Ministry of Health of the Republic of Belarus
Educational Institution
“Gomel State Medical University”

Department of Pathological Anatomy

Author:
Grigorii V. Tishchenko, Associate Professor of the Department of Pathological Anatomy, Candidate of Medical Sciences (Ph.D. in Medicine)

METHODICAL GUIDELINES

for conducting a practical class
in the academic discipline “Pathological Anatomy”
for students
of the 3rd year, Faculty of International Students (instruction in English),
enrolled in the specialty
7-07-0911-01 “General Medicine”

Topic: “Tumours. Mesenchymal (soft tissue) neoplasms, teratomas”

Duration: 3 hours

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EDUCATIONAL AND INSTRUCTIONAL GOALS, OBJECTIVES, AND MOTIVATION FOR MASTERING THE TOPIC

Educational Goal:

- To study the classification, morphology, and clinical features of mesenchymal (soft tissue) neoplasms and germ cell tumours (teratomas). To analyze benign and malignant soft tissue tumours arising from adipose tissue (lipoma, liposarcoma), fibrous tissue (fibroma, fibrosarcoma, desmoid tumour), smooth muscle (leiomyoma, leiomyosarcoma), skeletal muscle (rhabdomyoma, rhabdomyosarcoma), vascular tissue (haemangioma, angiosarcoma, Kaposi sarcoma), and peripheral nerve sheath (schwannoma, neurofibroma, malignant peripheral nerve sheath tumour). To discuss the histological grading, immunohistochemical markers (e.g., desmin, smooth muscle actin, S-100, CD34, CD31, MyoD1, myogenin), and molecular genetic features (e.g., translocations in Ewing sarcoma, synovial sarcoma, liposarcoma). To examine teratomas as germ cell tumours containing tissues from all three germ layers (ectoderm, mesoderm, endoderm), including mature teratomas (benign) and immature teratomas (malignant), as well as monodermal teratomas (e.g., struma ovarii, carcinoid). To discuss the anatomical distribution and clinical behaviour of these neoplasms.

Instructional Goal:

- Within the framework of the educational process for this academic discipline, the student must acquire not only theoretical knowledge, practical skills and abilities in the specialty but also develop their personal potential. They should cultivate qualities of responsibility and patriotism, be prepared to actively participate in the economic, socio-cultural, and public life of the country, recognize the social significance of their future professional activity, understand the norms of medical ethics and deontology, and learn to observe academic and labor discipline. In the course of studying the educational material, students should realize the importance of maintaining a healthy lifestyle and, as an example in the future, when performing professional duties, set an example for those around them and their patients.

Objectives: Upon completion of the practical session, the student must:

Know:

- The classification of benign and malignant soft tissue tumours;
- The morphological features of common soft tissue neoplasms (lipoma, liposarcoma, leiomyoma, leiomyosarcoma, rhabdomyosarcoma, angiosarcoma, schwannoma, neurofibroma);
- The immunohistochemical markers used to diagnose soft tissue tumours;
- The definition, classification, and morphological features of teratomas (mature, immature, monodermal);
- The clinical behaviour, outcomes, and complications of soft tissue sarcomas and teratomas.

Be able to:

- Identify benign and malignant soft tissue neoplasms on histological specimens;
- Diagnose teratomas based on the presence of tissues derived from multiple germ layers;
- Distinguish between mature (benign) and immature (malignant) teratomas using histological criteria;
- Diagnose pathological processes and diseases based on the description of macroscopic and microscopic changes in organs and tissues of the body.

***Master*:**

- Basic techniques for working with a microscope;
- Skills in clinical-anatomical analysis;
- The fundamentals of synthetic generalization of morphological diagnostic signs of diseases and their correct interpretation in cause-and-effect relationships.

Motivation for Mastering the Topic:

Soft tissue sarcomas, though relatively rare (approximately 1% of all adult cancers), are aggressive malignancies that require prompt and accurate diagnosis for optimal management. They can arise in any location and often present diagnostic challenges due to their morphological diversity and overlapping features with benign lesions. Teratomas are among the most common germ cell tumours, frequently encountered in the ovaries, testes, and sacrococcygeal region in children and adults. Understanding the histological spectrum of these neoplasms, from benign mature teratomas to malignant immature teratomas and sarcomas, is essential for appropriate surgical and oncological management. This knowledge is critical for pathologists, surgeons, oncologists, and other clinicians involved in the care of patients with these tumours.

QUESTIONS

1. Fibrous tissue tumors. Definition. Classification. Types and localization. Pathological features.
2. Adipose tissue tumors. Definition. Classification. Types and localization. Pathological features.
3. Muscle tissue tumors. Definition. Classification. Types and localization. Pathological features.
4. Nervous tissue tumors. Definition. Classification. Types and localization. Pathological features.
5. Tumors of blood vessels. Definition. Classification. Types and localization. Pathological features.
6. Tumors of lymphatic vessels. Definition. Classification. Types and localization. Pathological features.

