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Research Article

CORRELATION BETWEEN CT SCAN FINDINGS, HISTOPATHOLOGY AND DEMOGRAPHIC VARIABLES ASSOCIATED WITH LUNG CARCINOMA

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ABSTRACT

Lung cancer is one of the commonest causes of cancer mortality worldwide. During our six months study period all the lung biopsy specimens acquired through CT guided needle biopsies were included. The mean age incidence in our study was 58 years with a male preponderance. Male: female ratio was calculated as 2.5:1. The incidence of adenocarcinoma was higher and squamous cell carcinoma was seen with higher stage. Females had higher percentage of metastatic involvement of the lung. CT findings correlated with histopathological findings in 75% [p value 0.0010] of the cases in our study. CT scan and histopathology are complimentary in the diagnosis of lung tumors. However, histopathology is the gold standard in the diagnosis as it is used to advocate treatment based on the subtype. In case of uncertain histopathological findings or if there is discrepancy between CT scan findings and histopathological reports, repeat CT guided biopsies are advised.

INTRODUCTION

Lung cancer is the leading cause of morbidity and mortality with estimated new cases for the year 2016 are 224,390 and estimated deaths are158, 080 according to SEER study (WahbahM *et al*, 2007). Treatment of this dreaded tumor is based on the histopathological classification of the lung tumor – Small cell or Non-small cell carcinoma and among the Non-small cell carcinoma whether it is squamous cell carcinoma or adenocarcinoma. For small cell carcinoma the treatment is chemotherapy as the tumor is widely disseminated at the time of diagnosis, for localised Non-small cell squamous cell carcinoma the treatment is surgery and for advanced Non-small cell squamous cell carcinoma the treatment includes chemotherapy (Collins LG *et al*, 2007, Felip E *et al*, 2009). Among the Non-small cell tumors, if it is adenocarcinoma molecular tests like epidermal growth factor receptor [EGFR] and anaplastic lymphoma kinase [ALK] are advocated and if found positive the treatment includes targeted chemotherapeutic agents (Lindeman NI *et al*, 2013, MukhopadhyayS *et al*, 2012). Thus histopathological examination of the biopsies is the gold standard theranostic [Therapeutic and diagnostic] tool. Various demographics associated with lung cancer were analysed. The positive predictive value of CT in diagnosing lung cancer is said to be 100%. This study was done to correlate the CT findings of the suspected lung cancer patients with the histopathological examination of the core biopsy specimens.

MATERIALS AND METHODS

Inclusion criteria: CT guided biopsy specimens in suspected lung carcinoma patients were included.

Exclusion criteria*:* Lung biopsies acquired through other modalities

Other tumors

During our study period of six months from January 2016-June 2016 all the lung biopsy specimens acquired through CT guided needle biopsies were included. Eighteen gauge needles were used to acquire the specimen [Fig 1].

Age and sex was noted from the clinical data provided and their respective incidences were calculated. Received biopsy specimens were fixed in formalin and stained with haematoxylin and eosin and sections were studied.

Latest WHO recommendations for small biopsies were followed while reporting. The tumors were classified as small cell carcinoma [SCC] or Non-small cell carcinoma [NSCC]. If the tumor cell had neuroendocrine morphology it was classified as SCC [Fig 2]. Immunohistochemical markers like CD56 and TTF-1 were used in difficult cases.

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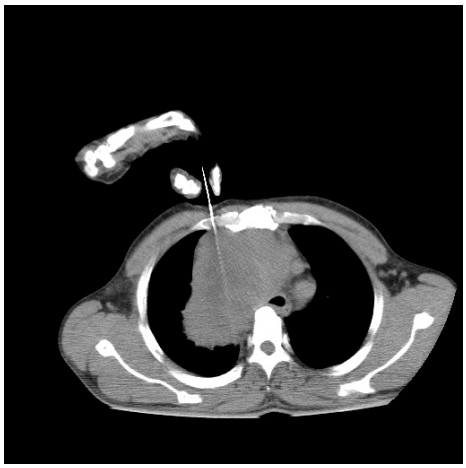

Fig 1 Shows needle biopsy being done on a suspected lung mass.

