# Soft tissue tumor

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**MSS lectures 2023**

# Introduction

- Soft tissue refers to non-epithelial tissue excluding the skeleton, joints, central nervous system, hematopoietic and lymphoid tissues Although nonneoplastic conditions can involve soft tissue, they are seldom confined to this compartment, so the area of soft tissue pathology is restricted to neoplasms.
- With the exception of skeletal muscle neoplasms, benign soft tissue tumors outnumber their malignant counterparts
- Most soft tissue tumors arise in the extremities, especially the thigh. Approximately 15% arise in children but the incidence increases with age.

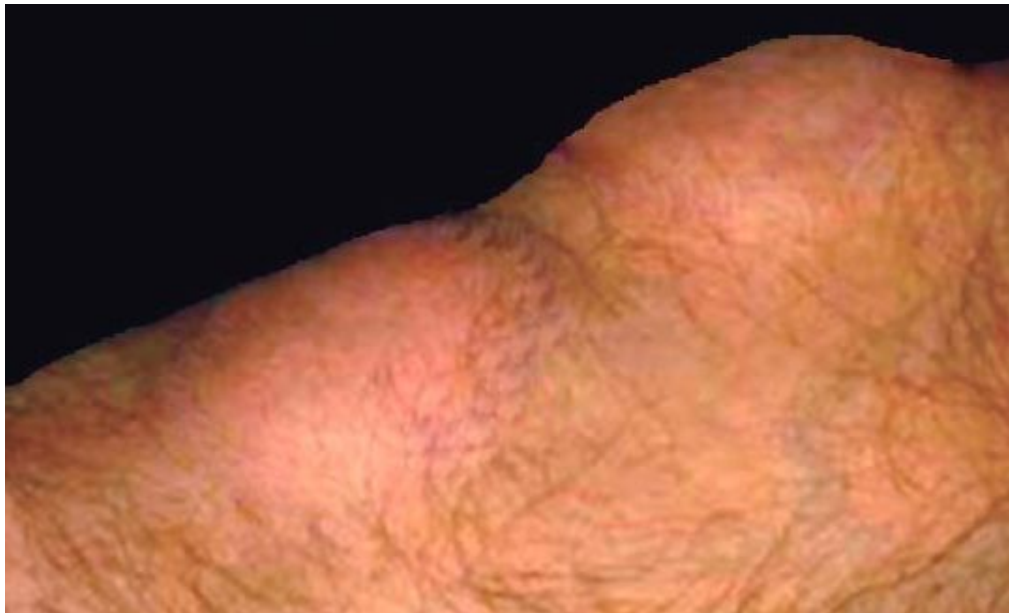
# Pathogenesis

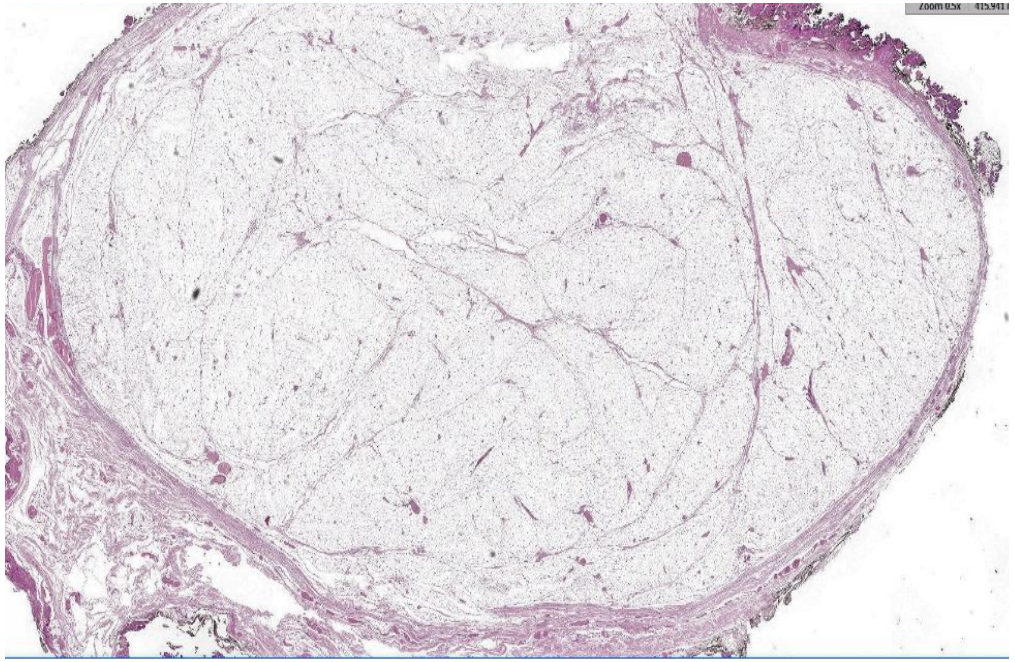
- Most sarcomas are sporadic and have no known predisposing cause.
- A small minority of soft tissue neoplasms are associated with germline mutations in tumor suppressor genes (neurofibromatosis 1, Gardner syndrome, Li-Fraumeni syndrome, Osler-Weber Rendu syndrome).
- A few tumors can be linked to known environmental exposure such as radiation, burns, or toxins.

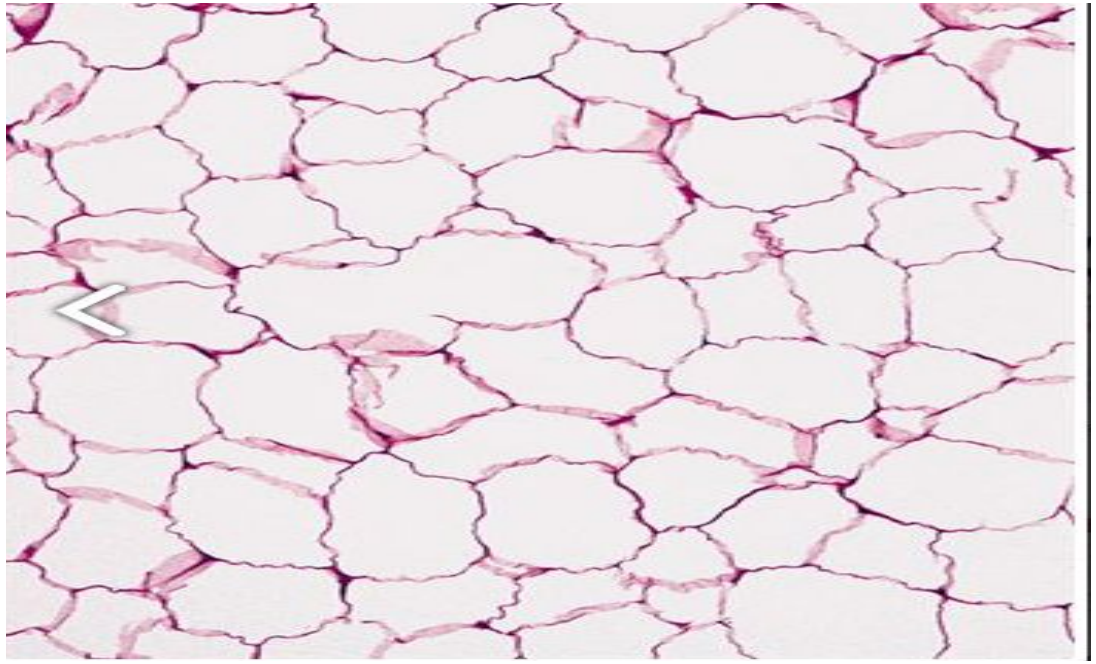
# TUMORS OF ADIPOSE TISSUE

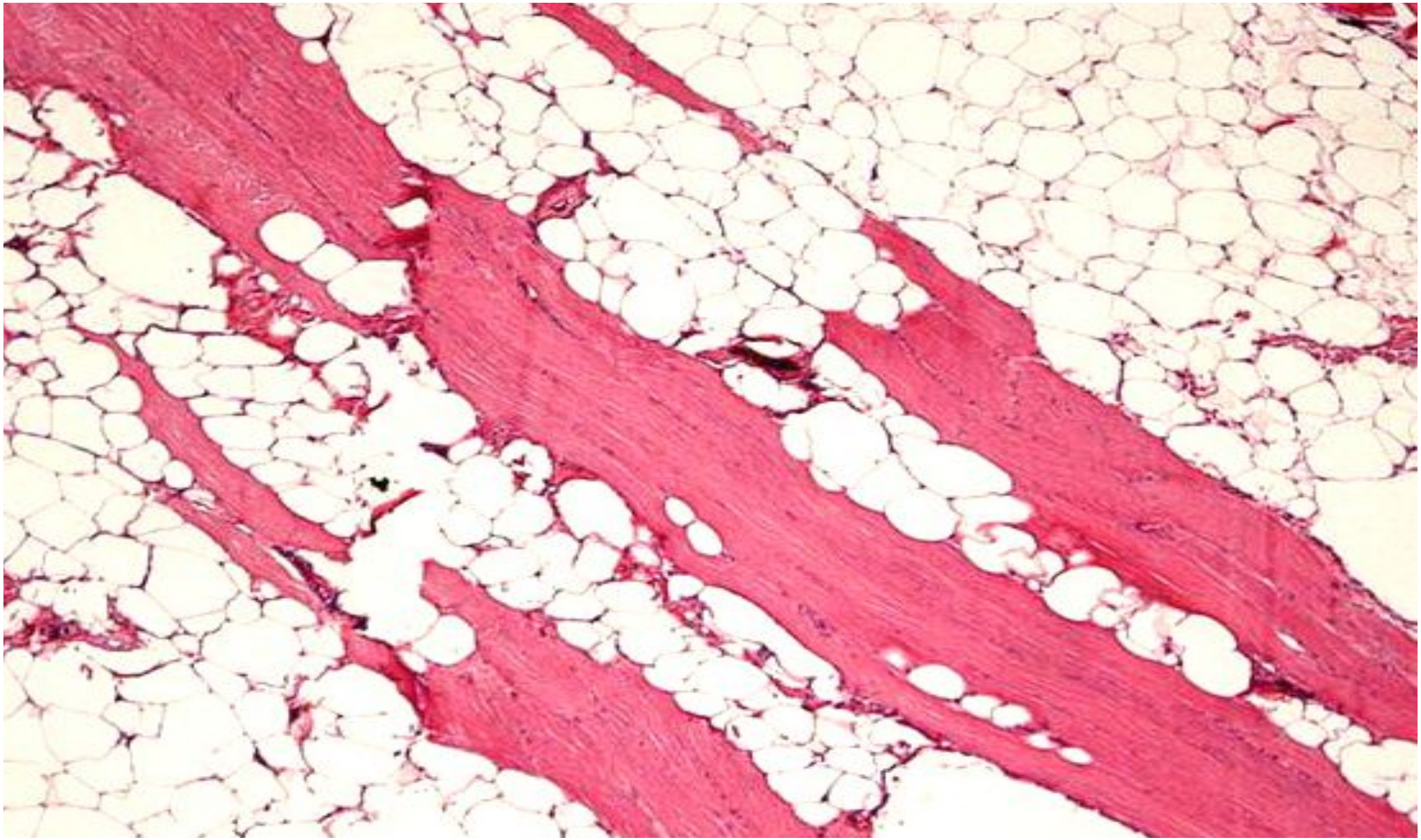
# Lipoma

- **Lipoma, a benign tumor of fat, is the most common soft tissue tumor in adults.** The conventional lipoma is the most common subtype, from which rare variants are distinguished according to characteristic morphologic or genetic features.
- Conventional lipoma is a well encapsulated mass of mature adipocytes. It usually arises in the subcutis of the proximal extremities and trunk, most frequently during middle adulthood. Infrequently, lipomas are large, intramuscular, and poorly circumscribed. Most lipomas are usually cured by simple excision.









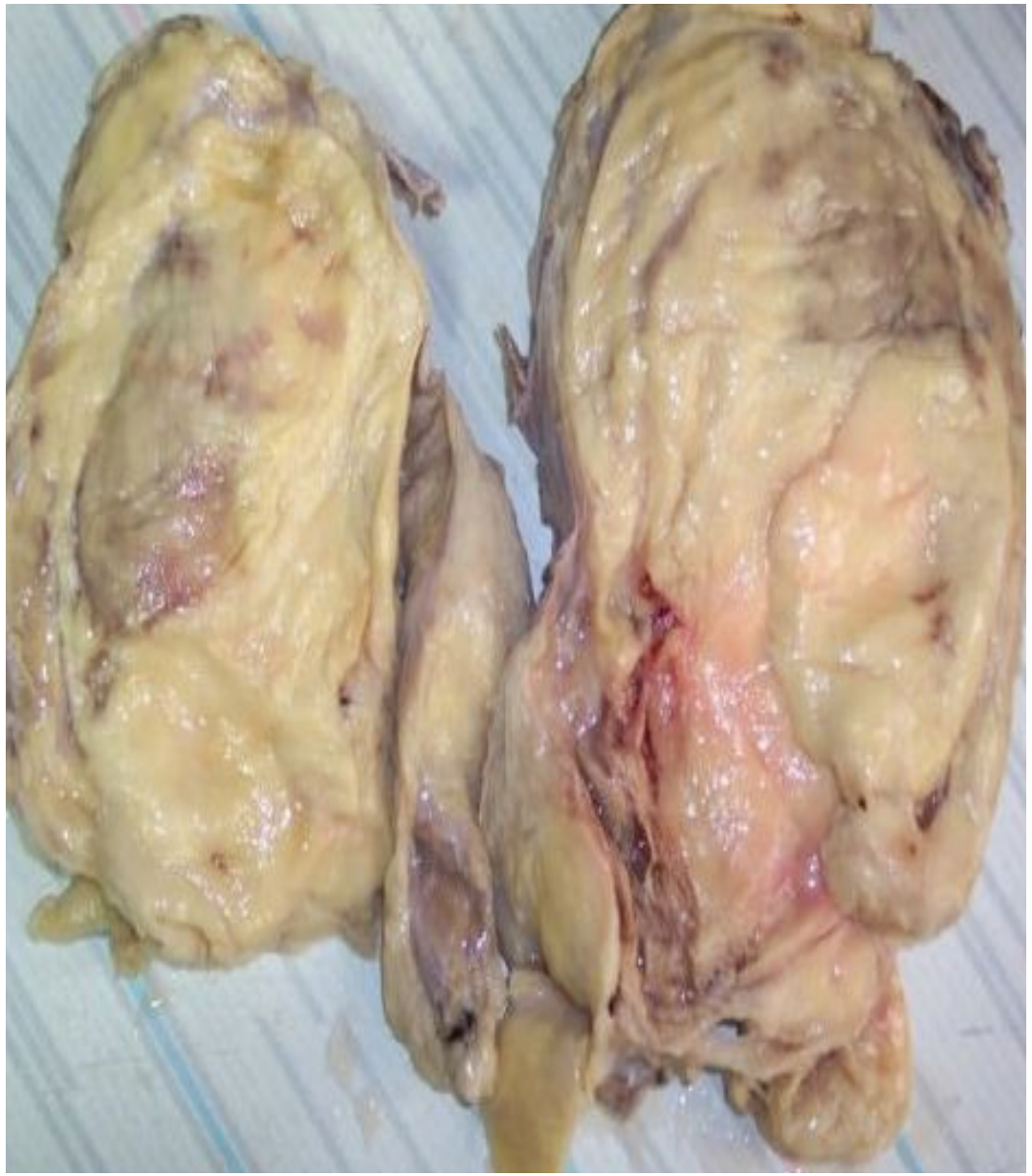
# Liposarcomas

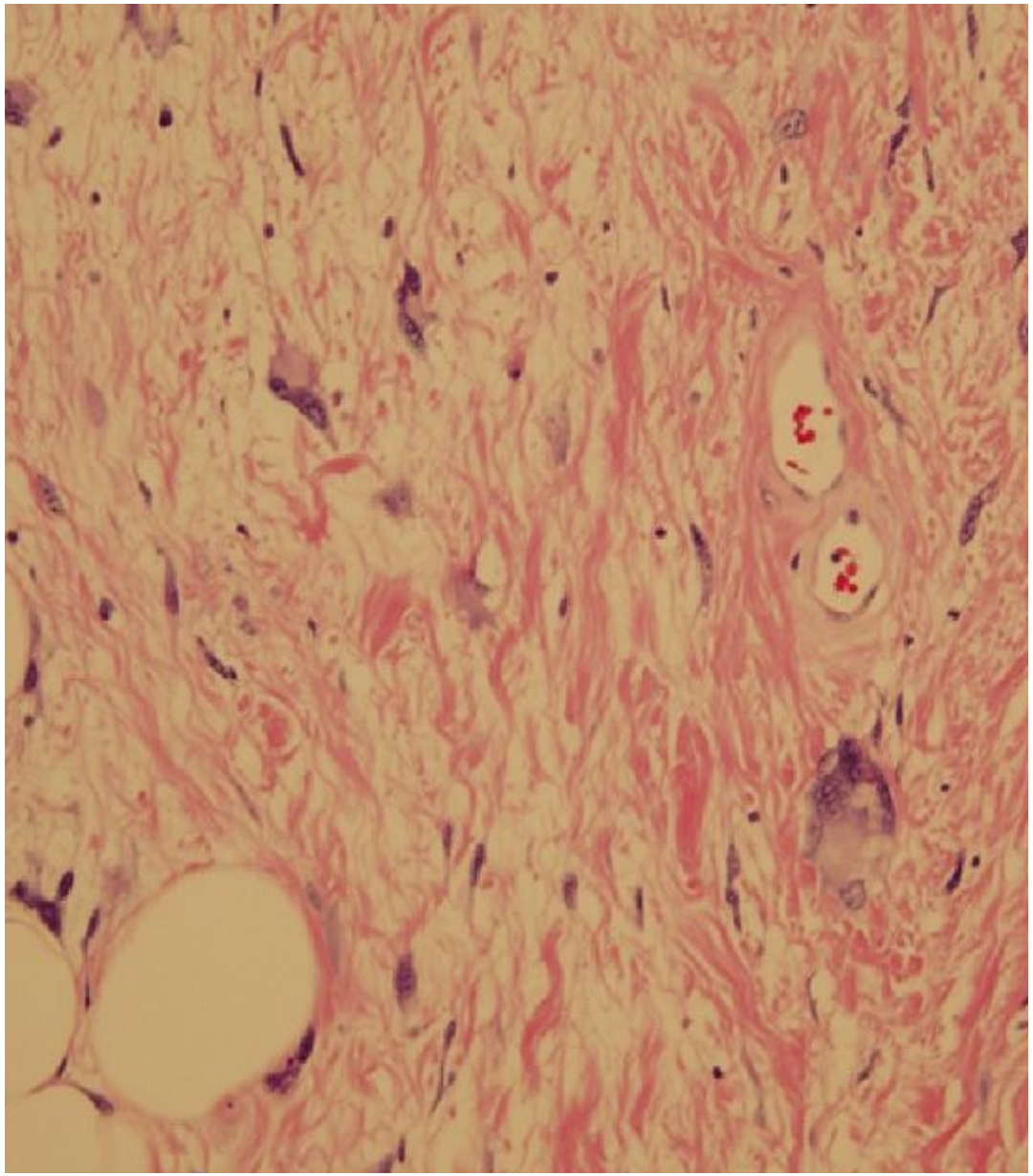
- **Liposarcomas are malignant tumors of adipose tissue**.
- One of the most common sarcomas of adulthood. It occurs mainly in people in their 50s to 60s in the deep soft tissues and retroperitoneum.
- All types of liposarcoma recur locally and often repeatedly unless adequately excised.
- The well-differentiated variant is relatively indolent, the myxoid/round cell type is intermediate in its malignant behavior, whereas the pleomorphic variant usually is aggressive and frequently metastasizes.

