Annals of R.S.C.B., ISSN: 1583-6258, Vol. 25, Issue 4, 2021, Pages. 18545-18561
Received 05 March 2021; Accepted 01 April 2021

Histo Pathological Study Of Malignant Tumours Of Lung-An Observational Study

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Abstract

TheCarcinoma of the lung is of varied variety based on histopathology. The precise identification of tumors is imperative to initiate specifictreatment under modern therapeutics measures. It is increasingly being recognized in India due to unabated smoking habits and urbanization. The present study includes all the malignant lesions of the lung,slides and blocks with histologically proven lung malignancy in the department of Pathologyin JJM Medical College Davangere. Cases were categorized based on new classification of lung tumoursas per WHO.In all25 malignant lesions of the lung was recorded, ofwhich 13(52%) were biopsies and 12 (48%) were lobectomy specimens. The most common was squamous cell carcinoma (40%)significantly correlated (p=0.001, odds 7.45) withmean age group of 59.52years. Most of the patients were in 6th decade, with male predominance. The common chief complaints presentedwere, cough with hemoptysis, chest pain and breathlessness, withsmoking as the most commonlyassociated risk factor.The other lesions encountered include,large cell carcinoma4(16%), adenocarcinoma2(8%), small cell carcinoma2(8%), carcinoid tumours14(%), unclassified tumours3(12%), pleuropulmonary blastoma1(4%) and metastatic tumours2(8%). Metastatic tumours were seen secondary to gestational choriocarcinoma; lung tumours are known for histologic heterogeneity and composed of different histological types and subtypes. Light microscopy examination is sufficient to diagnose lung cancer virtually in all cases, with a need for histochemical stains and immunohistochemistry.Limited histologic types weredifferentiated inpediatric tumours and small cell carcinoma of the lung.

Keywords: *Lung cancers; squamous cell carcinoma; smoking; large cell carcinoma.*

Introduction

Lung cancer is one of the most lethal cancers known to mankind, because of high incidence and grave prognosis of the disease[91, 92]. Lung cancer is increasingly becoming frequent in the past 60 years. The global incidence of lung cancer is increasing at the rate of (0.5%) per year[5, 10, 92]. With Indiancontext, the exact incidence of lung cancer is not known due mainly to lack of formal epidemiological data available across the country[2, 5, 11, 13, 21]. Majority of lung cancers at the time of presentation would have reached considerable size and about 60 per cent are incurable as a result of extensive local spread or distant metastasis.Overlapping signs and symptoms will vary with time and confuse with primary inflammatory process that commonly affect the lungs. Cancers of the lung are unfamiliar for producing paraneoplastic syndromes, which may be the presenting symptoms or first sign of recurrence[91],[92]. Lung cancer is more common in urban populationbecause of lifestyle and genetic complexity [91].In addition to immunohistochemistry, fluorescence bronchoscopy, bronchoscopic biopsy and cytological procedure like brush cytology, many other diagnostic procedures are used for the

detection of lungcancer at early stage *e.g.*, genetic markers and signatures. However, bronchioalveolar lavage will facilitate the early detection and diagnosis of lung diseases, yet histopathological study of resected specimens of lung would be gold standard not only for deferential diagnosis but also for classification of grading and management aspects of lung carcinoma[90]. In this proximity of the research intervention, the present study aims to correlate the gross and microscopic features of tumours of the lung and alsotocategorize them into different histological subtypes[10,15]

Methodology

Histopathological study of malignant tumours of the lung was undertaken at the Department of Pathology, JJMMedical College, Davangere. It includes all malignant lesions of the lung received during the study period from May 2004 to 2006, with diagnosis of primary malignant and metastatic tumours and slides and blocks prepared during 2000 to April 2004.The study material consisted of 25 lung tissue samples of histologically proven malignancy. It includes 12(48.0%) lobectomy specimens and 13 (52%) bronhcoscopic biopsy specimens.Inclusion and exclusioncriteria rulewas adopted for thestudy,inclusion criteria;both primary and metastatic tumours of the lungirrespective ofage group. Whereas, benign tumours, inflammatory lesions and biopsies which failed to show the different features of malignancywere excluded. The relevant data sets of clinical attributes were obtained from patient records (subjected to surgery and case review) which include age, sex, presenting symptoms, X-ray and CT findings*etc.*, The sample specimens were obtained from the patient subjected to naked eye examination for tumour involvement at the surgical resected line, including the resected end of bronchus, peribronchial and perivascular soft tissue and surface covering the tumour, such as pleura, thoracic wall or diaphragm and searched for resected lymph nodes. In case of biopsy, just morphological characteristics werecarefully recorded in separate sheet. The entire tissue was subjected for biopsy, although representative areas were selected from lobectomy specimens and fixed in 10 per cent formalin. Withdue procedure,4-6μ thick section was prepared and stained with hematoxylin and eosin stain. Where ever necessary, special stains like 'PAS' and mucicarmine was employed. All sections were subjected to detailed histopathologicalexaminationwith special reference mentioned in the Proforma (annexure) and all cases were categorized accordingly by using WHO criteria. The gross examinationwas done during the study process and documented inseparate annexure.Collected data was fed to the computer, compilation was done by using SPSS statistical software, binary logistic regression and multivariate analysis was employed to test the hypothetical results at greater accuracy.