7. Tumors of synovial tissue. Definition. Classification. Types and localization. Pathological features.

8. Bone tissue tumors. Definition. Classification. Types and localization. Pathological features.

9. Cartilage tissue tumors. Definition. Classification. Types and localization. Pathological features.

tumor may cause **pain** or **discomfort**, especially if it **impinges on nearby structures**, nerves, or blood vessels. Retroperitoneal liposarcomas, situated in the abdominal cavity, may grow to a significant size before causing symptoms, potentially leading **to abdominal pain or distension**. The dedifferentiated subtype, known for its aggressive behavior, may exhibit a combination of well-differentiated and high-grade components, impacting the clinical course.

Tumors of muscle tissue

Benign

1. **Leiomyoma** consists of smooth muscle with chaotic location of the muscular bands separated by the stroma with blood vessels and nerves. Secondary changes such as necrosis, hemorrhages, cysts, hyalinosis, petrifaction are characteristic for leiomyoma.

2. **Rhabdomyoma** consists of striated muscle fibers, which resemble to embryonic muscular fibers and myoblasts. Cardiac rhabdomyoma appears as a hamartomatous lesion and is accompanied by other developmental defects (large masses of striated muscles). Soft tissue rhabdomyomas are predominantly located in the head and neck, tongue, etc. and composed of large, round to oval cells, having abundant, granular cytoplasm.

3. **Granular-cell tumor** (Abrikosov's tumor) is a small tumor in a capsule, which consists of large, round or polygonal, uniform, with granular cytoplasm (no lipids) cells. Usually it occurs in the tongue, esophagus, and skin.

Leiomyoma: Morphology

Leiomyomas, also known as uterine fibroids, are **benign smooth muscle tumors** that commonly originate from the **myometrium** (muscle layer) of the uterus.

Morphologically, leiomyomas exhibit a distinctive appearance characterized by **whorled bundles of smooth muscle cells** surrounded by connective tissue.

These tumors can vary in size, ranging from **small nodules to large masses** that distort the shape of the uterus.

Microscopically, leiomyomas are composed of **elongated, spindle-shaped smooth muscle cells with centrally located nuclei**. The extent of collagen deposition within the tumor influences its consistency, with some leiomyomas appearing more solid, while others may have a more rubbery texture.

Different subtypes of leiomyomas, such as **intramural**, **submucosal**, and **subserosal**, are classified based on their location within the uterine wall.

Leiomyoma: Clinical Manifestations

Leiomyomas are most commonly found in the **uterus**, but they can also occur in other parts of the reproductive system and, more rarely, in **extrauterine locations**. Intramural leiomyomas are situated within the uterine wall, submucosal leiomyomas grow **into the uterine cavity**, and subserosal leiomyomas protrude **outward from the uterus**.

The clinical manifestations of leiomyomas can vary widely. While many leiomyomas are **asymptomatic**, those that cause symptoms often depend on their size, number, and location. Intramural and subserosal leiomyomas may lead to **pelvic pain** or **pressure**, while submucosal leiomyomas can cause abnormal **uterine bleeding**. Women with submucosal leiomyomas may experience fertility issues or **recurrent pregnancy loss**.

Additionally, leiomyomas can contribute to other reproductive health concerns, such as **difficulties with conception** or increased discomfort during menstruation. The severity and nature of symptoms can vary from individual to individual, and treatment options range from watchful waiting for asymptomatic cases to surgical interventions, such as myomectomy or hysterectomy, for those with significant symptoms or fertility concerns.

Rhabdomyoma: Morphology

Rhabdomyomas are rare benign tumors composed of **striated muscle cells**, or rhabdomyocytes.

Morphologically, these tumors often exhibit a characteristic appearance under the microscope, with **elongated cells that have cross-striations**, resembling skeletal muscle fibers.

The tumor cells are typically well-differentiated and may form **bundles or sheets within a myxoid or fibrous stroma**.

Rhabdomyomas can be further classified into **cardiac** and **extracardiac** types based on their localization. Cardiac rhabdomyomas, more commonly seen in pediatric patients, often arise within the walls of the heart, particularly the **ventricles**. Extracardiac rhabdomyomas occur outside the heart, typically in the **head and neck regions**, and are more frequently observed in adults.

Rhabdomyoma: Clinical Manifestations

Cardiac rhabdomyomas are most frequently encountered in the ventricles of the heart, particularly in the **walls of the left ventricle**. They can also occur in the atria and septum. These tumors are often **associated with tuberous sclerosis**, a genetic disorder characterized by the growth of benign tumors in multiple organs. Extracardiac rhabdomyomas, while less common, can be found in various locations outside the heart. Common extracardiac sites include the head and neck, particularly the **oral cavity, pharynx, and larynx**. These tumors may also arise in the extremities, trunk, and other soft tissues.

The **clinical manifestations** of rhabdomyomas depend on their location and size. Cardiac rhabdomyomas, when present in the heart, may lead to symptoms such as **arrhythmias**, **heart failure**, or **obstruction of blood flow**. In some cases, cardiac rhabdomyomas may be detected prenatally during fetal ultrasound examinations.

Extracardiac rhabdomyomas, particularly those in the head and neck region, can cause symptoms related to their anatomic location. For example, tumors in the oral cavity or pharynx may lead to **difficulty swallowing**, **breathing difficulties**, or a visible mass.

Tumors of muscle tissue

Malignant

1. **Leiomyosarcoma** is a tumor with cellular atypia, high mitotic index, necrosis.

2. **Rhabdomyosarcoma** is characterized by severe pleomorphism, loss of features of muscular tissue.