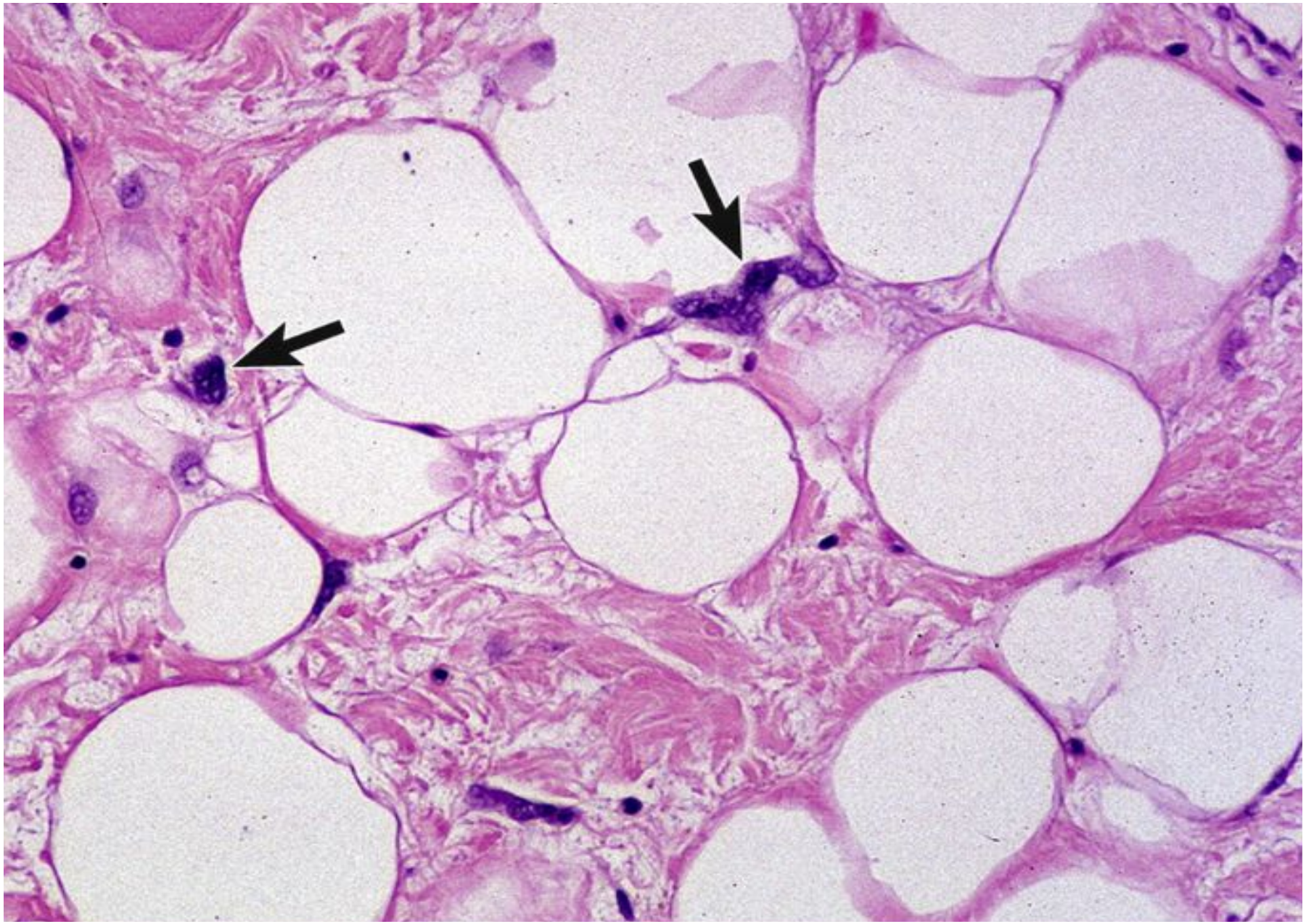
# MORPHOLOGY

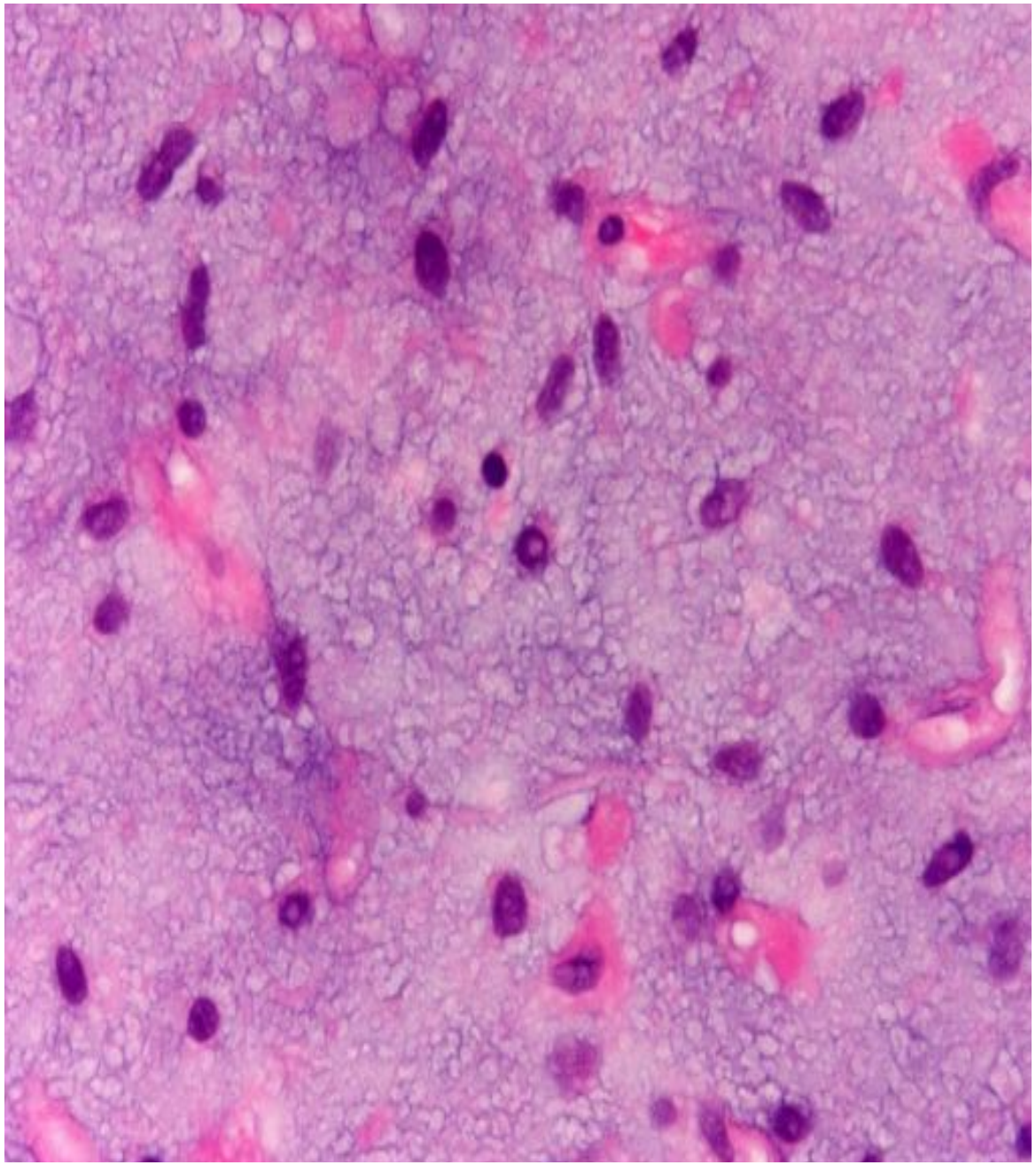
Liposarcomas are divided into three subtypes:

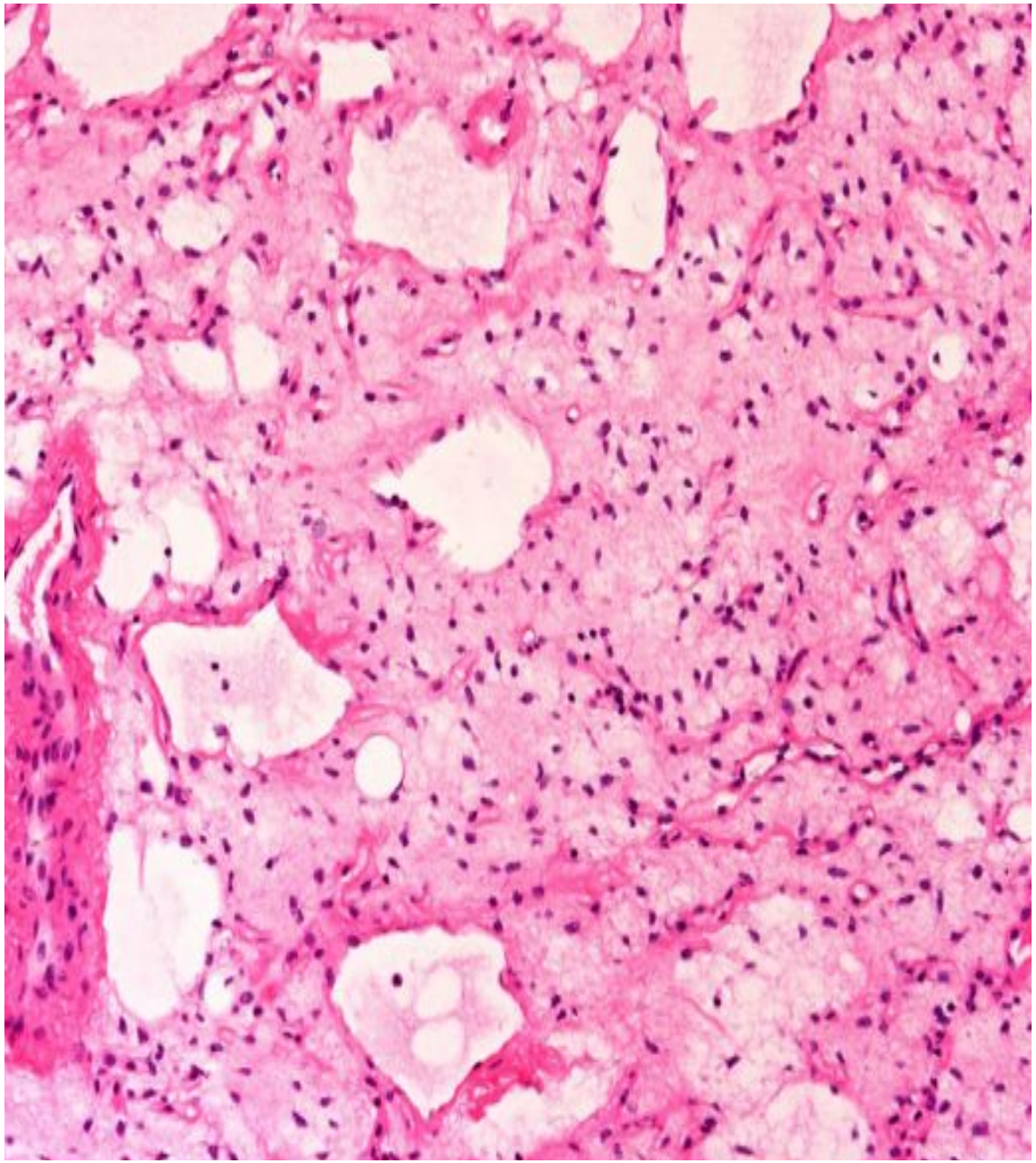
- Well-differentiated liposarcoma contains adipocytes with scattered atypical spindle cells. The tumors harbor amplification of chromosome region 12q13-q15, which includes the gene for *MDM2*. You will recall MDM2 encodes a potent inhibitor of p53.
- Myxoid liposarcoma contains abundant basophilic extracellular matrix, arborizing capillaries, and primitive cells at various stages of adipocyte differentiation reminiscent of fetal
- Pleomorphic liposarcoma consists of sheets of anaplastic cells, bizarre nuclei, and variable amounts of immature adipocytes (lipoblasts). These tumors have complex karyotypes.

