

WHO CLASSIFICATION OF ENDOCRINE TUMOURS Online PDF

WHO classification of endocrine tumours is a pivotal framework used by pathologists, oncologists, and medical professionals worldwide to categorize and understand the diverse spectrum of endocrine neoplasms. This classification system is continually updated by the World Health Organization (WHO) to incorporate new scientific insights, improve diagnostic accuracy, and guide effective treatment strategies. Endocrine tumours originate from hormone-producing glands, including the thyroid, parathyroid, adrenal glands, and neuroendocrine cells dispersed throughout various organs. Proper classification is essential for prognosis determination, therapeutic planning, and facilitating research efforts. In this comprehensive overview, we explore the WHO classification of endocrine tumours, detailing the categories, key features, diagnostic criteria, and latest updates to this vital system.

Understanding the WHO Classification of Endocrine Tumours

The WHO classification of endocrine tumours is a histopathological and molecular framework that categorizes tumors based on their origin, cellular differentiation, malignancy potential, and molecular features. The system emphasizes a multidisciplinary approach, combining morphological assessment with immunohistochemistry, molecular genetics, and clinical data.

Key objectives of the WHO classification include:

- Standardizing diagnosis across institutions and countries
- Facilitating research and clinical trials
- Improving patient management and prognosis prediction
- Incorporating advances in molecular pathology

The classification is periodically revised, with the latest edition published in 2022, reflecting significant advances in understanding endocrine tumours.

Major Categories in the WHO Classification of Endocrine Tumours

The classification broadly divides endocrine tumours into several main categories, each with specific subtypes, based on tissue of origin and biological behavior.

1. Tumours of the Thyroid Gland

Thyroid tumours are among the most common endocrine neoplasms. They are classified into benign and malignant categories.

Benign Tumours:

- Follicular adenoma
- Hürthle cell adenoma

Malignant Tumours:

- Papillary thyroid carcinoma (PTC)
- Follicular thyroid carcinoma (FTC)
- Medullary thyroid carcinoma (MTC)
- Anaplastic thyroid carcinoma (ATC)

Key features:

- Differentiation status
- Presence of specific genetic mutations (e.g., BRAF, RAS)
- Histological architecture

2. Parathyroid Tumours

Parathyroid tumours are predominantly benign but can occasionally be malignant.

Main types:

- Parathyroid adenoma (most common)
- Parathyroid hyperplasia
- Parathyroid carcinoma (rare but aggressive)

Diagnostic highlights:

- Elevated serum calcium and parathyroid hormone levels
- Histopathological features distinguishing benign from malignant

3. Adrenal Gland Tumours

Adrenal tumours include those arising from the cortex and medulla, with distinct classifications.

Adrenal Cortical Tumours:

- Adenomas (benign)
- Carcinomas (malignant)
- Myelolipomas and other rare tumours

Adrenal Medullary Tumours:

- Pheochromocytomas
- Paragangliomas (extra-adrenal sympathetic or parasympathetic)

Features:

- Hormone secretion profiles
- Malignancy potential based on invasion and metastasis
- Molecular markers (e.g., SDH mutations)

4. Neuroendocrine Tumours (NETs)

Neuroendocrine tumours are a diverse group originating from neuroendocrine cells scattered throughout the body.

Primary sites include:

- Gastroenteropancreatic (GEP) system
- Lung
- Thymus
- Other organs

Classification:

- Well-differentiated neuroendocrine tumours (NETs)

- Poorly differentiated neuroendocrine carcinomas (NECs)

Grading and staging:

- Based on mitotic count and Ki-67 proliferation index
- Graded as G1, G2, or G3

Key features:

- Hormone secretion (functional vs. non-functional)
- Morphological subtype (e.g., carcinoid, small cell carcinoma)

Histopathological and Molecular Features in WHO Classification

The latest WHO classification emphasizes integrating histopathology with molecular diagnostics. Key molecular markers and genetic alterations are now integral to tumor classification.

Common molecular features include:

- BRAF, RAS, RET mutations in thyroid carcinomas
- MEN1, DAXX, ATRX mutations in pancreatic NETs
- SDH mutations in paragangliomas and pheochromocytomas
- TP53 mutations in anaplastic carcinomas

This integration enhances diagnostic precision, allows for targeted therapies, and provides prognostic information.

