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Editorial

Warped and Contorted-Squamous Dysplasia Lung

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Squamous dysplasia and carcinoma *in situ* of bronchial mucosa preceding invasive squamous cell carcinoma and basaloid carcinoma configure as a spectrum of pulmonary pre-neoplastic alterations. Additionally, atypical adenomatous hyperplasia preceding bronchioloalveolar carcinoma and diffuse idiopathic pulmonary neuroendocrine cell hyperplasia may represent as possible precursor of carcinoid tumour.

Squamous dysplasia and carcinoma *in situ* emerge as a multifocal, clonal disorder intensely concurrent with cigarette smoking or tobacco consumption. Aforesaid contributory factors may configure 'field cancerization' of incriminated mucosa. Generally, squamous dysplasia or carcinoma *in situ* demonstrates a predilection for large, central airways.

Alternatively, high grade squamous dysplasia or carcinoma *in situ* appears associated with enhanced possible emergence of invasive squamous cell carcinoma.

Squamous dysplasia commonly configures as a component of squamous bronchial lesions. In contrast, angiogenic squamous dysplasia is composed of capillary vascular articulations intensely juxtaposed with and protruding into metaplastic or dysplastic squamous bronchial epithelium.

Squamous dysplasia of bronchial mucosa demonstrates a male predilection and an enhanced male to female proportion of disease emergence [1,2].

Squamous dysplasia or carcinoma *in situ* (CIS) delineates a propensity for large, central airways and is commonly exemplified around airway bifurcations. However, trachea is uncommonly incriminated.

Squamous dysplasia of bronchial mucosa may precede neoplastic emergence by an extensive duration [1,2].

Pre invasive epithelial lesions may appear clone specific and are concordant with subsequent occurrence of pulmonary carcinomas. Stepwise progression of epithelial dysplasia into frank, invasive carcinoma may ensue. However, 'field carcinogenesis' is posited as an intense, engendering factor [2,3].

Squamous dysplasia of bronchial mucosa exhibits sequential genetic alterations as encountered within pathogenesis of pulmonary carcinoma. Modifications such as loss of heterozygosity (LOH), microsatellite alterations or telomerase dysregulation may ensue. Besides, discordant genetic aberrations may occur within bronchial mucosa susceptible to diverse carcinogens [2,3].

Squamous dysplasia of bronchial mucosa is associated with cigarette smoking or tobacco consumption. Lesion demonstrates possible progression from basal cells or metaplastic goblet cells into squamous epithelial metaplasia and dysplasia followed by carcinoma *in situ*.

Singular lesions of squamous dysplasia of bronchial mucosa appear asymptomatic [2,3].

Grossly, squamous dysplasia manifests with an unremarkable mucosa. Alternatively, mucosa may appear granular or demonstrate papillary projections or an absence of mucosal folds [2,3].

Upon microscopy, bronchial epithelial dysplasia exhibits distinct morphological configurations as basal cell dysplasia, columnar cell dysplasia, bronchial epithelial dysplasia with transitional differentiation or squamous dysplasia [3,4].

Squamous dysplasia is comprised of focal or comprehensive replacement of bronchial epithelium with squamous epithelial cells. Constituent squamous epithelial cells are permeated with pleomorphic nuclei with enhanced nucleocytoplasmic ratio. Subjacent basement membrane appears intact. Mitotic activity appears enhanced.

Generally, invasive epithelial progression is absent. However, the neoplastic epithelium may expand into ducts of submucosal glands [3,4].