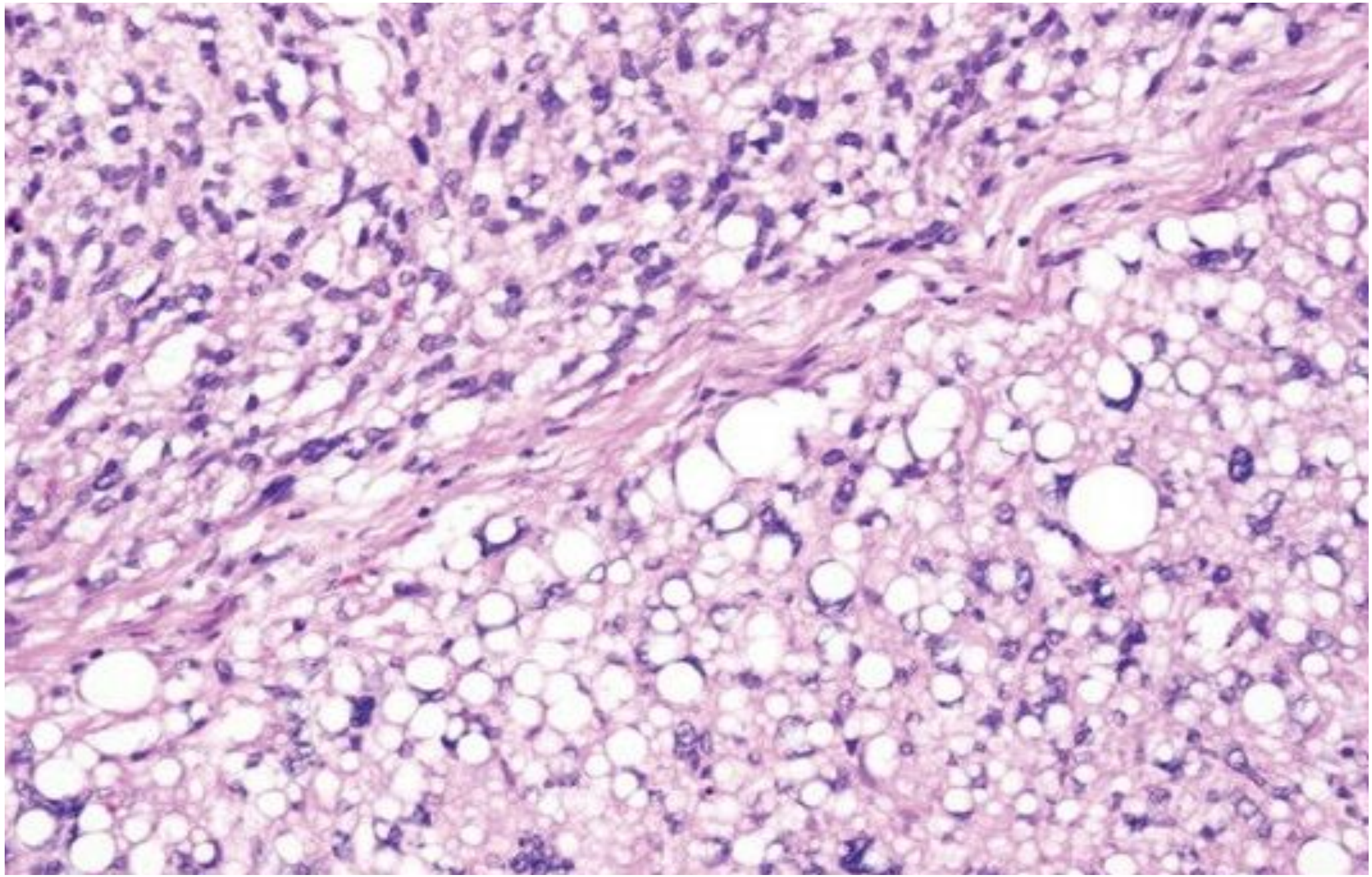


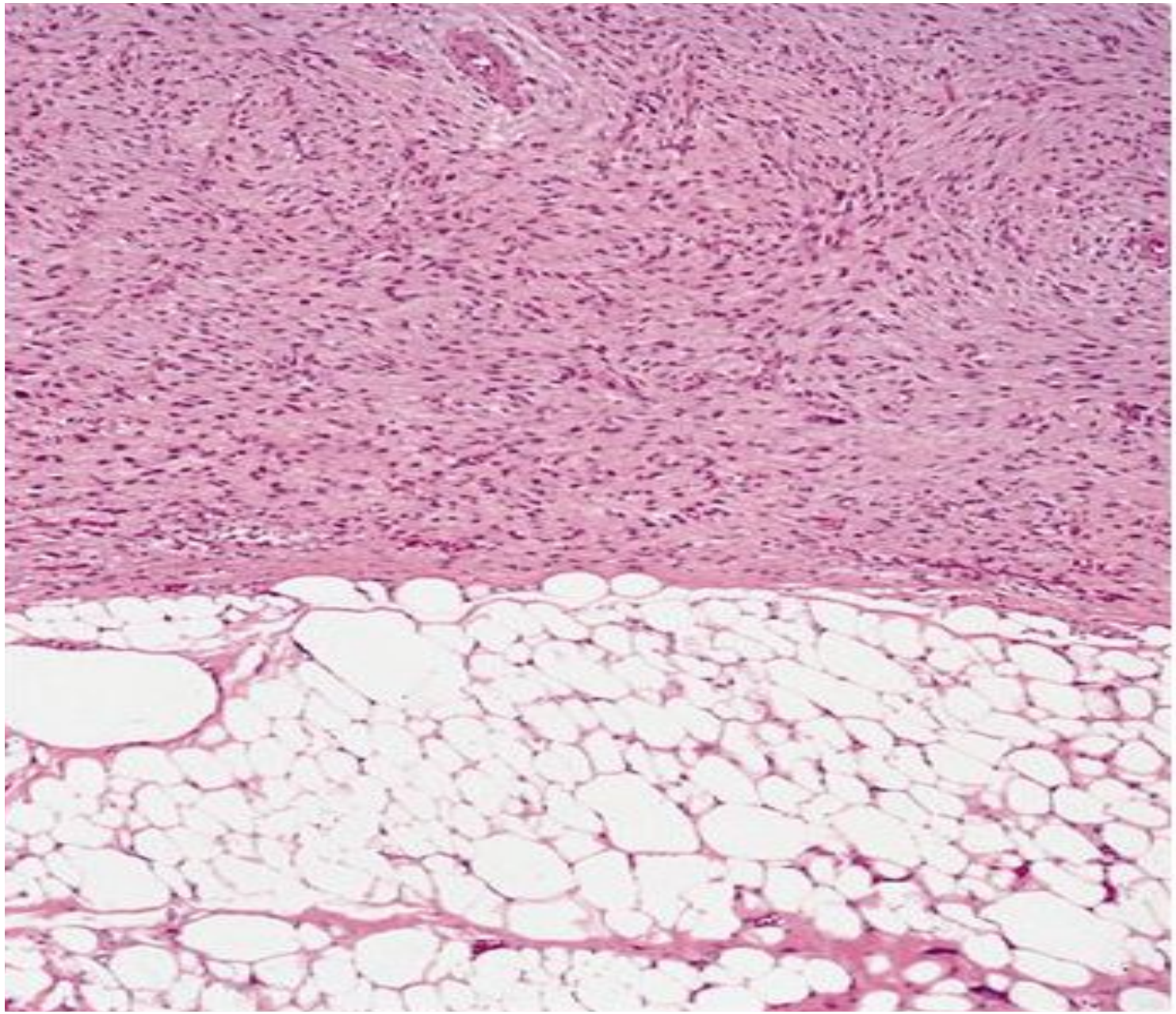












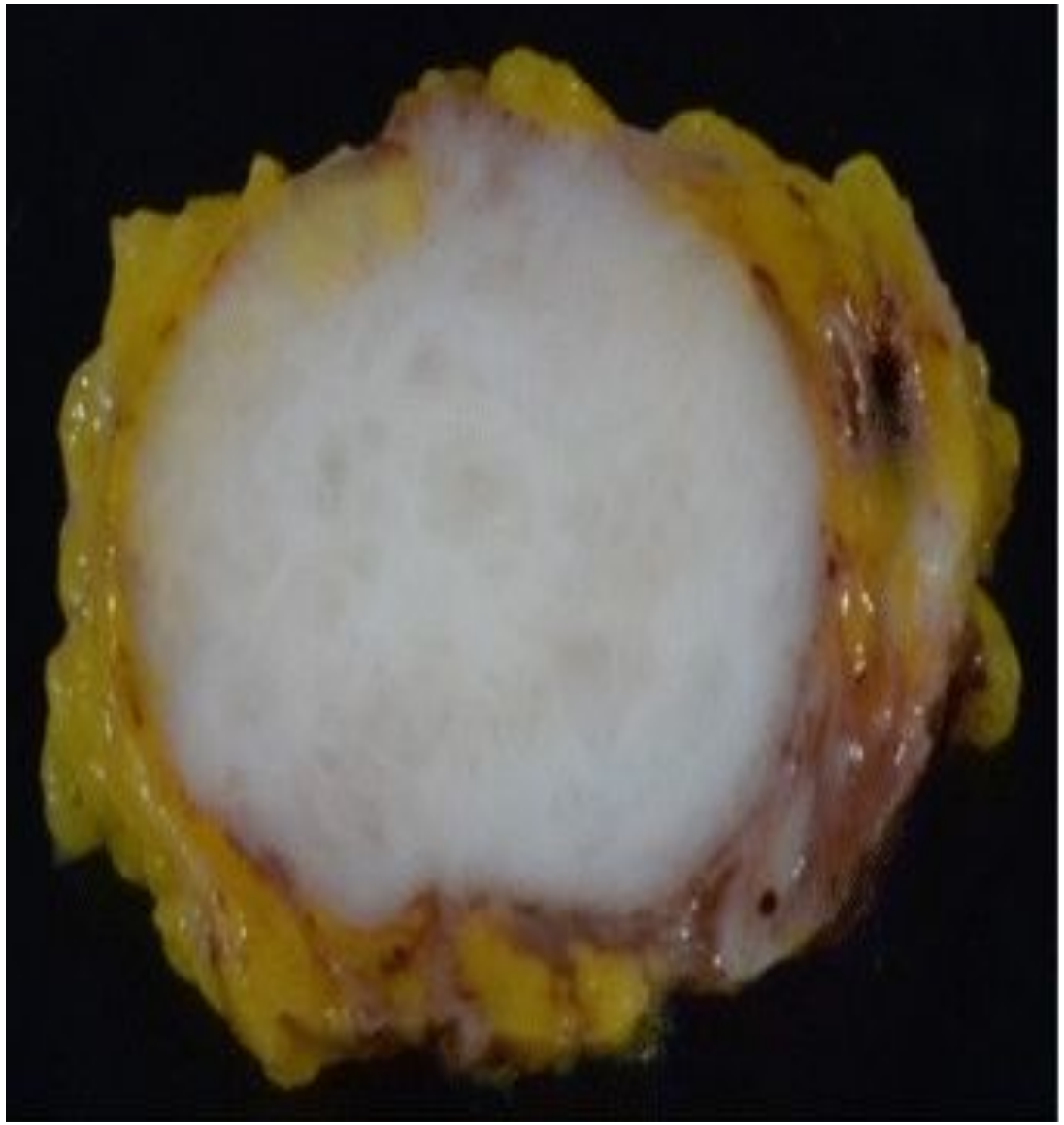
# FIBROUS TUMORS

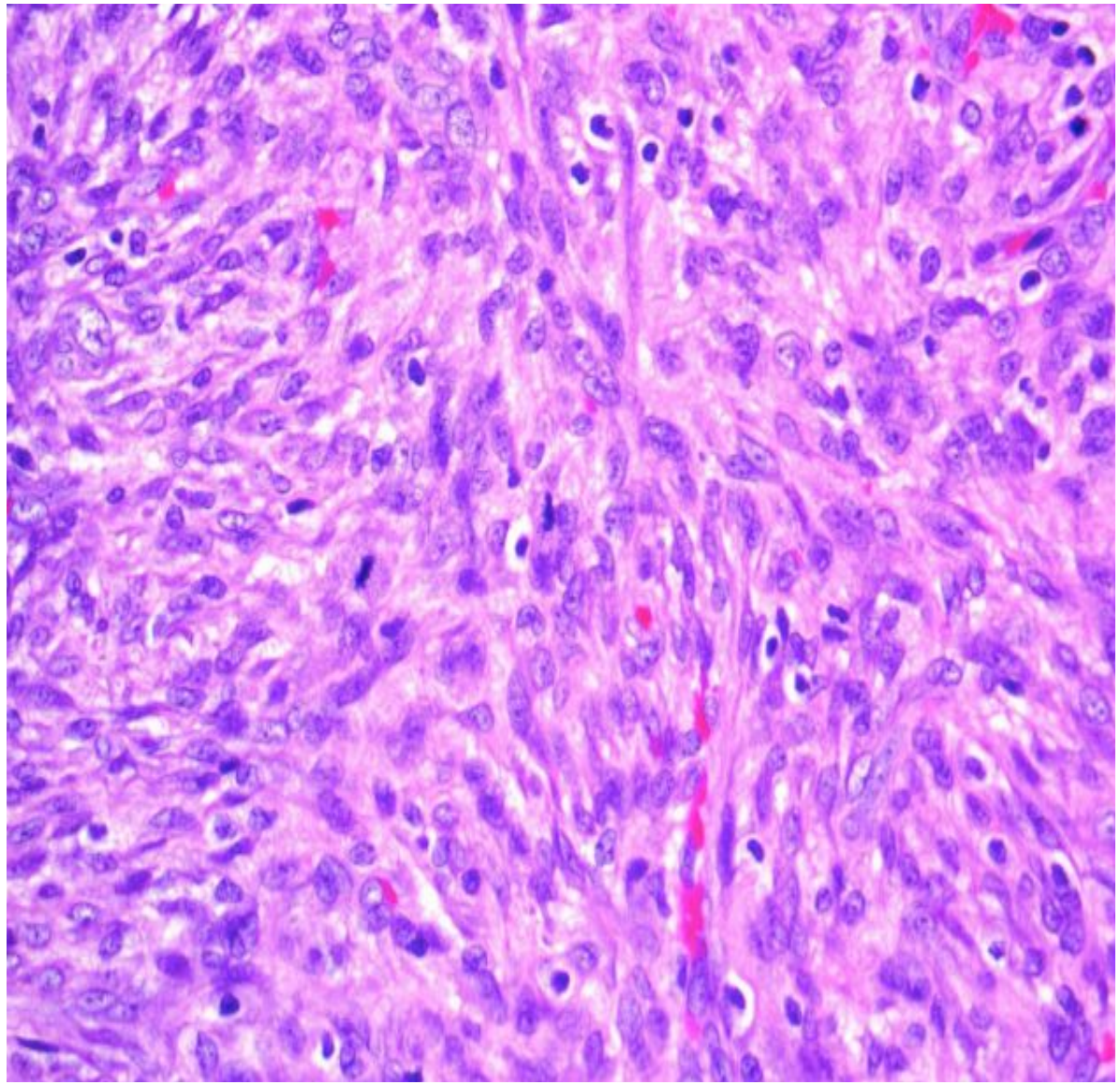
# Nodular fasciitis

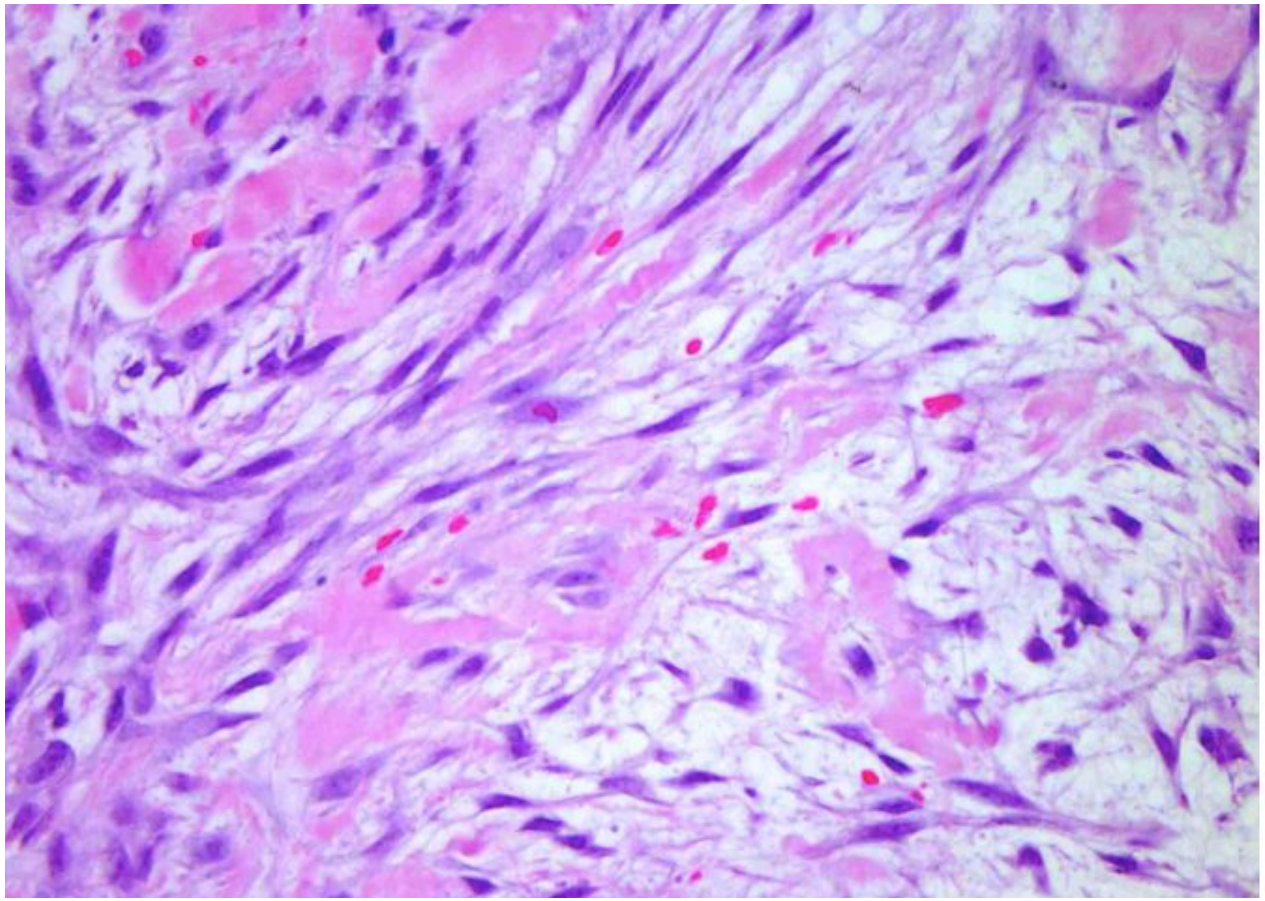
- **Nodular fasciitis is a self-limited fibroblastic and myofibroblastic proliferation that typically occurs in the upper extremities of young adults.**
- A history of trauma is present in approximately 25% to 50% of cases, and the tumors grow rapidly during a period of several weeks or months. Whereas nodular fasciitis was historically considered a purely reactive lesion, identification of a t(17;22) translocation producing a *MYH9-USP6* fusion gene indicates that it is a clonal, yet self-limited, proliferation. It is hypothesized that the proliferating cells lack some key hallmark of cancer, perhaps the ability to avoid senescence.
- Nodular fasciitis can spontaneously regress and, if excised, rarely recurs. Malignant transformation is virtually nonexistent.

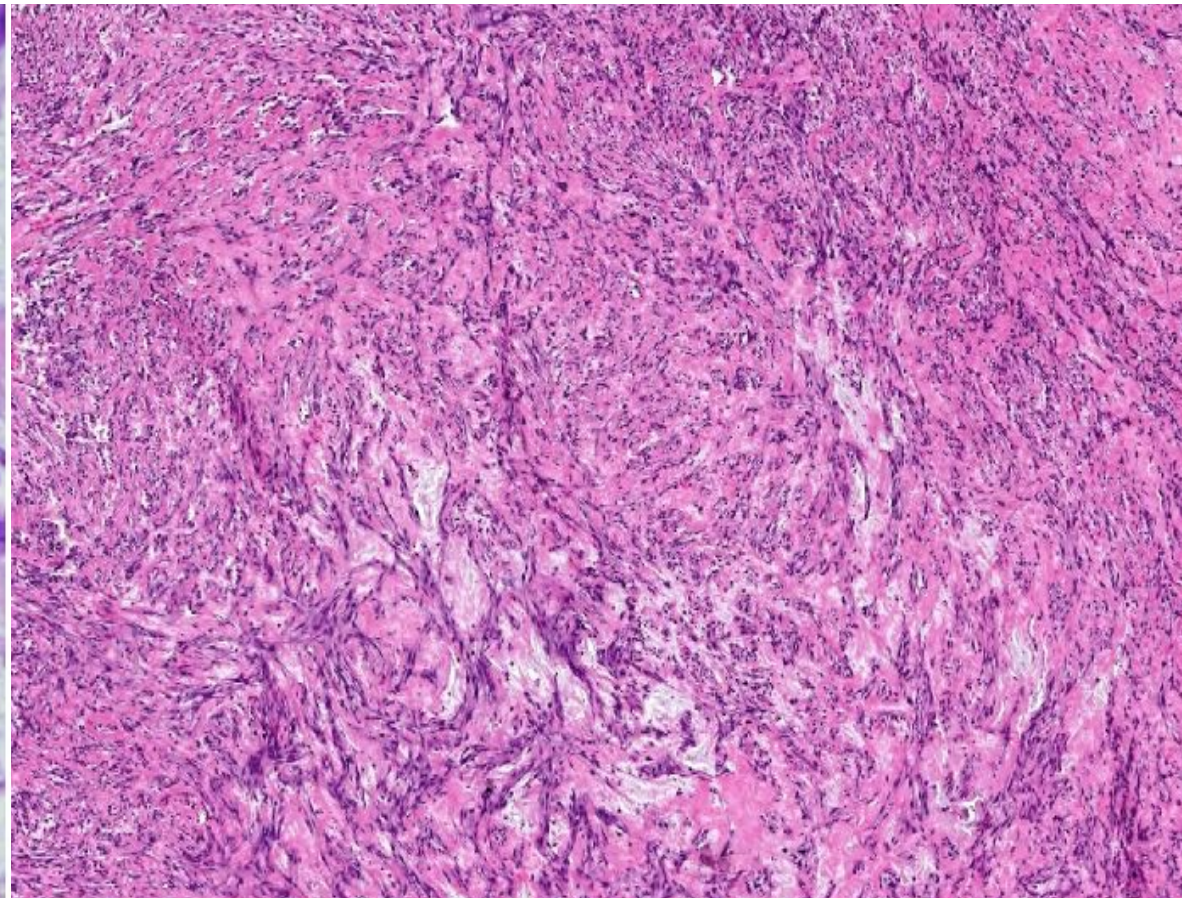
# MORPHOLOGY

- Nodular fasciitis arises in the deep dermis, subcutis, fascia, or muscle. Grossly the lesion is less than 5 cm, circumscribed, or slightly infiltrative. It is highly cellular containing plump, immatureappearing fibroblasts and myofibroblasts arranged in a pattern reminiscent of cultured fibroblasts.
- A gradient of maturation *(zonation)* from cellular, loose, and myxoid to organized and fibrous is typical. The cells vary in size and shape (spindle to stellate) and have conspicuous nucleoli; mitotic figures are abundant. Lymphocytes and extravasated red blood cells are common but neutrophils are unusual.