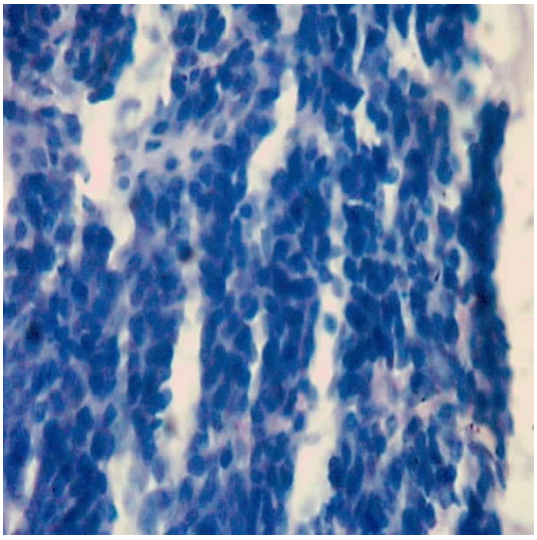

Fig 2 Shows tumor cells having scant cytoplasm, dispersed chromatin and exhibiting nuclear moulding- Small cell carcinoma [H&E, 40x]

In case of Non-small cell carcinoma further categorization of adenocarcinoma and squamous was made based on the morphology.

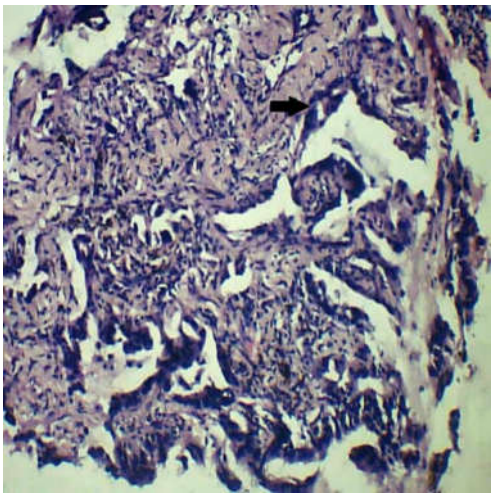

Fig 3 Shows tumor cells confined to the alveolar wall [Black arrow]- Lepidic predominant adenocarcinoma [H&E, 40x]

Adenocarcinoma was identified by the glandular pattern and further sub classified as Lepidic [formerly broncho alveolar] [Fig 3], acinar, papillary, solid and micropapillary. Individual cells having basophilic granular foamy to vacuolated cytoplasm, eccentrically placed nucleus and having macronucleoli was identified as adenocarcinoma cells. In difficult cases immunohistochemical stain NapsinA and TTF-1 were used to confirm the diagnosis (Moreira A *et al*, 2010, Jagirdar J *et al*, 2008).

Squamous cell carcinoma [SqCC] was identified by keratin, pearls and intercellular bridges [Fig 4]. In difficult cases, p40and cytokeratin were used to confirm squamous cell carcinoma (Pelosi G *et al*, 2012). If both histopathology and immunohistochemistry were inconclusive for adenocarcinoma and squamous carcinoma then it was classified as NSCC NOS and the possibility of adenosquamous carcinoma was considered.

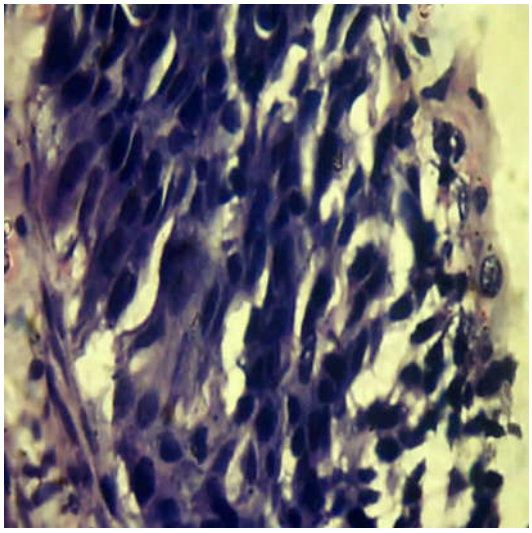

Fig 4 Shows non keratinised squamous cell carcinoma in which the cells exhibit hyperchromatic pleomorphic nuclei.

