1

ADIPOCYTIC TUMORS

Benign tumors and reactive conditions

Lipoma
Lipomatosis
  Multiple symmetric lipomatosis (Launois-Bensaude syndrome)
  Asymmetric lipomatosis
Lipomatosis of nerve
Adiposis dolorosa
Piezogenic pedal papules
Fat necrosis of the morbidly obese
Nevus lipomatosus superficialis
Fibrohistiocytic lipoma
Lipofibromatosis
Lipoblastoma/lipoblastomatosis
Lipoblastoma-like tumor of the vulva
Angiolipoma
Myolipoma of soft tissue
Myelolipoma
Chondroid lipoma
Spindle cell lipoma
Pleomorphic lipoma
Hibernoma

Malignant tumors

Atypical lipomatous tumor/well-differentiated liposarcoma/dedifferentiated liposarcoma
Spindle cell liposarcoma
Myxoid liposarcoma
Pleomorphic liposarcoma

LIPOMA

Definition
- A benign dermal or subcutaneous mesenchymal tumor composed of mature adult-type adipose tissue

Clinical features
Epidemiology
- The most commonly encountered mesenchymal tumor
- Majority of patients are adults
- No sex predilection

Presentation
- Most cases are asymptomatic
- Occasionally painful when compressing nerves
- Slowly growing, but size is variable
- Usually solitary
- Multiple lipomas may be associated with neurofibromatosis, multiple endocrine neoplasia syndromes, or Bannayan syndrome (hemangiomas and multiple lipomas)

Prognosis and treatment
- Treated mostly for aesthetic reasons
- Cured by conservative surgical excision
- Recur only if incompletely excised and then only rarely
- Not associated with progression to liposarcoma

Pathology
Histology
- Resemble normal adult-type adipose tissue
- Lobules of adipocytes bounded by thin fibrous septa
- Adipocytes have large single lipid vacuole in their cytoplasm and eccentrically located small nuclei
- May show areas of fat necrosis and increased fibrosis after trauma
- No atypia, pleomorphism, mitoses, or hyperchromasia

Immunohistochemistry/special stains
- Adipocytes express S100 protein

Genetic profile
- True neoplasms
- Translocation at 12q14 involving *HMGA2* gene is the most common aberration, often with *LPP* (3q27)
- 6p21-23 rearrangements involving *HMG1B* gene are also seen

Main differential diagnoses
- Normal adipose tissue
- Pseudolipomatosis cutis
- Atypical lipomatous tumor

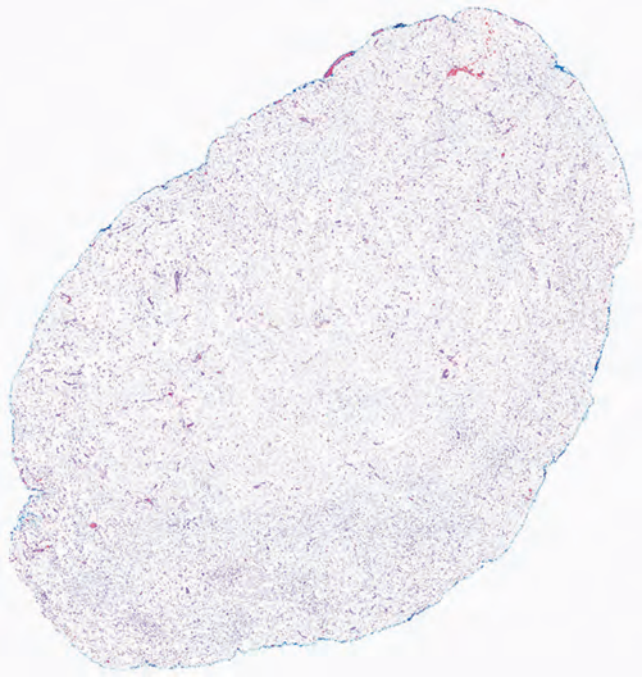

Fig. 1. **Lipoma.** Deeper lipomas are well-circumscribed neoplasms composed of mature adipose tissue essentially indistinguishable from normal fat.