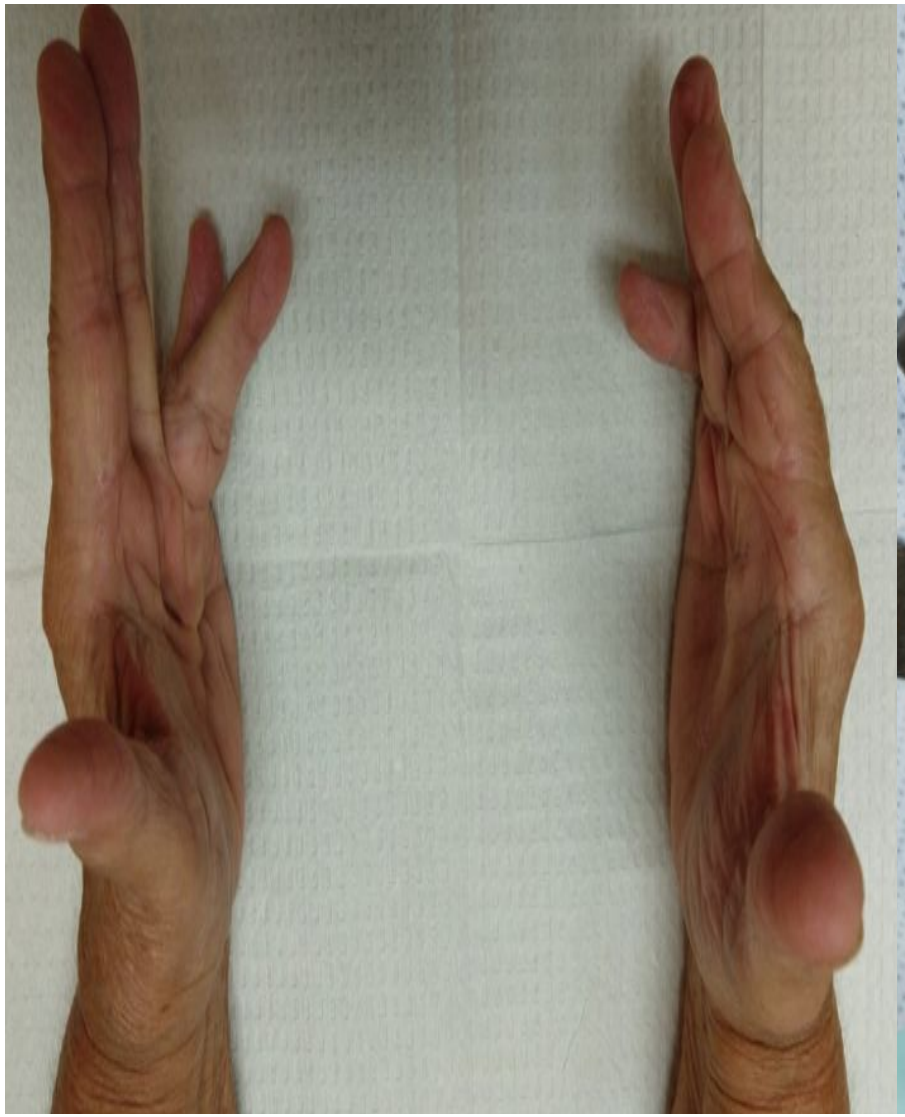
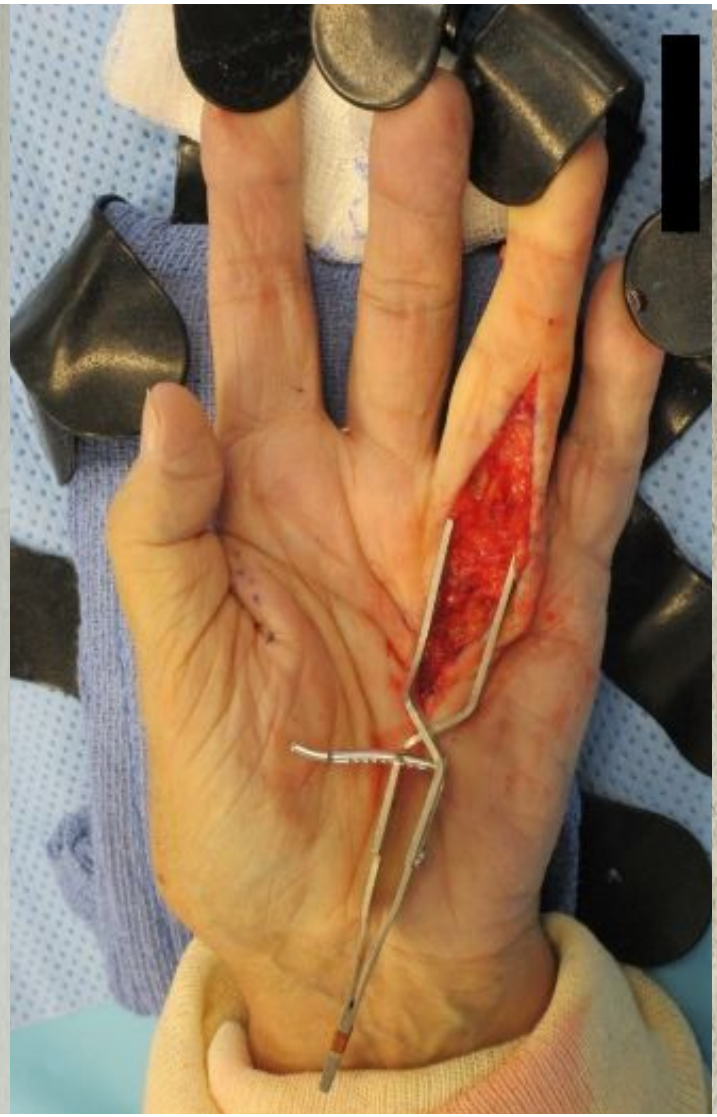
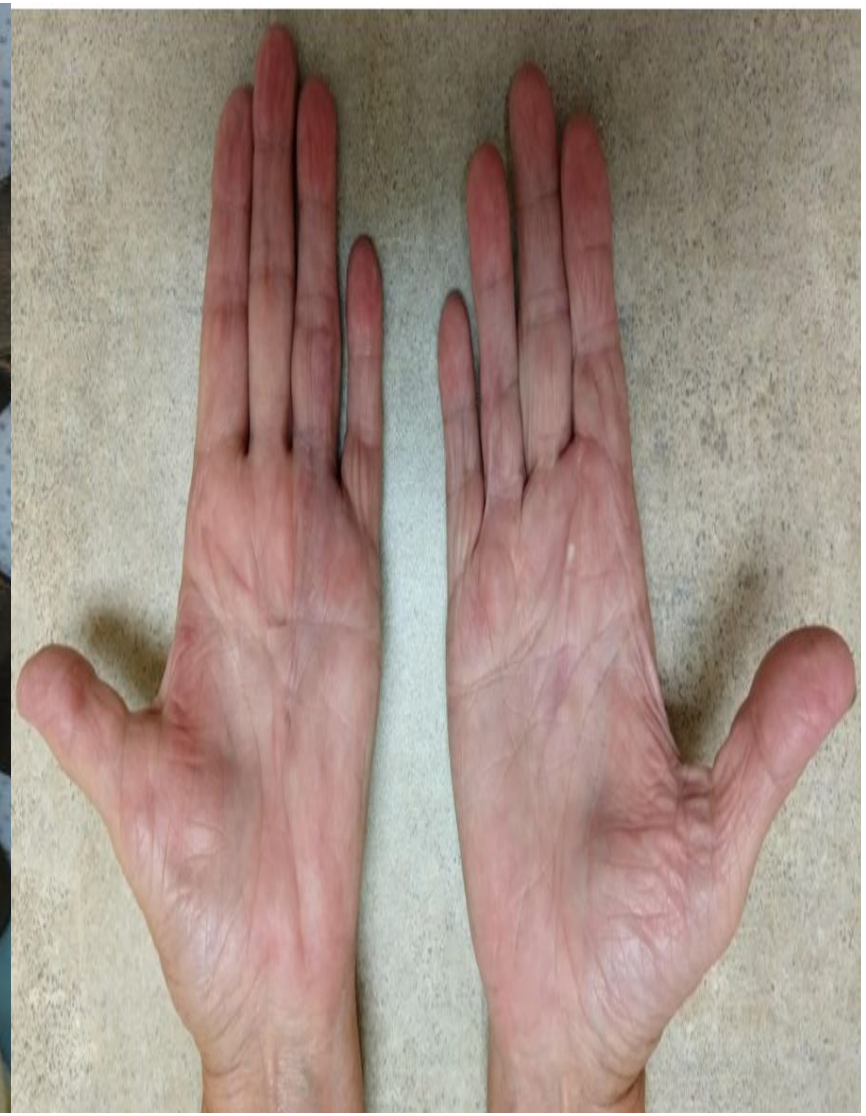


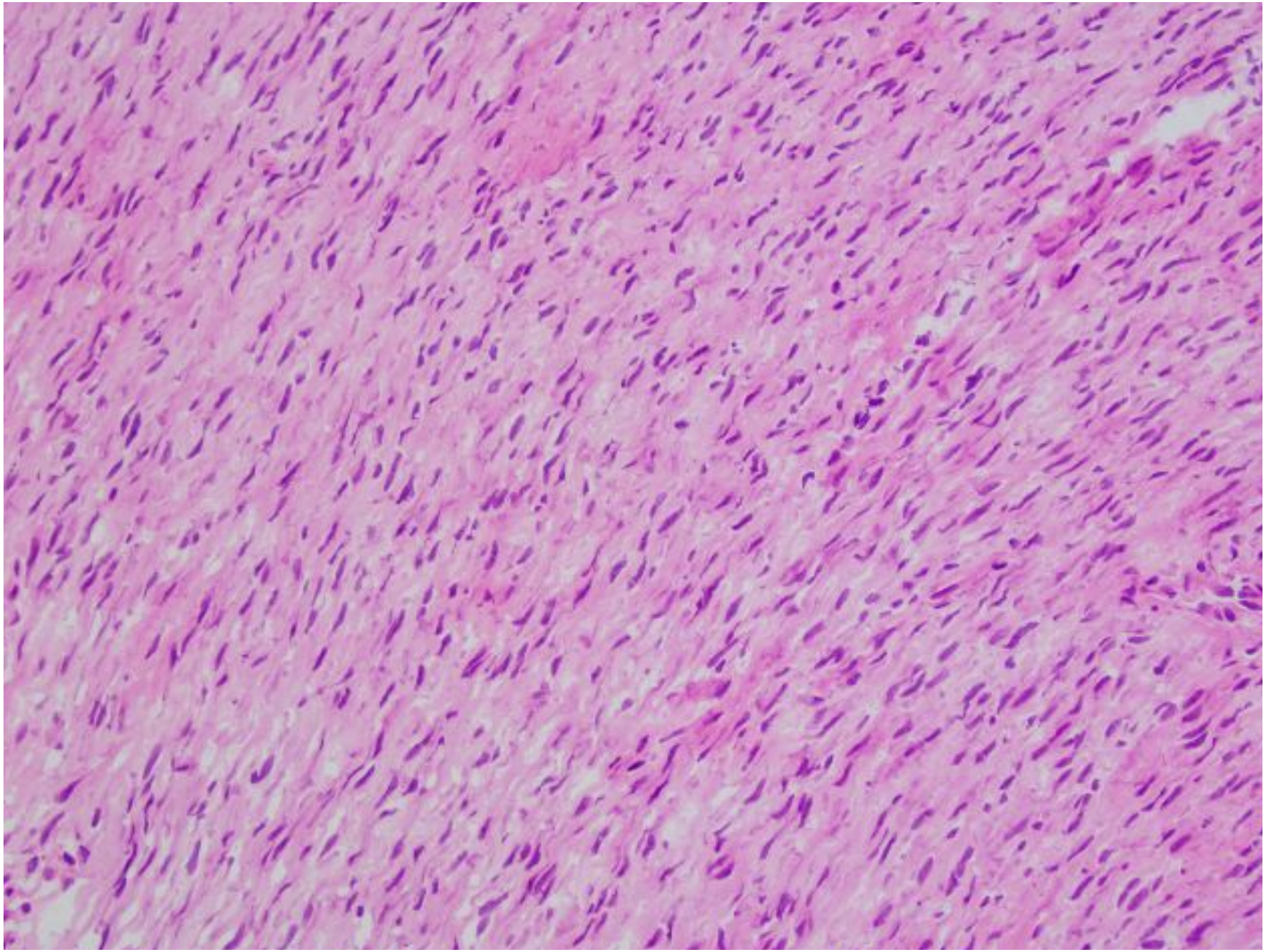


# Fibromatoses

- **Superficial fibromatosis is an infiltrative proliferation that can cause local deformity.**
- All forms of superficial fibromatosis affect males frequently than females. They are characterized by nodular or poorly defined broad fascicles of fibroblasts in long, sweeping fascicles, surrounded by abundant dense collagen. Several clinical subtypes have been identified:
- *Palmar (Dupuytren contracture):* Irregular or nodular thickening of the palmar fascia either unilaterally or bilaterally.
- *Plantar:* Common in young patients, unilateral and without contractures.
- *Penile (Peyronie disease)*: Palpable induration or mass on the dorsolateral aspect of the penis.

- In about 20% to 25% of cases, the palmar and plantar fibromatoses stabilize and do not progress, in some instances resolving spontaneously. Some recur after excision, particularly the plantar variant

