Original Article

Zahedan Journal of Research in Medical Sciences

Journal homepage: www.zjrms.ir

Primary Lung Cancer Subtypes: How Does Chest CT Scan Help to Differentiate them?

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Article information

Article history:
Received: 9 Feb 2013
Accepted: 1 May 2013
Available online: 1 Sep 2013
ZJRMS 2014; 16(1): 64-68

Keywords:
Adenocarcinoma
Small cell carcinoma
Squamous cell carcinoma
CT scan

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Abstract

***Background*:** Lung cancer has wide variety of clinical presentations and different imaging features relating its subtypes. This study is focused on the role of CT scan in differentiating primary lung cancer subtypes including adenocarcinoma, squamous cell carcinoma and small cell carcinoma.

***Materials and Methods*:** This retrospective study is conducted on 55 pathologically diagnosed primary lung cancer patients. Several CT features including lung mass and pleural effusion and parenchymal nodule characteristics, mediastinal and hilar involvement, pericardial effusion and thickening, chest wall invasion, reticulation, superior vena cava (SVC) syndrome and encasement of main bronchus were checked.

***Results*:** We enrolled 55 primary lung cancer patients including 29 adenocarcinomas, 19 squamous cell carcinomas and 7 small cell carcinomas, 36 males and 19 females with mean age of 60.3 years. Most common CT features of primary lung cancer were lung mass (94.5%) particularly located in hilum (51.9%) and irregular bordered (55.8%). Other prevalent findings included parenchymal nodules (60%), pleural effusion (41.8%), mediastinal adenopathy (47.3%), hilar adenopathy (42.9%), mediastinal invasion (43.6%) and reticulation (56.4%). Hilar adenopathy (47.4%), reticulation (48.3%) and parenchymal nodule (62.1%) in adenocarcinoma; hilar mass (57.9%) and parenchymal nodule (68.4%) in squamouos cell carcinoma; hilar and mediastinal involvement in small cell carcinoma were the most frequent findings.

***Conclusion*:** Comparing three subtypes, we found squamous cell and adenocarcinoma more similar regarding CT images parenchymal nodules, mass calcification and cavitation were more frequently seen in them compared to small cell lung cancer whereas hilar involvement, mediastinal involvement, irregular bordered mass and encasement of main bronchus were more prevalent in small cell carcinoma.

Introduction

Lung cancer is the leading cause of cancer death in women and men worldwide [1]. Lung cancer causes more deaths than the next three most common cancers combined (colon cancer, breast cancer and prostate) [2]. The incidence of lung cancer is increasing and only 10% has been mentioned as cured [3]. Two main groups of lung cancer are defined: small cell lung cancer (SCLC) and non small cell lung cancer (NSCLC). NSCLC includes several subtypes of tumor: adenocarcinoma, squamous cell carcinoma and large cell carcinoma. Majority of primary lung cancers include small cell carcinoma, squamous cell carcinoma, adenocarcinoma (including bronchioloalveolar) and large cell carcinoma [4]. NSCLCs represent almost 85% of all primary lung cancers [5], while small cell is less common but more often central mass and aggressive and tend to metastases more quickly compared with NSCLC [6]. About 5% of primary lung cancers are rare cell types like carcinoid tumor, lymphoma and others. Adenocarcinoma of the lung is the most common histopathologic type of lung cancer, and its prevalence is reported to be increasing. In addition, reports have shown that screening with low-dose CT can improve the detection of lung cancer, especially of adenocarcinoma [7, 8]. Lung cancer has wide variety of presentations and they may stay asymptomatic until well advanced or even after metastasis to other organs. It demonstrates the importance of early stage diagnosis of lung cancers. CT scan has notable role in early detection of lung cancers at an earlier and potentially more curable stage which can lead to more effective treatment and improve its prognosis [9, 10]. Lung cancer is usually suspected in individuals who have abnormal chest radiograph findings or have symptoms caused by either local or systemic effects of the tumor [11]. More accurate diagnosis and staging which is so important for treatment plan, necessitates more sensitive imaging modalities. CT scan is known as one of sensitive available imaging tools and there are different CT findings related to primary lung cancer subtypes. In this study we found important CT findings in three subtypes of primary lung cancer including adenocarcinoma, squamous cell carcinoma and small cell carcinoma and

compared them concerning their imaging findings as a guide in differential diagnosis.