Update Highlights from the 2022 WHO Classification

The 2022 edition introduced several notable updates:

- Refinement of grading criteria for neuroendocrine tumours, emphasizing proliferation markers
- Clarification of molecular subtypes within thyroid carcinomas, especially papillary and follicular types
- Recognition of new entities, such as well-differentiated grade 3 neuroendocrine tumours
- Inclusion of emerging molecular data supporting targeted therapies
- Standardization of terminology to reduce ambiguity in diagnosis

These updates reflect ongoing research and technological advances in molecular pathology.

Practical Implications of WHO Classification in Clinical Practice

Accurate classification per WHO standards influences every aspect of patient care:

Diagnosis:

- Guides biopsy interpretation
- Determines the need for molecular testing

Treatment planning:

- Surgical approach
- Use of targeted therapies
- Surveillance strategies

Prognosis estimation:

- Differentiation status
- Tumor grade and stage
- Molecular features

Research and clinical trials:

- Stratification of patients
- Development of novel therapies

Conclusion

The WHO classification of endocrine tumours is a comprehensive, dynamic system that plays a crucial role in the diagnosis, management, and research of endocrine neoplasms. Its integration of histopathology with molecular genetics has revolutionized understanding and treatment of these tumours. Staying updated with the latest WHO classifications ensures clinicians and pathologists can provide accurate diagnoses and optimal care, ultimately improving patient outcomes. As advancements continue, the classification will evolve further, incorporating new biomarkers and targeted therapies, reaffirming its importance in the field of endocrine oncology.

WHO classification of endocrine tumours

The WHO classification of endocrine tumours represents a critical framework used worldwide by pathologists, oncologists, and researchers to diagnose, categorize, and manage tumors originating from endocrine glands. These tumors encompass a diverse group of neoplasms arising from endocrine tissues such as the thyroid, parathyroid, adrenal glands, and neuroendocrine cells throughout the body. Over the years, this classification has evolved significantly, integrating advances in histopathology, molecular genetics, and clinical behavior to provide a comprehensive and standardized approach. Its importance lies not only in improving diagnostic accuracy but also in guiding treatment strategies and prognostication.

Historical Context and Development of WHO Classification

Understanding the evolution of the WHO classification helps appreciate its current utility. Initially, endocrine tumors were classified based solely on histological appearance and clinical features. However, as molecular biology advanced, it became evident that tumors with similar histology could have vastly different genetic profiles and behaviors. The first WHO classifications for endocrine tumors were published in the 1980s, with subsequent updates in 1992, 2004, 2010, and most recently in 2017.

Key milestones include:

- Integration of molecular markers to refine tumor subtypes.
- Emphasis on grading and staging systems to assess malignancy.
- Inclusion of new entities based on genetic alterations.

The latest WHO classification (2017) emphasizes a multidisciplinary approach, combining morphology, immunohistochemistry, and molecular findings.

Core Principles and Structure of the WHO Classification

The WHO classification is designed to be comprehensive yet adaptable, categorizing endocrine tumors based on:

- Histological features: cell morphology, architecture, mitotic activity.
- Immunohistochemical profiles: hormone production, neuroendocrine markers.
- Molecular genetics: presence of specific mutations or gene alterations.
- Behavioral criteria: benign, uncertain malignant potential, or malignant.

The classification groups endocrine tumors mainly into:

- Tumors of the thyroid gland
- Tumors of the parathyroid glands
- Tumors of the adrenal cortex and medulla
- Neuroendocrine tumors (NETs) of other sites

Each category includes specific tumor types with well-defined criteria, facilitating consistent diagnosis across institutions.

Thyroid Tumors

Thyroid neoplasms are among the most common endocrine tumors, and their classification is vital for prognosis and management.

Major Categories

- Differentiated thyroid carcinomas (DTCs)
 - Papillary thyroid carcinoma (PTC)
 - Follicular thyroid carcinoma (FTC)
 - Hurthle cell carcinoma
- Medullary thyroid carcinoma (MTC)
- Anaplastic thyroid carcinoma
- Thyroid adenomas

Features and Features of Each Type

- Papillary thyroid carcinoma:
 - Most common thyroid cancer (about 80%)
 - Characteristic nuclear features (orphan Annie eyes, nuclear grooves)
 - Often associated with BRAF mutations
 - Good prognosis with appropriate treatment

- Follicular thyroid carcinoma:
 - Accounts for ~10-15% of thyroid cancers
 - Distinguished from adenoma by capsular and vascular invasion
 - Associated with RAS mutations and PAX8-PPAR γ rearrangements