Results

A total 1539 malignant lesions were screened anddiagnosed during the study process.Of which,25were malignant lung tumours constituting 1.62 per centof total malignancieswith Indian perspective. Among the malignant tumours, 13 (52%) were biopsies and 12 (48%) were lobectomy specimens (Table 1). In the present study, carcinoma of the lung was more common in males with mean age of 55 years with SD 0.96 years(IQR 61-70 years) females mean age 58 years with SD 0.21 IQR (51-60 years), and the incidence declined withmean age of 70 years. Of 25 (1.60%) cases diagnosed as malignant neoplasms, 17 (68.0%) were from males and remaining 8 (32%) were from females, with male preponderance. Male to female ratio was 2.1:1.The most common presenting symptom was cough with hemoptysis seen in 15 (60%) followed by chest pain in 9 (36%) cases. Tobacco smoking is the major etiological factor for lung cancer. Risk factors were correlated byusing binarylogistic regression.Asper the analysis,22 (88%) patients were found to be smokers and only 3 (12%)

Annals of R.S.C.B., ISSN: 1583-6258, Vol. 25, Issue 4, 2021, Pages. 18545-18561
Received 05 March 2021; Accepted 01 April 2021

patients were non-smokers.In Indian perspective, risk factors are significantlycorrelated toincrease occurrenceof disease.Of which17 (77.3%) were males and 5 (22.7%) were females who consumed tobacco in the form of inhalation (snuff).Among the smokers, 15 (68.2%) patients had history of smoking more than 20 years and remaining 7 (31.8%) had smoked up to 20 years. The frequency of daily smoking, the tendency to inhale, and the duration of smoking habits shows strong relation to the incidence of lung cancers (p=0.001, hazard risk 18.52 ; odds 5.68).

Table1: Showing lung samples distribution

Specimen	Number of cases	Percentage	P value
Biopsy	13	52	≤0.001
Lobectomy	12	48	≤0.000
Total	25	100	

Histopathological examination was done in accordance with standard operating protocol of WHO and ICMR to study the lung tumour squamous cell carcinoma, it is the most common type of carcinoma found in the irrespective of age group.Among 25 cases, 4 cases (16%, ODDS 1.91, p<0.01)were carcinoma and 3 cases (12%, odds 1.56,p<0.01) were undifferentiated carcinoma (p=0.001). Lung tumour squamous cell carcinoma is the most common type of malignancy, accounted 10 (40%, odds 2.36, p<0.01)casesfollowed by large cell neuroendocrine carcinoma 4 (16%, odds 1.91, p<0.01) cases and undifferentiated carcinoma was seen in 3 (12%, odds 1.56, p<0.01) cases respectively. While, adenocarcinoma, small cell carcinoma and metastatic tumour were seen in2(8%, 1.47, p<0.01) cases each. Carcinoid tumour and pleuropulmonary blastoma were seen in one (4%, odds 0.93, p>0.01) case each (Table 2)

Table 2: Showing histological types of lung tumours

Histological type	Number of cases	Odds	P-value
Squamous cell carcinoma	10 (40%)	2.36	≤0.001
Adenocarcinoma	2(8.0%)	1.56	≤0.001
Large cell neuroendocrine carcinoma	4(16.0%)	1.91	≤0.001
Carcinoid tumour	1(4.0%)		
Small cell carcinoma	2(8.0%)	1.02	≤0.001
Undifferentiated carcinoma	3(12.0%)	1.56	≤0.001
pleuropulmonary blastoma	1(4.0%)	0.93	≥0.001
Metastatic tumour	2(8.0%)	1.47	≥0.001
Total	25.0		

Squamous cell carcinoma

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In this study, most common type of malignant lesion was squamous cell carcinoma, seen in 10 (40%) cases. Lesions in 4 (40%) of them were seen in left upper lobe, 2 (20%) each in right upper, middle and left lower lobe.

Table 2: Showing location of squamous cell carcinoma

Site of lesion	Number of cases	odds	P-value
RUL	2(%)	<1	≤0.001
RML	2(%)	<	≥0.001
RLL	0(%)	-	≥
LUL	4(%)	3.6	≤0.001
LLL	2(%)	<1	≥0.001
Total	10		

Central location of the lesion was more common than peripheral. Of these 10 cases, 7 (70%) lesions were seen inside lung while remaining 3 (30%) lesions were seen in peripheral location , results RUL and LUL was found that statistically significant (p ≤0.001).

Table 3: Showing distribution of lesions in squamous cell carcinoma

Distribution	Number of cases	odds	P-value
Central	7 (70%)	2.38	≤0.001
Peripheral	3(30%)	1.99	≤0.001
Total	10		

On radiological evaluation of squamous cell carcinoma the size ranged from 6-10cms in 8(50%) cases and < 5cms in remaining 2 (20%) cases.Of these lesions, 7 (70%) were well localized and well delineated, and the remaining 3cases (30%) (Table 4) showed diffuse infiltration of lung parenchyma. Since two cases were exhibits the adjoining area with consolidation.

