 76 neonates; reason being smaller organs and less experienced staff [9]. The sampling inadequacy rate in the present study was much less (9.6%); compared to other studies. High adequacy rate in our study showed more top technical experience, skilled personals; mainly include single organ or limited organ biopsy and predominance of the adult population with larger organs. A large number of non-representative cases belonged to lung and kidney. Procedures are unguided; thus deeply seated organ kidney has low adequacy rate. Guided (USG/MRI/CT) procedures will help in dealing with this. Lack of experience will lead to

Diagnostic entities	Number of biopsies
Acute hepatitis	35
Acute viral hepatitis	5
Autoimmune hepatitis	7 (1 necrosis, 1 bridging fibrosis)
HBV related hepatitis	2
HCV related hepatitis	1
Cholestatic liver disease	16
Extrahepatic biliary atresia	4
PFIC	2
PILBD	2
Neonatal hepatitis	1
Metabolic liver disease (GSD)	5
Niemen Pick disease	1
Indian childhood cirrhosis	2
Wilsons disease	3
Drug induced liver disease (DILI)	1
Steatohepatitis	4
Malarial hepatitis	1
Cryptococcus	1
Histoplasmosis	1
Tuberculosis	4
Amyloidosis	2
Multiacinar necrosis	100
Passive venous congestion	4
Lymphoma	6
Hepatocellular carcinoma	1
Hepatoblastoma	1
Metastatic carcinoma	3
Cirrhosis	33 [Cryptogenic (21); Autoimmune (6); Wilson disease (3); Alcoholic (1); EHBA (1); HBV related (1)]

[Table/Fig-2]: Diagnostic spectrum of post-mortem liver biopsies.
HBV: Hepatitis B virus; HCV: Hepatitis C virus; EHBA: Extrahepatic biliary atresia; PFIC: Progressive familial intrahepatic cholestasis; PILBD: Paucity of intralobular bile duct

Diagnostic entities	Number of biopsies
Acute tubular necrosis	3
Crescentic glomerulonephritis	1
Diffuse proliferative glomerulonephritis	3
Membranoproliferative glomerulonephritis	1
Focal proliferative glomerulonephritis	1
Tubulointerstitial nephritis	1
Fungal infection	4
Thrombotic microangiopathy	4

[Table/Fig-3]: Diagnostic spectrum of postmortem kidney biopsies (n=18).

Diagnostic entities	Number of biopsies
Alveolar hemorrhage	6
Bronchopneumonia	2
Fungal infection	1
Hyaline membrane disease	3
Interstial lung disease	3
Metastatic carcinoma	1
Tuberculosis	1
Pulmonary edema	2

[Table/Fig-4]: Diagnostic spectrum of postmortem lung biopsies (n=19).

Anatomic site	Clinical dagnosis	Disagreement diagnosis
Liver	Lymphomatous infiltrate	Multiacinar necrosis
Liver	Metabolic liver disease	Lymphomatous infiltrate
Kidney	Chronic kidney disease, Diabetes	Crescentic glomerulonephritis
Kidney	Henoch Schoenlen purpura	Membranoproliferative glomerulonephritis

[Table/Fig-5]: Disagreement diagnoses (n=4).

Anatomic site	Clinical diagnosis	Surprise diagnosis
Brain	Tubercular meningitis	Cryptococcal meningitis
Kidney	Perinephric haematoma,	Fungal infection (Mucormycosis)
Kidney	HUS, APLA	Fungal infection (Mucormycosis)
Kidney	Aplastic anaemia	Thrombotic microangiopathy
Kidney	Renal infarct	Fungal infection (Mucormycosis)
Kidney	Septic shock, MODS	Histoplasmosis
Liver	Acute liver failure, hepatomegaly	Lymphoproliferative disorder
Liver	Alcoholic liver disease	Metastatic carcinoma
Liver	Metabolic liver disease	Paucity of bile duct
Liver	Hepatomegaly, liver failure	Histiocytic infiltrative disorder
Liver	Glycoge storage disorder, hepatomegaly	Hepatoblastoma
Liver	Rheumatoid arthritis, methotrexate intoxication	Granulomatous inflammation
Liver	Pain abdomen, hepatomegaly	Metastatic carcinoma
Liver	Acute pancreatitis	Lymphoproliferative disorder
Liver	Inflammatory myositis, hepatomegaly (liver sols)	Metastatic carcinoma
Liver	Thalassemia major	Niemann pick disease
Liver	SLE, right lobar pneumonia	tuberculosis
Liver	Sepsitic shock	Histoplasmosis
Lung	Bronchopneumonia, Chronic renal failure	Metastatic carcinoma
Lung	SLE, AILD	Tuberculosis
Spleen	Septic shock, MODS	Histoplasmosis