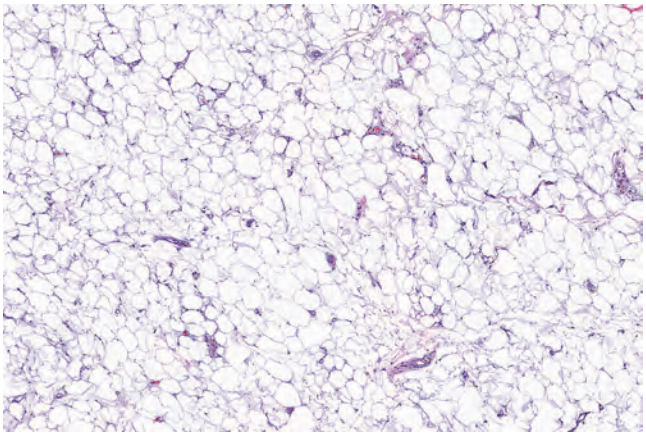

Fig. 2. **Lipoma.** High-power view of mature adipocytes exhibiting minimal size variation and small, eccentric nuclei.

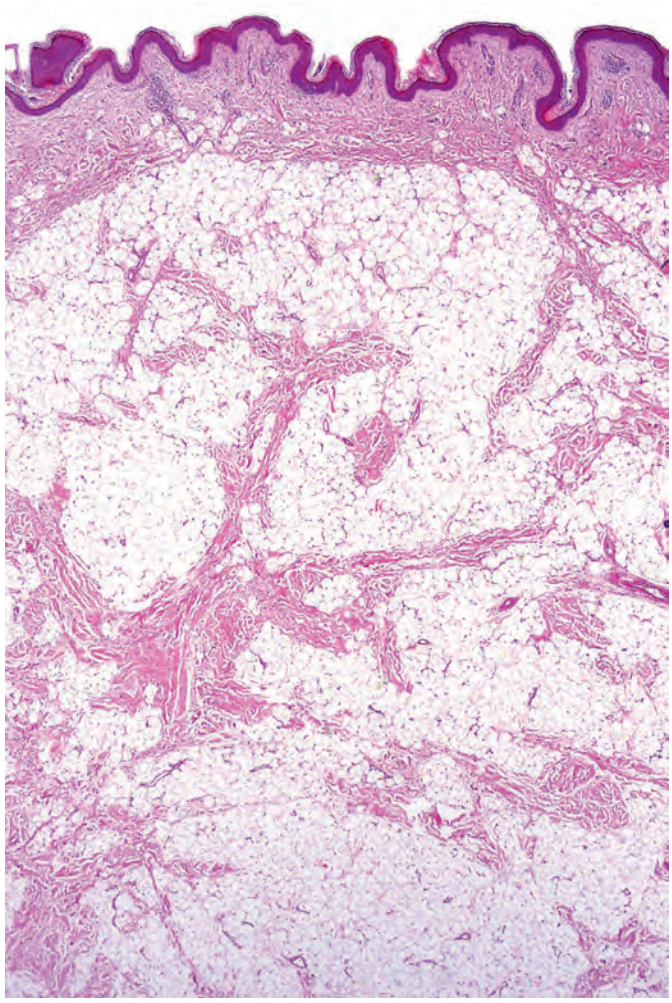

Fig. 3. **Lipoma.** Intradermal lipoma is a well-demarcated dermal neoplasm. It is composed of lobules of mature adipose tissue bounded by fibrous septa.