Table 4: Showing gross pattern of squamous cell carcinoma

Pattern	Number of cases	P-Value
Localized	7(30%)	≤0.001
Diffuse	3 (70%)	≤0.001
Total	10	

As per the study, the centrallesionswerelarger than the peripheral lesions. The central lesions varied from 7-10 cm while the peripheral lesions were 5-8cms. On gross examination of all 10 cases of squamous cell carcinoma, thebiopsy specimen was adequate with grey white in color. The X-ray of these lesions did notreveal any cavitating lesions attributing to central necrosis. Although, the squamous cell carcinoma was grouped based onextent of differentiation, it was moderately differentiated. In 9 cases the predominant cell type,the squamous cell carcinoma was poorly differentiated. Further, in 9 of the biopsy specimens pleomorphic cells were seen in sheets, along with areas of undifferentiated cells. These cells were large with vesicular nucleus and prominent nucleoli. Cytoplasm was abundant and pale, atypical mitoses 2-3/hpf was seen in 4 cases. Necrosis was observed in 7 cases and hemorrhagic area was seen in 5 cases. Intervening thin stroma showed inflammatory infiltrate. A solitary case of squamous cell carcinoma showed groups of clear cells, with centrally situated large nucleus, with abundant clear cytoplasm. In this case, mucicarmine was positive and PAS was negative and it was called as squamous cell carcinoma with clear

cell change. Other features noted were,abundant collagenized stroma in one case, whereas, other two cases showed arborizing capillaries and associated spindle cell component.In case of moderately differentiated squamous cell carcinoma**,** onlyOne case showed moderate differentiation where the tumour cells were distributed in groups and nests. The cells were large with round, vesicular pleomorphic nucleus, nucleoli were absent and occasional cells showed individual cell keratinization. Further histologic intervention corroboratedthe presence of small cell carcinoma.Results were statistically significant with age and gender with 8 (2 cases) per cent variation. Both were males in the age group of 40-60 years. Exposed cases had history of smoking for more than 20 years. Lesions were seen in middle lobe of right lung with central location, of which one was lobectomy and the other was biopsy specimen. On cut section the lobectomy specimen measured 15 x 13 x 8cm and was diffuse in distribution. Histologically both tumours showed small round to oval cells resembling lymphocytes, arranged in sheets and groups with very little intervening stroma. These cells have hyperchromatic nucleus, finely granular chromatin, inconspicuous nucleoli and scanty cytoplasm. Mitotic figures and individual cell necrosis were frequently seen. Squamous or glandular differentiation was not seen. In case of adenocarcinoma the malignant epithelial tumours with glandular differentiation or mucin production. In the present study 2 (8%) cases were diagnosed as adenocarcinoma. One case was well differentiated in 67 year old patient with the history of smoking. The specimenmeasuring 7.5 x 6 x 4.5cm was retrieved by lobectomy fromperiphery right lung upper lobe. Cut section showed poorly circumscribed grey yellow lesion; without any associated peripheral scarring or extension into the neibouring air spaces. Microscopically lesion showed glandular differentiation with formation of groups of acinar structure lined by columnar epithelium throwing at places into papillary infoldings. These epithelial cells have large, vesicular nucleus with prominent nucleoli and granular cytoplasm, a few cells showed clear cytoplasm indicating mucin production. Mitosis was occasionally seen. The glandular component is separated by wide area of fibrovascular stroma impregnated with anthrocotic pigments. Large areas of hemorrhage and necrosis were seen. Bronchioloalveolar junctions also revealed lesions. The other case in this study was papillary carcinoma lung diagnosed in 52 years old female who presented with chest pain and streaky hemoptysis. X-ray revealed homogenous opacity. A diffused tumour was seen in middle lobe of right lung. Cut section showed grey white firm mass measuring 4 x 3cms and there were 3 satellite nodules in adjoining parenchyma. Microscopically the tumour showed well delineated lesion consisting of well formed papillary fronds with thin fibrovascular core. These papillae were lined by classical overcrowded columnar to cuboidal epithelial cells with large ground glass nucleus. Mitosis was rare and psammoma bodies were not seen.Large cell carcinoma was confirmed with histopathology in 4 (16%) males cases aged between 50 and 65 years. Tumour size ranged from 6-15cms in diameter, 2 (50%) lesions were well localized and well delineated and remaining 2 (50%) was diffusedwith grey white surface.

