Differences in Ki67 Proliferation Index Between Peripheral and Central Small Cell Carcinomas of the Lung

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All authors have nothing to disclose.

Background

Traditionally, small cell carcinomas of the lung (SCC) were thought to occur predominantly in a central location, however recent studies have shown that a subset of SCCs occur peripherally, and these tumors may behave in a less aggressive manner. While endocrine marker expression has been compared in peripheral versus central SCC, differences in Ki67 proliferation rate have not been adequately assessed. We retrospectively compared Ki67 proliferation rates in peripheral versus central SCC in an institutional series.

Design

90 cases of SCC were identified using a CERNER database search. A radiologist specializing in thoracic radiology reviewed imaging associated with each case to determine a peripheral versus central location. Ki67 immunohistochemical (IHC) staining (clone 30-9) was performed on all cases. Cases were excluded if insufficient tissue for Ki67 staining or if localization of tumor (central/peripheral) was indeterminate by imaging. Scanscope Aperio software was used to quantify the proliferation index. If the tissue was crushed or otherwise unable to be quantified morphometrically, quantification was performed by visual inspection of glass slides. Endocrine markers (CD56, synaptophysin, chromogranin) and TTF1 were compared when available.

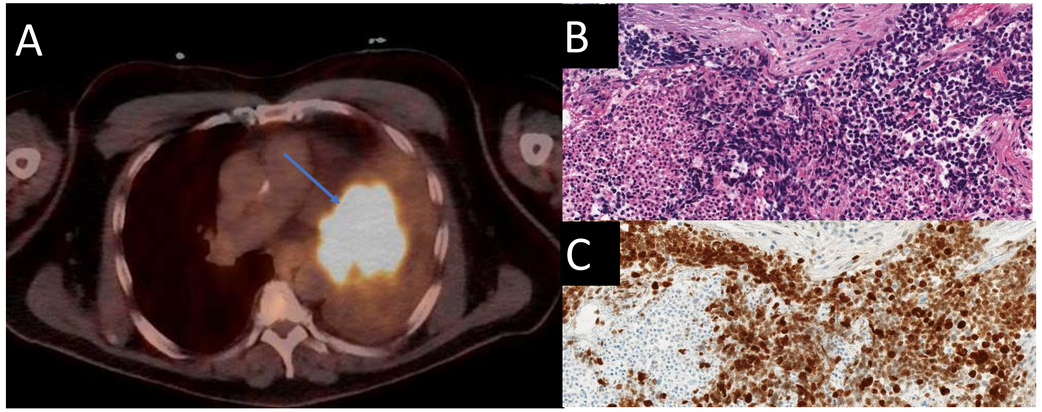

Figure 1: Central small cell carcinoma seen on PET scan (A), on routine stain (B), and on Ki67 immunostain (C).

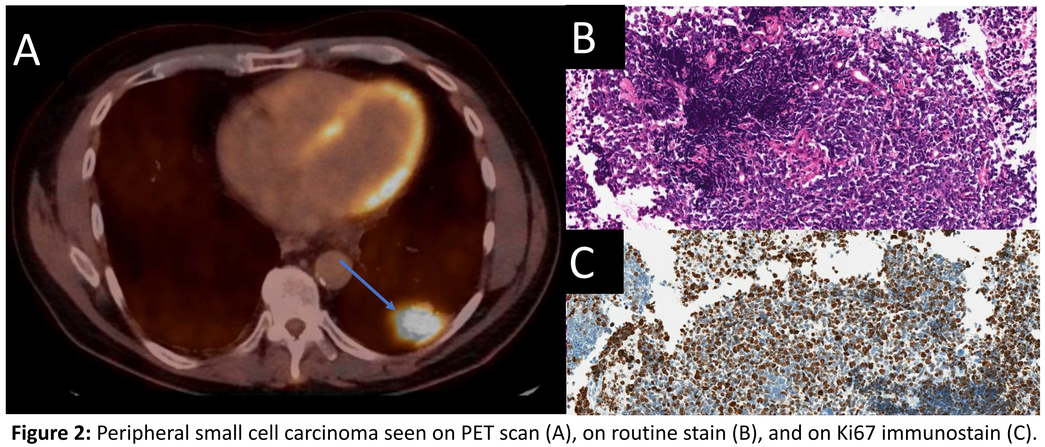

Figure 2: Peripheral small cell carcinoma seen on PET scan (A), on routine stain (B), and on Ki67 immunostain (C).

	Peripheral Tumor Immunostaining (%)	Central Tumor Immunostaining (%)	P-value
Mean Ki67	77.5 ± 2.5	84.1 ± 2.7	0.02
Endocrine Markers (Any)	89	91	NS
TTF1 Positivity (Any)	62	73	NS

Table 1: Immunostaining in peripheral vs. central tumors.

Results

Cases included 45 TBNA, 12 transbronchial biopsies, 9 core biopsies, 14 endobronchial biopsies, 9 resections, and 1 lymph node biopsy. Immunostains for endocrine markers (synaptophysin, chromogranin, CD56) and TTF- were reviewed in 31 cases. 44 cases were central (mean age 63.7 y, range 48-84; M:F = 13/31), and 47 were peripheral (mean age = 68.0 y, range = 52-85; M:F = 16/31). Mean Ki67 was 84.1 ± 2.7 for central and 77.5 ± 2.5 for peripheral tumors (p=.02). There was no difference in Ki67 values for lymph node samples (78.7 ± 3.1 v. 81.8 ± 2.3 for primary sampling). There was no significant difference in the rate of any endocrine marker staining in central v. peripheral tumors (91% v. 89%, respectively) and there was a statistically insignificant decrease in peripheral TTF-1 positivity (73% v. 62%, respectively).

Conclusions

When strict radiologic criteria are used, we found that more SCC are located peripherally versus centrally. The Ki67 proliferation rate is somewhat lower in peripheral tumors, which may explain their reportedly lesser aggressiveness. Further study is warranted, including survival data, to better define these differences.