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INTRODUCTION

- Lung cancer is the leading cause of cancer death in the United States and worldwide, the majority of which are non-small cell carcinomas (NSCLCs) including adenocarcinoma (ADC) and squamous cell carcinoma (SQCC).
- In light of discovery of molecular alterations associated with lung ADCs and advent of targeted therapies, further subtyping of NSCLCs has profound therapeutic implications.
- Differentiation of lung ADCs from SQCCs may sometimes be difficult to achieve based on cytomorphology alone, especially for those poorly differentiated carcinomas.
- A panel of TTF-1/p63 immunostains is the current recommendation for differentiation of ADC from SQCC in small biopsies or cytological specimens.
- However, p63 positivity, though seen in virtually all SQCCs, can be seen in as high as 30% ADCs. Furthermore, only up to 70% of ADCs show positive TTF-1.
- Recently, p40, a new antibody that targets one p63 isoform - ΔNp63, has been shown a promising marker in identifying SQCC with high sensitivity and specificity on surgically resected tumors.
- In this study, we evaluated p40 immunoreactivity in the fine needle aspiration (FNA) specimens of lung ADCs and SQCCs.

MATERIALS AND METHODS

- The cytopathology database was searched for the cases with FNA diagnosis of non-small cell carcinomas at the Yale-New Haven Hospital between January 2008 and July 2012.
- Only the cases with the diagnosis of either ADC or SQCC of the lung on surgical follow-up and sufficient cells on the cell blocks were included in the study.
- FNA biopsy of the lung and mediastinal lymph nodes was performed under the guidance of endobronchial ultrasound (EBUS) using 25-gauge needles. Diff-Quik and Papanicolaou stained smears were used for cytomorphologic analysis.
- Rapid on-site evaluation was performed by a cytopathologist in almost all cases to ensure adequate sampling and preliminary diagnosis.
- Additional aspirates were saved in the CytoRich Red fixative and processed for cell blocks for potential immunocytochemical studies.
- Histopathologic diagnoses were rendered on the core biopsy or resection specimens with or without ancillary immunohistochemical studies. The immuno markers may include p63, CK5/6, Napsin A and TTF1.
- The p40 immunostain was performed on the cell-block section of FNA specimens. Nuclear staining was semi-quantitatively evaluated as 0 (none), 1+ (1-25%), 2+ (25-50%), 3+ (50-75%), and 4+ (75-100%).
- The sensitivity and specificity of p40 immunostain for SQCC were calculated based on the expression of p40 in SQCC and ADC cases.

RESULTS

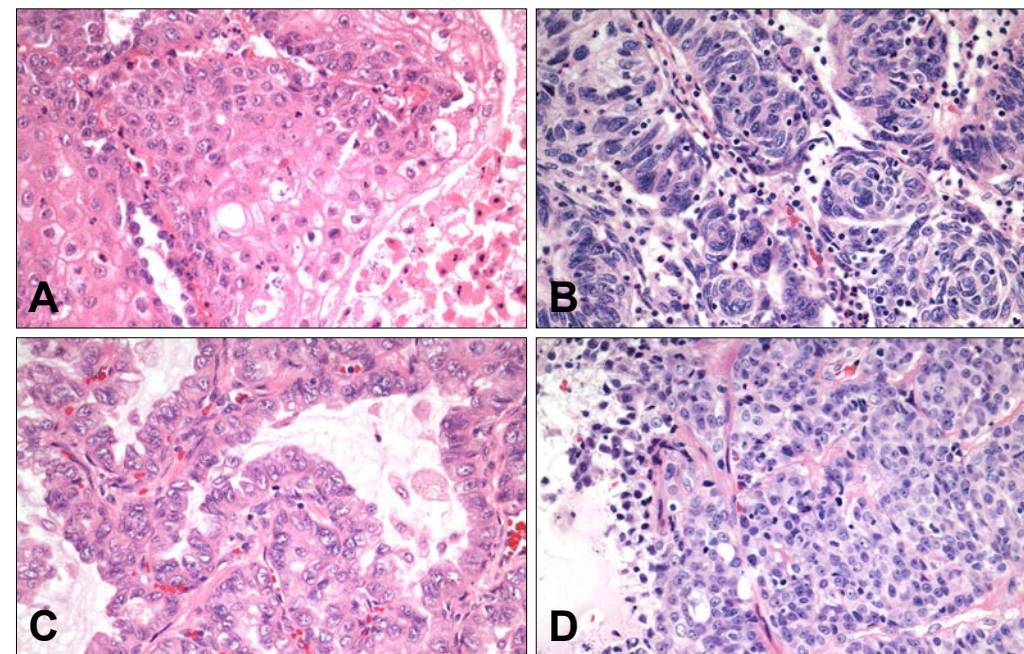


Figure 1. Histomorphologic features of well (A) and poorly (B) differentiated squamous cell carcinoma and well (C) and poorly (D) differentiated adenocarcinoma of the lung.