Table 5: Distribution of gross pattern of large cell carcinoma

Site of lesion	Number of cases	Percentage	P-value
Localized	2	50	≤0.001
Diffuse	2	50	
Total	4	100	

Histologically large cell carcinomas were composed of solid nests of polygonal cells with vesicular nucleus. Prominent nucleoli, and moderate cytoplasm, cell borders were well defined and showed scanty fibrovascular stroma. Two (50%) of the 4 lesions showed

organoid nesting, rosette like and palisading patern suggesting neuroendocrine differentiation. Of the remaining 2 (50%) lesions one showed sheets of large cells arranged in syncytial pattern with intervening stroma showing scanty lymphocytic infiltration, at places giving comedo pattern, while the other showed synctyial pattern of growth with intervening area showing dense lymphocytic infiltration and was subtyped as lymphoepithelioma like carcinoma (Table 5). All 4 (100%) lesions showed high mitotic index. Areas of hemorrhage and necrosis were also seen.

Table 6: Showing histological feature of large cell carcinoma

Histological features	Large cell carcinoma	No. of Cases
Organoid, nesting rosette like	Prominent	2
Syncytial sheets	Prominent	2
Cell size	Larger	4
Nuclear cytoplasmic ratio	Decreased	4
Nuclear chromatin	Vesicular	4
Nucleoli	Prominent	4
Lymphocytic infiltrate	Prominent	1
A typical mitosis	Present	4

Carcinoid tumour

A solitary carcinoid tumour was diagnosed in 70 years old male who presented with loss of weight and hemoptysis. Patient was a known smoker. The lesion was central and localized in right middle lobe and measured 6 x 5 x 3cm. Cut surface was grey white and was divided by fibrous septa. Microscopically the tumour showed small round uniform cells with central nucleus having fine chromatin network and scanty cytoplasm. Mitotic features were not seen. These cells were arranged in nests, ribbons and broad sheets. Areas of necrosis were not seen.

Pleuropulmonary blastoma

A solitary case of pleuropulmonary blastoma was diagnosed in 40 days old female babywho presented with respiratory distress since birth, X-ray showed homogenous mass occupying whole of right middle lobe. On lobectomy the lesion measured 11 x 9 x 5cms, it was well delineated with grey white cut surface with focal areas of hemorrhage and necrosis. Microscopically the lesion showed sheets of undifferentiated round to oval short spindle shaped cells having vesicular nucleus with ill defined cytoplasmic borders. These cells were arranged in fascicles running in different directions with intervening capillaries. At places there are entrapped normal bronchial epithelial cells. Blasteomatous like areas were seen. Skeletal muscle or cartilagenous differentiation were not appreciated.

Unclassified tumours

Threelung tumourscases (12%) could not be categorized into any of the above studied categories. All 3 cases were males, agedbetween 45 to 68 years; all were smokers. They presented with the history of cough, hemoptysis and dyspnoea. Among them one was lobectomy and two were biopsy specimens.Right middle lobe was involved in lobectomy specimen, where as in biopsy specimens both right and left upper lobes were involved.The lobectomy specimen measured 16 x 7 x 5cm was diffuse in distribution, with grey white cut surface. Microscopically, lesion showed sheets and nests of tumour cells, while the other two biopsy specimens showed small aggregates of tumour cells (Fig 1 &2). These cells were

Annals of R.S.C.B., ISSN: 1583-6258, Vol. 25, Issue 4, 2021, Pages. 18545-18561
Received 05 March 2021; Accepted 01 April 2021

round to oval, small to large, having vesicular to hyperchromatic large nucleus and scanty to moderate pale cytoplasm. Lobectomy lesion showed high mitotic figures ranging from 3-4/hpf. Background showed hemorrhage and necrosis with inflammatory cells.

