



HISTOPATHOLOGICAL STUDY OF LUNG LESIONS IN AUTOPSY CASES.

Pathology

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ABSTRACT

We conducted prospective, descriptive type of study in 300 consecutive autopsy cases over a span of two years. Out of 300 autopsy cases, lung lesions were encountered in 270 cases, benign lesions outnumbered malignant lesions. Pulmonary oedema was the most frequently encountered lesion followed by alveolar hemorrhage both of which usually represent the terminal end stage disease. Infectious causes like pneumonia and tuberculosis were the next culprits. Tuberculosis is a notorious infection not only in Indian community, but also worldwide. It is especially important due to its association with AIDS. Rare cases of disseminated infection with Cryptococcosis, candidiasis, microfilaremia as well as sickle cell disease can be a cause of death.

KEYWORDS

Autopsy, Pulmonary oedema, alveolar hemorrhage. Pg2

INTRODUCTION

Lung lesions form an important cause of morbidity as well as mortality. The lungs are vulnerable to a wide range of inflammatory, hemodynamic, neoplastic and other lesions.¹ Although lung cancer heads among the list of mortality worldwide accounting for 19.3% with similar increased incidence in India (9.3%), chronic lung diseases fare far more in morbidity.^{2,3} Also lungs are almost always involved secondarily by terminal events of cardiovascular diseases.⁴ A goal directed autopsy remains a vital component and hence this present study was undertaken for the study and evaluation of various lung diseases.

MATERIALS AND METHODS

In this study, lung specimens from 300 autopsy cases were studied over a period of 2 years from August 2014 to July 2016. An autopsy is performed in deaths that may have medical and legal issues. Autopsies done in our institution include cases of road / railway accidents, burns, drowning and poisoning. We also receive formalin preserved viscera from medicolegal cases of prison death and viscera from Primary Health Centers of nearby places. The specimens received in pieces or in toto were fixed in 10% formalin. Gross examination included recording of weight, assessment of the size, color change and texture. Photography of lesions were taken. Multiple longitudinal cuts were made to ensure maximum exposure and fixation. Microscopic study was done from representative tissue bits.

Routine tissue processing technique was done and paraffin blocks were prepared. Tissue sections of 3-5 microns thickness were cut. These sections were stained with routine Hematoxylin & Eosin stains. Special stains viz. (Z-N, PAS, and GMNS) were employed whenever needed. The stained sections were mounted with cover slips using DPX. The slides thus prepared, were studied under light microscope and diagnosis was rendered correlating the gross & microscopic findings.

RESULTS:

A total number of 312 lung specimens were received in our department. In 12 cases, lung was completely autolysed hence were excluded. Observations were tabulated according to the patient age, sex and pathological lesions. Out of 300 cases studied, lung lesions were noted in 270 cases. Distributions of various lesions encountered were tabulated accordingly (table1). Distribution of lesions according to age (table2) and gender was depicted. Wide age ranges from newborn up to 83 years was observed. However, maximum number of cases (85 cases) belonged to young adults within the age range of 21 to 30 years. Number of males affected was much higher than females; yielding a male: female ratio of 1.4:1. 130 cases of pulmonary oedema comprising 48.14% and 111 cases of intra-alveolar haemorrhage

comprising 41.1% ranked amongst the various benign pathological lesions.

Pneumonia constituted the second major benign lesion comprising 33.7%. Incidence of interstitial pneumonia and bronchopneumonia was higher as depicted in the pie-chart (fig.1). Bacterial pneumonia has two patterns: lobular bronchopneumonia and lobar pneumonia.⁵ Microscopically bronchioles and peribronchiolar alveoli are filled with inflammatory exudate as was seen in our case.

Emboic episodes were next common findings noted in 18 cases comprising 6.6%. Pulmonary embolism is a complication principally in patients who are suffering from cardiac disease or cancer, or who are immobilized, those with hip fracture being at highest risk. Hypercoagulable states, either primary or secondary are frequent risk factors. Indwelling central venous lines can be a nidus for right atrial thrombus.⁶ Grossly lung pieces appeared unremarkable however microscopic evidence of marrow embolism with fat and haemopoietic tissue was found (fig2). We also found one case each, of amniotic embolism and air embolism.