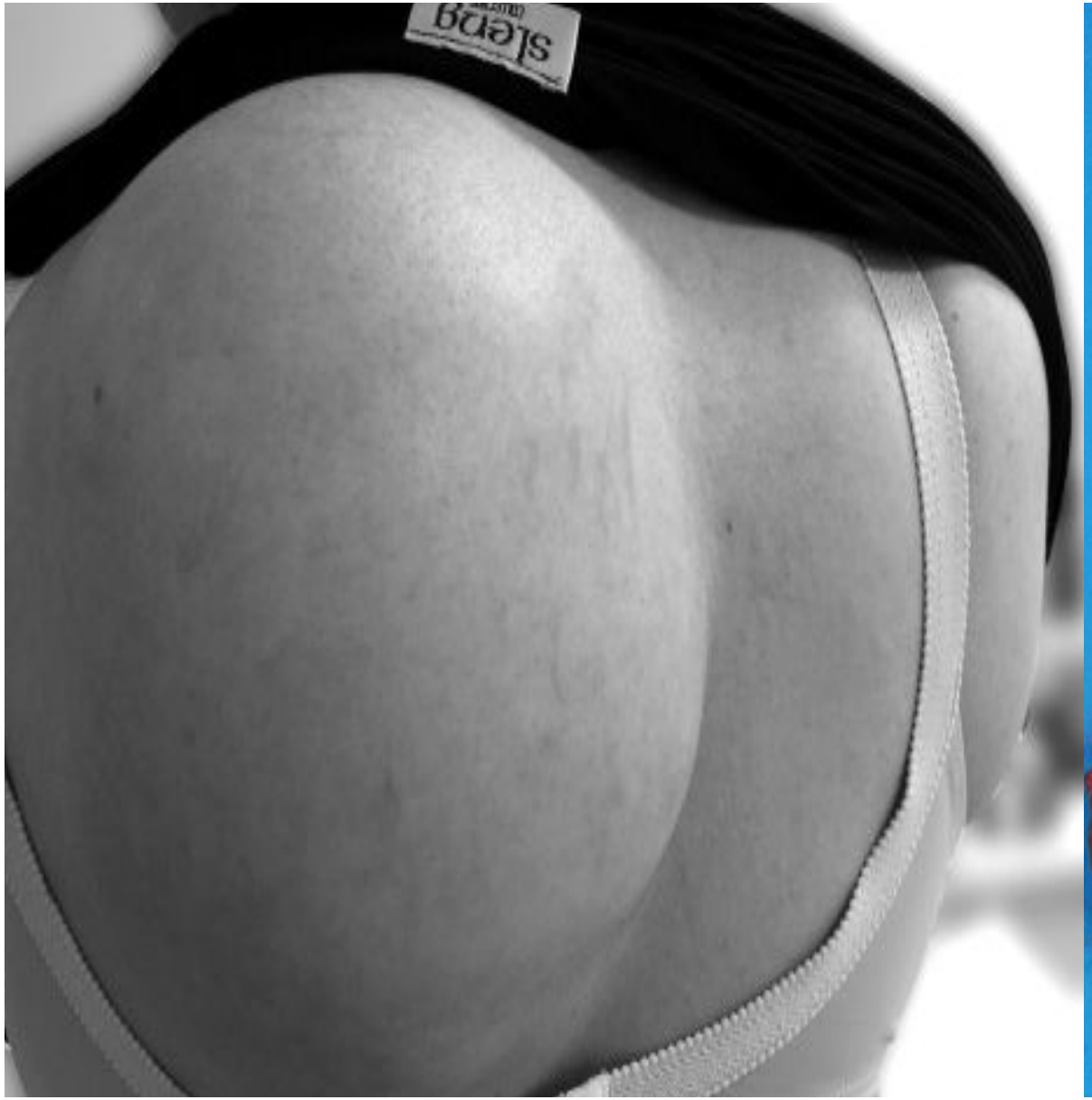




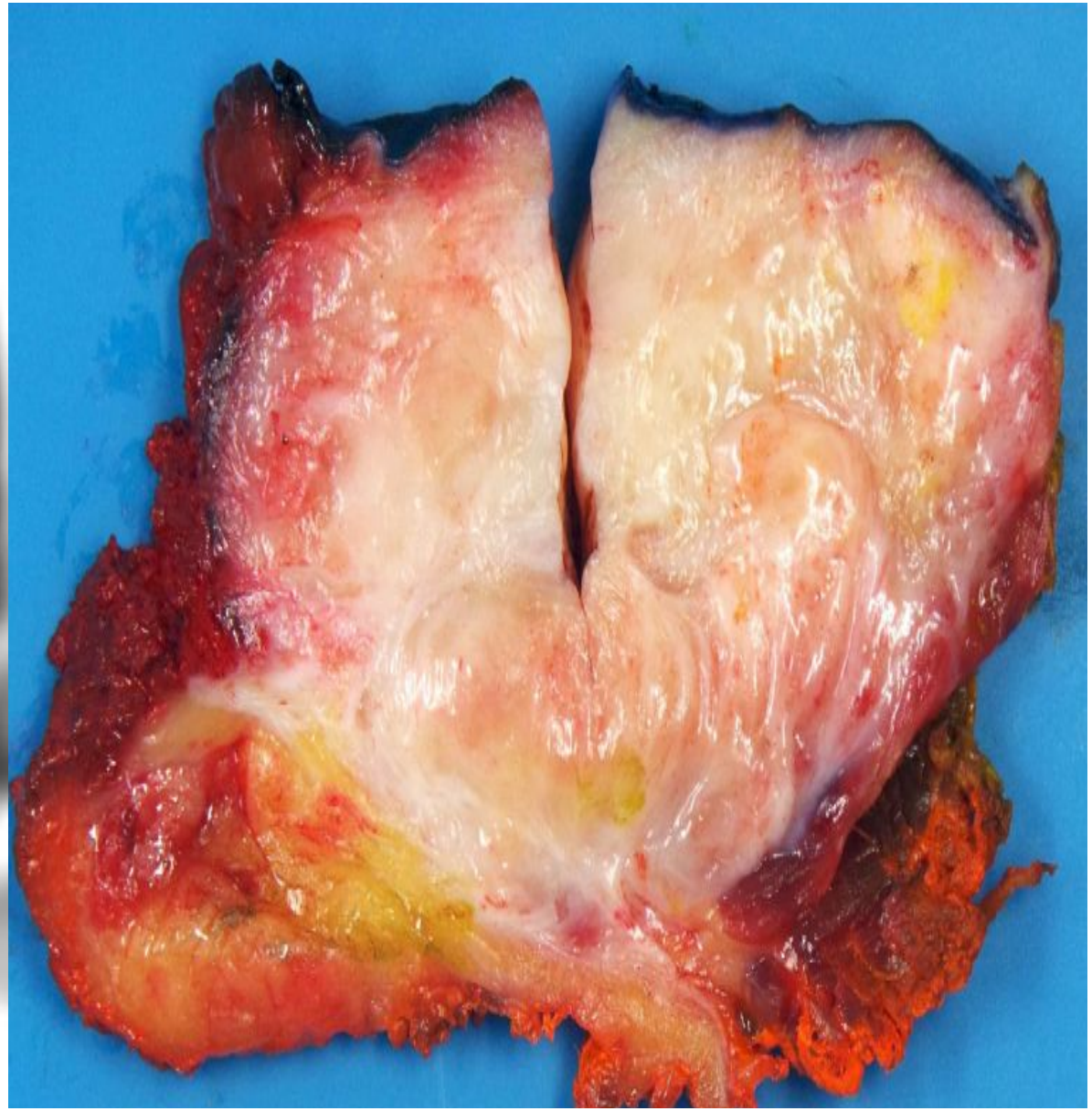


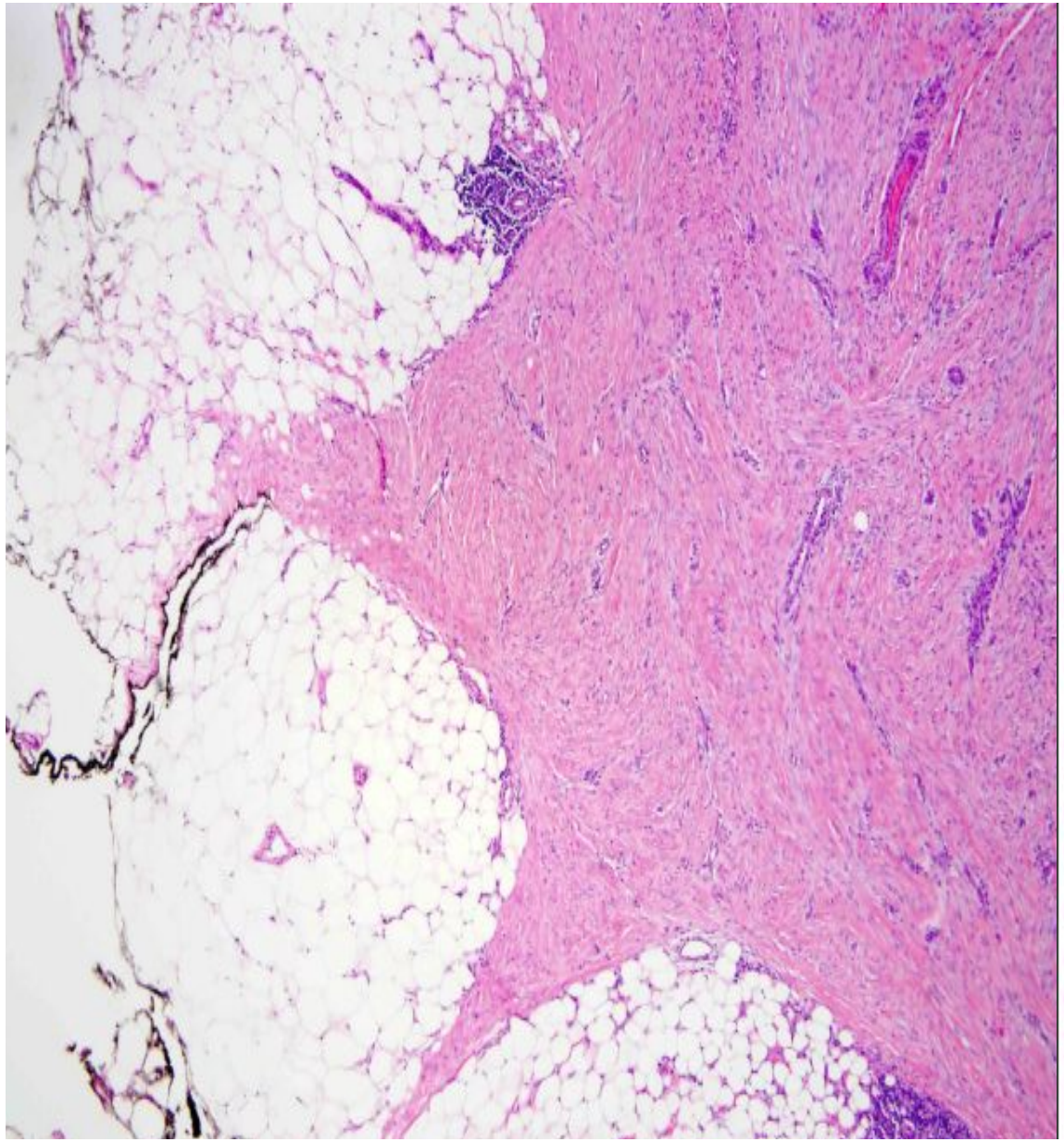
- **Deep fibromatoses, also called desmoid tumors, are large, infiltrative masses that frequently recur but do not metastasize.**
- They most frequently occur in the teenage years to 30s, predominantly in women. Abdominal fibromatosis generally arises in the musculoaponeurotic structures of the anterior abdominal wall but tumors can arise in the limb girdles or the mesentery. Deep fibromatoses contain mutations in the *CTNNB1* (β-catenin) or *APC* genes, leading to increased Wnt signaling. Most tumors are sporadic, but individuals with familial adenomatous polyposis (Gardner syndrome) who have germline *APC* mutations are predisposed to deep fibromatosis.

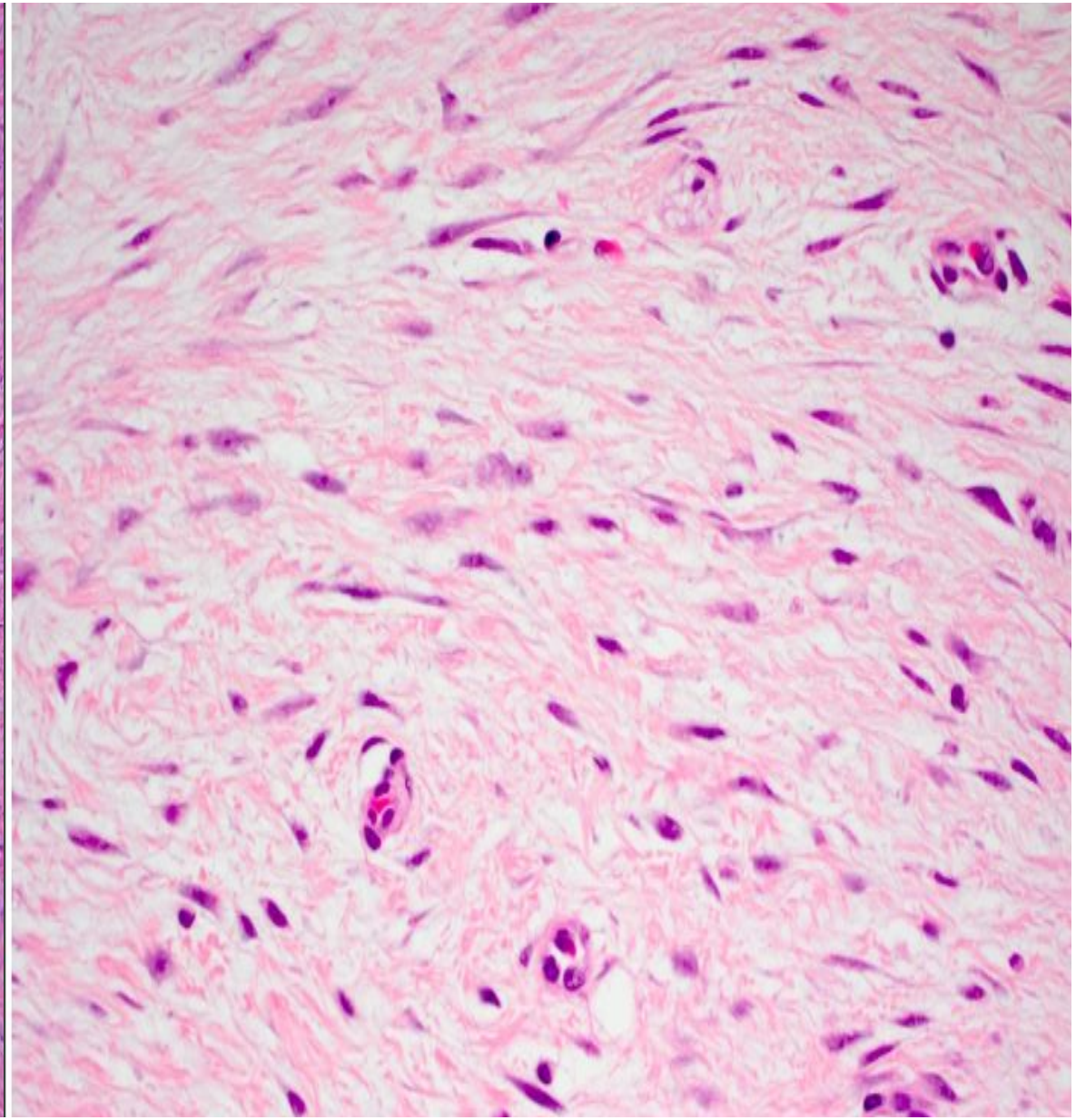
# MORPHOLOGY

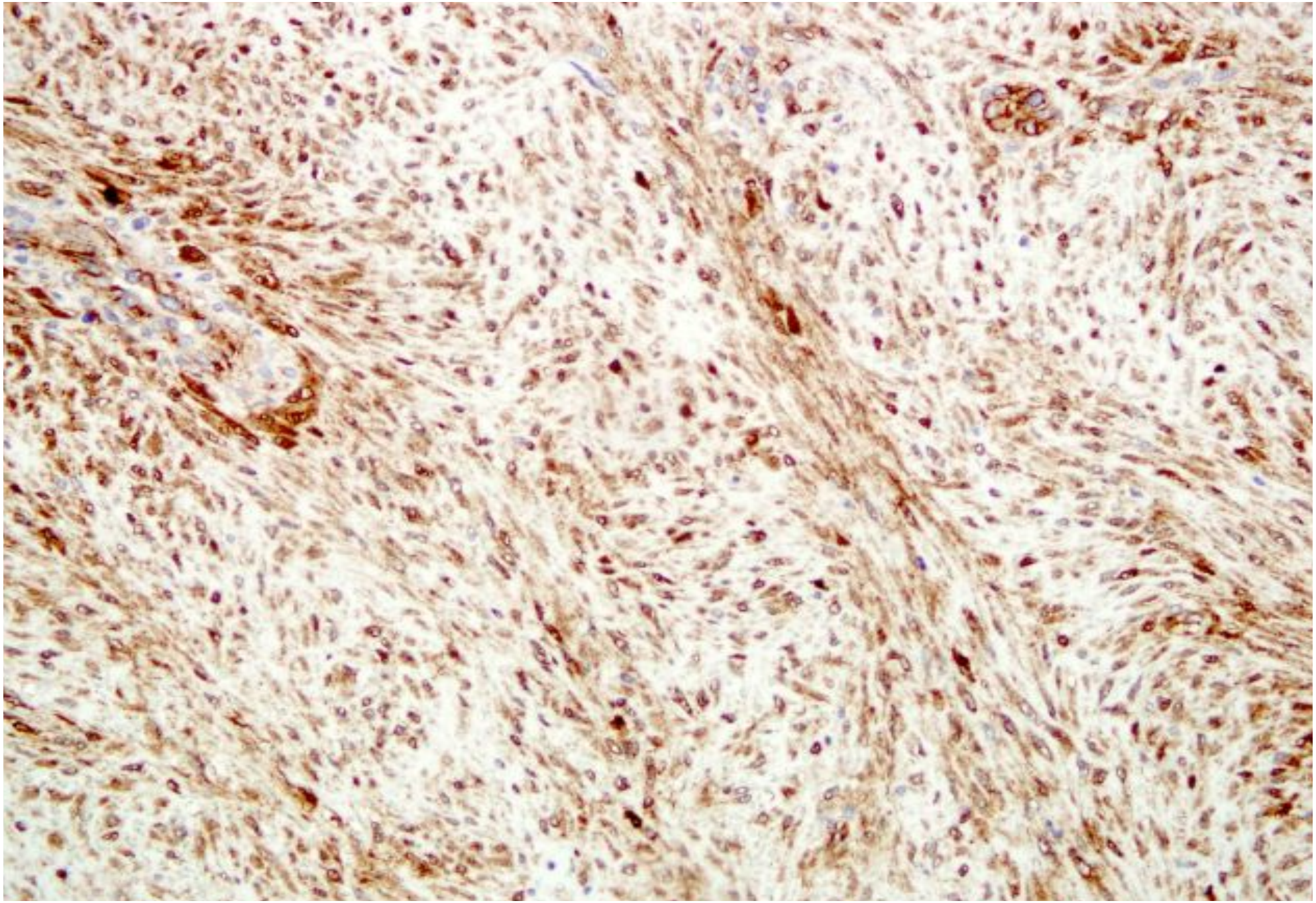
- Fibromatoses are gray-white, firm, poorly demarcated masses varying from 1 to 15 cm in greatest diameter. They are rubbery and tough, and have marked infiltration of surrounding muscle,  nerve and fat. Cytologically bland fibroblasts arranged in broad sweeping fascicles amid dense collagen are the characteristic histologic pattern. The histology resembles a scar.











# SKELETAL MUSCLE TUMORS

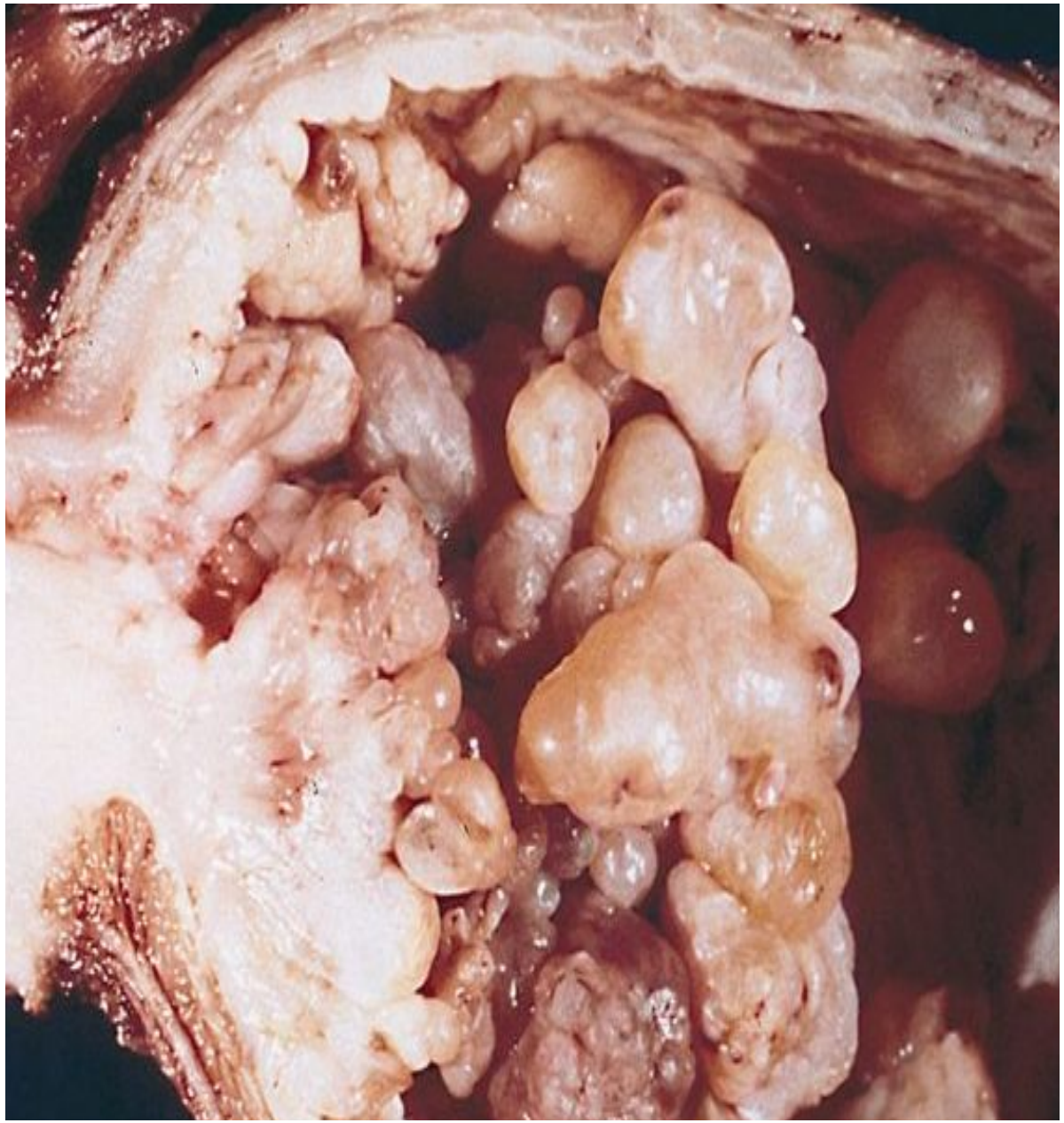
Skeletal muscle neoplasms, in contrast to tumors of other lineages, are almost all malignant. The benign rhabdomyoma is more frequent in individuals with tuberous sclerosis.