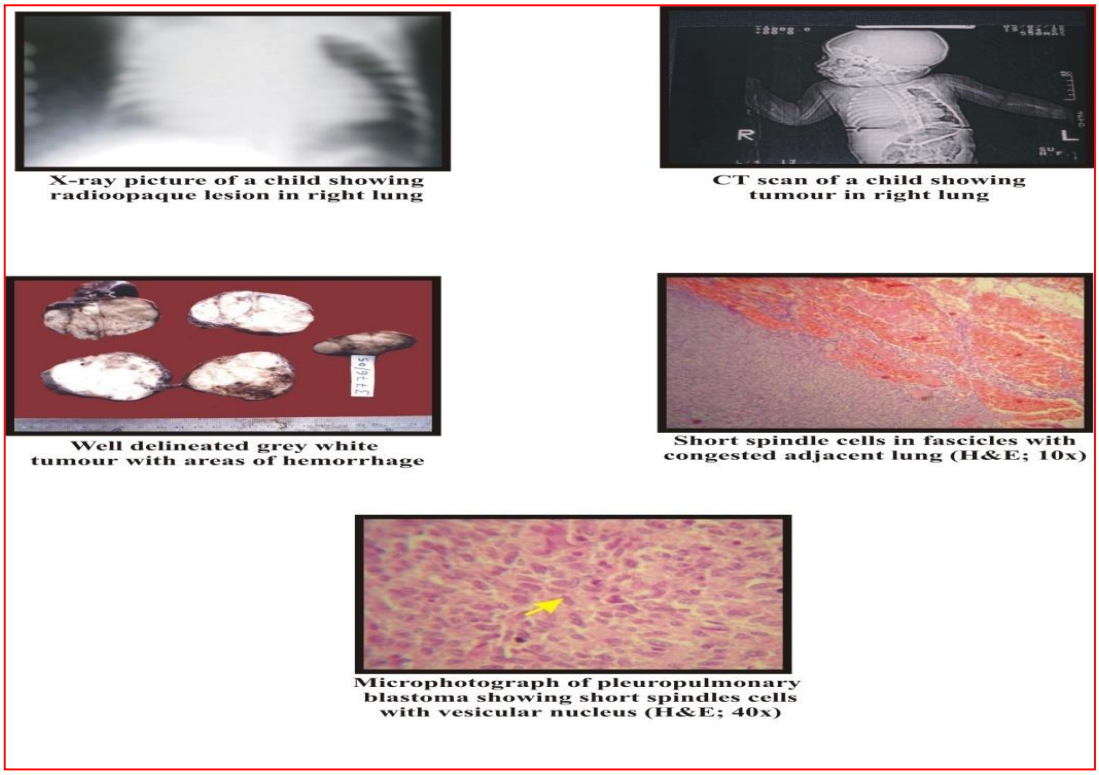

Fig 1: CT over view of tumour in right lung

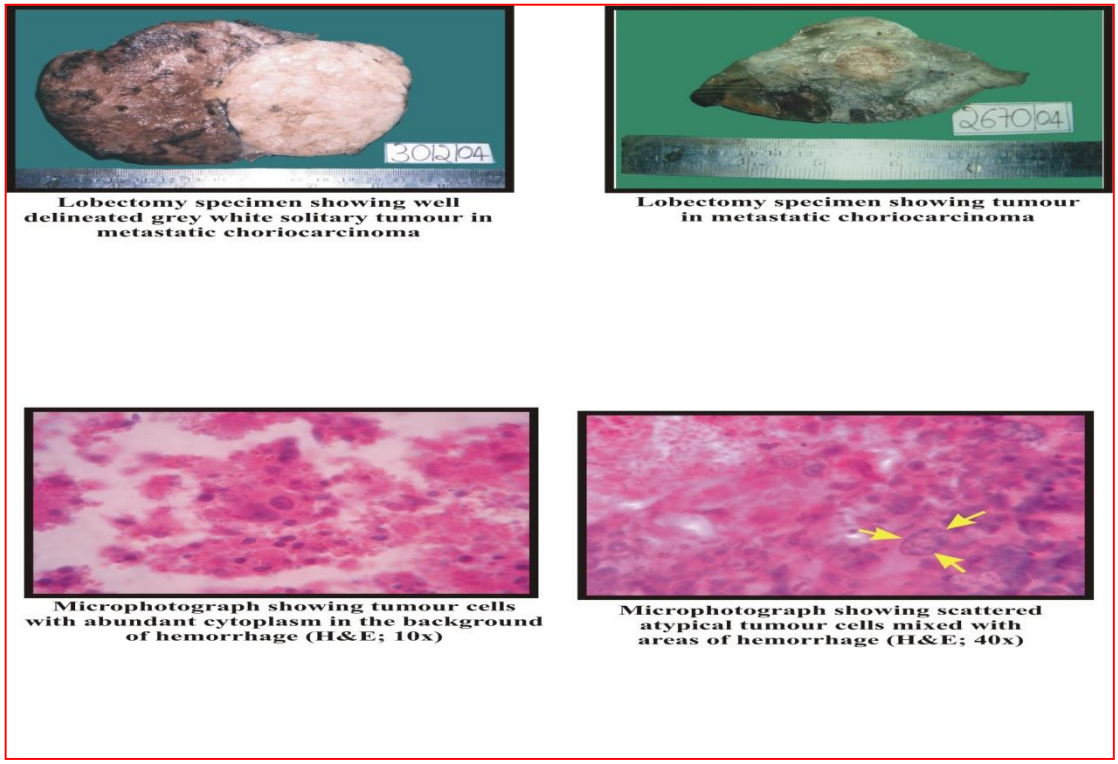

Fig 2: Morphological features of lung cancer

Annals of R.S.C.B., ISSN: 1583-6258, Vol. 25, Issue 4, 2021, Pages. 18545-18561
Received 05 March 2021; Accepted 01 April 2021

Metastatic choriocarcinoma

The most common malignant neoplasm of the lung is metastatic tumour. However in the present research intervention, only two metastatic tumours were encountered and both were diagnosed histologically as metastatic choriocarcinoma. Were young females, aged around 25-30 years, and presented with chest pain, streak of blood tinged sputum, loss of appetite and generalized weakness. There was history of bleeding per vagina on and off. One case presented with mass in cervix and liver with raised urinary HCG levels. Both were lobectomy specimens and presented as unilateral isolated lesions and grossly simulated primary lung lesions. In one case, tumour was seen in right lower lobe and in the other case tumour was seen in left upper lobe.On gross examination, one lesion measured 13 x 11 x 8cm and other measured 5 x 5 x 2cms. Cut surface of both these lesions showed grey white areas admixed with extensive areas of hemorrhage and necrosis. Surface was irregular in both the lesions. Microscopically both lesions showed groups and sheets of tumour cells with infiltrative growth into alveoli. These tumour cells were large and pleomorphic having vesicular nuclei and acidophilic cytoplasm. Many cells showed hyperchromatic bizarre nuclei resembling syncytial giant cells. Mitoses 1-2/hpf with atypical forms was seen.