- Medullary thyroid carcinoma:
 - Arises from parafollicular C cells
 - Produces calcitonin
 - Can be sporadic or familial (MEN 2 syndromes)
 - Associated with RET mutations

- Anaplastic thyroid carcinoma:
 - Highly aggressive and undifferentiated
 - Poor prognosis
 - Often arises from pre-existing differentiated carcinomas

Pros and Cons of WHO Classification for Thyroid Tumors

| Pros | Cons |

|-----|-----|

- | Clear histological and molecular criteria improve accuracy | Some tumors may have overlapping features, complicating diagnosis |

- | Guides targeted therapies (e.g., RET inhibitors for MTC) | Rare variants may not fit neatly into categories |

- | Facilitates prognostication and management planning | Requires specialized expertise and resources |

Parathyroid Tumors

Parathyroid neoplasms are relatively rare but clinically significant due to their role in primary hyperparathyroidism.

Types and Features

- Adenoma (most common)
- Hyperplasia
- Carcinoma (rare)

Features

- Parathyroid adenomas:
 - Usually solitary
 - Composed of chief cells, with a thin capsule
 - Typically benign with excellent prognosis
- Parathyroid carcinoma:
 - Larger, invasive, may invade surrounding tissues
 - Histologically challenging; criteria include capsular, vascular, or perineural invasion
 - Rare but aggressive

Strengths and Limitations

- The WHO classification emphasizes invasion and metastasis for malignancy diagnosis, which can sometimes be subtle histologically.
- Accurate diagnosis influences surgical management and follow-up.

Adrenal Tumors

Adrenal tumors are diverse, including cortical, medullary, and metastatic lesions.

Adrenal Cortical Tumors

- Adenomas (benign)
- Carcinomas (malignant)
- Myelolipomas and other benign lesions

Features

- Adrenal cortical adenomas:
 - Usually nonfunctioning or secreting cortisol, aldosterone, or androgens

- Well-circumscribed, benign features
- Adrenal cortical carcinomas:
 - Larger, irregular, invasive
 - Mitotic figures, nuclear atypia, necrosis, and invasion are hallmarks
 - Weiss criteria are used for diagnosis

Adrenal Medullary Tumors

- Pheochromocytomas:
 - Derived from chromaffin cells
 - Secrete catecholamines
 - Classified as benign or malignant based on invasion and metastasis

Features and Prognostic Indicators

- Malignancy in adrenal tumors is confirmed by invasion or metastasis, not solely histology.
- Molecular markers and scoring systems (e.g., PASS) assist in risk stratification.

Neuroendocrine Tumors (NETs) of Other Sites

NETs are characterized by neuroendocrine differentiation and can occur throughout the body.

Classification and Features

- Gastroenteropancreatic neuroendocrine tumors (GEP-NETs)
- Well-differentiated tumors (NETs) and poorly differentiated neuroendocrine carcinomas (NECs)
- Graded based on mitotic count and Ki-67 index into G1, G2, G3
- Pulmonary NETs
 - Typical carcinoid
 - Atypical carcinoid
 - Large cell neuroendocrine carcinoma
 - Small cell lung carcinoma

Advantages of WHO Classification

- Incorporates proliferation indices (mitotic rate, Ki-67) for grading, which correlates with prognosis.
- Recognizes distinct biological behaviors and treatment responses based on grade and differentiation.

Limitations

- Requires precise histological and immunohistochemical assessment.
- Some tumors demonstrate heterogeneity, complicating classification.

Molecular Advances and Future Directions

The WHO classification increasingly integrates molecular data, recognizing that genetic alterations can refine diagnosis and predict behavior.

- Mutations such as BRAF, RAS, RET, and TP53 are incorporated into diagnostic criteria.
- Gene expression profiles aid in subclassification, especially for poorly differentiated tumors.
- Targeted therapies are emerging based on molecular alterations, making these classifications clinically relevant.

The future of the WHO classification is likely to involve:

- More precise molecular subclassifications
- Personalized risk assessments
- Incorporation of emerging biomarkers

Conclusion

The WHO classification of endocrine tumours remains a cornerstone in endocrine pathology, providing a structured, evidence-based approach to tumor diagnosis and management. Its comprehensive nature—combining histological, immunohistochemical, and molecular features—enhances diagnostic precision, facilitates prognostication, and guides therapy. While it has notable strengths, including standardization and integration of advances, challenges such as evolving molecular data and tumor heterogeneity persist. Continued refinement, incorporating new molecular insights, will ensure that the WHO classification remains relevant and invaluable in the era of personalized medicine.