Leiomyosarcoma: Morphology

Leiomyosarcoma is a **malignant soft tissue tumor** arising from **smooth muscle cells**.

Morphologically, leiomyosarcomas are characterized by the presence of **elongated, spindle-shaped cells** with blunt-ended nuclei. The tumor cells often display a **fascicular or storiform growth pattern**, forming **bundles or whorls** within a collagenous stroma.

Cellular atypia, **increased mitotic activity**, and **areas of necrosis** are common features, distinguishing leiomyosarcoma from benign smooth muscle tumors such as leiomyomas.

Immunohistochemical staining for smooth muscle markers, such as **smooth muscle actin** and **desmin**, is used to confirm the smooth muscle origin of the tumor cells. Leiomyosarcomas can occur in various locations, including the uterus (uterine leiomyosarcoma) and soft tissues in other parts of the body.

Leiomyosarcoma: Clinical Manifestations

Leiomyosarcomas have a predilection for forming in the smooth muscle layers of the **uterus**, giving rise to uterine leiomyosarcoma. These tumors can also arise in other soft tissues, including those in the **extremities**, **retroperitoneum**, and **gastrointestinal tract**. Retroperitoneal leiomyosarcomas, which develop behind the abdominal cavity, are often challenging to diagnose early due to their deep-seated location. Leiomyosarcomas can also occur in the blood vessels, known as **vascular leiomyosarcomas**.

Clinical manifestations of leiomyosarcoma vary based on the tumor's location. Uterine leiomyosarcomas may present with **abnormal uterine bleeding**, **pelvic pain**, or a **palpable pelvic mass**. In soft tissues, leiomyosarcomas can present as painless **masses that may grow rapidly**. Pain or discomfort may arise if the tumor compresses nerves or other structures. Retroperitoneal leiomyosarcomas may remain asymptomatic until they reach a considerable size, causing **abdominal pain** or **distension**. The potential for local recurrence and distant metastasis, particularly to the lungs, liver, and bones, makes leiomyosarcoma a clinically challenging malignancy.

Tumors of blood vessels

Benign

1. **Hemangioma** is a benign tumor of blood vessels. There are several types of hemangioma: capillary, cavernous, venous, etc.

2. **Glomus tumor** (glomangioma). More often develops in hands and feet (fingers and toes). It consists of vessels with endothelium, surrounded by ferrules of epithelioid (glomus) cells. Tumor is rich in nerves thus it is usually painful.

Malignant

Angiosarcoma is a highly malignant tumor with high mitotic cells rate and areas of necrosis. It has early metastases.

Hemangioma: Morphology

Hemangiomas are common **benign vascular tumors** characterized by an overgrowth of blood vessels.

Morphologically, hemangiomas can be categorized into two main types: **capillary** hemangiomas and **cavernous** hemangiomas.

Capillary hemangiomas are composed of **small, closely packed capillaries**, often forming a red or purplish lesion.

Cavernous hemangiomas consist of **larger, dilated blood vessels**, and they may appear as deeper, blue-colored masses.

Microscopically, these tumors demonstrate **proliferation of endothelial cells** forming vascular channels. The endothelial cells are surrounded by connective tissue and may exhibit characteristic lobular patterns. Hemangiomas are often described based on their developmental stage, including the **proliferative phase**, in which active angiogenesis occurs, and the **involutive phase**, marked by regression of the vascular components.

Hemangioma: Clinical Manifestations

Hemangiomas can occur in various locations throughout the body, and their common localization often depends on the age of the individual. **Infantile hemangiomas** are the most prevalent vascular tumors in infants, typically appearing within the first few weeks of life. They commonly occur on the **skin** and **superficial soft tissues**, with a predilection for the head and neck region. While infantile hemangiomas often undergo spontaneous involution during childhood, some may require medical intervention or treatment due to complications such as ulceration or disfigurement. Cavernous hemangiomas can also affect internal organs, including the **liver, spleen,** or **brain**.

The **clinical manifestations** of hemangiomas vary depending on their type, size, and location. Infantile hemangiomas often manifest as **raised, red,** or **purplish nodules** on the skin. They may grow rapidly during the first months of life before entering a phase of spontaneous regression. Larger hemangiomas or those located in critical areas, such as around the eyes or mouth, may lead to functional impairment or **cosmetic concerns**. Cavernous hemangiomas in internal organs can be asymptomatic or present with symptoms related to the specific organ involved. For example, hepatic hemangiomas may cause **abdominal pain** or discomfort.

Glomus tumor

Glomus tumors are rare, benign neoplasms originating from the **glomus body**, a specialized **arteriovenous structure** involved in thermoregulation.

Morphologically, glomus tumors consist of **uniform**, **round** to **polygonal cells** with a characteristic **perivascular arrangement**. These cells are surrounded by a prominent layer of smooth muscle-like cells and a rich vascular network. Immunohistochemical markers, such as **smooth muscle actin** and **S100** protein, help confirm the diagnosis.

Clinically, glomus tumors often present as **small**, **painful nodules**, particularly in the **subungual region** of the fingers, where they are known as subungual glomus tumors. These tumors can cause localized tenderness and sensitivity to cold or pressure.

Though typically benign, glomus tumors can be challenging to diagnose due to their small size and the variability in clinical presentation. Surgical excision is the primary treatment, providing relief from symptoms and preventing recurrence.