Discussion

Lung cancer is one of the commonest malignant neoplasms all over the world. It is increasingly being recognized in India. In the present study too, it is peaking at an age group between 61-70 years. Of the 25 malignant lung tumours 17 (68%) were males and 8 (32%) were females with male to female ratio of 2.1:1 indicating male predominance[5,4,8,10].

Table showing comparison of age, sex and lung tumours

Authors	Total	Age (years)	Average	Male	Female	M:F
Narang RK et al[81]	58	18-70	51.3	52	6	8.7:1
Jindal SK et al[82]	150	51-60	-	127	23	5:1
Jindal SK et al[83]	336	51-60	53.3	282	54	5.2:1
Malhotra V et al[84]	70	51-60	-	62	8	7.7:1
Jindal SK et al[85]	1009	-	54.6	825	184	4.5:1
Arora VK et al[86]	100	40-60	-	82	18	4.5:1
Present study	25	61-70	65.5	17	8	2.1:1

Present study revealed that 5th to 6th decade is the common age group for carcinoma of the lung with male predominance[12,13,14]. This is in agreement with several researchers[21,22,26].However, Gupta *et al*. reported the lung carcinoma in 26 patients below the age of 35 years in which 17 were males and 9 were females. 16 out of 26 cases were non-smokers and the most frequent histological type was undifferentiated carcinoma[13,28,32,34,35]. 15 out of 26 cases had been incorrectly assessed at the time of first presentation, and were wrongly administered with antituberculosis drugs. Hence they advocated that, bronchogenic malignancy in young is not rare and should be suspected in patients with unusual pulmonary presentation.[87,88,93] However in the present study except a pediatric pleuropulmonary blastoma and metastatic choriocarcinoma, no primary malignant lung tumours were detected below the age of 40 years, indicating its rarity in younger age group. Majority of cancers of the lung are a consequence of smoking. Smokers to non-smokers ratio in our study was

7.3:1.Our finding of smoking to non-smoking ratio correlates well with other studies indicating smoking is an important contributory factor for lung carcinoma.In recent study by Gupta *et al* (80%) of men and (33%) of women among the patients were smokers compared to (60%) of men and (20%) of women among controls. The risk increases with both duration and frequency of smoking products.[45,47,52,88] 77.3 percent were male smokers while female constituted 22.7 per cent indicating similar prevalence.Clinical features; cough with hemoptysis was the most common presenting complaints seen in (60%) followed by chest pain in (36%).Other symptoms were weight loss, breathlessness and weakness. Similar findings were observed in other studies also. Symptoms such as fever, cough with expectoration, hemoptysis, weight loss and anorexia are common to both tuberculosis and lung cancer. Hence in India where tuberculosis is rampant it is not uncommon to find a lung cancer patient being treated for tuberculosis initially[75,7688,97,]. However in the present study no such incident is reported.Radiological and clinical findings suggested involvement of upper zone as a common site (44%) for carcinoma of lung followed by mid zone and lower zone. These findings are in agreement with Behera and Balamugesh.[54,65,6288]Squamous cell carcinoma of the lung is generally considered to be a tumour of central airways that frequently invades hilar structures and causes bronchial obstruction. Squamous cell carcinoma is a tumour of elderly age group usually seen above the age of 40 years, with male predominance. In our study in the age range of 61-70 years, with male to female ratio 1.5:7; 70 per cent of cases were located in central region and remaining 30 per cent in peripheral location indicating central predominance of the lesions[54,55,61,62,68]. Tomashefski *et al.* and Funai *et al.* have reported higher incidence of peripherally located lesions than in centre.[10,11,147,8] In this study squamous cell carcinoma of the lung was common in left lung (60%) with predominance of upper lobe involvement and majority of them were central in location.Tomashefski *et al.*in their study of 40 primary pulmonary carcinoma had found similar predominance of upper lobe involvement however in their study right lung was commonly involved with peripheral lesion and left lung was more commonly involved with central lesions.Peripheral location of squamous cell carcinoma is associated with improved survival and may be explained by smaller tumour size and lower prevalence of hilar node involvement[7,11,23,28,32,36,38]. However no survival correlation was deduced in our study.Histologically squamous cell carcinomas were categorized into well differentiated, moderately differentiated and poorly differentiated types depending on the differentiation of squamous cells in the lesions, which correlates with survival period.In the present study, poorly differentiated squamous cell carcinoma was the commonest type seen in 9 (90%) cases and remaining 1 (10%) case was diagnosed as moderately differentiated and no well differentiated squamous cell carcinoma were recorded.Funai *et al.*in their study of 204 cases, moderately differentiated squamous cell carcinoma was predominant type followed by poorly differentiated squamous cell carcinoma and well differentiated squamous cell carcinoma[7,8,25,33,36,37,38]. The variation in the present study may be attributed to late diagnosis of the lesions and smaller sample size. Microscopically the diagnosis of the malignancy was based on cell atypia and invasiveness and diagnosis of squamous cell type was on the detection of keratin/ intercellular bridges. Keratin formation may be seen in isolated cells or more commonly in the form of keratin pearls. Isolated necrotic cells should not be confused with keratinized cells. Whorl formation and definite stratification of tumour cells have been used by some as presumptive evidence of squamous differentiation in the absence of classical features, and according to WHO classification these tumours should be placed in undifferentiated large cell category[11,15,]. Such difficulties were encountered in 2 cases in this study; however they were included under unclassified category with added note of further evaluation by immunohistochemistry.A solitary case of squamous cell carcinoma showed group of clear cells with centrally situated large nucleus with abundant clear cytoplasm. In