[Table/Fig-6]: Surprise diagnoses (n=21).

high inadequacy rate in obtaining lung biopsy and usually contained pleural tissue only. A deeper and tru-cut biopsy is advised.

The bulk of the cases include liver (66.7%), lung (12.9%) and kidney (9.1%) biopsies. As post-mortem needle biopsies are not performed as a protocol in our institute, thus various departments have different criteria to carry out post-mortem needle biopsies. The procedure has been performed only by few departments such as gastroenterology, nephrology and critical care medicine which are an important reason for high sample rates from these departments resulting in sample variability.

The tissues such as liver and kidney are solid organs and are commonly investigated during the ante mortem phase and have a good diagnostic yield. The other tissues such as muscle, skin, lung, and GIT yield mostly tissues with non-specific findings, and brain tissue gets autolyzed if not fixed rapidly yielding non-specific findings. Primary constrain with needle autopsy is high false negativity rate particularly when the lesion is localised. This may lead to sampling error of both the target organ and the target lesion. In such cases, open autopsy or guided needle autopsy is more fruitful.

There will always be a possibility of missed vital pathologies with single organ needle biopsy which has similar connotations as in ante-mortem biopsies. Focal lesion/mass lesion can be identified by clinical and radiological examination during life Those lesions can be targeted during post mortem based on the antemortem imaging.

The cases with diffuse pathology have a lower chance of being missed on needle biopsy. Post-mortem biopsy was performed from a single site mostly for diffuse pathologies in the present study. Therefore we suggest performing multiple site biopsies in case of focal lesions to improve the diagnostic accuracy.

Smaller studies in various adult populations have shown successful biopsy rates of 98-100% for the liver, 76-94% for the lungs, 50-100% for the heart and 10-80% for the kidneys [3,4,10].

We found the diagnostic yield, highest in liver (89.2%) followed by the kidney (69.2%) and lung (50%). Biopsies from bone marrow, heart, colon, stomach, muscle, skin, and lip in the present study were very small in number, and the majority of them showed unremarkable morphology. Being a tertiary care center and dealing with severe, complex cases, most of the pathologies may involve liver and kidney. Some of the departments follow the protocol of doing postmortem biopsies from organs such as liver, lung, kidney and spleen, therefore, we are getting post mortem biopsies from lung, liver, kidney, brain, and spleen. Most of the organs are uninvolved, and pathology will be limited to the Liver and Kidney only.

Most successful post-mortem needle biopsy studies in newborns were from the liver (92%) and lung (84%), due to their superficial location, as studied by Garg S et al., [11]. A comparative study between minimal invasive autopsy and conventional autopsy in 44 fetal and neonatal cases showed most successful post-mortem needle biopsy was from the lung (86%) and liver (76%) [12]. We had 163 patients of the paediatric age group (age range <1 to 18 years) out of which 11 were infants (2.5%). Diagnostic yield was high in liver (89.2%) and kidney (61.2%).

The diagnosis offered on needle autopsy may not be the sole cause of death but may be helpful in the assessing diseases commonly affecting the visceral organs (lung, kidney, liver, etc,). Reported success rates to obtain tissue vary widely depending on the organ involved. This study shows that needle biopsies of the liver and kidney obtained in post-mortem patients are more diagnostic than other organ biopsies such as lung, spleen, and brain [13, 14].