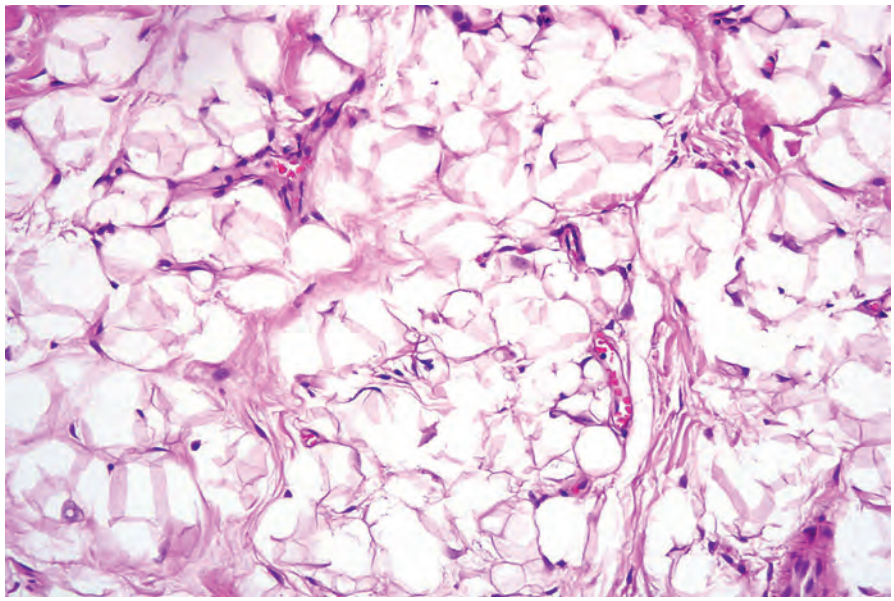

Fig. 4. **Lipoma.** High-power view of intradermal lipoma. Note the mature adipocytes.

LIPOMATOSIS

Definition
- Diffuse overgrowth of mature adipose tissue
- The disease presents in two forms: multiple symmetric lipomatosis (Launois-Bensaude syndrome) and asymmetric lipomatosis

Clinical features
Epidemiology
- Rare disorder, commonly associated with obesity
- Some familial cases show evidence of autosomal-dominant mode of inheritance
- Common in children less than 2 years of age
- Adults can occasionally be affected
- Can present in trunk, head and neck, and extremities

Presentation
- Painless, diffuse enlargement of affected area due to fat accumulation
- Rapid growth is characteristic

Prognosis and treatment
- Recurrence after palliative surgical removal is common
- Usually cured by radical surgical excision
- Although benign, can be fatal due to laryngeal obstruction

Pathology
Histology
- Sheets and lobules of mature adipocytes
- No encapsulation

Immunohistochemistry/special stains
- The mature adipocytes strongly express S100 protein

Main differential diagnoses
- Intramuscular lipoma
- Atypical lipomatous tumor

Multiple symmetric lipomatosis (Launois-Bensaude syndrome)

- The most common form of lipomatosis characterized by symmetrical deposition of adipose tissue in the trunk and head and neck area
- Two variants exist: diffuse and localized
- The diffuse variant usually affects the trunk of male children
- The localized variant characteristically affects the cervical area of adult males and can present with laryngeal obstruction
- Patients can present with neuropathy

Asymmetric lipomatosis

- Asymmetric deposition of adipose tissue affecting any part of the body
- Less common than the symmetric form of lipomatosis
- Can present with macrodactyly or gigantism of affected body area

LIPOMATOSIS OF NERVE

Definition
- A rare hamartomatous condition characterized by fatty infiltration of epineurium of a major nerve
- Also known as *fibrolipoma of nerve, fibrolipomatous hamartoma of nerve, macrodystrophia lipomatosa, perineural lipoma,* and *intraneural lipoma*

Clinical features
Epidemiology
- Affected individuals are mostly newborns and young children
- Female predilection

Presentation
- The median nerve is the most common location, followed by the ulnar nerve
- Slowly growing masses or macrodactyly
- Can be asymptomatic or associated with pain, paresthesia, or motor deficit

Prognosis and treatment
- Benign condition, but management can be challenging
- Surgical excision may result in permanent sensory and/or motor deficit
- Incomplete removal is associated with high rate of recurrence

Pathology
Histology
- Infiltration of epineurium and perineurium by mature adipose tissue admixed with fibrous tissue
- Metaplastic bone formation is rarely seen

Main differential diagnoses
- Intraneural lipoma
- Diffuse lipomatosis
- Traumatic neuroma

