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Commentary

Intramural and Transmogrified-Adenocarcinoma *In Situ* Lung

Anubha Bajaj*

Department of Histopathology, Panjab University, A.B. Diagnostics, India

***Corresponding Author**: Anubha Bajaj, Department of Histopathology, Panjab University, A.B. Diagnostics, India.

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Adenocarcinoma *in situ* and minimally invasive adenocarcinoma manifest up to 14% of primary pulmonary malignancies. Alternative terminology of bronchioloalveolar carcinoma is considered as obsolete.

Adenocarcinoma *in situ* lung is an uncommon variant of bronchial carcinoma. Adenocarcinoma *in situ* manifests as a pre-invasive pulmonary adenocarcinoma of magnitude ≤ 30.0 millimetres. The subcategory of pulmonary adenocarcinoma represents with significantly diverse clinical manifestations, applicable therapeutic options and prognostic outcomes.

Tumefaction exhibits a pure 'lepidic' pattern of tumour evolution wherein tumour infiltration is absent. Appropriate discernment of adenocarcinoma *in situ* necessitates thorough sampling of the entire neoplasm. Adequate tumour detection upon evaluation of miniature tissue samples or cytological smears may be challenging.

Characteristically, neoplasm exhibits a lepidic pattern of tumour evolution along with an absence of tumour invasion within subjacent stroma, vascular spaces or pleura. Classically, tumour magnitude is ≤ 30.0 millimetres [1,2].

An estimated 50% lesions of adenocarcinoma *in situ* delineate EGFR genetic mutations. Additionally, KRAS genomic mutations are encountered.

Incidence of aforesaid EGFR mutation appears enhanced in incriminated Asians whereas KRAS mutations are frequently observed in Caucasians. Besides, molecular assessment is recommended while treating subjects with cogent targeted therapy.

Genetic mutations within TP53 and NF1 contribute to frequent emergence of adenocarcinoma *in situ* and minimally invasive adenocarcinoma lung.

Adenocarcinoma *in situ* and minimally invasive adenocarcinoma lung are associated with significant copy number loss, in contrast to occurrence of deleterious chromosomal mutations [1,2].

Adenocarcinoma *in situ* exhibits diverse subtypes as

- Non-mucinous subtype is frequent.
- Mucinous subtype is exceptional.
- Mixed subtype is infrequent.
- Lepidic histological configuration is characteristically accompanied by an absence of tumour necrosis or invasion.

Adenocarcinoma *in situ* configures ~ 5% of non-small cell lung carcinomas (NSCLC). A mild female predominance or an equivalent gender predilection is observed.

Adenocarcinoma *in situ* lung frequently emerges within non smokers, female subjects and Asian population. Besides, adenocarcinoma *in situ* may arise within preceding focus of pulmonary fibrosis as enunciated with scarring of tuberculosis, pulmonary infarct or scleroderma.

Adenocarcinoma *in situ* is commonly confined to peripheral pulmonary lobes [1,2].

Emergence of adenocarcinoma *in situ* is concordant with multistep tumour progression denominated as

- Adenocarcinoma *in situ* (AIS) configures as an intermediate lesion between atypical adenomatous hyperplasia (AAH) and minimally invasive carcinoma (MIA).
- Incidence of EGFR chromosomal mutations within atypical adenomatous hyperplasia towards adenocarcinoma *in situ* and minimally invasive carcinoma demonstrates an increasing order of frequency.
- KRAS and BRAF genetic mutations may not display concordant progression, thereby indicating activation of alternative molecular alterations within neoplastic emergence.
- EPPK1, KMT2C, KMT2D, NOTCH3 and NF1 chromosomal mutations may manifest as preliminary elements within progression of pulmonary adenocarcinoma [1,2].

Akin to invasive pulmonary adenocarcinoma, cigarette smoking or tobacco consumption is posited to induce adenocarcinoma *in situ*.

Non-smokers may depict neoplastic appearance due to exposure to passive smoke or radon. Besides, occupational exposure or air pollution may configure the lesion [1,2].

Majority of pulmonary carcinomas encountered within non smokers emerge as idiopathic neoplasms and depict varied chromosomal mutations, in contrast to cigarette smoking induced pulmonary carcinoma.

