
Appendices

Appendix A. Template for Interpreting Pulmonary Cytology Using the New Standardized Terminology of the Papanicolaou Society of Cytopathology (PSC)

Nondiagnostic (Check all that Apply)

- Cellularity insufficient for diagnosis
- Tissue obscured by (air drying, mechanical, blood) artifact
- Presence of only normal epithelial elements or alveolar macrophages when a discrete nodule, mass, or cyst is identified on imaging

Negative for Malignancy

- Acute inflammation
- Granulomatous inflammation
- Amyloid
- Viral cytopathic effect
- Benign epithelial elements only (when no discrete nodule, mass, or cyst is seen on imaging)
- Fungal elements
- *Pneumocystis jirovecii*
- Pulmonary infarction

Atypical

- Atypical epithelial elements (see note)
 - Note: The sample shows atypical respiratory epithelial cells, pneumocytes, or metaplastic squamous cells showing greater degrees of cytologic dysmorphism than expected for benign and reactive conditions but falling short of that needed for a suspicious for malignancy diagnosis
- Cell population suspicious for a benign neoplasm or neoplasm of undetermined malignant potential but lacking sufficient diagnostic criteria for a definitive diagnosis

Neoplastic

- Benign
 - Pulmonary hamartoma
 - Granular cell tumor
 - Squamous papilloma
- Neoplasms of undetermined malignant potential
 - Epithelioid hemangioendothelioma
 - Clear cell tumor of the lung
 - Sclerosing pneumocytoma
 - Primary pulmonary meningioma
 - Langerhans cell histiocytosis
 - Solitary fibrous tumor
 - Inflammatory myofibroblastic tumor
 - Myoepithelial neoplasms

Suspicious for Malignancy

- Markedly atypical epithelial cells showing marked cytomorphologic changes suspicious for an adenocarcinoma, squamous cell carcinoma, small cell carcinoma, carcinoid tumor, large cell neuroendocrine carcinoma, adenosquamous carcinoma, or a metastatic carcinoma, but features fall short of those necessary for a definitive diagnosis
- Atypical lymphoid population (flow cytometry either not performed or results are equivocal)
- Atypical mesenchymal cells suspicious for a primary or metastatic sarcoma (immunohistochemistry and molecular studies either not performed or equivocal)

Positive for Malignancy

- Epithelial cell population showing cytomorphologic abnormalities sufficiently severe to be diagnostic of an adenocarcinoma (specify type when possible),

squamous cell carcinoma, small cell carcinoma, carcinoid tumor, large cell neuroendocrine carcinoma, adenosquamous carcinoma, or a metastatic carcinoma (immunohistochemistry useful to clarify site of origin)

- Atypical lymphoid population diagnostic of lymphoma (flow cytometry and/or molecular studies should be performed to confirm diagnosis)
- Atypical mesenchymal cells diagnostic of a sarcoma (immunohistochemistry and/or molecular studies can be performed to confirm diagnosis and establish type of sarcoma present)

Appendix B. Useful Ancillary Tests in the Diagnosis of Pulmonary Lesions

Ancillary test	Target	Diagnostic utility
<i>Histochemical stains</i>		
Bacterial culture	Aerobic and anaerobic bacteria and acid-fast bacteria	Bacterial pneumonia, abscesses, and granuloma
Fungal culture	Fungal organisms	Fungal abscesses, granuloma
Periodic acid-Schiff with diastase	Mucin	Mucin-producing adenocarcinomas and adenosquamous carcinomas
Mucicarmine	Mucin	Mucin-producing adenocarcinomas and adenosquamous carcinomas
Alcian blue pH 2.5	Mucin	Mucin-producing adenocarcinomas and adenosquamous carcinomas
<i>Immunohistochemical stains</i>		
TTF-1	Positivity supports pulmonary adenocarcinoma	Pulmonary adenocarcinoma
P40	Positivity supports squamous cell carcinoma	Squamous cell carcinoma
P63	Positivity supports squamous cell carcinoma	Squamous cell carcinoma
Synaptophysin	Strong diffuse staining supports neuroendocrine differentiation	Small cell carcinoma, carcinoid tumor, large cell neuroendocrine carcinoma
Chromogranin	Strong diffuse staining supports neuroendocrine differentiation	Small cell carcinoma, carcinoid tumor, large cell neuroendocrine carcinoma
GATA-3	Positivity supports urothelial or breast primary	Breast or urothelial primary
CDX2	Positivity supports GI and pancreatic primaries	Colonic or pancreatic primary
ALK	ALK-rearranged adenocarcinoma	ALK-positive adenocarcinoma
ROS-1	ROS-1-positive adenocarcinoma	ROS-1-positive adenocarcinoma
S100	Positivity supports diagnosis of melanoma	Melanoma, schwannoma
SOX10	Positivity supports diagnosis of melanoma	Melanoma

(continued)

Ancillary test	Target	Diagnostic utility
A103	Positivity supports diagnosis of melanoma	Melanoma
PAX-8	Positivity supports diagnosis of renal cell carcinoma or carcinoma of thyroid	Renal cell carcinoma, thyroid carcinoma
<i>Molecular tests</i>		
EGFR	Drug susceptibility	Mutation-positive adenocarcinoma
ROS-1	Drug susceptibility	Mutation-positive adenocarcinoma
ALK	Drug susceptibility	Mutation-positive adenocarcinoma
<i>Flow cytometry</i>	Atypical lymphoid populations	Lymphoma

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