Incidence of Chronic venous congestion (CVC) was 4.81 %.

Tuberculosis is a systemic disease caused by Mycobacterium tuberculosis (M. Tb).^{6,7} The organisms are usually found extracellularly within the debris of the necrotic granulomas. Typical from atypical mycobacterium cannot be distinguished on the basis of their microscopic appearance. Acid fast stain brings out typical organisms. However, for definitive differentiation culture and/or polymerase chain reaction is necessary.^{6,7} We found military tubercles in lung showing epithelioid granulomas with central caseation, Langhan's type of giant cell, surrounded by mantle of lymphocytes.

Aspiration as well as aspiration pneumonia can lead to choking syndrome. Two cases of aspiration of vegetable matter were found. One case had a history of alcoholism, aspiration of gastric contents could be the culprit in this case. Other case was a 16-year-old male with history of breathlessness. Microscopic examination showed plugging of bronchioles with vegetable matter (fig3).

Fetal distress initiates vigorous respiratory movement leading to aspiration of amniotic fluid containing vernix caseosa, epithelial cells, meconium and blood which blocks small airways. Pathogenic bacteria may accompany and pneumonitis may ensue.⁸ One case of aspiration pneumonitis was found in a newborn female baby and other was 12 hours old female. Grossly, lungs were unremarkable in both cases. Microscopically, alveoli were filled with squames, keratin, few neutrophils and macrophages. Single case of acute respiratory distress

was found in a 25-year-old female with 8 months pregnancy and history of breathlessness. Microscopically, there was evidence of hyaline membrane disease, with accumulation of neutrophils, macrophages and red blood cells.

Pulmonary hypertension was seen in four cases (1.48%). Histologic findings of arterial intimal fibrosis and medial thickness with arteriolar occlusion leading to onion skin appearance⁹ as was seen in our case.

Emphysema was seen in 3 cases (1.1%). Emphysema is defined as an abnormal permanent enlargement of airspaces distal to terminal bronchioles with destruction of alveolar walls without obvious fibrosis.⁸ Gross appreciation of bullae is better than microscopic evidence. We appreciated distended multiple tiny bullae on the surface of lower lobe (fig4). Microscopically, abnormally large alveoli were seen separated by thin septae which appear to be floating or protrude blindly into alveolar spaces.

Other rare lesions encountered were single cases of disseminated cryptococcosis, disseminated microfilaremia, and disseminated candidiasis.

Cryptococcal infection was observed as opportunistic infection in a 42-year-old male, a known case of HIV infection with abdominal and CNS Tuberculosis. Microscopically disseminated cryptococcal infection involving lung, liver, spleen & kidney was found.

We encountered an interesting autopsy case of disseminated microfilaremia in a 30-year-old unknown male with no clinical details. Grossly, the organs were unremarkable. Microscopically, there was extensive tissue damage with eosinophils, micro abscess and fibrin-rich inflammatory exudate in the lung, heart, liver, spleen & kidneys with the presence of microfilariae (fig5).

Another case of disseminated infection – candidiasis was seen in 21 years PNC female who died with postpartum hemorrhage. The alveoli were studded with yeast and pseudo-hyphae morphologically consistent with candidiasis.