Squamous dysplasia is graded as:

- Mild dysplasia wherein squamous epithelial cells exhibit minimal anomalies confined to lower one third of epithelial thickness. The cellular lesion exhibits surface maturation. Constituent cells exemplify basal expansion. Epithelial cells are pervaded with vertical nuclei. Mitotic figure are absent or infrequently discerned.
- Moderate dysplasia is comprised of squamous epithelial cells demonstrating cellular and nuclear anomalies and mitotic figures expanding into lower two thirds of epithelial thickness. Surface maturation is partial.
- Severe dysplasia exhibits constituent squamous epithelial cells permeated with coarse nuclear chromatin and prominent nucleoli. Cellular pleomorphism is significant. Epithelial alterations are confined to basal zone and extend into upper one third of superimposed epithelial cell layer along with flattening of superficial epithelium. Mitotic activity is confined to lower two thirds of epithelium.
- Carcinoma *in situ* is comprised of squamous epithelial cells depicting lack of maturation with significant cytological anomalies. Squamous epithelial cells are imbued with coarse nuclear chromatin and delineate inconsistent nuclear orientation. Mitotic figures invade comprehensive epithelial thickness. Alternatively, low grade or high grade lesions may ensue [3,4].

TNM staging of non small cell carcinoma lung as per American Joint Committee on Cancer 8th Edition [3,4].

Primary tumour

- TX: Primary tumour cannot be assessed or tumour discerned by malignant cells encountered within sputum or bronchial washings although non visualized upon imaging or bronchoscopy.
- T0: No evidence of primary tumour.
- Tis: Carcinoma *in situ*, squamous cell carcinoma *in situ*, adenocarcinoma *in situ* or a 'pure' lepidic pattern with tumour magnitude ≤ 3 centimetres.
- T1mi: Minimally invasive adenocarcinoma ≤ 3 centimetre diameter with a predominantly lepidic pattern and ≤ 5 millimetres depth of invasion.

- T1a: Tumour ≤ 1 centimetre magnitude OR exceptionally, a superficial, spreading tumour of variable magnitude with tumour invasion confined to bronchial wall which extends proximal to main bronchus.
- T1b: Tumour magnitude > 1 centimetres and ≤ 2 centimetres.
- T1c: Tumour magnitude > 2 centimetres and ≤ 3 centimetres.
- T2: Tumour magnitude > 3 centimetres and ≤ 5 centimetres or tumour incriminates main bronchus irrespective of distance to carina in the absence of involvement of carina. Tumour invades visceral pleura OR is associated with atelectasis or obstructive pneumonitis which extends to hilar region and confined to partial or comprehensive (100%) pulmonary parenchyma.
- T2a: Tumour magnitude > 3 centimetres and ≤ 4 centimetres along with minimally a singular aforesaid features.
- T2b: Tumour magnitude > 4 centimetres and ≤ 5 centimetres.
- T3: Tumour magnitude > 5 centimetres and ≤ 7 centimetres OR tumour directly invades parietal pleura, chest wall OR tumour confined to superior sulcus, phrenic nerve or parietal pericardium or presence of disparate tumour nodule within singular pulmonary lobe.
- T4: Tumour magnitude > 7 centimetres or tumour of variable magnitude with invasion into diaphragm, mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, oesophagus, vertebral body or carina or presence of disparate tumour nodule within an ipsilateral, different pulmonary lobe.

Regional lymph nodes

- NX: Regional lymph nodes cannot be assessed.
- N0: Regional lymph nodes metastasis absent.
- N1: Tumour metastasis into ipsilateral peribronchial, ipsilateral hilar or intrapulmonary lymph nodes along with direct tumour extension into lymph nodes.
- N2: Tumour metastasis into ipsilateral mediastinal or subcarinal lymph nodes.
- N3: Tumour metastasis into contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene or supraclavicular lymph nodes.

Distant metastasis

- M0: Distant metastasis absent.
- M1a: Distant metastasis with disparate tumour nodules within contralateral pulmonary lobe, pleural nodules, pericardial nodules, malignant pleural effusion or malignant pericardial effusion.
- M1b: Distant metastasis into singular extra-thoracic metastasis confined to singular organ or singular non regional lymph node.
- M1c: Distant metastasis into multiple extra-thoracic sites confined to singular organ or multiple organs.

Prognostic staging of non small cell carcinoma lung as per American Joint Committee on Cancer 8th Edition:

- Occult carcinoma: TX, N0, M0.
- Stage 0: Tis, N0, M0.
- Stage IA1: T1mi, N0, M0 OR T1a, N0, M0.
- Stage IA2: T1b, N0, M0.