Angiosarcoma: Morphology

Angiosarcomas are aggressive **malignant tumors** that arise from the **endothelial cells** lining blood vessels or lymphatic vessels.

Morphologically, angiosarcomas exhibit considerable variability, with features ranging **from well-differentiated to highly anaplastic and pleomorphic**.

Microscopically, these tumors often display **irregular, anastomosing vascular channels** lined by atypical endothelial cells.

The cells may show **hyperchromatic nuclei**, **cellular atypia**, and **frequent mitotic figures**.

The tumor stroma can be **hemorrhagic**, and areas of **necrosis** may be present.

Angiosarcoma: Clinical Manifestations

Angiosarcomas can arise in various locations throughout the body, but they most commonly affect the **skin** and soft tissues. **Cutaneous angiosarcomas** often manifest as bruise-like lesions on the head and face and are associated with chronic sun exposure. **Soft tissue angiosarcomas** may develop in the deep tissues of the extremities or trunk. Another distinct subtype is **breast angiosarcoma**, which can occur de novo or as a complication of prior radiation therapy for breast cancer. Additionally, angiosarcomas can arise in visceral organs such as the **liver**, **spleen**, or **heart**.

The clinical manifestations of angiosarcomas depend on their location and can be nonspecific, contributing to delayed diagnosis. Cutaneous angiosarcomas may present as purplish or **bruise-like lesions** that may be mistaken for benign conditions. Soft tissue angiosarcomas can present as **painless masses** or **swelling**, while visceral angiosarcomas may cause symptoms related to the affected organ's dysfunction. Breast angiosarcomas may present as **rapidly growing masses in the breast**, sometimes with associated skin changes. Due to their aggressive nature, angiosarcomas have a high potential for local recurrence and distant metastasis, particularly to the lungs.

Kaposi's sarcoma: Morphology

Kaposi's sarcoma (KS) is a **vascular tumor** associated with human herpesvirus 8 (**HHV-8**) infection.

Morphologically, Kaposi's sarcoma can be categorized into **several subtypes**, with the most common form being classic Kaposi's sarcoma, often affecting elderly individuals.

The tumor is characterized by **spindle-shaped cells**, **abnormal blood vessels**, and **inflammatory infiltrates**.

In endemic regions, particularly in Sub-Saharan Africa, epidemic Kaposi's sarcoma occurs in individuals with **immunosuppression**, such as those with **HIV/AIDS**. The morphology of these lesions is more aggressive, with a higher number of spindle cells and increased mitotic activity.

AIDS-related Kaposi's sarcoma, seen in the context of HIV infection, often presents as **multifocal skin lesions** but can involve internal organs, demonstrating a more aggressive clinical course.

Kaposi's sarcoma: Clinical Manifestations

Classic Kaposi's sarcoma frequently involves the **lower extremities**, presenting as reddish or purple plaques or nodules. Endemic Kaposi's sarcoma is more widespread in Sub-Saharan Africa and typically affects **mucosal surfaces**, often presenting with lesions in the oral cavity. AIDS-related Kaposi's sarcoma commonly manifests as cutaneous lesions but can involve internal organs such as the **gastrointestinal tract**, **lungs**, and **lymph nodes**. Kaposi's sarcoma has also been observed in **transplant recipients**, where it may arise as a **consequence of immunosuppressive therapy**.

The **clinical manifestations** of Kaposi's sarcoma depend on the variant and the immunologic status of the affected individual. Classic Kaposi's sarcoma is usually **indolent**, with **slow progression** and a relatively favorable prognosis. In endemic regions, epidemic Kaposi's sarcoma associated **with HIV/AIDS can be more aggressive**, causing widespread skin lesions and visceral involvement, leading to complications. Lesions may vary **from macules and papules to nodules and plaques**. The disease course in AIDS-related Kaposi's sarcoma can be rapidly progressive, and internal organ involvement can result in significant morbidity and mortality.

Tumors of lymphatic vessels

Benign tumors from lymphatic vessels

Lymphangioma is characterized by growth of lymphatic vessels. Microscopically tumor looks consists of cavities filled with lymph.

Malignant tumors from lymphatic vessels

Lymphangiosarcoma. It is composed of lymph clefts with proliferating atypical endothelial cells.

Lymphangioma: Morphology

Lymphangiomas are benign tumors that arise from the abnormal proliferation of lymphatic vessels.

Morphologically, these tumors are characterized by **thin-walled channels** or **cysts filled with lymphatic fluid**.

Lymphangiomas can be classified into **three main types**: *cystic hygromas*, *capillary lymphangiomas*, and *cavernous lymphangiomas*.

Cystic hygromas consist of large cystic spaces, while capillary lymphangiomas are composed of smaller, more tightly packed vessels. Cavernous lymphangiomas contain larger, dilated lymphatic spaces.

Microscopically, the lining of these vessels consists of endothelial cells. Lymphangiomas often **lack smooth muscle in their walls**, which differentiates them from blood vessels.