Lung cancer remains one of the leading causes of cancer mortality worldwide.^{10,11} Literature study has stated a strong association between lung cancer and cigarette smoking. 80 to 85% of cancer mortality is directly attributable to smoking.¹²

In our study no, primary lung cancer was seen. All cases were secondary tumors (0.74%) with a known primary in one case and unknown primary in other. The case with unknown primary was a 60-year male with mucinous adenocarcinoma in pleura. Grossly, the pleural surface showed multiple tiny irregular nodules, largest measuring 3x2x0.5cm. Histologic examination showed mucinous adenocarcinoma. The other case was a known case of carcinoma ovary in a young 15-year-old female. We found metastatic mixed germ cell tumor in lungs. Grossly, cut section of both lungs showed hemorrhagic dark brown appearance. Microscopically, metastatic mixed germ cell tumor (Yolk sac tumor +Choriocarcinoma) involving both lungs showing tumor cells arranged in microcystic, glandular and papillary pattern. At places, syncytiotrophoblastic and cytotrophoblastic cells were seen arranged in biphasic plexiform pattern (fig6).

Two cases (0.74%) of Coal workers' pneumoconiosis (CWP) were found. Coal being an important global commodity, mining of coal is important. Despite improvements in exposure assessment, ventilation controls and the existence of protective government regulations, coal miners are still at risk for respiratory diseases and their associated morbidity and mortality.¹³ Microscopically, there was presence of carbon laden macrophages, forming macules. BOOP is a chronic lung disease. Patients present with respiratory distress.^{6,14} Chronic inflammatory cells and plugs of loose, matrix rich connective tissue (Masson bodies) are distributed throughout the terminal bronchi, bronchioles, alveolar ducts and alveolar spaces.¹⁴ Alveoli show foamy cells, inflammatory cells and cellular debris.

Sickling of red blood cells was evident in one case. A young 25-year-old female, G4P3L2A1 with 32-33 weeks' pregnancy induced hypertension and pre-eclampsia had HELLP syndrome with IUD with severely deranged liver function tests. She vaginally delivered a still

born female baby & died the very next day. Grossly, cut surface of lungs was dark brown to black. Microscopically, blood vessels of all organs revealed sickled RBCs (fig7).

DISCUSSION

Out of 300 cases studied, lesions were noted in 270 (90%) cases, our findings are comparable with study of Selvambigai G. et al¹⁵ Hanmante R.D et al,¹⁶ Kalpana Mangal et al.¹⁷ (table no.3) Male preponderance was noted. Male affection was 58.33% while female affection was 41.67%.

In our study, the most common histopathological lesion found was pulmonary edema, which is similar to the study by Hanmante R D et al¹⁶, Uday Shankar et al¹⁸ and Soeiro AM et al¹⁹

Amongst the Infectious diseases, pneumonia headed the list and accounted for 30.33% which is similar to the findings of UdayShankar et al.¹⁸ The relative higher frequency of pneumonia cases in our setup might be due lack of knowledge or ignorance. were affected by pneumonia.

It is estimated that 10% of the cases of symptomatic pulmonary thromboembolism (PTE) will result in death within the first hour after the onset of symptoms. Patients who do not succumb during the acute phase usually present nonspecific symptoms.²⁰ In our study incidence of pulmonary thromboembolism is 4.6%. Hanmante et al (2014)¹⁶ found incidence of 2.5%. Bone-marrow embolism may occur during convulsions which impart shock to the skeleton or may follow bone fracture dislodging fragments of haemopoietic tissue into the veins by the increased pressure.²¹

Bone-marrow embolism was seen in 3 cases (1%). In one of the case, deceased was 65-year-old male, who died immediately after knee joint replacement. Schenken and Coleman²² stating similar case postulated that, fragments of marrow are forced into the veins mechanically by the wooden bone screws. In our case it is tempting to accuse similar theory.^{21,22} Amniotic fluid embolism usually present as sudden, unexpected maternal death that may occur during labour or postpartum period.²³ In present study, one case of amniotic fluid embolism was found in a postpartum death of a 30-year-old female.