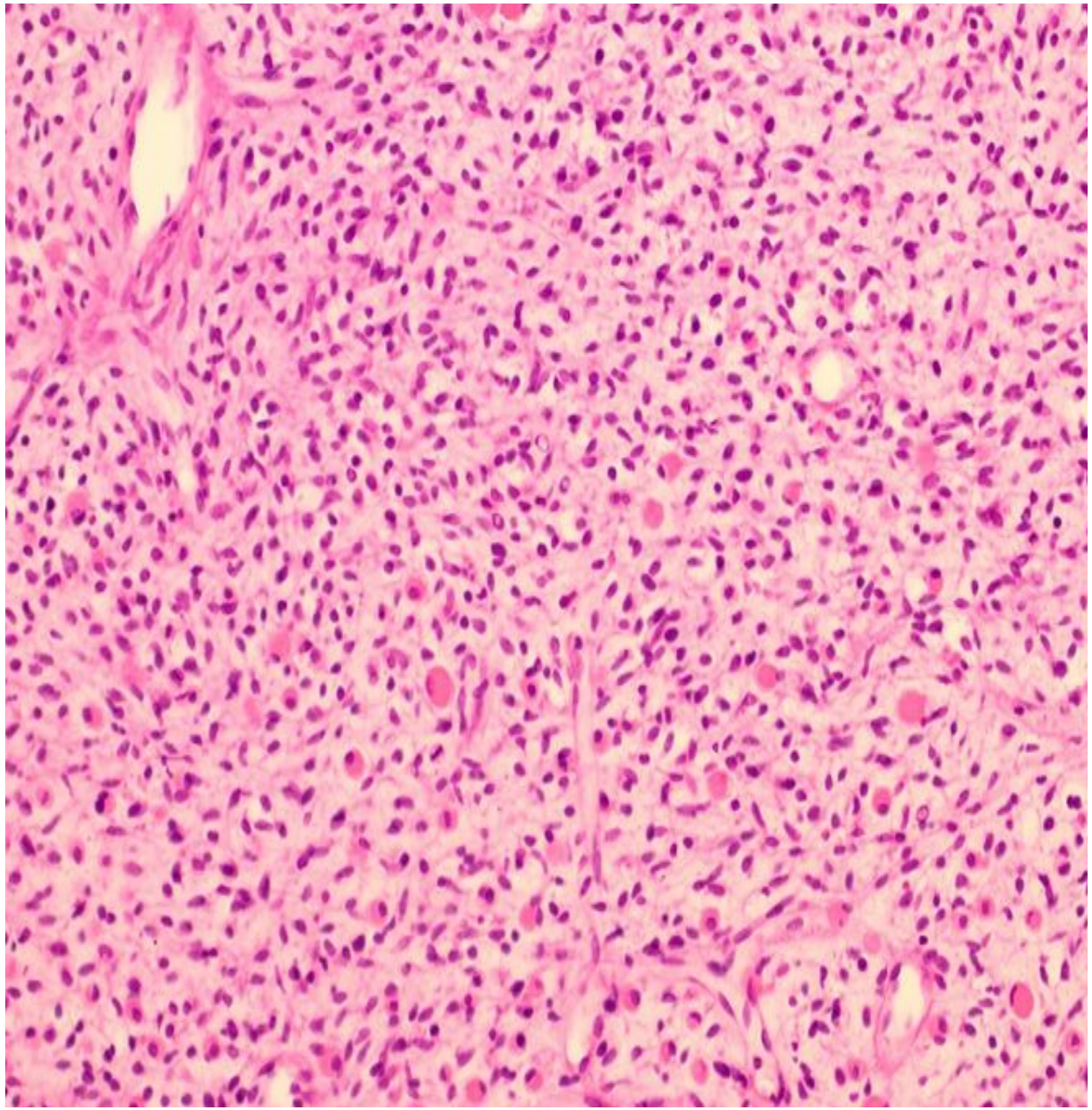
# Rhabdomyosarcoma

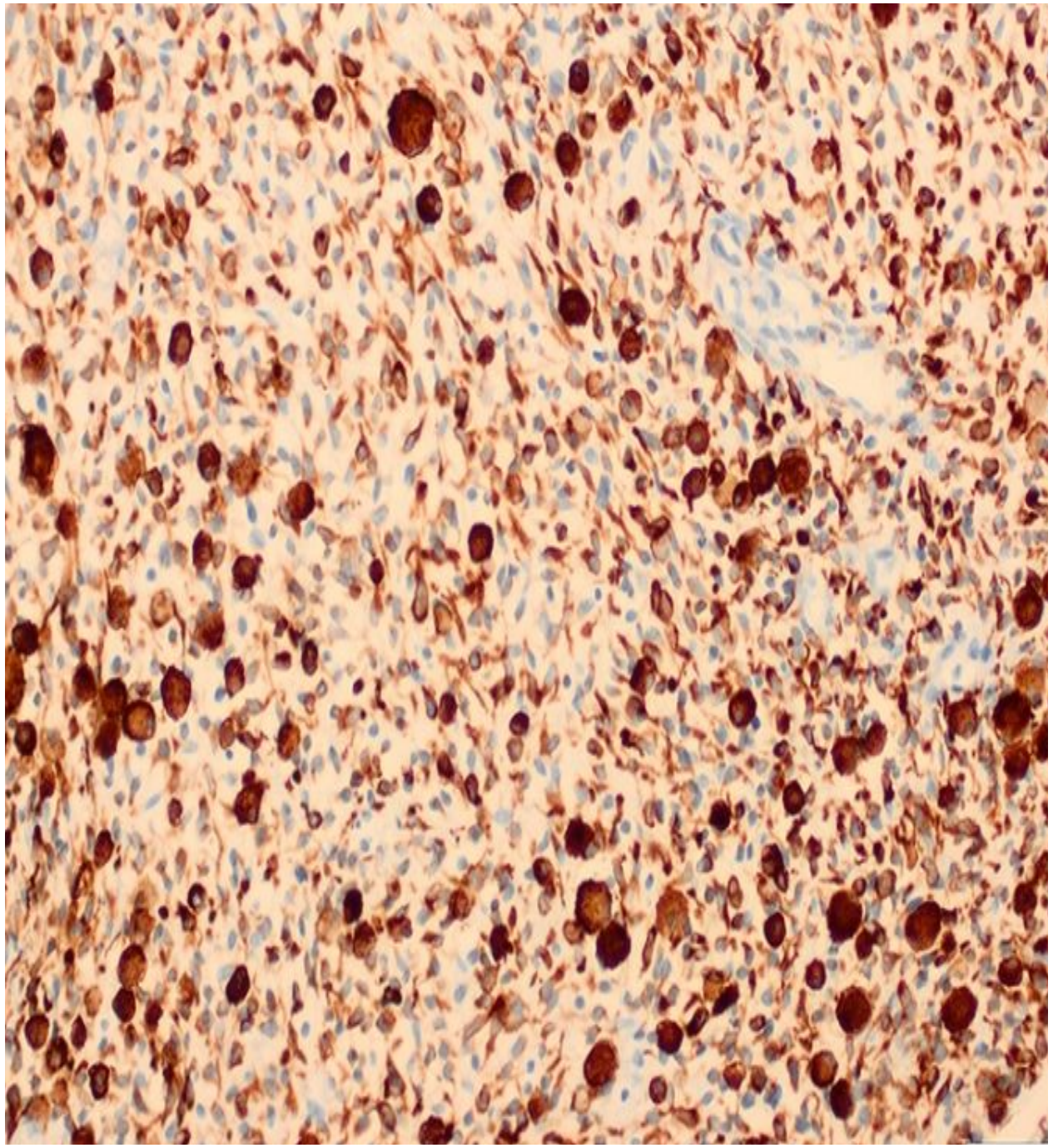
- **Rhabdomyosarcoma is a malignant mesenchymal tumor with skeletal muscle differentiation.**
- Three main subtypes are recognized: *alveolar* (20%), *embryonal* (60%), and *pleomorphic* (20%). Rhabdomyosarcoma (alveolar and embryonal) is the most common soft tissue sarcoma of childhood and adolescence, usually appearing before age 20. Pleomorphic rhabdomyosarcoma is seen predominantly in adults.
- The pediatric forms often arise in the sinuses, head and neck, and genitourinary tract, locations that do not normally contain much skeletal muscle, underscoring the notion that sarcomas do not arise from mature, terminally differentiated mesenchymal cells.

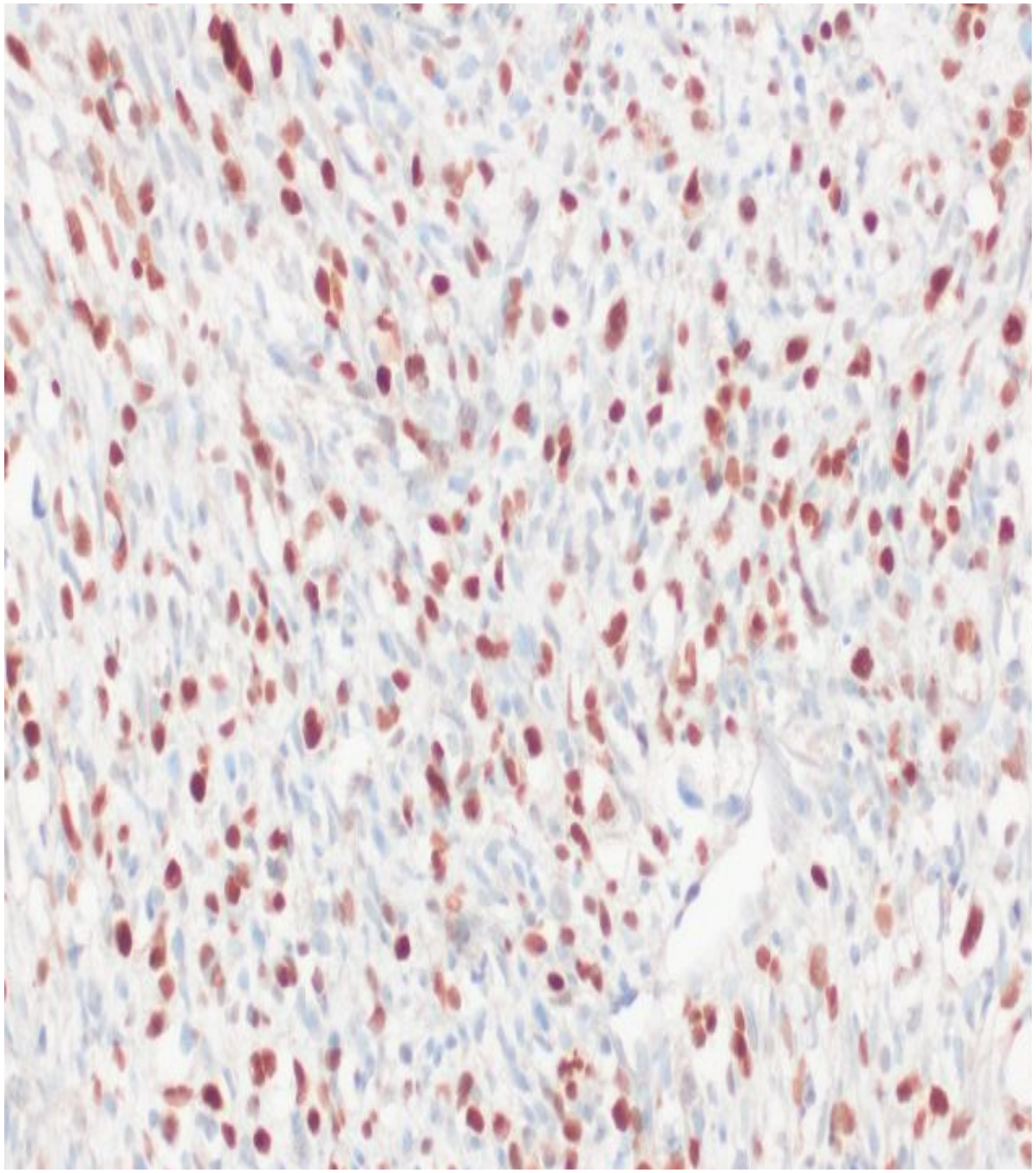
- Alveolar rhabdomyosarcoma frequently contains fusions of the *FOXO1* gene to either the *PAX3* or the *PAX7* gene, rearrangements marked by the presence of (2;13) or (1;13) translocations, respectively. PAX3 is a transcription factor that initiates skeletal muscle differentiation, and it appears that the chimeric PAX3-FOXO1 fusion protein interferes with differentiation.

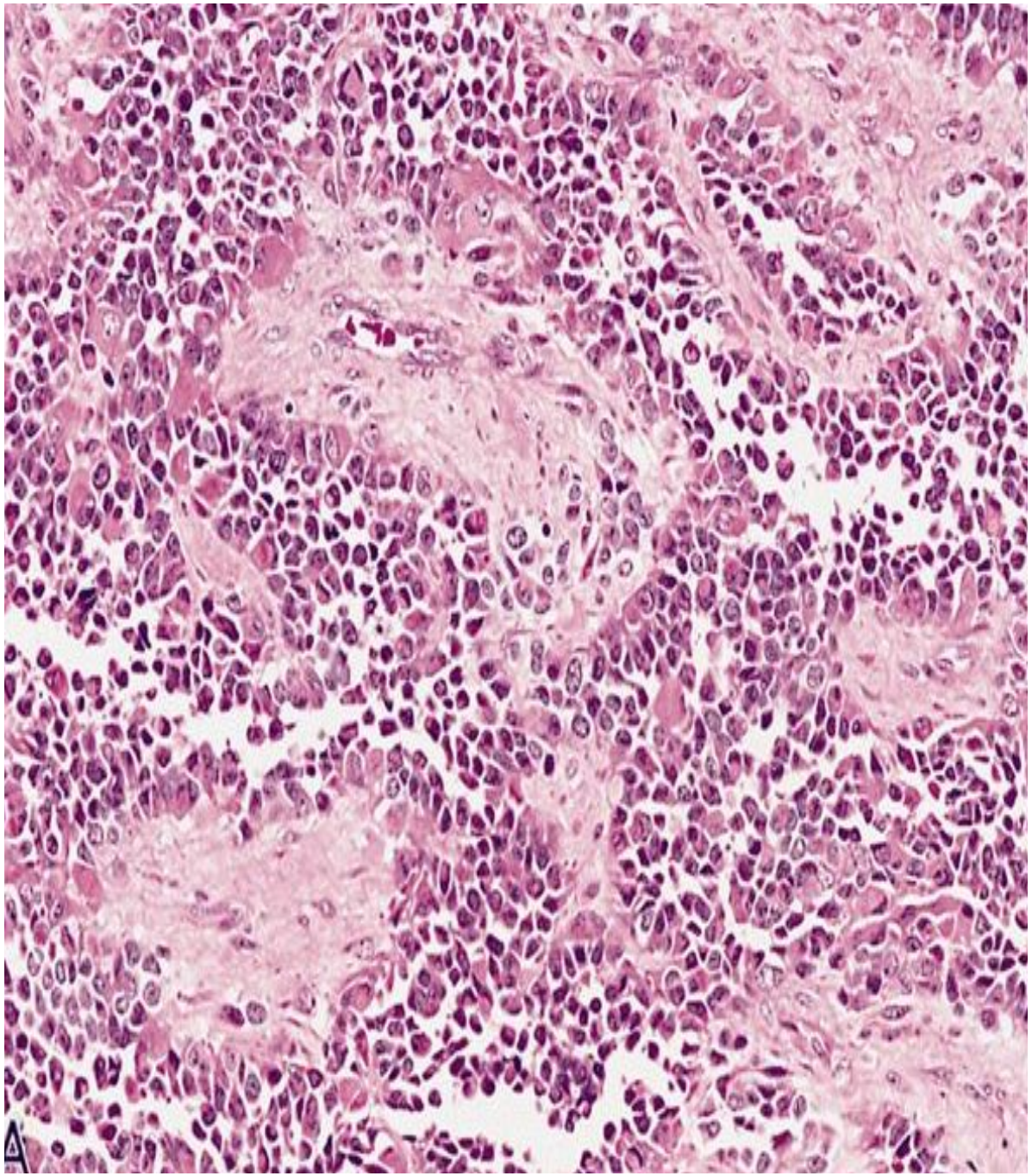
- **Embryonal rhabdomyosarcoma** presents as a soft gray infiltrative mass. The tumor cells mimic skeletal muscle at various stages of differentiation and consist of sheets of both primitive round and spindled cells. Rhabdomyoblasts with straplike cytoplasm and visible cross-striations may be present.
- **Sarcoma botryoides** is a variant of embryonal rhabdomyosarcoma that develops in the walls of hollow viscera such as the urinary bladder and vagina.
- **alveolar rhabdomyosarcoma,** a network of fibrous septae divide the cells into clusters or aggregates, creating a crude resemblance to pulmonary alveoli. The tumor cells are uniformly round with little cytoplasm and they are only minimally cohesive.
- **Pleomorphic rhabdomyosarcoma** is characterized by numerous large, sometimes multinucleated, bizarre eosinophilic tumor cells that can resemble other pleomorphic sarcomas. Immunohistochemical identification of muscle specific proteins such as myogenin is usually necessary to confirm rhabdomyoblastic differentiation.

