

BRIEF REPORT

The changing anatomic position of squamous cell carcinoma of the lung – a new conundrum

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Background: Traditionally, squamous cell carcinoma (SCC) of the lung is a central rather than a peripheral form of lung cancer. Rates of SCC in the lung periphery are typically sited in the 15–30% range. Recently, we observed that a significant portion of newly diagnosed SCC was located on a periphery. A comprehensive review of the tumor data at our facility, a busy teaching hospital with a large cohort of cancer patients, was undertaken to assess whether there had been a substantive change in the traditional epidemiologic distributions of the lung cancer, specifically with respect to SCC. Given the differences in cell biology and carcinogenesis of central versus peripheral SCC, a potential epidemiologic shift might suggest a change in tumor biology.

Methods: From May 12, 2012 through May 13, 2013, all histopathologically confirmed diagnoses of SCC of the lung were retrospectively reviewed. Each patient's lesion was then classified as peripheral or central based on CT evidence.

Results: A total of 56 patients were diagnosed with SCC. Of these, 55% ($n = 31$) had peripheral and 45% ($n = 25$) had central SCC. Twenty-nine patients did not have any prior history of malignancy. Of this subset of patients, 62% ($n = 18$) had peripheral SCC, and 38% ($n = 11$) had central SCC.

Conclusion: Our findings appear to correlate with our initial observation that, within our institution, there has been a substantive shift in the traditional distribution of SCC with the majority of these cancers now being diagnosed in the lung periphery as opposed to the more central locations.

Keywords: *squamous cell carcinoma; lung cancer epidemiology; squamous cell carcinoma epidemiology; lung cancer; peripheral location cell carcinoma*

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Received: 29 August 2016; Revised: 23 October 2016; Accepted: 25 October 2016; Published: 15 December 2016

Non-small cell lung cancer (NSCLC) is the most common type of lung cancer accounting for nearly 85% of the cases (1–3). Although adenocarcinoma has replaced squamous cell carcinoma (SCC) as the most common histological type of lung cancer, SCC accounts for 30% of the NSCLC cases. SCCs are classified into central (*c*-type) arising from the main stem, lobar, and segmental bronchi; and peripheral (*p*-type) based on the location of the primary lesion. Traditionally, in literature, the *c*-type has been reported to be the more common type accounting for nearly two-thirds of the cases, but we have noticed at our medical center, a busy outer city teaching hospital, a trend toward an increase in

the occurrence of peripheral squamous cell cancers. Given the considerable differences in the clinicopathologic and presenting features of *c*-type SCC and *p*-type SCC, and the potential differences in carcinogenesis (4–7), we believe it is important to acknowledge to the fact that the *p*-type of SCC is on the rise and may account for more than 50% of the cases of SCC.

Materials and methods

Study population

All the patients aged 18 and above with a histopathologic diagnosis of pulmonary SCC between May 12, 2012 and

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May 13, 2013 at our medical center were identified retrospectively from the pathology database.

Procedure

The medical records of the 56 patients were retrospectively reviewed. The diagnosis of squamous cell lung cancer was confirmed by a pathologist. The chest CT scans of all the patients were reviewed by a pulmonologist. The midline of each lung in the axial CT scan views was used as a definition point, the tumors medial to the midline were classified as being centrally located, and those lateral to the midline were classified as peripherally located tumors. Of the 56 patients, 27 patients were found to have a prior history of malignancy of various organs. The patients without prior history of malignancy were also analyzed as a separate subset. Demographic information of all the 56 patients, as well as other pertinent information including smoking history, inhaled steroid use, and proton pump inhibitor (PPI) use, was collected and described.

Statistical analysis

The data were collected and analyzed using Microsoft Excel 2010. Student's *t*-test was used to compare the means

for the ages of the two study groups, and a chi-square test was used to compare the rest of the demographic features and risk factors mentioned above. A *p*-value of <0.05 was used for all the analyzed data.

Results

From May 12, 2012, through May 13, 2013, a total of 56 patients with new diagnosis of SCC were identified. Of them, 44.6% ($n = 25$) were found to have tumors arising from the center, and the rest 55.4% ($n = 31$) had tumors arising from the periphery of the lungs (Table 1).