Incidence of chronic venous congestion was 4.3%. These findings are close to findings of Shweta et al.²⁴

Tuberculosis is a treatable disease; its fatality is attributed to its association with HIV infection cases. Prateek Rastogi et al²⁵ found that tuberculosis was the single most important cause of sudden unexpected death involving the respiratory system. Tuberculosis of lung was seen in 3% cases in our study which is similar with Selvam et al²⁶ Soeiro AM et al¹⁹ and Bal MS et al.²⁷ With HIV infection on the rise, a high suspicion of concurrent multiple opportunistic infections should be kept in mind.^{28,29}

We came across a case of disseminated cryptococcosis in a 42-year-old male, a known case of HIV with abdominal and CNS Tuberculosis. Microscopic examination of CSF or India ink preparation highlights the organism. A definitive diagnosis is made on culture. Cryptococcal antigen assay is helpful.²⁹ Prognosis is grave without treatment, as was observed in our case.

W. bancrofti is a nematode causing lymphatic filariasis though tropics and subtropics. The adult worm inhabits the lymphatics and produces lymphangitis and lymphadenitis, & the female produces sheathed microfilariae which circulate in the peripheral blood. Unlike lymphatic disease syndromes, the extra lymphatic manifestations of Bancroftian filariasis are not caused by the adult worm per se, but by diffusible products or by immune complexes.³⁰ In our case, the extensive inflammatory responses due to disseminated microfilarial infection may have resulted in toxemia which together with pulmonary thromboembolism could have led to demise. Kirti Gupta et al³⁰ reported a similar case of disseminated microfilaremia.

Candida species are important opportunistic pathogens that can invade the vascular space giving rise to disseminated candidiasis in kidneys, liver, spleen, retina and occasionally the heart and brain.³¹ We found a similar case of disseminated candidiasis involving lungs, heart and spleen.

Four cases of pulmonary hypertension were observed.

Two cases of aspiration of vegetable matter were found. One case was 43 years old male with history of alcoholism. Other case was 16-year-old male with history of breathlessness.

Amongst the malignant lesions, surprisingly we found no primary lung tumor, rather we met with two metastatic tumors. One was case of metastatic mixed germ cell tumor (choriocarcinoma + yolk sac tumor) Yet al³² reported fifteen patients of metastatic ovarian germ cell tumor (MOGCT) with lung metastasis. The other was metastatic mucinous adenocarcinoma of pleura with unknown primary. et al³³ encountered a male patient with pulmonary mucinous carcinoma with a known rectal cancer.

Sickle cell disease is characterized by recurrent episodes of ischemic reperfusion injury to multiple vital organ systems & a chronic hemolytic anemia. Vaso-occlusive crisis occurs due to obstruction of microcirculation by sickled RBCs. The death in sickle cell disease occurs due to acute chest syndrome, sickle cell crisis, chronic organ damage, painful & splenic sequestration crisis & bone marrow embolism.³⁴In our case sickle cell crisis was noted.

Manish B. Shrigiriwar et al³⁴ stated importance of considering sickle cell disease as cause of death in cases with no apparent cause especially in highly prevalent areas.

In our study, we came across a single of BOOP.

Take home message: Lung is seat of various benign as well as malignant lesions and is secondarily involved invariably as terminal event. Hence, autopsy study is a bliss in revealing undetected as well as rare causes of death.

Tables

Table no.1. Showing incidence of various pathological lesions in lung.

Sr no	Type of lesion	No. of cases	Percentage%
1	Pulmonary oedema	130	48.14
2	Alveolar hemorrhage	111	41.1
3	Pneumonia		
	Interstitial pneumonia		
	Bronchopneumonia		
	Lobar pneumonia		
	Organizing pneumonia		
	Total	91	33.7
4	Embolism		
	Thromboembolism		
	Bone marrow embolism		
	Amniotic fluid embolism		
	Total	18	6.6
5	CVC lung	13	4.81
6	Tuberculosis lung	9	3.3
7	Pulmonary Hypertension	4	1.48
8	Emphysema	3	1.1
9	Diffuse alveolar damage	3	1.1
10	Disseminated infections	3	1.1
11	Aspiration of vegetable matter 2		0.74
12	Aspiration pneumonitis	2	0.74
13	Malignancy	2	0.74
14	Coal worker's pneumoconiosis	2	0.74
15	BOOP	1	0.37
16	Sickle cell RBCs	1	0.37