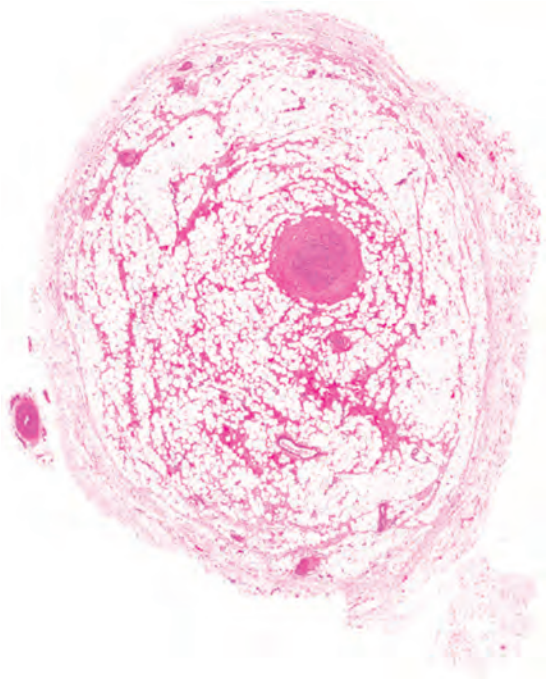

Fig. 1. **Lipomatosis of nerve.** Mature adipose tissue surrounds individual nerve branches but is bounded by epineurium.

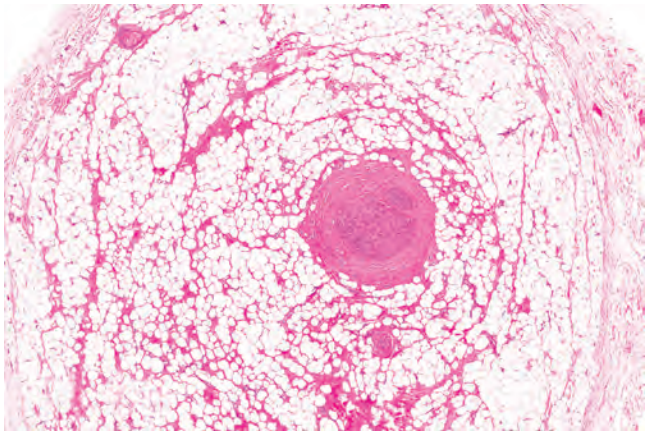

Fig. 2. **Lipomatosis of nerve.** Fibrosis of the surrounding adipose tissue is often seen.

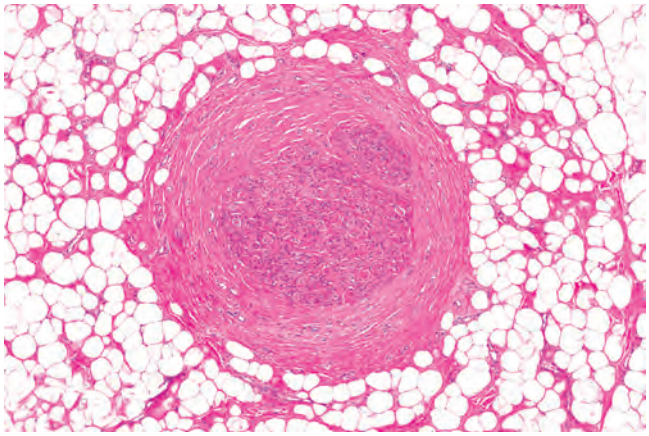

Fig. 3. **Lipomatosis of nerve.** Extensive concentric fibrosis of the largest central nerve bundle.

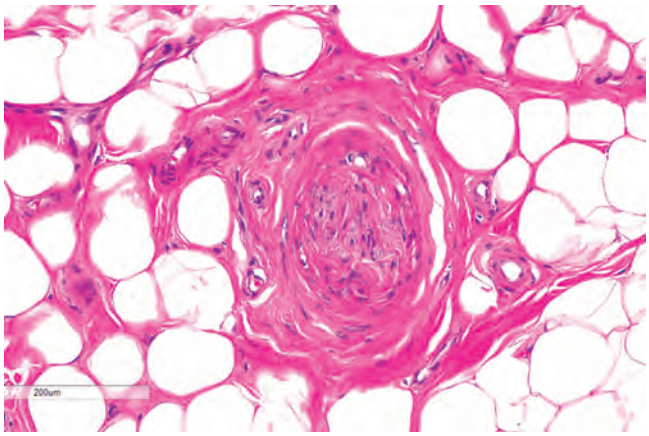

Fig. 4. **Lipomatosis of nerve.** A small nerve bundle with less surrounding fibrosis.