Incidence of various histopathological subtypes, correlation between age and sex with histopathological subtypes was done based on the histopathological reports.

CT scan was used to measure the mass and to locate the tumor. Along with that node involvement and metastasis was assessed using the CT scan. The provisional diagnosis given by the radiologists based on the CT findings were noted and correlation of CT findings with the histopathological study was done. Statistical significance of this correlation was calculated using Fischer's exact value and the two tailed p value was derived.

The tumor was staged based on TNM staging.T1a- Tumor is <2cm and not involving the main bronchus.T1b-Tumor is 2-3cm and not involving the main bronchus.T2a- Tumor is 3-5cm, involving the main bronchus2cm or more distal to the carina and the visceral pleura.T2b- Tumor is 5-7cm,involving the main bronchus 2cm or more distal to the carina and the visceral pleura.T3- Tumor is > 7 cm or directly invades any of the following: parietal pleura, chest wall (including superior sulcus tumors), diaphragm, phrenic nerve, mediastinal pleura, parietal pericardium or tumor in the main bronchus less than 2 cm distal to the carina.T4-Tumor of any size that invades any of the following: mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, esophagus, vertebral body, carina,

separate tumor nodules in a different ipsilateral lobe.Distribution of various histopathological subtypes along various TNM stages of the disease was tabulated.

RESULTS

Forty lung biopsy specimens were received. All forty cases were suspected as carcinoma based on the clinical history and CT findings. On histopathological examination thirty out of forty specimens received were malignant. Out of the remaining ten, one was diagnosed as having tuberculosis, one had aspergillous infection and the rest had nonspecific pneumonitis [Table 1].

Table1 CT diagnosed cases and Histopathological diagnosis of the received biopsy specimens

CT diagnosed malignant cases	Histopathologically diagnosed cases										
	Malignant								Non Malignant		
	Adenocarcinoma	Sq CC	NSCC NOS	Metastasis			Mesothelioma	SCC	TB	Aspergillous infection	Non-specific Penumonitis
				Melanoma	Follicular carcinoma	Sq CC cervix					
40	11	7	4	1	2	1	1	3	1	1	8

Most of the cases occurred around 70-80 years [Table2]. Mean age of occurrence in our study was 58 years. When male: female ratio was calculated, the ratio was 2.5:1.When age and sex was compared male: female ratio was equal among 61-70 years category.

Statistics

CT findings correlated with histopathological findings in 75% of the cases in our study [Table 1]. When the statistical significance of these two was assessed by Fisher exact test the two-tailed P value was 0.0010. This is statistically a significant value there by emphasizing the complimentary nature of these diagnostics.

Table 2 Age and sex distribution seen in the patients with malignant tumors of the lung

AGE IN YEARS	No of cases	Male	Female	SqCC	Adenocarcinoma	NSCC NOS	SCC	Mesothelioma	Metastasis	Infections
30-40	4	3	1	-	1	-	1	-	-	2
41-50	6	6	-	1	2	1	1	-	-	4
51-60	10	8	2	2	4	2	-	-	-	2
61-70	8	2	2	-	-	-	-	-	2	2
71-80	12	8	4	4	4	1	1	1	1	-
Total	40	29	11	7	11	4	3	1	4	10

Table 3 Correlation between the histological tumor type and sex in our study

Tumor	Male	Female
Adenocarcinoma	9	2
Squamous cell carcinoma	4	3
NSCC NOS	4	-
SCC	2	1
Mesothelioma	1	-
Metastasis	1	3