Materials and Methods

This retrospective study done in 2012 and we evaluated 55 patients, 36 males and 19 females, diagnosed as primary lung cancer. During a 3 years period from 2009 to 2012, all patients with a the diagnosis of lung carcinoma based on pathology study of brochoscopic, CT guided or open lung biopsies, extracted from the pathology department archive and some reviewed by the pathologist to reassess morphologic and IHC (immunohistochemistry) features leading to a more definite diagnosis. We revised patients' files and histories when needed as well. Fifty five patients full filled the inclusion criteria. The latter included a rather definite primary lung carcinoma of three mentioned categories and the necessity of an appropriate chest CT scan. All CT scans were reviewed by an expert radiologist, unaware of pathologic diagnosis; and a check list of expected findings including an open option for other findings was filled for each one. We evaluated CT scans for lung mass and its characteristics, pleural effusion and presence of parenchymal nodules and their characteristics, pericardial thickening and effusion, mediastinal and hilar involvement, chest wall invasion, reticulation, SVC syndrome and encasement of main bronchus. Data analysis was carried out using SPSS-16 and all findings were reported totally. In addition, we analyzed findings of three groups separately and the comparison analysis was performed between them (p-Value≤0.05).

Results

This study is conducted on 55 primary lung cancer patients, diagnosed by pathologic assessment. Thirty six males and 19 females enrolled with mean age of 60.3 years, age ranged from 32 to 81 year. According to their pathology reports, we classified them to three groups: 29 adenocarcinomas, 19 squamous cell carcinomas and 7 small cell carcinomas. Fifty two patients showed mass on their CT-scan and only 3 adenocarcinoma cases were found without mass lesion on imaging. Regarding location, hilum was the most common involved part followed by LLL (left lower lobe), RLL (right lower lobe), RUL (right upper lobe), LUL (left upper lobe), and RML (right middle lobe) respectively. Concerning different pathologies, hilum had highest involvement rate in each group as well. The mass characteristics are summarized in table 1. Assessing the mass borders, showed: 55.8% irregular, 30.8% lobulated and 13.5% smooth borders. Regarding irregular border as the most prevalent one, 50% of adenocarcinomas, 71.4% of small cells and 57.9% of SCCs (squamous cell carcinoma) were found with this feature. Evaluating mass location, 46.2% of primary lung cancers were central and 23.1% peripheral and others could not be classified as just central or peripheral. Thirty three patients showed parenchymal nodules, 48.5% of them were multiple, and 27.3% single and 24.2% diffuse. Characteristics of the nodules are mentioned in table 2. Pleural effusion was seen in 23 patients, mainly free (87%) ipsilateral (60.9%) and mild (69.6%) same deal in three groups. Table 3 demonstrates pleural effusion findings. Twelve adenocarcinomas, 6 small cells and 8 squamous cells, demonstrated mediastinal adenopathies and 12 out of 28 non hilar mass cases, showed hilar adenopathies, mostly ipsilateral. Mediastinal invasion in 24 (43.6%) of all cases and reticulation suggestive of lymphangitic carcinomatosis in 31 (56.4%) are other almost common findings of our cases. Comparing three groups these two findings (mediastinal adenopathy and reticulation) revealed statistically significant difference in different pathologic categories which is shown in table 4.