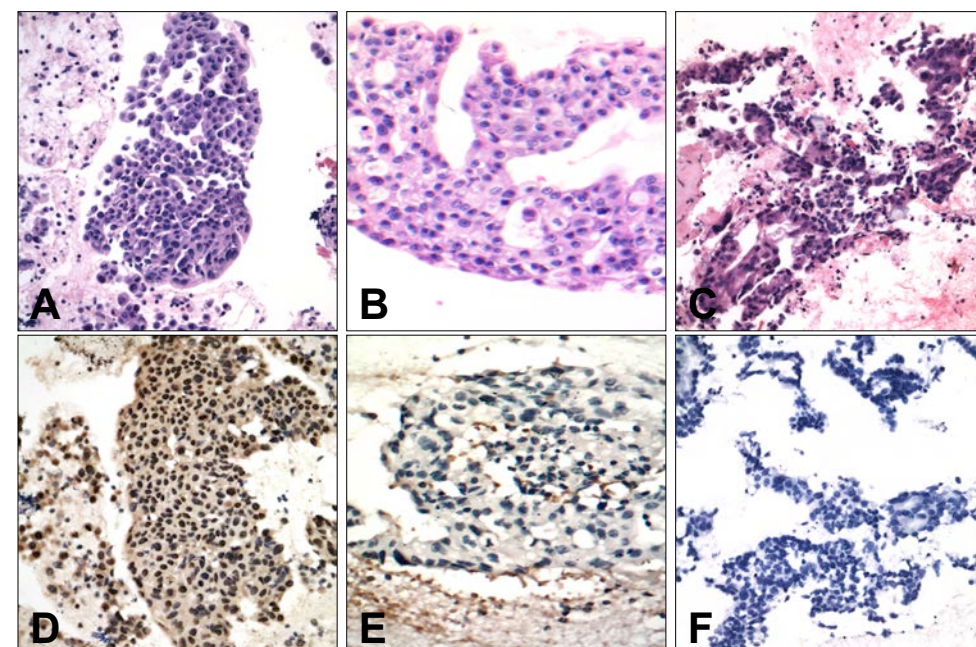


Figure 2. Cytomorphologic features and p40 immunostain of poorly (A, D) and well (B, E) differentiated squamous cell carcinoma and moderately differentiated adenocarcinoma (C, F) of the lung.

- A total of 63 cases were identified. The patients included 32 males and 31 females with the age ranging from 33 to 86 years old.
- The specimens included 26 lung and 37 mediastinal lymph node FNAs with final cytological diagnosis of NSCLCs, SQCC and ADC.
- Histopathologic diagnoses on follow-up were ADCs in 34 cases including 6 poorly differentiated tumors and SQCCs in 29 cases including 9 poorly differentiated tumors (Figure 1).
- Positive p40 immunoreactivity was seen in 26 of 29 SQCC cases (90%) while only one of thirty-four ADCs (3%) was positive for p40 (Table 1, Figure 2).
- Interestingly, two of three SQCCs with a negative p40 result were well differentiated SQCC.
- The only positive ADC case had a focal positive p40 stain.
- The calculated sensitivity and specificity of p40 immunostain for differentiation of SCCs from ADCs were 90% and 97%, respectively.

Table 1. p40 Expression in the Cytological Specimens of Squamous Cell Carcinoma and Adenocarcinoma of the Lung

Histopathologic Diagnosis	Case	p40 Immunostain				
		n	0	1+	2+	3+
Squamous Cell Carcinoma	29	3	3	5	6	12
Adenocarcinoma	34	33	1	0	0	0

CONCLUSIONS

- p40 immunostain has high sensitivity and specificity for identifying lung SQCCs on the FNA cell-block materials, which might be superior to p63 immunostain in the subtyping of NSCLCs.
- The study suggests that p40 be used as the first line antibody cocktail to differentiate SQCCs from ADCs in the cytological specimens.

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