Lymphangioma: Clinical Manifestations

Lymphangiomas can be found in different anatomical regions, with a predilection for the **head and neck**, **axilla**, and **mediastinum**. In infants and children, cystic hygromas are commonly seen in the neck and may present as soft, compressible masses. Capillary lymphangiomas may occur in the **skin** or **mucous membranes**, often affecting the head and neck. Cavernous lymphangiomas, characterized by larger cystic spaces, are more commonly found in deeper tissues such as the retroperitoneum or within organs like the spleen.

The **clinical manifestations** of lymphangiomas depend on their size, location, and involvement of surrounding structures. In the head and neck region, lymphangiomas may present as **painless**, **soft masses** that are often discovered at birth or in early childhood. These tumors may grow slowly over time and can be associated with **cosmetic concerns** or functional impairment if they compress adjacent structures. Lymphangiomas in deeper tissues or internal organs may be asymptomatic or cause symptoms related to the compression of organs or vessels. Complications can include infection, bleeding, or impaired organ function, depending on the extent of the lymphangioma.

Tumors of synovial tissue

1. **Tenosynovial giant cell tumor** develops in the tendons and tendon sheath. It contains a lot of stroma with hyalinosis, and a little number of vessels. It may have xanthoma cells and clefts.

2. **Synovial sarcoma** (malignant synovioma) develops in the large joints. Some tumors have pleomorphic cells and pseudoglandular formations with cysts, the other have fibroblast-like atypical cells and collagen fibers, structures resembling tendons.

TGCT: Morphology

Tenosynovial giant cell tumor (TGCT), also known as giant cell tumor of the tendon sheath (GCT-TS) or pigmented villonodular synovitis (PVNS), is a **benign proliferative disorder** involving the synovium and tendon sheaths.

Morphologically, TGCT is characterized by the presence of **giant cells**, **hemosiderin deposition**, and a **mononuclear cell component**.

The giant cells are multinucleated and can be observed within a background of **synovial-like stroma**. The mononuclear cells consist of fibroblast-like synoviocytes.

These tumors can be classified into *localized* and *diffuse types*, with the localized form primarily affecting the digits, while the diffuse form involves larger joints such as the knee.

The histological appearance and classification help guide treatment decisions and predict the potential for local recurrence.

TGCT: Clinical Manifestations

Tenosynovial giant cell tumors most commonly occur in the **hand** and **fingers**, particularly around the **flexor tendons**. The diffuse form is more frequently found in **large joints**, with the knee being a common site of involvement. While TGCT is generally considered benign, its local invasiveness and potential for recurrence underscore the importance of appropriate management and monitoring.

Clinical manifestations of TGCT can vary based on the tumor's location and type. In the localized form, patients may notice a **painless**, **firm mass** or nodule in the affected digit, often causing cosmetic concerns. Joint movement may become restricted as the tumor enlarges. The diffuse form, commonly affecting the knee, can lead to pain, **swelling**, and **decreased range of motion**. In some cases, patients may experience mechanical symptoms such as catching or locking of the joint. If left untreated, TGCT can cause **joint damage**, leading to functional impairment.

While TGCT is not typically associated with systemic symptoms, its local aggressiveness necessitates appropriate management.

Synovial sarcoma: Morphology

Synovial sarcoma, often referred to as synovioma, is a **malignant soft tissue tumor** that arises from the synovial tissue in joints, tendons, or bursae. Despite its name, synovial sarcoma does not originate from the synovial membrane of joints.

Morphologically, synovial sarcoma is characterized by a **biphasic pattern**, featuring both **epithelial** and **spindle cell components**.

The epithelial cells form glandular or tubular structures, while the spindle cells exhibit a fibrosarcoma-like appearance. Another subtype, monophasic synovial sarcoma, is composed solely of spindle cells.

Immunohistochemical staining for specific markers, such as **cytokeratins** and epithelial membrane antigen (**EMA**), aids in confirming the diagnosis.

Synovial sarcoma: Clinical Manifestations

Synovial sarcoma can arise in diverse soft tissue locations, most commonly occurring **near large joints**, especially the lower extremities, followed by the upper extremities. Despite its name, it can develop in proximity to, rather than directly within, synovial joints. Synovial sarcoma can also be found in the **trunk**, **head and neck**, and other less common sites.

Clinical manifestations of synovial sarcoma are often **nonspecific**, and the tumor may be asymptomatic initially. As it grows, patients may notice a **painless**

swelling or mass in the affected area. **Pain** may develop as the tumor enlarges and compresses adjacent structures or involves nerve structures. The tumor has a propensity for **local recurrence and metastasis**, particularly to the lungs, which can contribute to respiratory symptoms. The age of onset is typically in adolescents and young adults, but synovial sarcoma can occur at any age.

Mesothelioma: Morphology

Mesothelioma is a **malignant tumor** arising from the **mesothelial cells** that line the serosal surfaces of the pleura, peritoneum, pericardium, and tunica vaginalis.

Morphologically, mesotheliomas are characterized by a **diffuse**, **infiltrative growth** pattern with a propensity for local invasion.

The tumor cells demonstrate a variety of patterns, including **tubular**, **papillary**, or **solid** structures.

Mesothelioma cells are typically **cuboidal** to **columnar** in shape, with eosinophilic cytoplasm and prominent nucleoli. Immunohistochemical staining is crucial for diagnosis, with markers such as **calretinin**, **WT-1**, and **cytokeratin** commonly used to confirm the mesothelial origin of the tumor.