- Stage IA3: T1c, N0, M0.
- Stage IB: T2a, N0, M0.
- Stage IIA: T2b, N0, M0.
- Stage IIB: T1a, T1b, T1c, N1, M0 OR T2a, T2b, N1, M0 OR T3, N0, M0.
- Stage IIIA: T1a, T1b, T1c, N2, M0 OR T2a, T2b, N2, M0 OR T3, N1, M0 OR T4, N0, N1, M0.
- Stage IIIB: T1a, T1b, T1c, N3, M0 OR T2a, T2b, N3, M0 OR T3, T4, N2, M0.
- Stage IIIC: T3, T4, N3, M0.
- Stage IVA: Any T, any N, M1a OR any T, any N, M1b.
- Stage IVB: Any T, any N, M1c.

Squamous bronchial dysplasia demonstrates patchy, disseminated immune staining with p53 and Ki67. Besides, Ki67 labelling index is significantly elevated in instances with severe dysplasia, in contrast to mild dysplasia or moderate dysplasia [5,6].

Squamous dysplasia of bronchial mucosa requires segregation from lesions such as squamous metaplasia, reactive atypia, reparative atypia, basal cell hyperplasia or squamous papilloma confined to bronchial mucosa. Squamous dysplasia of bronchial mucosa may be appropriately discerned by invasive manoeuvers such as image enhanced endoscopy, auto-fluorescence bronchoscopy (AFB), high magnification bronchovideoscopy (HMS), narrow band imaging (NBI), endobronchial ultrasonography (EBUS) or optical coherence tomography (OCT).

Squamous dysplasia of bronchial mucosa may be frequently enunciated within surgical resection specimens. However, endoscopic tissue specimens may not appropriately exemplify precise mucosal alterations. Squamous dysplasia of bronchial mucosa may be optimally subjected to meticulous and extended monitoring with bronchoscopy. Lesions such as severe squamous epithelial dysplasia and carcinoma *in situ* (CIS) necessitate extensive follow up. Additionally, endobronchial techniques or surgical intervention are recommended to suitably alleviate the condition [5,6].

Few pre-neoplastic lesions may retrogress. Certain lesions may gradually progress. Proportionate lesion progression appears contingent to initial histological grading along with duration of lesion evolution and emergence. However, appropriate detection of potentially malignant lesions may be challenging [5,6].

Persistently occurring squamous dysplasia is concurrent with emergence of invasive squamous epithelial carcinoma.

Squamous dysplasia accompanied by enhanced telomerase activity, elevated Ki67 proliferation index and immune reactive p53 may persist with consequent progression into invasive carcinoma.

Carcinoma *in situ* emerges as a significant predictor of lesion progression into invasive squamous epithelial carcinoma [5,6].

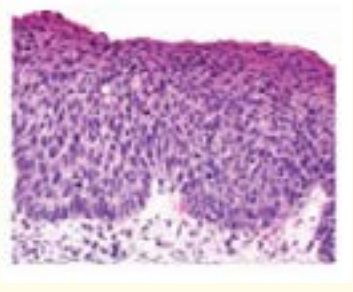

Figure 1: *Squamous dysplasia displaying epithelial anomalies comprised of full thickness cellular and nuclear atypia, pleomorphic nuclei with prominent nucleoli and mitotic figures [7].*

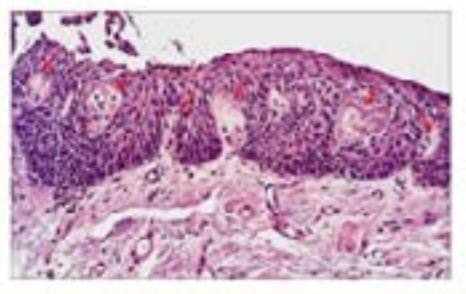

Figure 2: *Squamous dysplasia delineating epithelial cellular abnormalities with full thickness cellular and nuclear atypia, pleomorphic nuclei and pleomorphic nuclei. Mitotic figures are plentiful. Subjacent parenchyma is vascular [8].*

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7. Image 1 Courtesy: Oncohema key.
8. Image 2 Courtesy: Research gate.

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