ADIPOSIS DOLOROSA

Definition
- A rare condition characterized by multiple painful plaques of accumulated subcutaneous fat
- Also known as *Dercum disease*

Clinical features
Epidemiology
- Rare disorder, commonly associated with obesity
- Affected individuals are mainly postmenopausal women

Presentation
- Painful and tender plaques
- Usually multiple
- Most cases are located in the lower extremities and pelvic area

Prognosis and treatment
- Benign condition cured by surgical excision

Pathology
Histology
- Subcutaneous lobules of mature adipocytes
- Fat necrosis can be seen

Immunohistochemistry/special stains
- The mature adipocytes strongly express S100 protein

Main differential diagnoses
- Lipoma
- Other forms of lipomatosis

PIEZOGENIC PEDAL PAPULES

Definition
- Multiple papules located at the internal aspects of the heels

Clinical features
Epidemiology
- Commonly affects athletes, particularly marathon runners
- Associated with Ehlers-Danlos and Prader-Willi syndromes as well as rheumatoid arthritis
- Rarely familial

Presentation
- Multiple asymptomatic skin-colored papules
- Lesions become more pronounced after prolonged standing
- Pressure may elicit pain

Prognosis and treatment
- Conservative management includes intralesional steroid and anesthetic injection or compression treatment
- Therapy outcome might not be satisfactory
- Surgical intervention is usually more effective

Pathology
Histology
- Mature adipose tissue herniating into the dermis

Immunohistochemistry/special stains
- The mature adipocytes strongly express S100 protein

Main differential diagnoses
- Intradermal lipoma

FAT NECROSIS OF THE MORBIDLY OBESE

Definition
- Necrosis of subcutaneous adipose tissue as a result of obesity
- It is thought to result from medial calcification of subcutaneous arterioles with subsequent ischemic necrosis of fat

Clinical features
Epidemiology
- Usually affects distal extremities
- Can affect thighs, abdomen, and other areas
- Associated with chronic renal failure and hyperphosphatemia

Presentation
- Painful induration and purplish discoloration of skin
- Associated skin necrosis can lead to ulcer formation
- Skin ulceration progresses rapidly as level of phosphate peaks

Prognosis and treatment
- High mortality rate due to development of secondary infection

Pathology
Histology
- Massive necrosis of subcutaneous adipose tissue with minimal inflammatory reaction
- Calcification of subcutaneous arterioles with luminal narrowing

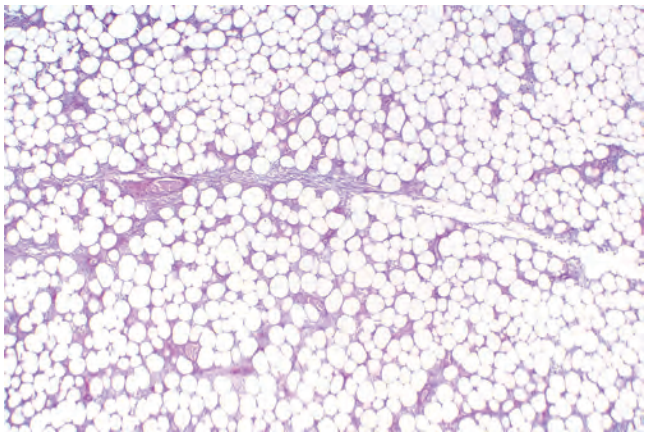

Fig. 1. **Fat necrosis of the morbidly obese.** Low-power view showing extensive fat necrosis.