The association with **asbestos exposure**, a known risk factor for mesothelioma, is often considered in the clinical context and history.

Mesothelioma: Clinical Manifestations

The most common site for mesothelioma is the pleura, resulting in **pleural** mesothelioma. **Peritoneal** mesothelioma, affecting the lining of the abdominal cavity, is the second most common form. **Pericardial** mesothelioma, arising in the lining of the heart, is rare but can occur. Mesothelioma of the **tunica vaginalis**, which covers the testes, is exceedingly rare. The primary cause of mesothelioma is **asbestos exposure**, and individuals with occupational or environmental exposure to asbestos are at an increased risk.

Clinical manifestations of mesothelioma depend on the specific location of the tumor. Pleural mesothelioma typically presents with **respiratory symptoms** such as **dyspnea**, **chest pain**, and **persistent cough**. Peritoneal mesothelioma may cause **abdominal pain**, **distension**, **weight loss**, and **gastrointestinal symptoms**. Pericardial mesothelioma can lead to chest pain, palpitations, and shortness of breath.

The latency period between asbestos exposure and the development of mesothelioma is often several decades, contributing to a delayed diagnosis. Unfortunately, mesothelioma is often diagnosed at an advanced stage, limiting treatment options and resulting in a poor prognosis.

Bone tumors

Benign

Osteoma develops as a rule in spongy and tubular bones, skull. It is common in young persons, mostly males. Macroscopically, an osteoid osteoma appears as a small round or oval mass containing a central red-brown, friable area. Microscopically, the tumor appears as a mass of irregular bone trabeculae, fibrous

tissue, and vessels. The center of the tumor is rich in osteoblasts, calcification, and multinucleate giant cells.

Malignant

Osteosarcoma consists of osteogenic tissue rich in atypical cells of osteoblastic type with a lot of mitoses. Two types of osteosarcoma are known: a) osteoblastic type (bone formation), b) osteolytic type (bone destruction). Most osteosarcomas arise in the metaphyseal end of long bones (predominantly the femur, humerus, and tibia), but they can involve any bone, including the small bones of the hands, feet and face.

Osteoma: Morphology

Osteomas are **benign bone tumors** characterized by the proliferation of compact or cancellous bone.

Morphologically, osteomas are typically **well-circumscribed**, **slow-growing** lesions that exhibit a homogeneous appearance on imaging studies.

These tumors may present as either ivory-like compact osteomas or spongy cancellous osteomas. Compact osteomas are composed of **dense**, **mature bone**, while cancellous osteomas contain a network of trabeculae resembling normal cancellous bone.

Osteomas most commonly involve the **craniofacial skeleton**, particularly the paranasal sinuses and the bones of the skull.

Histologically, osteomas show a **well-differentiated bony structure** with mature lamellar bone, and they lack the cellular atypia seen in malignant bone tumors.

Osteoma: Clinical Manifestations

Osteomas frequently localize to the **bones of the skull and face**. Frontal and ethmoid sinuses are common sites for paranasal sinus osteomas. In addition to the sinuses, osteomas can occur on various craniofacial bones, including the mandible, maxilla, and temporal bones. These tumors are often **incidental findings** on imaging studies conducted for unrelated reasons, as they tend to be slow-growing and asymptomatic. While craniofacial osteomas are the most common, osteomas can also occur in other parts of the skeleton, such as **long bones** or the **axial skeleton**.

Clinical manifestations of osteomas depend on their location and size. In many cases, osteomas are asymptomatic and discovered incidentally on imaging studies. When symptoms do occur, they are often related to the tumor's mass effect on surrounding structures. For example, **osteomas in the sinuses** may cause **sinusitis**, **nasal congestion**, or **headache**. In cases where the osteoma affects the skull bones, cosmetic concerns may arise due to visible or palpable masses. Osteomas that involve the **temporal bones** can cause **hearing loss** or **tinnitus**.

Overall, the prognosis for osteomas is excellent, and recurrence after complete excision is rare.

Osteosarcoma: Morphology

Osteosarcoma is a **malignant bone tumor** characterized by the production of osteoid, which is immature bone tissue, by the tumor cells.

Morphologically, osteosarcoma exhibits considerable **heterogeneity**, with various subtypes identified based on the predominant cellular components.

Conventional osteosarcoma, the most common form, typically presents with spindle-shaped tumor cells that produce osteoid. Other subtypes include **osteoblastic**, **chondroblastic**, and **fibroblastic** osteosarcomas, which display additional differentiation toward bone, cartilage, or fibrous tissue, respectively.

The tumor cells often show **high-grade cellular atypia**, numerous **mitotic figures**, and areas of **necrosis**. Osteosarcomas most commonly arise at the metaphysis of long bones, with a predilection for the distal femur, proximal tibia, and proximal humerus. The presence of osteoid-producing tumor cells is essential for the diagnosis of osteosarcoma.

Osteosarcoma: Clinical Manifestations

Osteosarcoma primarily affects the **metaphyseal regions of long bones**, where rapid bone growth occurs during adolescence and young adulthood. The tumor often arises near the knee joint, with the distal femur being the most common site, followed by the proximal tibia and proximal humerus. Osteosarcoma can also occur in other bones, such as the pelvis or jaw, but these occurrences are less frequent.