In summary, understanding the WHO classification of endocrine tumors is essential for clinicians

and pathologists alike, enabling consistent diagnosis, better patient outcomes, and the advancement of research in endocrine oncology.

Question What is the WHO classification of endocrine tumours based on? The WHO classification of endocrine tumours is based on histopathological features, cellular origin, differentiation status, and molecular characteristics to categorize tumours into benign, uncertain malignant potential, and malignant types. How does the WHO classification differentiate between benign and malignant endocrine tumours? The WHO classification uses criteria such as cellular atypia, mitotic activity, invasion, and metastasis presence to distinguish benign from malignant endocrine tumours, with specific categories like neuroendocrine tumors, carcinomas, and neoplasms of uncertain malignant potential. What are the key updates in the latest WHO classification of endocrine tumours? The latest updates incorporate molecular profiling, grading systems based on proliferation indices (like Ki-67), and refined criteria for borderline or uncertain malignant potential tumours to improve diagnostic accuracy and prognostication. How does the WHO classification impact clinical management of endocrine tumours? It guides treatment decisions by providing a standardized framework for diagnosis, grading, and staging, helping clinicians determine prognosis and appropriate therapeutic strategies for patients with endocrine tumours. Which endocrine tumours are most commonly classified under the WHO system? Commonly classified tumours include thyroid carcinomas (papillary, follicular, medullary, anaplastic), neuroendocrine tumours of the pancreas, adrenal cortical tumours, and parathyroid neoplasms. What role does molecular pathology play in the WHO classification of endocrine tumours? Molecular pathology aids in identifying genetic mutations and molecular subtypes, which refine classification, improve diagnostic precision, and can influence targeted therapy options in endocrine tumours.

Related keywords: endocrine tumors, WHO tumor classification, neuroendocrine tumors, endocrine neoplasms, tumor grading, tumor staging, endocrine pathology, tumor histology, neuroendocrine carcinoma, tumor biomarkers

Who Classification Of Tumours Of The Lung Pleura

WHO classification of tumours of the lung pleura

The World Health Organization (WHO) classification of tumours of the lung and pleura provides a comprehensive framework for diagnosing, categorizing, and understanding the diverse neoplasms that originate in these regions. This classification is pivotal for clinicians, pathologists, and researchers because it standardizes terminology, facilitates accurate diagnosis, guides treatment strategies, and aids in prognostication. This article delves into the detailed WHO classification of lung and pleural tumours, exploring the various tumour types, their histopathological features,

clinical relevance, and updates from the latest WHO editions.

Overview of WHO Classification of Lung and Pleural Tumours

The WHO classification system for lung and pleural tumours was first established to address the heterogeneity of neoplasms arising within these thoracic structures. It is periodically updated to incorporate advances in pathology, molecular biology, and clinical insights. The latest WHO classification categorizes tumours into benign, borderline, and malignant entities, based on histological features, behaviour, and molecular characteristics.

The classification encompasses tumours originating from:

- Lung parenchyma (primarily epithelial tumours)
- Pleura (mesothelial tumours)
- Other rare tumours of the lung and pleura

Understanding these categories is essential for accurate diagnosis and appropriate management.

Classification of Tumours of the Lung

Lung tumours are predominantly epithelial in origin, with non-small cell lung carcinomas (NSCLCs) being the most common, followed by small cell lung carcinomas (SCLCs). The WHO classification emphasizes histological subtypes, molecular alterations, and clinical implications.

Benign Lung Tumours

Benign lung tumours are rare and usually asymptomatic. They are often discovered incidentally during imaging studies. Main benign tumours include:

- Bronchial adenomas (now termed neuroendocrine tumors of low malignant potential)
- Hamartomas
- Leiomyomas
- Hemangiomas

Malignant Lung Tumours

Malignant tumours are classified primarily based on histological features into non-small cell lung carcinomas and small cell lung carcinomas.

Non-Small Cell Lung Carcinomas (NSCLCs)

This group includes the most prevalent lung cancers and is subdivided into:

- adenocarcinoma
- squamous cell carcinoma
- large cell carcinoma

Adenocarcinoma: The most common type, especially among non-smokers. It originates from glandular epithelium and often occurs peripherally.