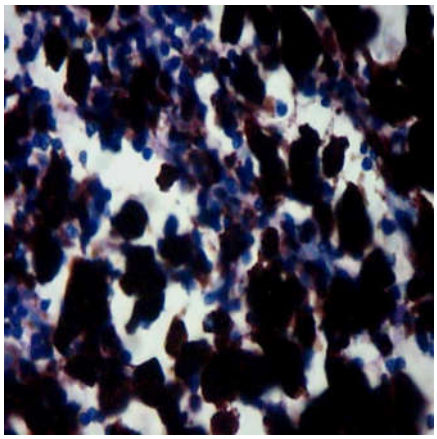

Fig 5 Shows melanoma cells exhibiting nuclear pleomorphism and atypia- Malignant melanoma deposits in the lung.

In our study, females had higher percentage of metastatic involvement of the lung [Table3]. Adenocarcinoma was seen more in male compared to females in our study. In the malignant tumor category, adenocarcinoma was the most common malignancy we had encountered [27.5%]. Squamous cell carcinoma contributed around 17.5% of all the tumors we had analysed. 10% of the cases were metastatic deposits. Two were from follicular carcinoma thyroid, one was malignant melanoma [Fig 5] and the other was from squamous cell carcinoma cervix [Table 1]. Right lung was most commonly affected than left and right apex was involved more among the right lung lesions [Table 4]. All the squamous cell carcinoma cases were seen involving the right lobe of the lung.

Table 4 Distribution of the malignant lung tumors in our study

Right	Left
Apical 13	
Upper 11	
Middle 9	
Hilum 1	
Lower 5	
Lower 1	

When staging of the tumor was analysed, most of the cases with squamous cell carcinoma was in stage T3. Adenocarcinoma cases were in stage T1b [Table 5].

DISCUSSION

Lung carcinoma is the commonest tumor seen in industrialised nations. Smoking is one of the predisposing factors for squamous cell carcinoma and small cell carcinoma (Morabia A *et al*, 1991). Loss of chromosome 3p and various tumor suppressor genes in the chromosome 3p region are seen in smoking associated lungcarcinoma (Girard L *et al*, 2000). Among non-smokers, adenocarcinoma associated with EGFR mutation, EML4-ALk fusion or amplification of c-MET are common and these markers have diagnostic and therapeutic implications. Clinical history, histological categorization,

Table 5 Stage wise distribution of the lung tumors in our study

Tumor	T1a <2cm	T1b 2-3cm	T2a 3-5cm	T2b 5-7cm	T3	T4	N0	N1	N2	N3	M0	M1a	M1b
SqCC	-	1	1	1	4	-	2	-	3	2	5	2	-
Adenocarcinoma	-	6	3	-	2	-	6	-	5	-	9	1	1
NSCC NOS	-	-	1	1	2	-	1	-	3	-	3	-	1
SCC	-	-	1	1	-	1	2	-	-	1	3	-	-
Mesothelioma	-	1	-	-	-	-	-	1	-	-	1	-	-

immunohistochemistry and molecular study are important in the diagnosis of lung carcinoma.

Age at which the tumor is diagnosed has an impact in survival. For every 10-year increase in age there was 30-40% increase in the mortality rate according to Tammenagi *et al*, 2004 and Toh *et al*, 2004. Adenocarcinoma associated with molecular abnormalities is seen in younger individuals where as other lung tumors are seen in older individuals. The age incidence of our study was compared with other studies seen in literature. Roy S *et al* in their study had stated that the mean age at which the lung cancer was diagnosed in their study group was 57.6 years which correlated with our study [58 years] (Roy S *et al*, 2015). In Noronha *et al*'s study the mean age group affected was 60.98 years in contrast to our study group (Noronha v *et al*, 2012). According to Das *et al*'s study (2015), the age incidence ranged from 35-80 years which correlated with our study.