Table 1. Radiological features of different lung masses

Radiologic finding	Total (%)	Adenocarcinoma (%)	Small cell carcinoma (%)	Squamous cell carcinoma (%)
Mass	94.5	89.7	100	100
Right upper lobe	17.3	23.1	0	15.8
Right middle lobe	3.8	3.8	0	5.3
Right lower lobe	19.2	19.2	28.6	15.8
Left upper lobe	13.5	15.4	0	15.8
Left lower lobe	19.2	23.1	14.3	15.8
Hilum	51.9	38.5	85.7	57.9
Smooth	13.5	11.5	0	21.1
Lobbulated	30.8	38.5	28.6	21.1
Irregular	55.8	50	71.4	57.9
Calcification	11.5	15.4	0	10.5
Cavitation	13.5	15.4	0	15.8

Table 2. Parenchymal nodule

Radiologic finding		Total (%)	Adenocarcinoma (%)	Small cell carcinoma (%)	Squamous cell carcinoma (%)
Parenchymal nodule		60	62.1	28.6	68.4
Nodule pattern	Single	27.3	27.8	50	23.1
	Multiple	48.5	38.9	0	69.2
	Diffuse	24.2	33.3	50	7.7
Nodule location	Same side	87.9	77.8	100	100
	Contralateral	60.6	72.2	50	46.2

Table3. Characteristics of pleural effusion

Radiologic finding		Total (%)	Adenocarcinoma (%)	Small cell carcinoma (%)	Squamous cell carcinoma (%)
Pleural effusion		41.8	41.4	42.9	42.1
Effusion location	Ipsilateral	60.9	58.3	100	50
	Contralateral	4.3	8.3	0	0
	Bilateral	34.8	33.3	0	50
Effusion volume	Mild	69.6	75	66.7	62.5
	Moderate	30.4	25	33.3	37.5
	Massive	0	0	0	0
Type of effusion	Free	87	83.3	100	87.5
	Locculated	17.4	16.7	0	25

Table4. Other findings in chest CT scans

Radiologic finding		Total (%)	Adenocarcinoma (%)	Small cell carcinoma (%)	Squamous cell carcinoma (%)
Pleural thickening		36.4	27.6	24.9	47.4
Pericardial effusion or thickening		14.5	17.2	14.3	10.5
Mediastinal adenopaty		47.3	41.4	85.7	42.1
Hilar adenopathy(out of 28 cases)		42.9	47.4	100	25
Hilar	Ipsilateral	81.1	87.5	100	50
	Bilateral	18.2	12.5	0	50
Mediastinal invasion		43.6	27.6	85.7	52.6
Chest wall invasion		5.5	6.9	0	5.3
Reticulation		56.4	48.3	57.1	68.4
SVC syndrome		5.5	3.4	14.3	5.3
Encasement main bronchus		21.8	10.3	71.4	21.1