Clinical manifestations of osteosarcoma typically include **localized pain** and **swelling** near the affected bone. The pain may be intermittent initially but can progress to become more persistent and severe. Swelling may be accompanied by a palpable mass or fullness around the affected joint. As the tumor enlarges, it can cause limitations in joint movement. Systemic symptoms such as fatigue or weight loss are less common but may be present in advanced disease. Osteosarcoma has a **propensity for early metastasis** to the lungs, which can lead to respiratory symptoms such as cough and shortness of breath.

Diagnosis involves imaging studies such as X-rays and MRI, and a biopsy is necessary for confirmation.

Cartilage tumors

Benign

1. **Chondroma** derives from hyaline cartilage in the feet, spine, breastbone, and pelvis. If tumor is located in the peripheral area of the bone it is termed exchondroma, if in the center area of the bone - enchondroma.

2. **Osteochondroma** is the most common benign tumor of bone affecting patients under age 20-21. The lesions may be single or multiple and predominantly involve the metaphysis of long bones.

Malignant

Chondrosarcoma is a malignant cartilaginous tumor. The most common locations are the spine, pelvic bones, and upper ends of the femur and humerus.

The neoplasm grows slowly and can remain locally aggressive for years, with a high tendency to recur and implant into soft tissues. The 10-year survival rate ranges from 50% to 60%.

Chondroma: Morphology

Chondromas are **benign cartilaginous tumors** that typically arise from the medullary cavity of bones.

Morphologically, chondromas are characterized by the presence of **mature hyaline cartilage**. These tumors often display a lobulated architecture with well-defined borders.

Histologically, chondromas consist of **chondrocytes** embedded in a **hyaline cartilage** matrix. The cells may be arranged in nodules or clusters, and the matrix may show varying degrees of cellularity and calcification.

Chondromas are generally **slow-growing** and **well-circumscribed**, with a low likelihood of malignant transformation.

They are classified into **enchondromas**, which are central cartilaginous tumors within the medullary cavity of bones, and **peripheral chondromas**, which arise from the surface of bones or within soft tissues.

Chondroma: Clinical Manifestations

Enchondromas, the more common type of chondroma, are frequently found in the **small bones of the hands and feet**, particularly the phalanges and metacarpals. Long bones such as the femur and humerus can also be affected. These tumors are often asymptomatic and discovered incidentally on imaging studies conducted for unrelated reasons. **Peripheral chondromas** can arise on the **surface of bones** or within the soft tissues and are more commonly found in the axial skeleton, particularly the chest wall and ribs.

Most chondromas are **asymptomatic**, and their discovery is often incidental during imaging studies or pathological examination of removed tissues. When symptoms do occur, they are typically related to the location and size of the tumor. Enchondromas in the small bones of the hands and feet may present with **pain** or **swelling**, especially if they lead to pathological fractures. In some cases, enchondromas can cause deformities if they affect the growth plates of bones in children. Peripheral chondromas occurring in the soft tissues may present as painless masses. The clinical course of chondromas is generally **indolent**, and the **risk of malignant transformation is low**.

Chondrosarcoma: Morphology

Chondrosarcoma is a **malignant tumor of cartilaginous origin**, characterized by the production of hyaline cartilage by the tumor cells.

Morphologically, chondrosarcomas exhibit a spectrum of features, ranging from **well-differentiated tumors** with mature cartilage to more **anaplastic forms** with increased cellular atypia and mitotic activity.

The tumor cells are typically arranged in **lacunae**, surrounded by a **hyaline or myxoid cartilaginous matrix**.

Chondrosarcomas can be classified into *central* or *medullary chondrosarcomas*, which arise within the medullary cavity of bones, and peripheral chondrosarcomas, which occur on the surface of bones or within soft tissues.

Histological grading is crucial for prognostication, with low-grade tumors having a more favorable outcome compared to high-grade or dedifferentiated chondrosarcomas.

Chondrosarcoma: Clinical Manifestations

Chondrosarcomas most commonly arise in the **axial skeleton**, including the pelvis, spine, and ribs. They also frequently occur in the long bones, such as the femur and humerus. Within the axial skeleton, the pelvis is a common site, and chondrosarcomas arising from the ilium or sacrum are often encountered. Peripheral chondrosarcomas can occur in the **hands**, **feet**, and **flat bones of the chest wall**. Chondrosarcomas are more prevalent in adults and are rare in children.

Clinical manifestations of chondrosarcoma are often related to the tumor's location and its effects on surrounding structures. **Pain** is a common symptom, especially in larger tumors or those involving weight-bearing bones. **Swelling** and a **palpable mass** may be noted, and in some cases, the tumor can cause deformities or functional impairment. Chondrosarcomas arising in the pelvis may compress nearby nerves, leading to sciatic pain or other neurological symptoms. **Pathologic fractures** can occur in the affected bone, as the tumor weakens the bone structure.

Imaging studies, such as X-rays, CT scans, and MRI, are essential for diagnosis and staging.

Schwannoma: Morphology

Schwannomas, also known as **neurilemmomas**, are **benign nerve sheath tumors** that arise from Schwann cells, which form the myelin sheath covering peripheral nerves.