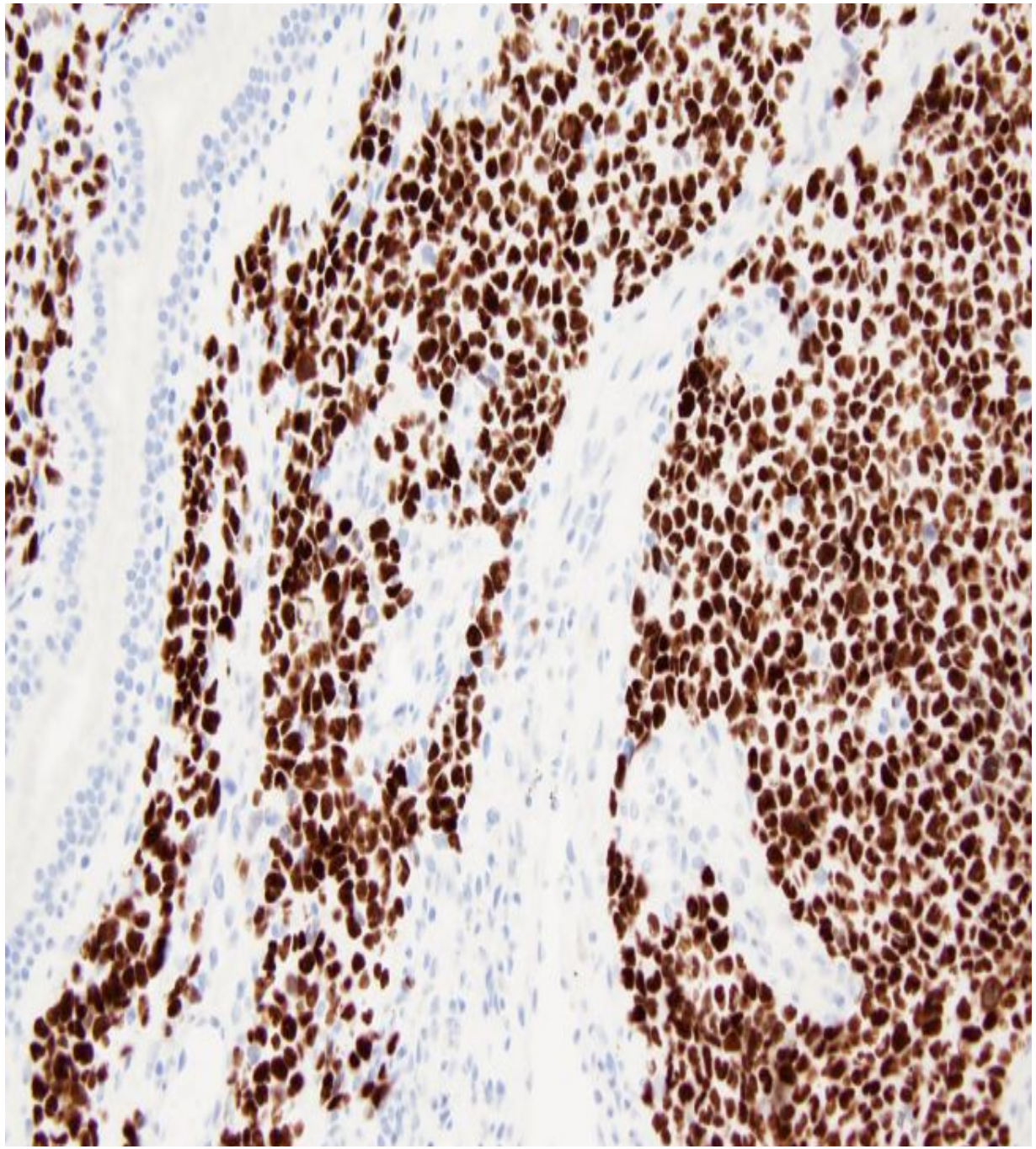


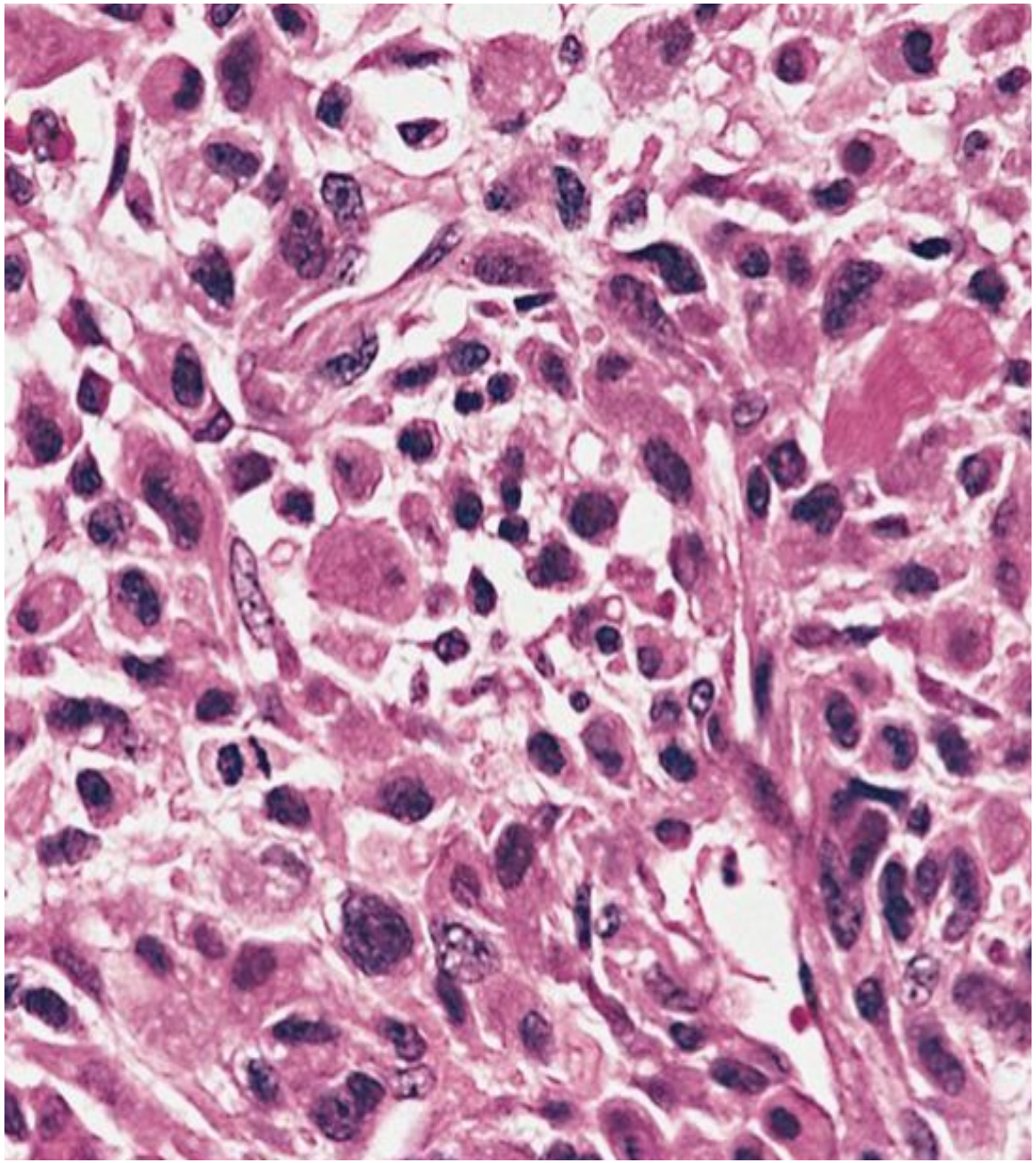


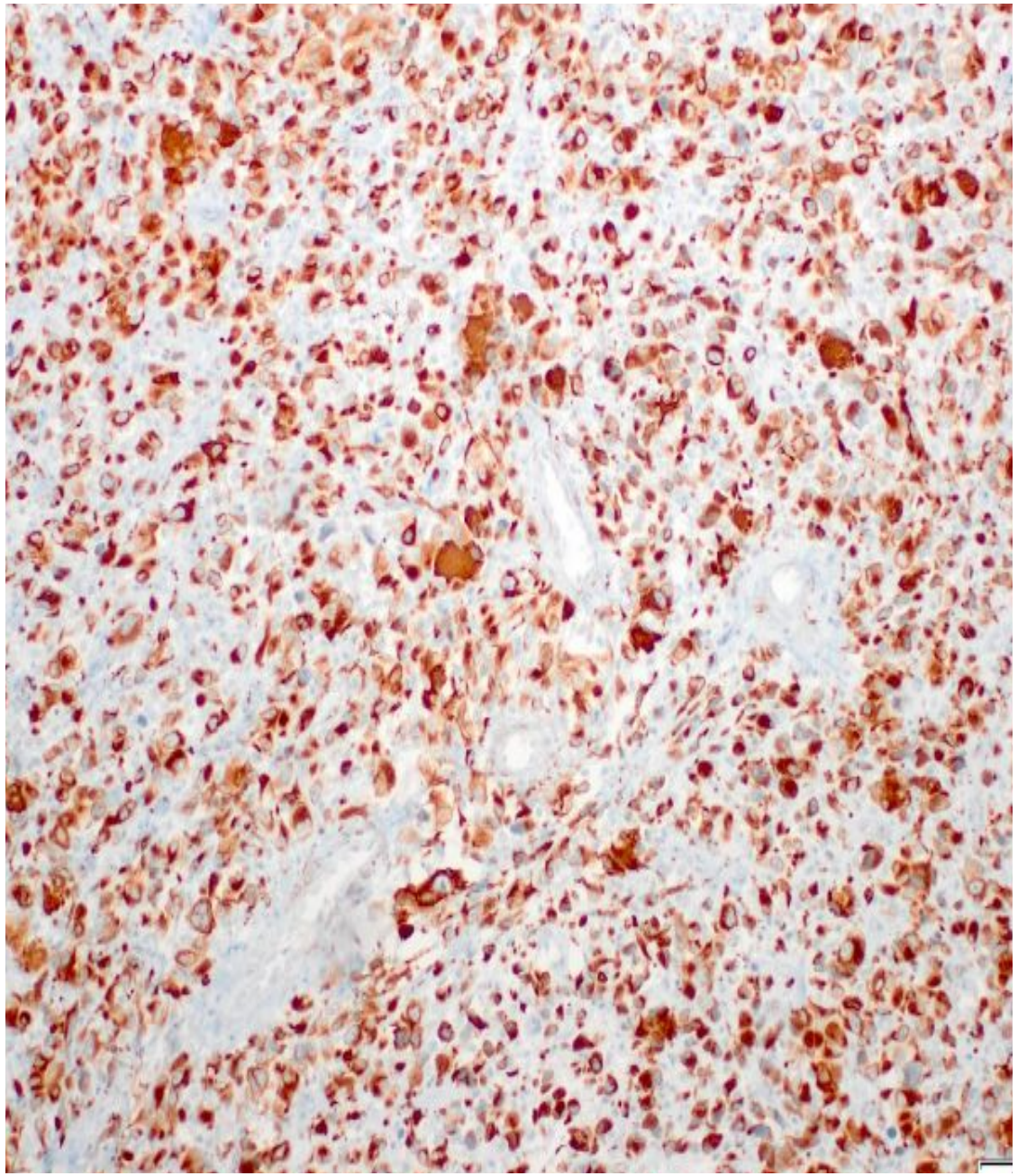












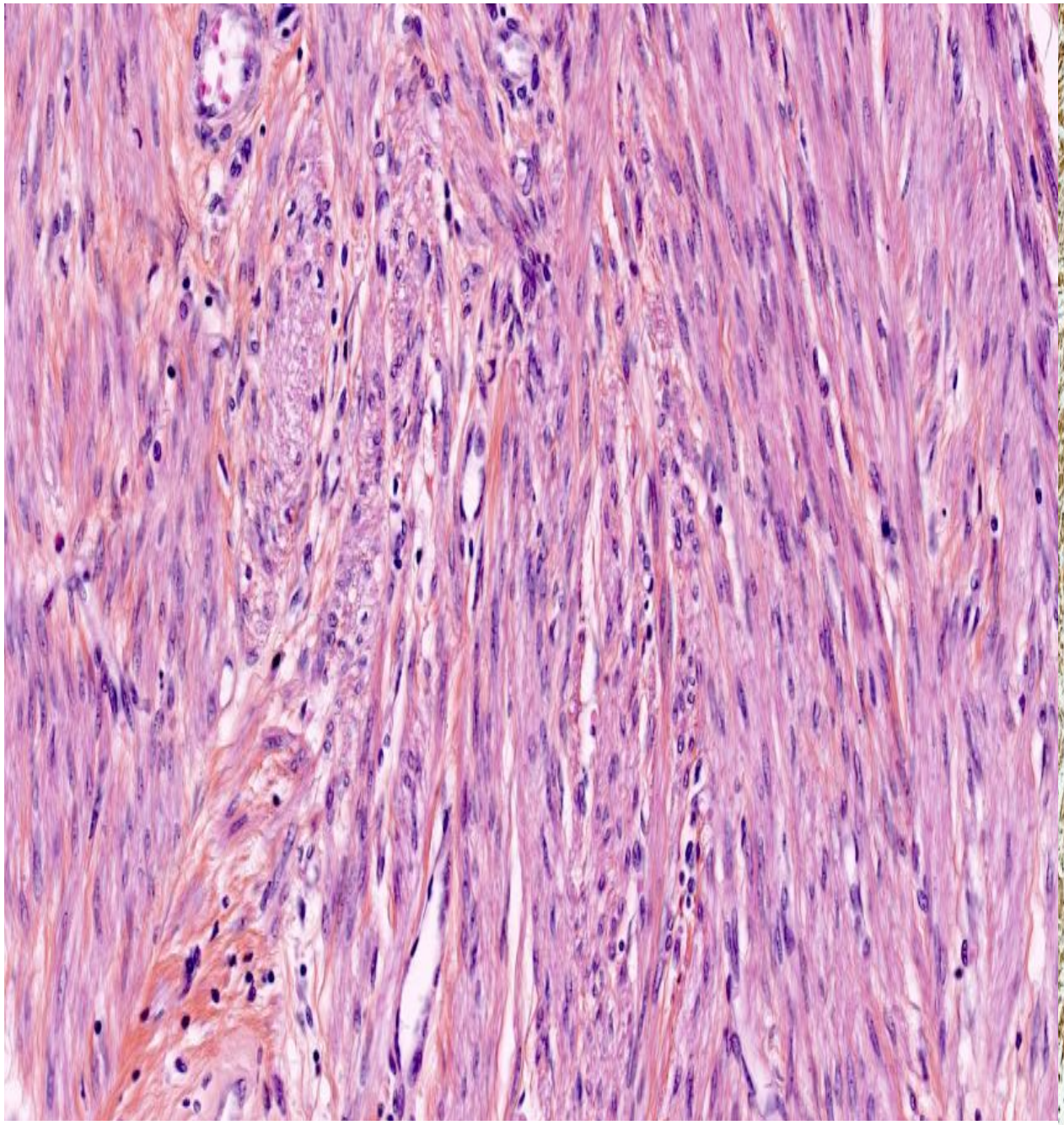
- Rhabdomyosarcomas are aggressive neoplasms that are usually treated with surgery and chemotherapy, with or without radiation therapy. The botryoid variant of embryonal rhabdomyosarcoma has the best prognosis, whereas the pleomorphic subtype is often fatal.

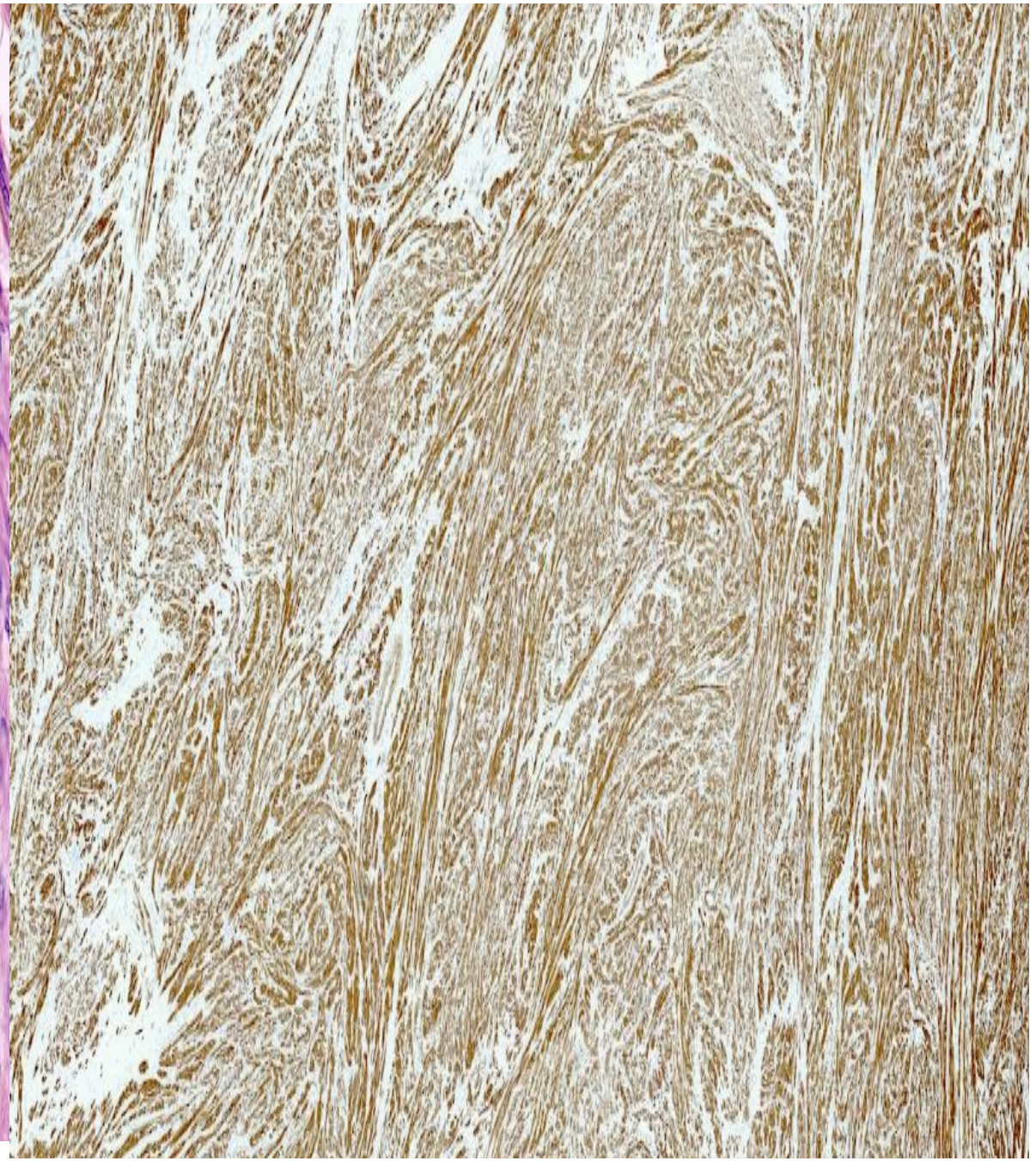
# SMOOTH MUSCLE TUMORS

# Leiomyoma

- Leiomyoma, a benign tumor of smooth muscle, is most common in the uterus but can arise in any soft tissue site.
- Uterine leiomyomas are common and may cause a variety of symptoms including infertility and menorrhagia.
- Leiomyomas also may arise from the erector pili muscles *(pilar leiomyomas)* in the skin and rarely in the deep somatic soft tissues or gastrointestinal tract. A germline loss-of-function mutation in the fumarate hydratase (FH) gene located on chromosome 1q42.3 leads to multiple cutaneous leiomyomas, uterine leiomyomas, and renal cell carcinoma.
- FH is an enzyme of the Krebs cycle, and this association constitutes another example of the link between metabolic abnormalities and neoplasia.

- Soft tissue leiomyomas are usually 1 to 2 cm in size and are composed of fascicles of densely eosinophilic spindle cells that tend to intersect each other at right angles. The tumor cells have blunt-ended, elongated nuclei and show minimal atypia and few mitotic figures. Solitary lesions are cured with surgery.



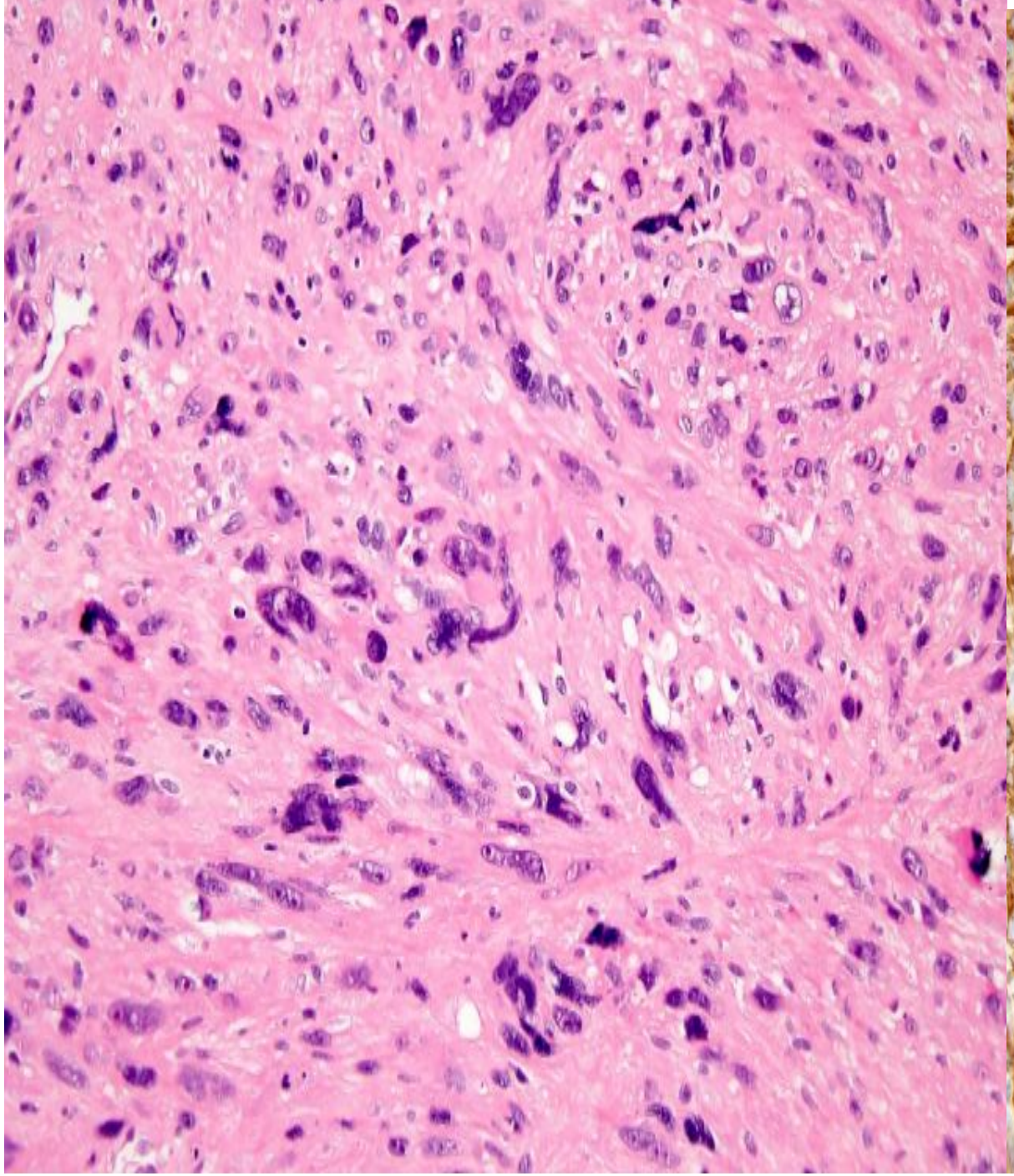


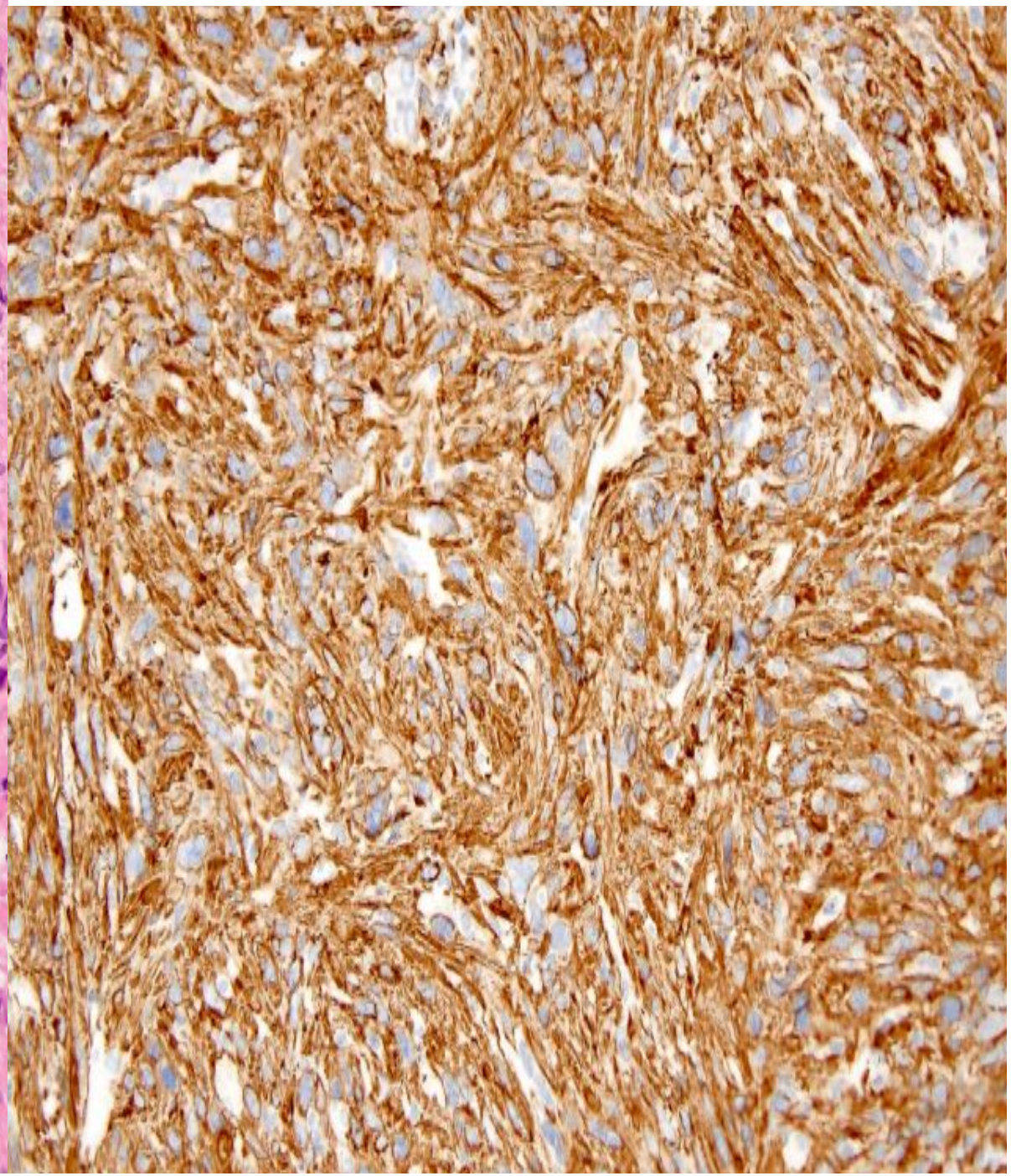
# Leiomyosarcoma

- Soft tissue leiomyosarcoma accounts for 10% to 20% of soft tissue sarcomas. They occur in adults and affect women more frequently than men. Most develop in the deep soft tissues of the extremities and retroperitoneum or arise from the great vessels. Leiomyosarcomas have complex genotypes that stem from acquired defects that lead to profound genomic instability.