Adenocarcinoma *in situ* is an incidentally discovered, gradually progressive lesion and may configure a singular tumefaction. Alternatively, lesion may concur with distinct focus of invasive adenocarcinoma [3,4].

Cytological examination exhibits mild to moderate cellular and nuclear atypia. Nuclear membrane appears irregular. Nuclear grooves and intra-nuclear pseudo-inclusions, reminiscent of papillary thyroid carcinoma may be observed. Categorical neoplastic discernment mandates histological evaluation of surgical tissue samples [3,4].

Upon frozen section, adenocarcinoma *in situ* exhibits lepidic pattern of tumour evolution. Mild to moderate cytological atypia is observed. Notwithstanding, appropriate categorization as adenocarcinoma *in situ* upon frozen section may be challenging. Besides, tumour invasion may emerge within deep seated neoplastic foci or tumour unassessed by frozen section examination [3,4].

Neoplasm diagnosed by singular frozen section devoid of tumour invasion may be labelled as adenocarcinoma *in situ* with lepidic pattern wherein additional evaluation with permanent, formalin fixed paraffin embedded sections obtained from residual tumour appears imperative.

Grossly, adenocarcinoma *in situ* emerges as a poorly defined nodule. Collapsed or compressed tumour nodules may appear solid.

Tumefaction may be associated with a scar. Tumour magnitude is ≤ 30.0 millimetres [3,4].

Upon microscopy, lesions demonstrate:

- Lepidic growth pattern configured of intensely adherent, back to back neoplastic cells singularly expanding along pre-existing alveolar structures. Tumour magnitude is ≤ 30.0 millimetres. Foci of stromal, vascular or pleural tumour invasion or tumour necrosis appear absent. Neoplasm may be detected singularly upon thorough sampling of surgical resection specimens. Neoplastic determination upon evaluation of miniature tissue samples, cytological smears or frozen section appears challenging. Distinction is necessitated from minimally invasive adenocarcinoma or invasive adenocarcinoma lung.
- Non-mucinous adenocarcinoma *in situ* exhibits mild to moderate cytological atypia and represents with an amalgamation of morphological features as hobnail cells, anisocytosis, irregular nuclear membrane, intra-nuclear pseudo-inclusions, nuclear grooves, hyperchromatic nuclei, miniature nucleoli or elevated nucleocytoplasmic ratio.
- Mucinous adenocarcinoma *in situ* is an extremely exceptional mucinous neoplasm demonstrating infiltration of adjacent pulmonary parenchyma. Mucinous tumour cells are permeated with abundant intracellular mucin and basal nuclei. Neoplastic cells exhibit minimal cellular and nuclear atypia.
- Adenocarcinoma *in situ* is constituted of lesion ≤ 3.0 centimetre magnitude. Neoplasm demonstrates lepidic pattern of tumour evolution and disseminates along alveolar walls wherein pulmonary architecture remains unaltered. Characteristically, absence of stromal, vascular or pleural invasion is enunciated [4,5].

	Magnitude ≤ 30 mm	**Magnitude ≥ 30 mm**
Singular lepidic pattern	Adenocarcinoma *in situ*	Adenocarcinoma lepidic predominant, stage T1a
Invasion ≤ 5.0 mm	Minimally invasive adenocarcinoma	Adenocarcinoma lepidic predominant
Invasion > 5.0 mm	Adenocarcinoma lepidic predominant	Adenocarcinoma lepidic predominant

Table: *Lepidic predominant pulmonary carcinomas [3,4].*

Adenocarcinoma *in situ* lung demonstrates immune reactivity characteristically simulating the immune reactive pattern of adenocarcinoma lung. Tumour cells appear immune reactive to CK7, thyroid transcription factor-1 (TTF-1) or Napsin A.

Neoplastic cells appear immune non reactive to CK20 or p40 [5,6].

Adenocarcinoma *in situ* lung requires segregation from pulmonary neoplasms such as atypical adenomatous hyperplasia, minimally invasive adenocarcinoma, adenocarcinoma, lepidic predominant, bronchiolar adenoma, glandular papilloma, papillary adenoma or peribronchial metaplasia. Besides, demarcation from lesions manifesting with solitary pulmonary nodule, chronic alveolar opacity or ground glass opacity is required [5,6].