This will serve as upper hand for histopathological, microbiological, immunological and molecular studies. Conceiving the idea that relatives often refuse to give consent for post mortem investigation, mainly because of the mutilation due to conventional autopsy, Van der Linden A et al., did a prospective study by performing a Minimally Invasive Autopsy (MIA) in 24 cases. They measured tissue quality for molecular studies and found MIA samples showed better RNA quality than conventional autopsy samples, probably due to the shorter post-mortem interval. This will again solidify our hypothesis of performing needle autopsy in institutes where a conventional autopsy has not done for better patient care in the future [15].

Twenty three (23) biopsies were found where post-mortem needle biopsy played a significant role. Four cases showed discrepancy with had clinical diagnosis, and 19 biopsies surprise diagnosis, some of which if diagnosed in antemortem, could have been treated antemortem.

Many studies were done in the past reflecting the disparity between clinical and autopsy diagnosis where the patient would potentially have survived if the clinical diagnosis had been correct. Shojania KG et al., conducted a systematic literature search from 1966 to 2002 and identified 45 studies reporting 53 distinct autopsy series meeting prospectively defined criteria. The median discrepancy rates were 23.5% (range, 4.1%-49.8%). All these studies performed complete clinical autopsies to establish autopsy diagnoses [16]. Bansal MG et al., prospectively studied the correlation between clinical diagnosis and needle autopsy diagnosis despite conventional autopsy in 50 cases from the emergency department with a discrepancy rate of 32% [17].

In our study, needle autopsy was done in place of a complete autopsy, and the discrepancy for major errors noted was just 6.3% as opposed to other studies where error varied between 10-60% [Table/Fig-7] [8,11,17-21]. Being a super-specialty institute, skilled staff, experienced clinicians and integrated approach towards diagnosis may account for the low rate of major diagnostic discrepancies.

Author	Year	Number of patients	Type of Autopsy	Discrepancy (%)	Group of patients
Goldman L et al. [8]	1983	300	Open, Invasive	10.3	All
Mercer J et al., [18]	1985	400	Open, Invasive	13	Adults
Battle RM et al., [19]	1987	2067	Open, Invasive	13.2	All
Shanks JH et al., [20]	1990	213	Open, Invasive	20.6	Perioperative deaths
Bernicker EH et al., [21]	1993	152	Open, Invasive	10	Medical Patients
Garg S et al., [11]	2009	25	Needle autopsy, Minimally Invasive	60	Neonates
Bansal MG et al., [17]	2015	50	Needle autopsy, Minimally Invasive	32	Emergency patients
Present Study	2017	334	Needle autopsy, Minimally Invasive	6.3	All

[Table/Fig-7]: Cases where the patient would potentially have survived if the clinical diagnosis had been correct [8,11,17-21].

Many known lesions are diagnosed in conventional autopsy which is essential for learning but not for usual pathological diagnosis. In some cases ante-mortem biopsies are not a routine procedure such as acute hepatitis, alcoholic hepatitis, etc., however the post-mortem biopsies available in these cases form an important source of learning for pathology residents [22].

LIMITATION

- It is a retrospective study, therefore adherence to hospital records and biopsy records of patients.
- Being a super specialty tertiary care center, we deal with severe and complicated cases, so may not reflect the deaths in other hospitals in India.
- No comparison was done between needle autopsy and conventional autopsy.
- Not having fixed protocol for post-mortem biopsies.

CONCLUSION

Post-Mortem needle biopsy is an important tool to reach at a diagnosis and determine cause of death where conventional autopsy is a limitation. The diagnostic yield and diagnostic accuracy of post-mortem needle biopsies were 79.4% and 93.2% respectively; in the present study. Surprise diagnosis was seen in 5.4% cases where either there was no diagnosis ante-mortem or the diagnosis changed post-mortem. The idea behind this study was to audit our post-mortem needle biopsy sampling to evaluate its utility.

It improves the decision making in future cases and lends a cause of death, thereby improving quality of patient care and teaching.

Future recommendation: We suggest the practice of post-mortem needle biopsies to be practiced in places where conventional autopsy is a limitation. Radiologically guided needle biopsies may further reduce inadequacy rates.

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