this case mucicarmine was positive and PAS was negative and it was called as squamous cell carcinoma with clear cell change.Luise *et al.*in their study noted significance of presence of clear cells in all types of lung carcinoma except small cell carcinoma and (< 50%) of cases showed clear cell areas in squamous cell carcinoma. Among them around (50%) were positive for glycogen and remaining cases showed scattered mucicarmine positivity. They were unable to explain these differences in staining characters.[16 ,17,23,27,29,31]

Small cell carcinoma is a highly malignant tumour with distinct cell type. Small cell carcinomas have strong relationship to cigarette smoking. Only about 1per centoccurs in non-smokers. They are the most aggressive lung tumours.[10,11,17,27,32] In the present study there were two male cases of small cell carcinoma with mean age of 50.5 years. Constituting 8 per cent of the lung cancers both were smokers. Both tumours were central in location one lobectomy specimen was bulky. There were no clinical symptoms suggestive of paraneoplastic syndrome or symptoms of early dissemination of the tumours.Small cell carcinoma is known for intracranial metastasis. However, Hirsch *et al.*could not diagnose brain metastasis by CSF examination and opinioned that careful clinical examination by neurooncologist is of great value in the early detection of brain metastasis[21,44,56,65]. Clinicians should be aware of transformation of NSCLC to small cell carcinoma and this can occur any time during the treatment and accumulation of the pluripotent cells indicate the genetic alterations that help them to transform into different lineages without the signal from EGFR. (Histopathological transformation to small-cell lung carcinoma in non-small cell lung carcinoma tumors 2016). Sheikh *et al.*in their study observed male sex predominance, mean age was sixth to seventh decade and squamous cell carcinoma was the most common histopathological types in both the sexes and they had seen this type both in smokers as well as in non-smokers. (Histological Pattern of Primary Malignant Lung Tumours Diagnosed in a Tertiary Care Hospital: 10 Year Study 2010). Further, recent study by Radhakrishnan. s *et al.* undermined the need for diagnosis of histological subtype at the onset of clinical presentation of suspected cases of lung cancer and opined that therapeutic regimen is to be initiated at the earliest to increase the longevity of the patient. (Original Research Article Histopathological subtypes of lung cancer presented at a tertiary care cancer hospital in Kerala: a cross sectional study 2021). Histological features in our study were well correlated with other studies. Adenocarcinoma of the lung usually occurs peripherally in the upper lobes. They are common in younger age group and in women, in contrast to squamous cell carcinoma. In the present study there were two cases of adenocarcinoma,one was well differentiated adenocarcinoma which was seen in male patient aged 67 years old, while the other was papillary carcinoma seen in female patient of 52 years old. Both were peripherally located which correlates with other studies except the age and sex.Dacosta *et al.*encountered adenocarcinoma as the most frequent histological types. The distribution of the lesion was both central and peripheral in location with mean age of 50.24 years.[34,36,37,38,41,46]Large cell undifferentiated carcinoma is a diagnosis by default. They occur either centrally or peripherally. They grow rapidly and are usually large tumours at the time of diagnosis. In this study, four cases (16%) were large cell carcinoma located equally in location with mean age of 57.5 years. All were males and were smokers. Two lesions were bulky, other two were moderate in size. Microscopically there were monomorphous large undifferentiated cells with high mitotic index. Vast areas of hemorrhage and necrosis were seen. Ultrastructural study was not possible. However 3 of 4 lesions were showing features of neuroendocrine differentiation and remaining one showed syncytial sheets of large cells, intervened by abundant lymphocytes and was subtyped as lymphoepithelioma like carcinoma.Although large cell tumours are apparently monomorphous at light microscopic level ultrastructural examination by electron microscopy revealed three types of morphologic differentiation.