Squamous cell carcinoma: Typically arises centrally within the bronchi and is strongly associated with smoking.

Large cell carcinoma: A diagnosis of exclusion characterized by undifferentiated malignant cells without glandular or squamous differentiation.

Small Cell Lung Carcinoma (SCLC)

SCLC accounts for approximately 15% of lung cancers. It is characterized by small, round to oval cells with neuroendocrine features, high mitotic rate, and aggressive behavior. It often presents with extensive disease at diagnosis and responds initially to chemotherapy and radiotherapy.

Other Rare Lung Tumours

The WHO also recognizes rare tumours such as carcinoid tumours, sarcomatoid carcinomas, and lymphomas involving the lung.

Classification of Tumours of the Pleura

Pleural tumours primarily originate from mesothelial cells lining the pleura. The WHO classification emphasizes mesothelial tumours, their benign, borderline, and malignant categories.

Benign Pleural Tumours

The most common benign pleural tumour is:

- Localized fibrous tumour of the pleura (also called solitary fibrous tumour)

These are usually asymptomatic, slow-growing, and incidentally found.

Borderline and Intermediate Tumours

This category includes tumours with uncertain malignant potential, though they are less well-defined compared to malignant tumours.

Diffuse Mesothelioma of the Pleura

While classified as malignant, mesotheliomas are a distinct entity with unique pathological features.

Malignant Pleural Tumours

The most significant malignant pleural tumour is:

- Malignant mesothelioma

This tumour arises from mesothelial cells and is strongly associated with asbestos exposure.

WHO Classification of Mesothelial Tumours

Mesothelial tumours are categorized based on histological subtypes, differentiation, and cellular features:

- Epithelioid mesothelioma: The most common form, characterized by epithelial-like cells.
- Sarcomatoid mesothelioma: Composed of spindle-shaped cells resembling sarcomas.
- Biphasic (mixed) mesothelioma: Contains both epithelioid and sarcomatoid components.

Additional features include the grading of cellular atypia, mitotic activity, and invasion patterns, which influence prognosis.

Key Features and Diagnostic Criteria in WHO Classification

The WHO classification emphasizes several diagnostic criteria:

- Histopathological features: Cell morphology, growth patterns, invasion depth.
- Immunohistochemistry: Markers such as calretinin, WT-1, cytokeratin 5/6 for mesothelial origin; TTF-1, Napsin A for adenocarcinomas; p40, p63 for squamous cell carcinomas.
- Molecular features: Genetic alterations, e.g., EGFR mutations in adenocarcinoma, BRAF, KRAS mutations, and PD-L1 expression relevant for targeted therapy.

Importance of WHO Classification in Clinical Practice

The WHO classification guides clinicians by:

- Providing a standardized terminology for diagnosis and communication.
- Informing prognosis; for example, adenocarcinomas generally have better outcomes compared to small cell carcinomas.
- Influencing treatment decisions; targeted therapies depend on molecular subtypes.
- Facilitating research and epidemiological studies through consistent categorization.

Updates in the Latest WHO Classifications

The WHO periodically revises its classification to incorporate advances in pathology and molecular biology. Notable updates include:

- Recognition of new subtypes of lung adenocarcinoma (e.g., lepidic, acinar, papillary).
- Inclusion of molecular markers as diagnostic criteria.
- Clarification of borderline and pre-invasive lesions.

- Better characterization of mesothelial tumours, including epithelioid, sarcomatoid, and biphasic variants.

Conclusion

The WHO classification of tumours of the lung and pleura remains a cornerstone in thoracic pathology, fostering precise diagnosis, guiding treatment, and improving understanding of tumour biology. Its systematic approach to categorizing benign, borderline, and malignant neoplasms based on histological, immunohistochemical, and molecular features ensures consistency across institutions and enhances patient care. Staying updated with WHO revisions is essential for healthcare professionals involved in the management of thoracic tumours, ultimately leading to better outcomes for patients.