Table no.2 Distribution of lung lesions according to age

Lesion	0-9yrs	10-19	20-29	30-39	40-49	50-59	>60yrs	total
Pulmonary oedema	5	6	32	33	25	10	19	133
Alveolar hemorrhage	6	14	26	32	20	8	5	111
Pneumonia	5	7	30	16	15	8	10	91
Embolism	0	1	4	4	5	1	3	18

Chronic venous congestion	1	1	1	4	2	2	2	13
Tuberculosis	0	0	2	1	4	2	0	9
Malignant lesions	0	1	0	0	0	1	0	2
Normal	0	1	10	7	0	6	6	30

Table 3 Comparison of distribution of lung lesions in autopsy cases

Study group	Total cases	Lung lesions present	Lung lesions absent
Shweta et al (2016) ⁶¹	150	138(92%)	12(8%)
Hanmante et al (2014) ³⁴	120	110(91.7%)	10(8.3%)
Tariq Tahir et al (2013) ⁵⁹	810	648(80%)	162(20%)
Present study	300	270(90%)	30(10%)

Figures

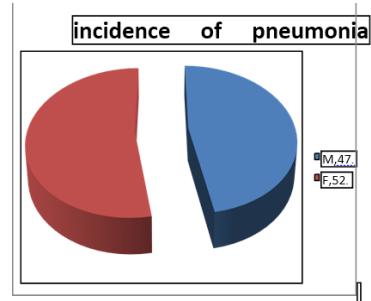


Fig 1.

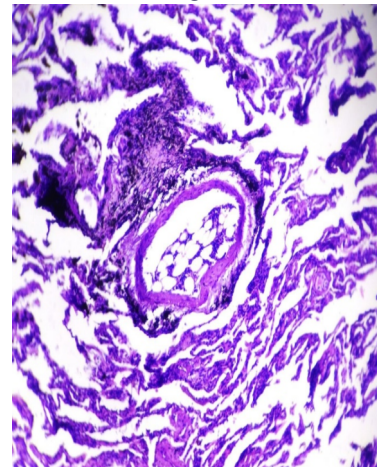


Fig 2

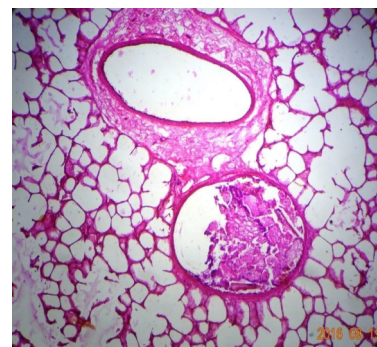


Fig 3



Fig 4

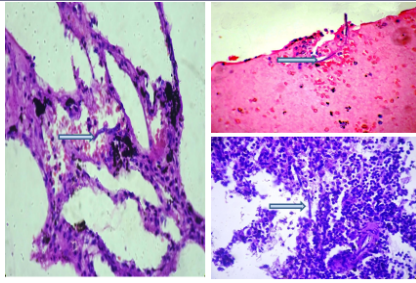


Fig 5

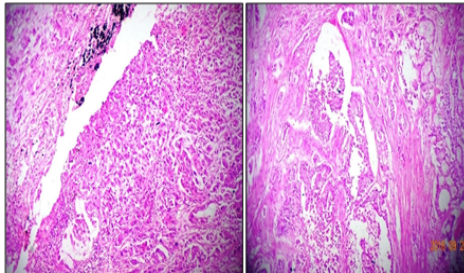


Fig 5

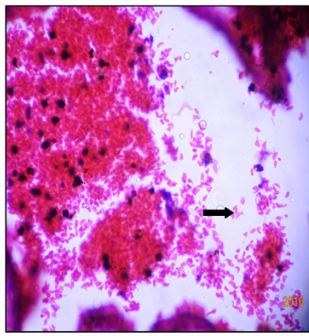


Fig 6

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