The incidence of lung cancer in women has increased by 134%, whereas it has increased by only 57% in men which is contributed to the rising smoking habit among women according to Blot WJ *et al*, 2004. When age and sex were correlated in our study, women had this tumor around 60-80 years of age. But according to FergusonMK *et al* (1990) and OslenJH (1995) women were affected at comparatively lower age group compared to male. Gastrin releasing protein receptor [GRPR] gene, a bronchial epithelial cell proliferation stimulant is activated early in women who smokes and this is the reason for lower age incidence among women. Women with NSCLC had better survival rates than men according to Radzikowska E *et al*, 2002. In contrast to our study group [Male: Female 2.5:1] Male: female ratio was 4.2:1 in Roy S. *et al*'s study (2015). According to Das *et al*'s study, male to female ratio was 4.25:1which was higher when compared with our study (2015).

When histological type was correlated, there is an increase in the incidence of adenocarcinoma among the lung tumors according to Etzel CJ, *et al* (2006) which correlated with our study. The increase in the incidence of adenocarcinoma is due to improvement of diagnostic methods for detecting peripheral lesions, exposure to passive smoking, diet, hormones, family history and occupational exposure (Lubin JH *et al*, 1984, McDuffie HH 1991, Weiss W *et al*, 1979).

When age and histopathological subtype was correlated, adenocarcinoma incidence had two peaks in our study, one was among 51-60 age groups and the other was in the 71-80 age groups. Two cases with adenocarcinoma were seen in younger individuals around 30-40 years in our study group which was also seen in Pemberton JH's study (1983). In Ramalingam S *et al* (1998) and McDuffie HH *et al*'s studies (1987) also adenocarcinoma occurred in relatively younger age group.

Squamous cell carcinoma was seen in relatively older individual in our study.The reason for the delayed occurrence of SQCC may be because induction of squamous cell carcinoma requires long exposure to carcinogens. When histological subtypes were correlated with sex, squamous cell carcinoma among women was seen in 7% of the cases in our study group. This is in correlation with Olak *et al* (2004) and Raùl Barrera *et al*'s (2012) study groups. SCC was seen more in female according to El-Torky *et al*'s study (1990) in contrast to our study group where males were commonly diagnosed with SCC.

When Sensitivity and adequacy of the image guided biopsies of our study was analysed, Yeow KM, *et al* (2003)and Arslan S, *et al*'s studies(2002) correlated with our study [75%] Klein *et al* (2000) in their study had mentioned that the diagnostic efficacy of CT guided biopsy was 70-100% which also correlated with our study. Quint *et al* (2006) in their study had reported diagnostic sensitivity, accuracy, and negative predictive value of the CT guided biopsies in the diagnosis of malignancy as 91%, 92%, and 68%, respectively. Loh *et al* (2013) had reported a diagnostic sensitivity, accuracy, and negative predictive value of CT-guided biopsies for malignant lesion as 96%, 97%, and 88%, respectively and they also had recommended on site FNAC along with the biopsies for increasing the diagnostic accuracy. Montaudon *et al* (2004) in their study had stated that higher rate of false negative diagnosis of malignancy was seen if the lesion size was equal to or smaller than 10 mm in diameter. Lee *et al* (2010) and Khouri *et al* (1985) had recommended repeat biopsies under CT guidance in case of inconclusive results that will help to reduce the disparity between the histopathological report and the CT reports.

When staging of the tumor was correlated with the histological subtype, squamous cell carcinoma was most commonly seen in the advanced stage in our study. The high prevalence of advanced stages at the time of diagnosis reflects the late onset of symptoms and the highly aggressive clinical course and this needs further evaluation.

CT scan and histopathology is complimentary to each other in the diagnostics and histopathology remains the gold standard supplemented by immunohistochemistry and molecular studies.

CONCLUSION

The most prevalent lung tumor in our study was adenocarcinoma. Squamous cell carcinoma presented in advanced stage in our study. Immunohistochemistry is a valuable tool to categorize when morphology is equivocal. The correlation of CT scan findings with histopathological diagnosis was 75% with a p value of 0.0010 in our study. In

case of inconclusive histopathological results repeat CT guided biopsies are advocated for better results.

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