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Commentary

Abeyant and Inhaling-Bronchiolar Adenoma Lung

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Bronchiolar adenoma emerges as a contemporary, exceptionally discerned neoplasm incriminating the bronchioles. Characteristically, neoplasm delineates as double layered, cellular configuration demonstrating specific phenotype and immune reactivity.

Previously contemplated as a benign neoplasm, bronchiolar adenoma is currently envisaged as a neoplasm with indeterminate malignant potential.

Initially scripted by Chang., *et al*. in 2017, bronchiolar adenoma or ciliated muconodular papillary tumour emerges as a bi-layered neoplasm comprised of epithelial cells and basal cells [1].

The frequently misinterpreted bronchiolar adenoma exhibits macroscopic features, histological manifestations and ultrasonography which appears reminiscent of diverse pulmonary conditions or malignant disorders.

Bronchiolar adenoma demonstrates distinctive, non specific genetic alterations within BRAF V600E, EGFR, ALK and KRAS genes, thereby indicating a neoplastic countenance [2,3].

Driver mutations or malignant metamorphosis is documented wherein malignant transformation is associated with lack of contiguous basal cells and emergence of driver mutations as L858R genomic mutation. Besides, genetic mutation of exon 19 and L858R gene may occur within concurrent adenocarcinoma *in situ* component [2,3].

Neoplasm may represent with cogent clinical symptoms as intermittent, productive cough and coarse crepitation incriminating pulmonary parenchyma. Pertinent history of cigarette smoking or alcohol consumption appears absent. Features such as cyanosis, sternal pain or respiratory distress are absent. Regional lymph node enlargement is absent [2,3].

Typically, bronchiolar adenoma represents with fusion of several pulmonary nodules. Alternatively, a singular tumefaction may be confined to pulmonary parenchyma adjacent to the bronchioles. Bronchiolar adenoma associated with diffuse pulmonary nodules is exceptionally exemplified.

Appropriate tumour discernment upon frozen section examination appears challenging [2,3].

Grossly, needle biopsy samples obtained from incriminated lung appear solid and grey/white.

Upon microscopy, tumefaction depicts irregular adenoid structures intermingled with foci of fibrosis and inflammation. Neoplasm exhibits dual cellular layer comprised of basal layer and luminal layer. Papillary configurations are absent [4,5].

Occasionally, micro-papillae may be configured with non-ciliated cells entrenched and germinating within the alveolar cavity. Luminal cellular layer is comprised of type II alveolar cells and club cells. However, flattened zones enunciate ciliated columnar cells and mucous cells.

Tumefaction appears non encapsulated, exhibits a distinct perimeter and manifests with papillary articulations or flattened neoplastic cells abutting walls of alveoli.

Contingent to composition of epithelial cells and proportion of luminal mucinous cells and ciliated cells, bronchiolar adenoma is subdivided into proximal subtype and distal types. Majority of instances configure as proximal subtype. However, aforesaid dual subtypes manifest with a bi-layered architecture constituted of luminal cells and contiguous basal cells [4,5].

Proximal subtype is composed of an admixture of mucous cells and ciliated cells. Distal subtype is composed of type II alveolar epithelium and club cells. As a commixture of proximal subtype and distal subtype is commonly encountered, neoplasm is contemplated to represent a contiguous disease spectrum [4,5].

Proximal subtype and distal subtype neoplasms are bi-layered with distinct foci of basal cells and commingled zones imbued with and devoid of columnar epithelial cells and mucous cells.

Additionally designated as ciliated muconodular papillary tumour, proximal subtype and constituent luminal cells are comprised of ciliated columnar epithelial cells and mucinous cells.

In contrast, luminal cells of distal subtype are configured of type II alveolar cells and club cells.

Foci of alveolar destruction and stromal expansion may be observed, akin to adenocarcinoma. Stromal expansion emerges due to oedema and infiltration of an inflammatory cell infiltrate. Stroma appears devoid of thick collagen fibres [4,5].

Tumour cells appear to lack cellular and nuclear atypia. Besides, mitotic figures and tumour necrosis appear absent. Basement membrane-like substance encompasses basal cell layer. Occurrence of contiguous layer of basal cells circumscribing the luminal cell layer is a pathognomonic morphological feature [4,5].

Gene	Molecular alteration
EGFR	Mutation (~35%)
KRAS	Mutation (25%)
HER2	Mutation (~6.7%), amplification (~22%), overexpression (~23%)
ALK	Chromosomal rearrangement (~8%)
MET	Amplification (~4%), mutation (~4%)
BRAF	Mutation (~5%)
RET	Chromosomal rearrangement (~2%)
ROS1	Chromosomal rearrangement (~1.7%)
NTRK	Gene fusions (~1%)

Table: *Driver mutations within non small cell carcinoma lung [5].*

Tumour cells appear immune reactive to p63, p40 and cytokeratin or CK5/6 within contiguous basal cells.