Morphologically, schwannomas are encapsulated tumors composed of spindle-shaped cells with elongated nuclei arranged in a palisading pattern, known as **Verocay bodies**. **Antoni A areas** consist of densely packed spindle cells, while **Antoni B areas** are more loosely arranged and may contain microcysts or myxoid changes.

Verocay bodies, formed by **parallel rows of nuclei** with **intervening cytoplasmic processes**, are a hallmark of schwannoma histology.

Immunohistochemical staining for **S100** protein is commonly positive, aiding in the diagnosis and differentiation from other soft tissue tumors.

Schwannoma: Clinical Manifestations

Schwannomas can occur **throughout the peripheral nervous system**, arising from cranial, spinal, or peripheral nerves. Intracranial schwannomas often involve the vestibular nerve (**acoustic neuroma**), **trigeminal nerve**, or other cranial nerves. **Spinal schwannomas** commonly affect the nerve roots and may occur along the spinal column. Peripheral schwannomas can develop in any peripheral nerve, with the most frequent locations including the extremities, particularly the flexor surfaces of the upper and lower limbs. These tumors are generally slow-growing and solitary,

although multiple schwannomas **can be associated with neurofibromatosis type II**.

The **clinical manifestations** of schwannomas depend on their location and size. Intracranial schwannomas may present with **hearing loss**, **tinnitus**, **imbalance**, or **facial weakness**, depending on the involved cranial nerve. Spinal schwannomas can cause **pain**, **sensory disturbances**, or motor deficits corresponding to the affected nerve root. Peripheral schwannomas often present as painless, slow-growing masses or nodules along the course of a peripheral nerve.

Malignant transformation is rare, but it can occur in a small percentage of cases.

GCT: Morphology

Granular cell tumors (GCTs), also known as Abrikosov tumors, are uncommon neoplasms that typically arise from **Schwann cells**, which are cells that form the protective sheath around nerves.

Morphologically, GCTs are characterized by **large, polygonal cells with abundant granular eosinophilic cytoplasm**.

These granules, which appear microscopically as fine and coarse **eosinophilic granules**, represent lysosomes within the tumor cells.

GCTs often exhibit a nested or sheet-like growth pattern and are surrounded by a fibrous or collagenous stroma.

The nuclei of the tumor cells are typically small and round. While GCTs are commonly associated with **nerves**, they can also occur in a variety of tissues, including the **skin**, **tongue**, **breast**, and internal organs.

GCT: Clinical Manifestations

Granular cell tumors can be found in various locations throughout the body, but they most commonly affect the skin and **subcutaneous tissues**. Within the skin, GCTs often present as painless nodules that are usually slow-growing and may have a firm consistency. They can also occur in the **oral cavity**, particularly on the tongue, where they may be discovered during routine dental examinations. Additionally, GCTs can arise in the **gastrointestinal tract**, **respiratory tract**, and other internal organs.

Clinical manifestations of granular cell tumors vary depending on their location. In the skin, these tumors often present as **solitary**, **painless nodules** or **plaques** that may be pigmented or non-pigmented. Oral cavity GCTs can be detected as painless masses on the tongue, gums, or other oral structures. While these tumors are typically benign, they can cause functional impairment or cosmetic concerns based on their location. In the gastrointestinal tract, granular cell tumors may lead to symptoms such as **abdominal pain**, **dysphagia**, or **obstruction**. The majority of GCTs are benign, but in a small percentage of cases, they may exhibit malignant behavior, including aggressive growth and the potential for metastasis.

Teratoma: Morphology

Teratomas are unique **germ cell tumors** that demonstrate remarkable **histological diversity**, as they can contain tissues derived from all **three embryonic germ layers**: ectoderm, mesoderm, and endoderm.

Morphologically, teratomas exhibit a **wide range of tissues**, including skin, hair, teeth, muscle, bone, and various glandular structures.

They can be classified into **mature** (benign) and **immature** (malignant) teratomas based on the presence of tissues resembling adult structures or more embryonic, primitive elements.

Mature teratomas often show **well-differentiated tissues**, while immature teratomas may contain **undifferentiated** or **embryonic-like elements**.

Teratomas can occur in various locations in the body, and their morphological appearance can vary depending on the specific tissues present and the degree of differentiation.

Teratoma: Clinical Manifestations

Teratomas can arise in both **gonadal** and **extragonadal locations**. Gonadal teratomas occur in the **ovaries** and **testes**, with ovarian teratomas being more common. Ovarian teratomas, also known as dermoid cysts, are frequently discovered during reproductive years and often contain a variety of mature tissues. Testicular teratomas are rare but may present with a mixture of tissues similar to ovarian teratomas. Extragonadal teratomas can occur in various sites, including the **sacrococcygeal region**, **mediastinum**, **retroperitoneum**, and central nervous system. Sacrococcygeal teratomas are often diagnosed in neonates and infants and can be associated with fetal anomalies.

The **clinical manifestations** of teratomas depend on their location, size, and the tissues they contain. Ovarian teratomas may be **asymptomatic** or present with **abdominal pain**, **pelvic discomfort**, or an **abdominal mass**. Testicular teratomas may present as painless testicular masses. Teratomas in the central nervous system may present with neurological symptoms such as **headaches**, **seizures**, or **motor deficits**.

The risk of malignancy is higher in immature teratomas, particularly when presenting in adult patients.

INFORMATIONAL AND METHODOLOGICAL PART

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