Such histological subtyping is necessary for tumour behaviour and responsiveness to therapy as well as patient prognosis.[39,49,51,52]

A solitary carcinoid tumour was encountered in our study constituting 4 per cent which was seen in male patient aged 70 years. Patient presented with cough, expectoration and dysponea. There were no symptoms of carcinoid syndrome. The tumour was located centrally in the right middle lobe and it showed all the classical histological features.Histological interpretation of bronchoscopic specimen of carcinoid may be difficult and misleading owing to crushing of the tissue during its removal and improper fixation. The nuclei becomes more homogeneous and hyperchromatic; such alterations leads to misinterpretation as undifferentiated carcinoma. In such cases Hira *et al.*opinioned that they should be surgically explored to diagnose carcinoid tumour.[89,90,91,92]

Pleuropulmonary blastoma was diagnosed in one case in present study, in a 40 days old baby who presented with respiratory distress. Tumour was seen in right middle lobe of lung. Microscopy showed sheets of short spindle shaped cells with vesicular nucleus and ill defined cytoplasmic borders. However the child was referred to higher centre along with resected specimen, where immunohistochemistry revealed features of congenital periobronchial myofibroblastic tumour. This case emphasized the importance of application of immunohistochemistry in certain lung tumours. Till now the baby is doing well.This stopathological study is based on light microscopic features only.

Unclassified tumours were encountered in 12 per cent of total malignant lung tumours. all were males and were smokers with median age of 56.5 years. Histologically features were not suggestive or correlated with any of the types described in WHO classification and were grouped as unclassified tumours. However there is no literature available describing these entities. Application of ultrastructural studies to this tumour would have helped them to classify into one of the known categories.

Lung is a very common sight of metastatic disease. Metastatic tumours were encountered in 8 per cent of the total malignant lung tumour in this study. Both were young females, who presented with history of chest pain, streak of blood tinged sputum, loss of appetite and weakness. Both were lobectomy specimens. One was seen in right lower lobe and other in left upper lobe. Histopathological features were suggestive of metastatic choriocarcinoma which showed presence of extensive necrosis with entangled cytotrophoblasitc and syncytiotrophoblastic cells. Following histological diagnosis, patients were advice for urinary HCG estimation which showed positivity in high titres in both these cases. One case had extensive metastasis into the liver and cervix and the patient died of respiratory complications in post operative period while the other patient was lost during follow-up. In both these cases diagnosis of metastatic choriocarcinoma was supported based on histological findings and the urinary HCG levels. Mazur *et al.*had encountered two similar cases of pulmonary metastasis of gestational choriocarcinoma but they were associated with low serum levels of β-subunit of HCG. Hence they felt that both immunohistochemistry and electron microscopy can be used as an additional supportive study in establishing the diagnosis of metastatic choriocarcinoma in difficult cases. Although it is known that HCG and HPL can be present at times in variety of other carcinoma, the combined presence of these two substance in tumours from patients with known gestation trophoblastic disease provides solid evidence that these are a form of choriocarcinoma.[77,82,86] However in our study histology itself was suggestive of metastatic choriocarcinoma and investigated for serum levels of HCG which showed very high levels.

Conclusion

Lung tumors are known for histologic heterogeneity and it was composed of many histological types and subtypes. Light microscopy is sufficient for the diagnosis of lung cancer virtually in all cases, with a need for histochemical stains or immunohistochemistry, in only a few histologic types, particularly in differentiating pediatric tumours and small cell carcinoma lung. Histologic evaluation for lung cancer diagnosis should be done at the early stage of disease applying in various procedures like brochoscopic or needle biopsies and surgical biopsy (thoracoscopy).

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Proforma

Type of surgical excision: Pneumectomy / Lobectomy / Bilobectomy / Segmentectomy / Wedge excision / biopsy / others

Location of tumour: Right lung / Left lung
a) RUL / RML / RLL b) LUL / LLL

Distribution of tumour- Central / Peripheral
Tumour size
Surface: Smooth/irregular/nodular/well circumscribed/poorly circumscribed/others
Cut section: Size

Colour

Circumscription

Cavitation

Hemorrhage and necrosis

Associated lesions: Fibrosis / atelectosis / consolidation
Local infiltration: Absent / Present

Microscopy

Tumour type: Squamous differentiation / glandular differentiation / neuroendocrine spindle cell type / giant cell type / bronchial gland type / other type.
Differentiation: Well / Moderately / Poorly differentiated
Histological grade: High grade / intermediate grade / low grade
Pattern: Diffuse / rosette / trabecular / nests / acinar / solid / papillary / sheets
Cell border: Distinct / indistinct / overlapping
Nuclear features:
Size : Small / medium / large

Shape : Round / oval / irregular / others

Atypia : Slight / moderate / high

Chromatia: Hyperchromatic / bland / optically clear / granular / vesicular /others.

Nucleoli : Absent / present, single / multiple

Nuclear membrane: Thin / thick / regular / irregular

Nuclear groove: Absent / present

Mitoses: Absent / present
Typical / atypical /HPF

Cytoplasm: Scanty / abundant / granular / pale / clear
Stroma: Scant / abundant
Inflammatory infiltrate: Absent / present
Necrosis: Absent / present – focal / extensive
Metaplastic change: Absent / present
Lymph node metastasis: Present / absent
Associated changes: fibrosis / aclectosis / pneumonic consolidation / hemorrhage / necrosis
Special stains employed
Histopathological diagnosis