Luminal cells and few basal cells appear immune reactive to thyroid transcription factor-1 (TTF-1). Luminal cells express immune markers discerned with terminal bronchioles as pan-cytokeratin, CK7, Napsin A and carcinoembryonic antigen (CEA) [6,7].

Luminal cells articulating proximal subtype appear immune non reactive or minimally reactive to thyroid transcription factor-1 (TTF-1) and Napsin A. In contrast, luminal cells configuring distal subtype are intensely immune reactive to thyroid transcription factor-1 (TTF-1) and Napsin A.

Basal cells configuring proximal subtype and distal subtype appear immune reactive to p40, p63 and CK5/6 with weak immune reactivity to thyroid transcription factor-1 (TTF-1).

Mucous cells may be highlighted with periodic acid Schiff's (PAS) stain. Ki-67 proliferation index is minimal and appears < 10%.

Serum levels of carcinoembryonic antigen (CEA) or non-small cell lung cancer associated antigen (CYFRA21-1) appear elevated [6,7].

Bronchiolar adenoma requires segregation from diverse benign and malignant conditions such as invasive mucinous adenocarcinoma, adenocarcinoma *in situ*, bronchiolar metaplasia, mixed squamous cell and glandular papilloma, sclerosing pneumocytoma or mucoepidermoid carcinoma [6,7].

Upon radiographic imaging, tumefaction may represent with several nodules confined within upper and lower pulmonary segments.

Computerized tomography (CT) may exemplify multiple, solid nodules confined within upper and lower pulmonary segments. Tumour nodules of variable magnitude appear irregular wherein a few demonstrate central cavitation.

Contrast enhanced computerized tomography (CECT) enunciates multiple, 'cauliflower-like', partially fused soft tissue nodules confined to pulmonary parenchyma. Tumefaction adheres to adjacent, irregularly thickened pleura wherein distinction between tumour mass and pleura may be challenging. Regional lymph node enlargement appears absent.

Ultrasound-guided percutaneous needle tissue sampling of incriminated lung may be optimally employed for diagnosis [6,7].

Bronchiolar adenoma may be appropriately treated by wedge resection of pulmonary parenchyma along with excision of wide margin of uninvolved tissue. However, emergence of diffuse pulmonary nodules may mandate extermination of entire lung [6,7].

Aforesaid surgical manoeuver may significantly impair quality of life. Therapeutic strategies are necessitated to regulate normal daily activities, muscular strengthening, preserve mechanism of respiration and circumvent respiratory infections along with adoption of agents which relieve dyspnoea and cough.

Bronchiolar adenoma demonstrating an indeterminate malignant potential may undergo tumour reoccurrence and distant metastasis [6,7].

Appropriate discernment of bronchiolar adenoma necessitates comprehensive analysis with cogent history, assessment of imaging features along with evaluation of macroscopic and histopathological manifestations with precise immunohistochemistry.

Misinterpretation is to be circumvented in order to prevent non required surgical intervention or adjuvant radiotherapy and chemotherapy [6,7].

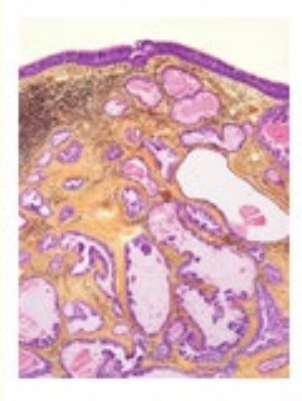

Figure 1: *Bronchiolar adenoma demonstrating adenoid structured lined by basal layer and luminal layer surrounded by a fibrotic stroma infiltrated by chronic inflammatory cells. Papillary articulations are absent [8].*

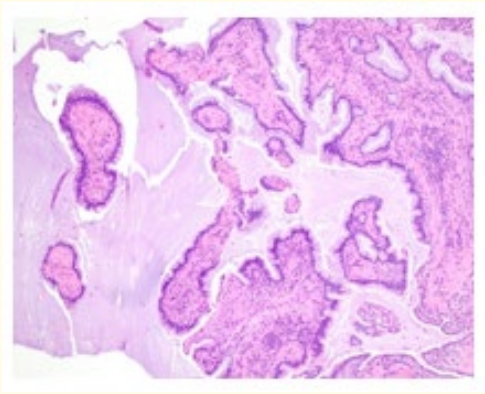

Figure 2: *Bronchiolar adenoma delineating adenoid articulations lined by basal layer and luminal layer surrounded by a fibrotic stroma infiltrated by chronic inflammatory cells. Papillary configurations are absent [9].*

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8. Image 1 Courtesy: Science photo library.

9. Image 2 Courtesy: Twitter.com.

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