Keywords: WHO classification, lung tumours, pleural tumours, mesothelioma, lung carcinoma, benign lung tumours, malignant lung tumours, thoracic pathology, tumour histology, thoracic neoplasms

WHO Classification of Tumours of the Lung Pleura

The World Health Organization (WHO) classification of tumours of the lung and pleura represents a comprehensive framework that guides pathologists, oncologists, and researchers in diagnosing, categorizing, and managing thoracic neoplasms. This classification system, regularly updated to incorporate advances in molecular pathology and histopathology, provides a standardized language that enhances clinical decision-making and facilitates epidemiological studies. In this review, we explore the detailed taxonomy of pleural tumours as outlined by the WHO, emphasizing their histopathological features, molecular characteristics, and clinical implications.

Introduction

The pleura, a vital serous membrane enveloping the lungs and lining the thoracic cavity, is a site for a diverse array of benign and malignant tumours. Malignant pleural mesothelioma (MPM) is the most notorious primary neoplasm arising from the mesothelial cells, but secondary tumours such as metastases from lung, breast, and other carcinomas also involve the pleura. The WHO classification provides a structured approach to distinguish these entities, primarily focusing on mesothelial neoplasms, fibrous tumours, and other rare variants.

Understanding the WHO classification is essential for accurate diagnosis, prognostication, and therapeutic planning, especially given the heterogeneity of pleural tumours and the evolving landscape of molecular diagnostics.

Primary Tumours of the Pleura

Primary tumours originate from the mesothelial lining or associated stromal components. They are classified based on histopathological features, immunohistochemical profiles, and molecular alterations.

Mesothelial Tumours

Mesothelial neoplasms are the most common primary pleural tumours and encompass benign, borderline, and malignant categories.

Benign Mesothelial Tumours

- Localized Mesothelial Hyperplasia: Reactive proliferation of mesothelial cells often associated with inflammation or trauma.
- Well-Differentiated Papillary Mesothelial Tumour (WDPMT): A rare benign entity characterized by papillary proliferation of mesothelial cells with minimal atypia and no invasion.

Malignant Mesothelial Tumours

- Malignant Mesothelioma (MM): The most significant primary malignant tumour of the pleura, with distinct histological subtypes and molecular features.

Malignant Mesothelioma Subtypes

The WHO recognizes three main histological subtypes, each with differing prognosis and therapeutic responses:

- Epithelioid Mesothelioma
- Sarcomatoid Mesothelioma
- Biphasic (Mixed) Mesothelioma

Epithelioid Mesothelioma:

Most common (~60-70%), characterized by polygonal cells forming tubules, papillae, or solid sheets. Frequently exhibits a prominent fibrous stroma and tends to have a better prognosis.

Sarcomatoid Mesothelioma:

Less common (~10-20%), composed of spindle-shaped cells resembling sarcoma. These tumours

are often more aggressive and less responsive to therapy.

Biphasic Mesothelioma:

Contains both epithelioid and sarcomatoid components, with prognosis depending on the proportion of each.

Molecular and Immunohistochemical Features of Mesothelioma

- Key Immunohistochemical Markers:
 - Positive: Calretinin, WT1, D2-40 (podoplanin), Cytokeratin 5/6, Mesothelin
 - Negative: Carcinoma markers such as TTF-1, CEA, Ber-EP4
- Molecular Alterations:
 - Loss of BAP1 expression
 - CDKN2A (p16) deletion detectable via FISH
 - Rare mutations in BRAF, NRAS

Other Mesothelial Tumours

- Localized Malignant Mesothelioma: Rare, similar to diffuse but confined to localized areas.
- Multicystic Mesothelioma: Generally benign, presenting as multicystic lesions.

Fibrous and Other Tumours of the Pleura

Aside from mesothelial origins, the pleura can host fibrous and miscellaneous tumours.

Solitary Fibrous Tumour (SFT)

- Originates from fibroblastic mesenchymal cells.
- Usually benign but can be malignant.
- Features: Well-circumscribed, spindle cells with high vascularity, "patternless" pattern, and CD34 positivity.

- Malignant SFTs show increased cellularity, atypia, mitoses, necrosis.
- Molecular hallmark: NAB2-STAT6 gene fusion detectable via immunohistochemistry (STAT6 nuclear positivity).

Fibrosarcoma and Other Sarcomas

Rare; includes fibrosarcoma, malignant peripheral nerve sheath tumour, and angiosarcoma. These are generally distinguished through histomorphology and immunoprofile.

Mesenchymal Tumours with Other Differentiations

- Lipomas and Liposarcomas
- Hemangiopericytoma

Secondary Tumours of the Pleura

Metastatic involvement of the pleura is common, especially from lung, breast, and other carcinomas.