Discussion

We evaluated 55 pathologically diagnosed primary lung cancer patients by reviewing their chest CT-scans. The most prevalent histopathologic subtype was adenocarcinoma (52.7%), similar to 53.9% adenocarcinoma in Nanguzgambo et al. study [12]. Except three adenocarcinoma patients, all presented with parenchymal mass with highest involvement rate in hilum comparing three pathology groups, hilar mass in small cell was notably frequent compared with others (85.7% hilar mass in small cell vs. 57.9% in squamous cell and 38.5% in adenocarcinoma). Similarly, among 24 out of 55 cases that had only central mass, 6 cases were diagnosed small cell carcinoma while only 9 squamous cell carcinoma and 9 adenocarcinomas presented with central mass. It demonstrates that small cell is mostly central tumor and central neoplasms of lung are more probable to be determined as small cell than peripheral ones. Regarding mass shape and feature, most of them had irregular border. It is considerable that 5 out of 7 small cell cases showed irregular masses (71.4%) and 2 had lobulated mass borders, whereas among adenocarcinoma patients. We found irregular mass in 13 cases (50%), lobulated ones in 10 and smooth borders in 3 patients. Among squamous cell carcinomas we had 11 irregular (57.9%), 4 lobulated and 4 smooth bordered masses. In a study by Lindell et al. on 61 cancers, 33% of BAC (bronchioloalveolar carcinoma) and 56% of non BAC adenocarcinoma showed irregular borders respectively which is close to our result while they found 71% of squamous cell cases with irregular mass borders which differs from our result that is 57.9% [13]. So we see irregular border more often in small cell carcinomas; and squamous cell and adenocarcinomas are ranked as second and third pathologies considering this feature. Mass calcification was seen in 6 cases (11.5%) and cavitation in 7 patients (13.5%) of 55 cases with similar prevalence in squamous cell and adenocarcinomas while no small cell carcinoma presented with these findings. Hollings and Shaw concluded in their article that cavitation is a rare finding in small cell carcinoma, a result similar to ours, but in their conclusion it is seen in 4% of adenocarcinomas and in 82% of squamous cell carcinomas which is different from our findings [14]. We observed parenchymal nodule in 60% of all cases in which small cell represented lowest rate (28.6%) while higher prevalence in squamous and adenocarcinoma were detected. Excluding small cell carcinomas, nodules were mostly seen in multiple patterns (48.5%) particularly in squamous cell cases where 9 out of 13 cases had multiple nodules (69.2%) in comparison with adenocarcinomas which equal to 38.9%. Therefore we can take multiple nodules more in favor of squamous cell carcinoma rather than adenocarcinoma or small cell carcinoma. Eighty seven point nine percent of all nodules were ipsilateral to mass and 60.6% presented contralaterally. Four patients with adenocarcinoma showed contralateral nodules without any nodule in the same side. The most common contralateral nodules belonged to adenocarcinoma that was equal to 72.2%. We found pleural effusion in 23 patients (41.8%), 60.9% of them were ipsilateral. This finding differs from Bouchard et al. article results that showed pleural effusion in 5% to 10% of patients with lung cancer [15]. One adenocarcinoma case had only contralateral effusion and none of small cell cases had effusion contralateral to mass side. Bilateral effusion was identified in 33.3% of adenocarcinomas and 50% of squamous cell carcinomas. It suggests that contralateral effusion supports the diagnosis of squamous cell or adenocarcinoma and we do not expect this in small cell carcinomas based on our study. It's notable that no massive effusion were observed and pleural effusion were mostly appeared as mild, 69.6% (1/3 of lung volume) and

moderate, 30.4% (1/3-2/3 lung volume), with similar results in three mentioned categories. According to our study pleural effusion in primary lung cancer was often free, just two adenocarcinomas and two squamous cell carcinomas demonstrated locculated effusion. We appraised mediastinal adenopathies in all cases (55 cases) and hilar adenopathies in non hilar masses (28 cases). Totally, 26 cases were found with mediastinal adenopathy with almost two times higher prevalence in small cell carcinomas in comparison with squamous cell carcinomas and adenocarcinomas (85.7% vs. 42.1% and 41.4%). Twelve out of 28 patients (non hilar mass cases) were identified with hilar adenopathies, 9 adenocarcinomas, and 2 squamous cell carcinomas. Similarly, it's written in Hollings and Shaw article that mediastinal and hilar or hilar involvement is seen in 51% of cases [14]. Generally, all small cell carcinoma cases had hilar involvement including adenopathy or mass and it was two times more frequent in adenocarcinomas compared to squamous cell carcinomas (47.4% vs. 25%). To sum up, small cell carcinoma was mainly determined as central mass which had hilar or mediastinal involvement. We looked over mediastinal invasion and found it almost common, about 43.6%, in order of frequency: in small cell (85.7%), squamous cell (52.6%) and adenocarcinomas (27.6%) and considering, higher prevalence of mediastinal invasion in small cell carcinoma was statistically significant. Another significant difference was encasement of main bronchus in 71.4% of small cell carcinomas in comparison with 21.1% in squamous cell and 10.3% in adenocarcinomas. Therefore these two parameters can be mentioned as important findings which support the diagnosis of small cell carcinomas. Furthermore, our study demonstrated rather high prevalence of reticulation in primary lung cancers, which equaled to 56.4% of all cases, almost similar prevalence in three separate groups.