# MORPHOLOGY

- Leiomyosarcomas present as painless firm masses. Retroperitoneal tumors may be large and bulky and cause abdominal symptoms. They consist of eosinophilic spindle cells with blunt-ended, hyperchromatic nuclei arranged in interweaving fascicles.
- They express smooth muscle proteins (actin, desmin, caldesmon), which can be detected by immunohistochemistry. Unlike leiomyomas, mitotic activity and necrosis are common in leiomyosarcoma.





# Clinical Course

- Treatment depends on tumor size, location, and grade. Superficial leiomyosarcomas are usually small and have a good prognosis, whereas those of the retroperitoneum are difficult to control and cause death by both local extension and metastatic spread, especially to the lungs.

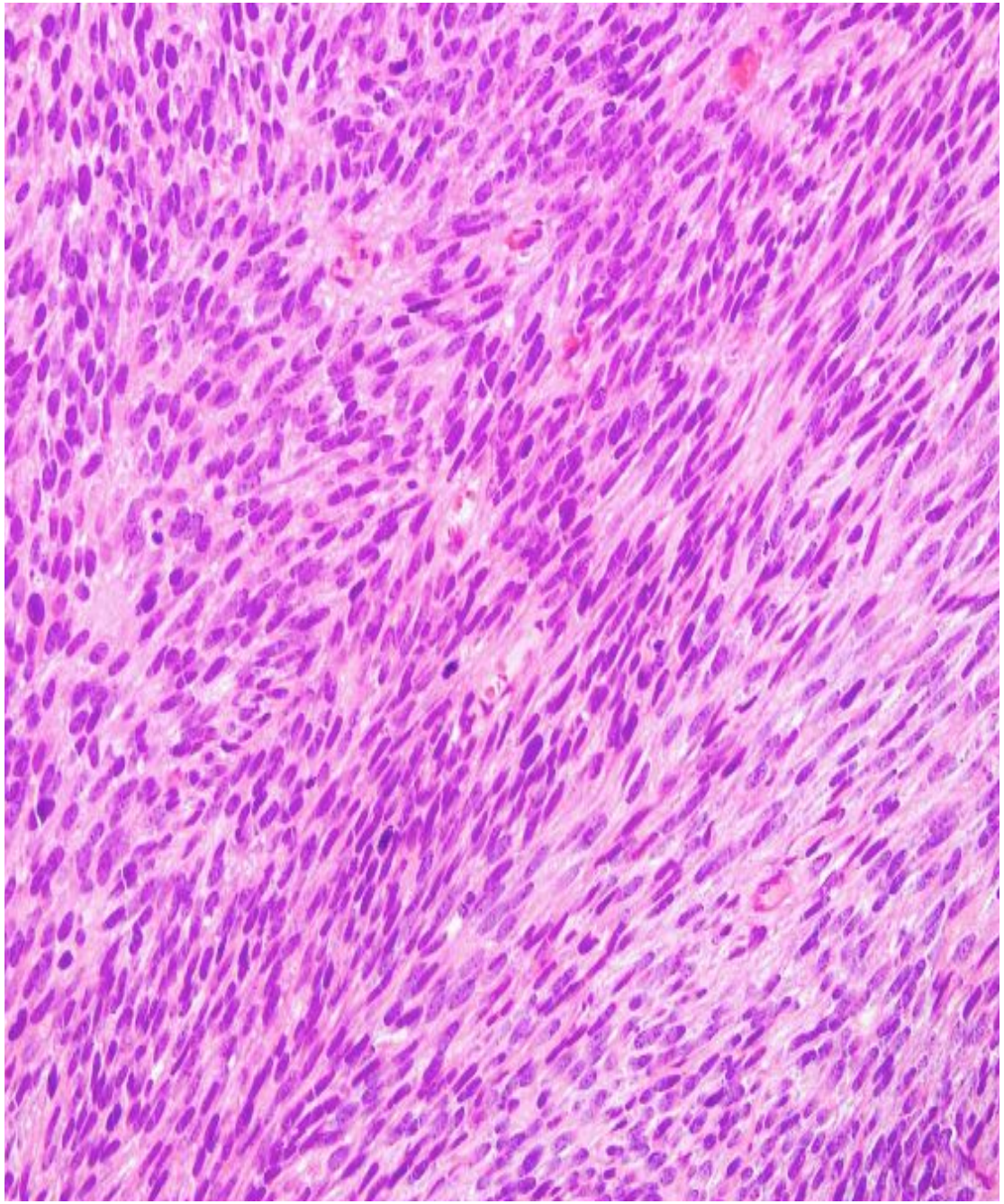
# TUMORS OF UNCERTAIN ORIGIN

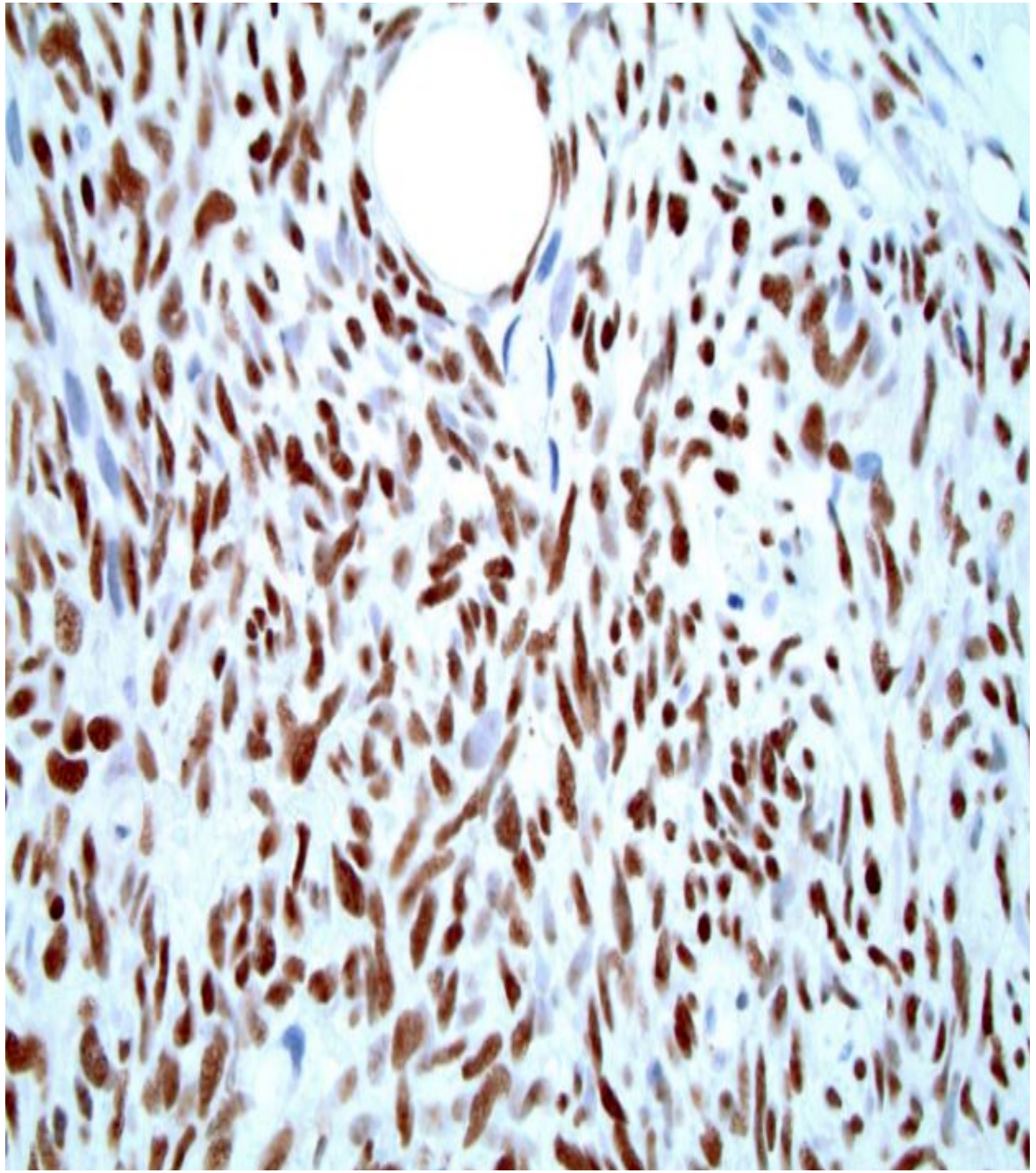
# Synovial Sarcoma

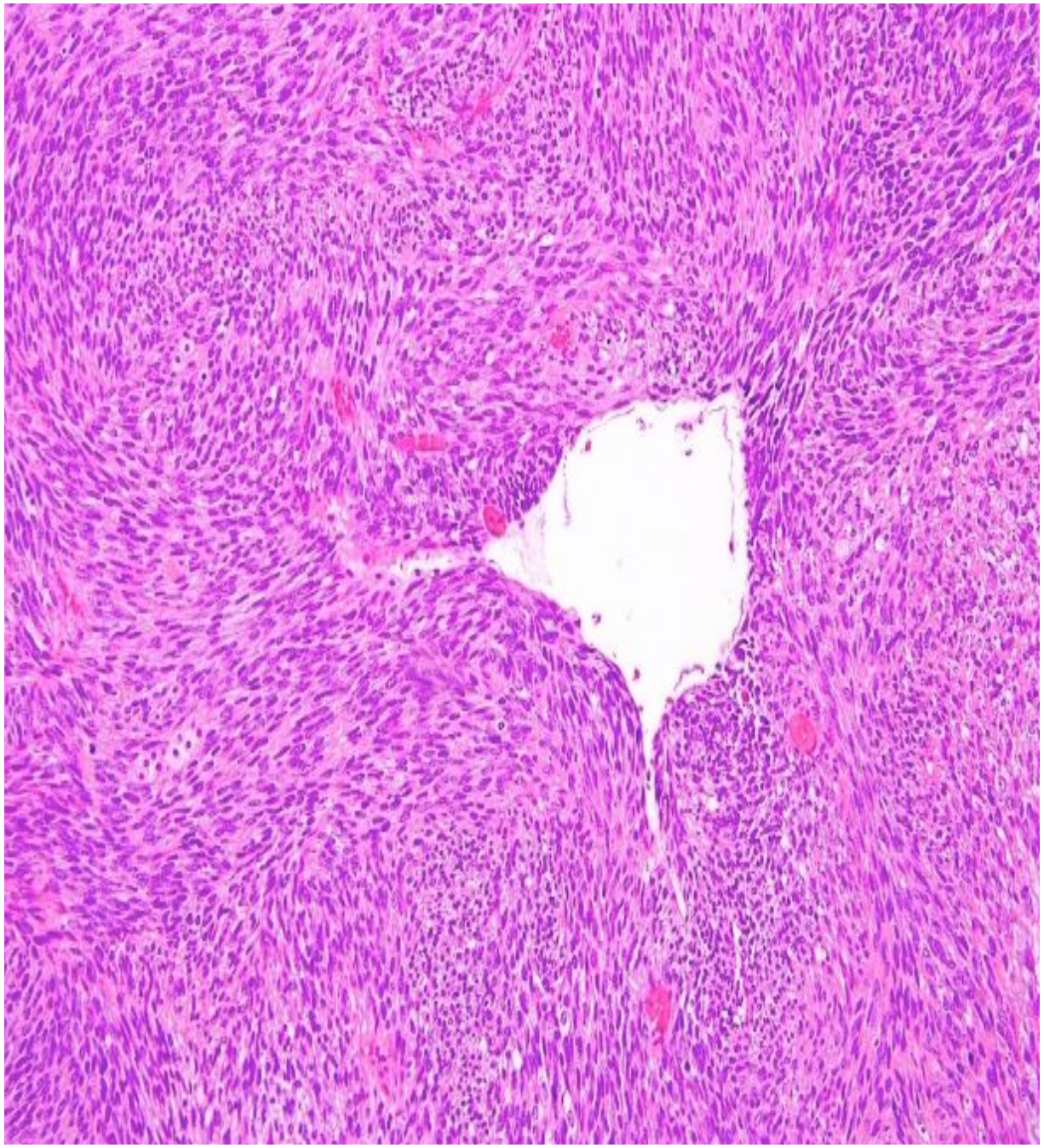
- *Synovial sarcoma* was so-named because the first described cases arose in the soft tissues near the knee joint and a morphologic relationship to synovium was postulated.
- However, this name is a misnomer, as these tumors can present in locations that lack synovium and their morphologic features are inconsistent with an origin from synoviocytes.
- Synovial sarcomas account for approximately 10% of all soft tissue sarcomas. Most occur in people in their 20s to 40s. Patients usually present with a deep-seated mass that has been present for several years.
- Synovial sarcomas show a characteristic chromosomal translocation t(x;18)(p11;q11) producing fusion genes composed of portions of the *SS18* gene and one of three *SSX* genes.

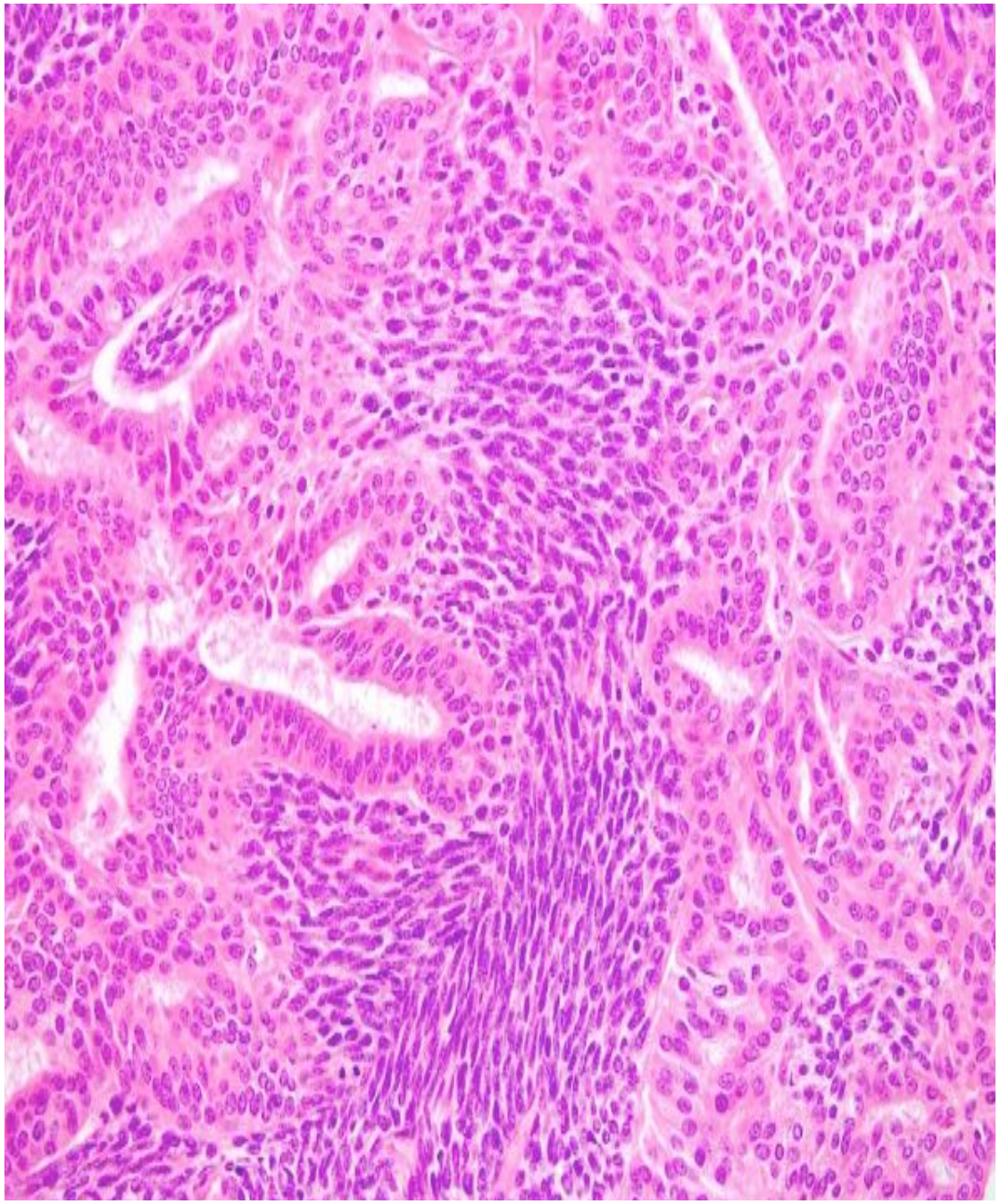
# MORPHOLOGY

- Synovial sarcomas are microscopically monophasic or biphasic.
- Monophasic synovial sarcoma consists of uniform spindle cells with scant cytoplasm and dense chromatin growing in short, tightly packed fascicles.
- The biphasic type contains glandlike structures composed of cuboidal to columnar epithelioid cells in addition to the aforementioned spindle cell component.
- Immunohistochemistry is helpful in identifying these tumors, since the tumor cells, especially in the biphasic type, are positive for epithelial antigens (e.g., keratins), differentiating them from many other sarcomas.









- Synovial sarcomas are treated aggressively with limbsparing surgery and frequently chemotherapy. The 5-year survival varies from 25% to 62%, related to stage and patient age. Common sites of metastases are the lung and, unusual for sarcomas, regional lymph nodes.