Adenocarcinoma *in situ* lung may or may not be discernible upon computerized tomography (CT) or magnetic resonance imaging (MRI). Appropriate detection is contingent to tumour magnitude and accompanying scar tissue.

Indolent lesions delineate:

- Miniature magnitude.
- Extended volumetric doubling time exceeding > 400 days.
- Maximum standardized uptake value (SUV) < 1 [5,6].

Nevertheless, definitive lesion discernment necessitates surgical extermination followed by cogent histopathological evaluation.

Plain radiographs depict a non solid, partially solid or solid tumefaction. Additionally, neoplasm may be mucinous or demonstrates a scar. Adenocarcinoma *in situ* lung can be optimally treated with comprehensive surgical eradication, a manoeuver which is diagnostic and may appropriately alleviate the lesion [5,6].

Adjuvant chemotherapy or radiotherapy remains superfluous. Comprehensive surgical extermination of lesion is associated with 100% disease free and reoccurrence free proportionate survival.

Tumours unamenable to surgical eradication may progressively enlarge, contingent to factors such as initial tumour magnitude, history of cigarette smoking and status of chromosomal mutations [5,6].

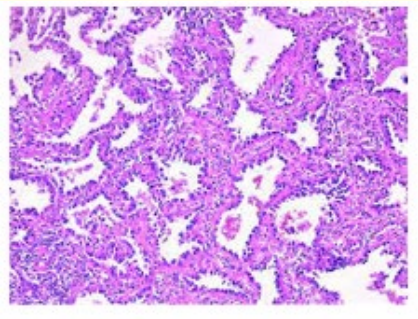

Figure 1: *Adenocarcinoma in situ delineating alveolar spaces lined by neoplastic epithelial cells with cellular and nuclear atypia, hyperchromatic nuclei with prominent nucleoli. Foci of stromal invasion are absent [7].*

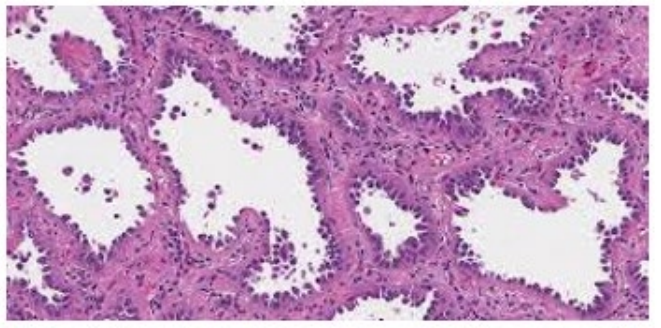

Figure 2: *Adenocarcinoma in situ demonstrating alveolar spaces lined by neoplastic epithelial cells incorporated with abundant, eosinophilic cytoplasm, hyperchromatic nuclei and prominent nucleoli. Foci of stromal invasion are absent [8].*

Bibliography

1. Zhu J., *et al*. "Evolution of lung adenocarcinoma from preneoplasia to invasive adenocarcinoma". *Cancer Medicine* 12.5 (2023): 5545-5557.

2. Myers DJ and Wallen JM. "Lung Adenocarcinoma". Stat Pearls International, Treasure Island, Florida (2023).

3. Zhang K., *et al*. "Treatment options and prognosis of patients with lung squamous cell cancer *in situ*: a comparative study of lung adenocarcinoma *in situ* and stage IA lung squamous cell cancer". *Translational Lung Cancer Research* 12.6 (2023): 1276-1292.

4. Zhang Y., *et al*. "Excellent prognosis of patients with invasive lung adenocarcinomas during surgery misdiagnosed as atypical adenomatous hyperplasia, adenocarcinoma *in situ*, or minimally invasive adenocarcinoma by frozen section". *Chest* 159.3 (2021): 1265-1272.

5. Yotsukura M., *et al*. "Long-term prognosis of patients with resected adenocarcinoma *in situ* and minimally invasive adenocarcinoma of the lung". *Journal of Thoracic Oncology* 16.8 (2021): 1312-1320.

6. Wang BY., *et al*. "The comparison between adenocarcinoma and squamous cell carcinoma in lung cancer patients". *Journal of Cancer Research and Clinical Oncology* 146.1 (2020): 43-52.

7. Image 1 Courtesy: Twitter.com.

8. Image 2 Courtesy: My pathology report.com.

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