Generally, the most common CT finding in primary lung cancer is lung mass particularly in hilum and with irregular borders. Other common findings of primary lung cancer are multiple parenchymal nodules and mild free pleural effusion, both of them occurring more often ipsilateral to mass side. Furthermore mediastinal adenopathy, hilar adenopathy, mediastinal invasion and reticulation are almost common CT features in these three groups of primary lung cancers. According to our study, comparing these three pathologic groups reveals that adenocarcinomas and squamous cell carcinomas show similar CT features and parenchymal nodules, mass calcification and cavitations are considerably more common in them than small cell lung cancer whereas hilar involvement, mediastinal involvement, irregular mass border and encasement of main bronchus are found more common in small cell carcinoma. In this study we compared CT findings of adenocarcinoma and squamous cell carcinoma. Both these pathologies are classified as NSCLC and present with almost similar CT features and we reported most considerable differences between them to find probable CT scan clues to differentiate them. Considering mass location, hilum showed most significant difference, because 57.9% of squamous cell cases had hilar masses in contrast to 38.5% of adenocarcinomas. Irregular mass border had almost similar prevalence between them but smooth borders were more frequent in squamous cell carcinoma cases (21.1% vs. 11.5%) while lobulated borders were more prevalent in adenocarcinoma (38.5% vs. 21.1%).

We found multiple nodules more common in squamous cell carcinoma but diffuse nodules were notably more common in adenocarcinoma (33.3% vs. 7.7%). Besides, contralateral nodules were more popular in adenocarcinomas (72.2% vs. 48.2%). On the other hand, bilateral pleural effusion was more common in squamous cell carcinomas (50% vs. 33.3%). Regarding pleural thickening, it was almost twice more prevalent in squamous cell carcinoma group, 47.4% in squamous carcinomas compared to 27.6% in adenocarcinoma. Mediastinal invasion, reticulation and encasement of main bronchus were other findings which were more common in squamous cell carcinoma comparing with adenocarcinoma. None of these differences were statistically significant, but multiple nodules and mediastinal invasion were most considerable different findings. Primary lung cancer mostly appears as hilar mass with irregular borders and massive pleural effusion is almost rare in that. We found parenchymal nodules, mass calcification and cavitations more related to adenocarcinoma and squamous cell carcinomas which have generally similar CT features. Central mass particularly with hilar involvement, mediastinal involvement, irregular mass borders and encasement of main bronchus are more probable to appear in small cell carcinoma. Comparing adenocarcinoma and squamous cell carcinoma reveals that, adenocarcinoma is seen as peripheral mass with lobulated borders and diffuses parenchymal nodules more commonly while a central mass with smooth borders is more probable to be diagnosed as squamous cell carcinoma pathologically. In addition, multiple nodules, pleural thickening and mediastinal invasion are more common in squamous cell carcinoma than adenocarcinoma. Considering comparison analysis, it’s concluded that CT scan findings can be used to differentiate small cell carcinoma from other primary lung carcinomas but it's not recommended to use computed tomography to differentiate adenocarcinoma and squamous cell carcinoma radiologically.

Acknowledgements

We would like to express our sincere gratitude and appreciation to Dr Bakhshayesh Karam, head of radiology depertment, and Dr Shirin Karimi, head of pathology depertment, for their valuable support on this study.

Authors’ Contributions

All authors had equal role in design, work, statistical analysis and manuscript writing.

Conflict of Interest

The authors declare no conflict of interest.

Funding/Support

This project was done by personal expenses.

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Please cite this article as: Mehrian P, Mosadegh L, Poorabdollah M. Primary lung cancer subtypes: How does chest CT scan help to differentiate them? Zahedan J Res Med Sci (ZJRMS) 2014; 16(1): 64-68.