Subgroup analysis

We also analyzed a subgroup with no prior history of any malignancy, and a total of 29 patients were included in this subset. Of the 29 patients, 37.9% ($n = 11$) were found to have centrally located tumors, and the rest 62.1% ($n = 18$) were found to have tumors arising from the periphery. The mean age was 68 (± 6.73) for the patients with central tumors, whereas the mean age was 69 (± 8.36) for the patients with peripheral tumors, and no statistically significant difference was found on the *t*-test. The rest of the variables including gender, race, smoking status, PPI use, and inhaled steroid use were analyzed in the subset of

Table 1. Statistical analysis

		Central		Peripheral		Total	
		Count	Percent	Count	Percent	Count	Percent
No. of patients		25	44.6	31	55.4	56	
Age	Range	52–88		52–82		52–88	
	Mean	67		70		69	
Sex	Male	19	76.0	19	61.3	38	67.9
	Female	6	24.0	12	38.7	18	32.1
Race	Caucasian	23	92.0	24	77.4	47	83.9
	African American	2	8.0	5	16.1	7	12.5
	Other	1		1	3.2	2	3.6
Smoking status	Current	8	32.0	12	38.7	20	35.7
	Past (quit > 6 months)	16	64.0	19	61.3	35	62.5
	Never	1	4.0	0	0.0	1	1.8
PPI use		7	28.0	6	19.4	13	23.2
Inhaler use		14	56.0	18	58.1	32	57.1
Right lung	Total	13	52.0	16	51.6	29	51.8
	Upper	5	38.5	9	56.2		
	Middle	8	61.5	0	0.0		
	Lower	0	0.0	7	43.8		
Left lung	Total	11	44.0	14	45.2	25	44.6
	Upper	4	36.4	11	78.6		
	Lower	7	63.6	3	21.4		

Data were managed with Microsoft Excel 2010. Student's *t*-test was used to compare the means for the ages of the two study groups, and a chi-square test was used to compare the rest of the demographic features and risk factors mentioned above. A *p*-value of <0.05 was used for all the analyzed data.

Table 2. *De novo* subgroup analysis

		Central		Peripheral		Total	
		Count	Percent	Count	Percent	Count	Percent
No. of patients		11	37.9	18	62.1	29	100
Age	Range	54–76				52–81	
	Mean	68		69		68	
Sex	Male	8	72.7	10	55.6	18	62.1
	Female	3	27.3	8	44.4	11	37.9
Race	Caucasian	11	100.0	13	72.2	24	82.8
	African American	0	0.0	5	27.8	5	17.2
	Others	0	0.0	0	0.0		
Smoking status	Current	4	36.4	5	27.8	9	31.0
	Past (quit >6 months)	7	63.6	13	72.2	20	69.0
	Never	0		0		0	
PPI use		3	27.3	2	11.1	5	17.2
Inhaler use		6	54.5	10	55.6	16	55.2
Right lung	Total	5	45.5	8	44.4	13	44.8
	Upper	3	27.3	4	22.2		
	Middle	2	18.2	0	0.0		
	Lower	0	0.0	4	22.2		
Left lung	Total	6	54.5	9	50.0	15	51.7
	Upper	2	18.2	1	5.6		
	Lower	1	9.1	8	44.4		

patients without previous history of malignancy, and no significant difference was found as well (Table 2).

Discussion

Lung cancer is the leading cause of cancer-related death among both men and women in the United States, of which SCCs account for a significant proportion. Traditionally, SCCs of the lung have been believed to arise from the central airways, with the prevalence of peripheral SCC among all SCC has been reported to range from 15 to 30% (8, 9). But recently, a few reports have documented a change in this distribution (4, 10, 11) with the peripheral form of SCC accounting for nearly 50% of SCC of the lung. We found in our study that the peripheral SCC accounted for 55% of the SCC in the entire study population and for 62% in the new lung cancer subgroup.

Our study has limitations. First, the study was a retrospective chart review. Second, only a small number of patients were studied. Finally, most of the study patients were Caucasians with a minor representation from African American and other races, and as a consequence, the results may not be generalizable.

Despite the limitations, our study correlates with the recent reports of increasing number of peripherally arising squamous cell cancers of the lung. Though we looked at some of the demographic variables and other factors that may be influencing this change in distribution, we were unable to identify a causative factor for this shift. As these

two forms of SCC have considerable differences in clinicopathologic features and presentation, we believe larger prospective studies are needed to further delineate the causative factors for this change in distribution.

Conflict of interest and funding

The authors have not received any funding or benefits from industry or elsewhere to conduct this study.

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