Common Metastases

- Lung Carcinomas: Adenocarcinoma, squamous cell carcinoma
- Breast Carcinoma
- Gastrointestinal Tumours
- Lymphomas and Leukemias

Immunohistochemistry and molecular studies help determine the primary site, especially in poorly differentiated tumours.

Rare and Unusual Pleural Tumours

- Mesenchymal chondrosarcoma
- Malignant fibrous histiocytoma
- Synovial sarcoma

These are exceedingly rare but are recognized within the WHO framework based on histopathology and molecular features.

Diagnostic Challenges and Advances

Accurate classification relies on a combination of histopathology, immunohistochemistry, and increasingly, molecular diagnostics.

Role of Molecular Diagnostics

- Detection of BAP1 loss and CDKN2A deletions for mesothelioma
- Identification of NAB2-STAT6 fusion in SFT
- Next-generation sequencing panels for rare entities

Diagnostic Algorithms

- Use of panel immunohistochemistry to differentiate mesothelioma from metastatic carcinoma
- Employing molecular markers for ambiguous cases

Clinical Implications of WHO Classification

The WHO classification informs prognosis and guides management strategies:

- Benign vs. Malignant: Surgery for benign tumours; multimodal therapy for mesothelioma.
- Histological Subtypes: Epithelioid mesotheliomas have better outcomes.
- Molecular Features: Potential targets for novel therapies.

Conclusion

The WHO classification of tumours of the lung and pleura offers a detailed and nuanced taxonomy that reflects advances in our understanding of thoracic neoplasms. It emphasizes the importance of integrating histopathological, immunohistochemical, and molecular data to achieve accurate diagnosis. As research continues to evolve, especially in molecular genetics and targeted therapies, this classification will likely undergo further refinements, ultimately improving patient outcomes through tailored treatment approaches.

Understanding the diverse spectrum of pleural tumours aids clinicians and pathologists in making precise diagnoses, prognostic assessments, and guiding appropriate management. The ongoing evolution of the WHO classification underscores the importance of multidisciplinary collaboration in thoracic oncology.

Question What is the WHO classification of tumors of the lung and pleura? The WHO classification of tumors of the lung and pleura is a standardized system that categorizes benign and

malignant tumors based on histological features, genetic profiles, and clinical behavior to guide diagnosis and treatment. How are mesotheliomas classified in the WHO system? In the WHO classification, mesotheliomas are categorized into epithelioid, sarcomatoid, biphasic (mixed), and rare variants, based on their cellular morphology and immunohistochemical profiles. What are the main types of primary lung carcinomas according to WHO? The main types include non-small cell lung carcinomas (adenocarcinoma, squamous cell carcinoma, large cell carcinoma) and small cell lung carcinoma, each with distinct histological and molecular features. How does the WHO classify benign tumors of the lung and pleura? Benign tumors are classified as hamartomas, papillomas, lipomas, and other rare benign neoplasms, characterized by their benign histological appearance and non-invasive behavior. What is the significance of the WHO classification in clinical management? The WHO classification helps in accurate diagnosis, prognosis, and selection of appropriate treatment strategies by providing a standardized framework for tumor categorization. Are genetic features incorporated into the WHO classification of lung and pleural tumors? Yes, the WHO classification increasingly incorporates molecular and genetic markers that aid in subclassification, prognosis, and targeted therapy options. How are metastatic tumors to the lung and pleura classified in the WHO system? Metastatic tumors are classified based on their primary origin and histological similarity, with common types including metastases from breast, colon, and other cancers, but they are not part of the primary WHO tumor classification. What updates have recent WHO classifications introduced for lung and pleural tumors? Recent updates include enhanced molecular characterization, recognition of new tumor variants, and refined criteria for differentiating benign from malignant lesions to improve diagnostic accuracy. How does the WHO classification address rare tumors of the lung and pleura? The WHO classification provides specific categories for rare tumors such as solitary fibrous tumors, carcinoids, and other uncommon neoplasms, facilitating their recognition and management. Why is the WHO classification important for pathologists and clinicians? It ensures consistent diagnosis, informs prognosis, guides treatment decisions, and fosters research by providing a comprehensive, evidence-based framework for tumor categorization.

Related keywords: lung tumors, pleural tumors, WHO classification, thoracic oncology, mesothelioma, lung cancer types, pleural mesothelioma, malignant pleural effusion, tumor histology, lung neoplasms

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