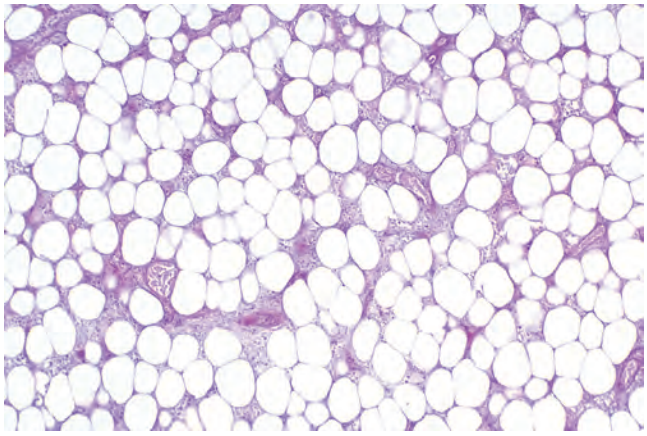

Fig. 2. **Fat necrosis of the morbidly obese.** Necrosis involving the adipocytes as well as the vascularized fibrous septa.

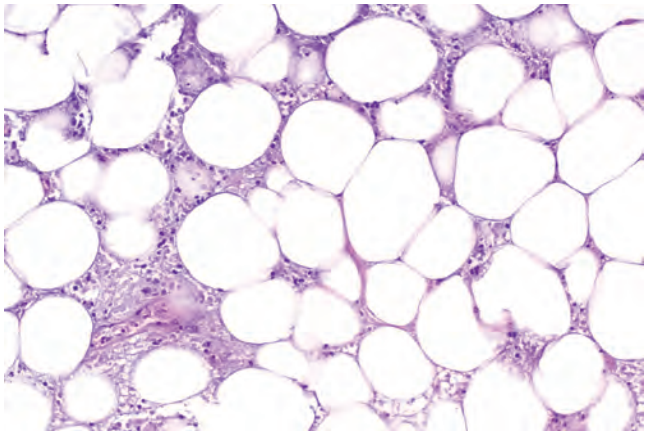

Fig. 3. **Fat necrosis of the morbidly obese.** Necrotic adipocytes and necrotic connective tissue septa are seen in this image.

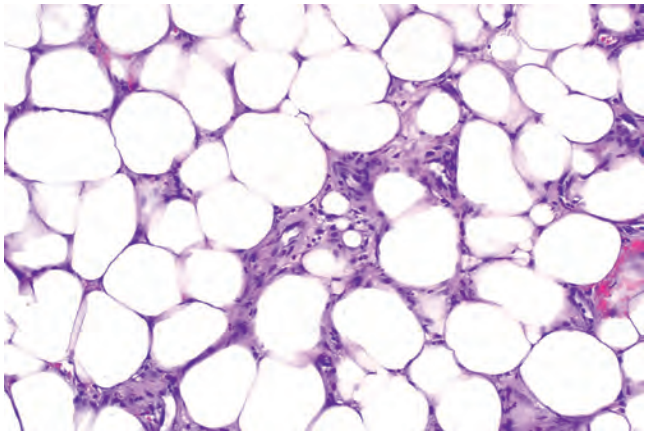

Fig. 4. **Fat necrosis of the morbidly obese.** Viable adipocytes can be seen in a patchy or geographical distribution.

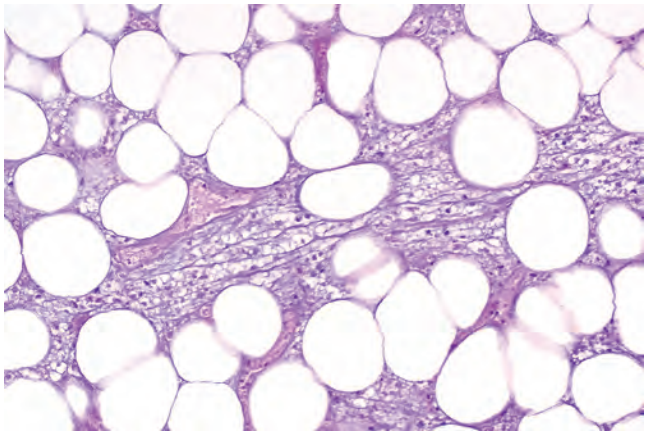

Fig. 5. **Fat necrosis of the morbidly obese.** Necrotic adipocytes often retain their shape but lose nuclear staining.

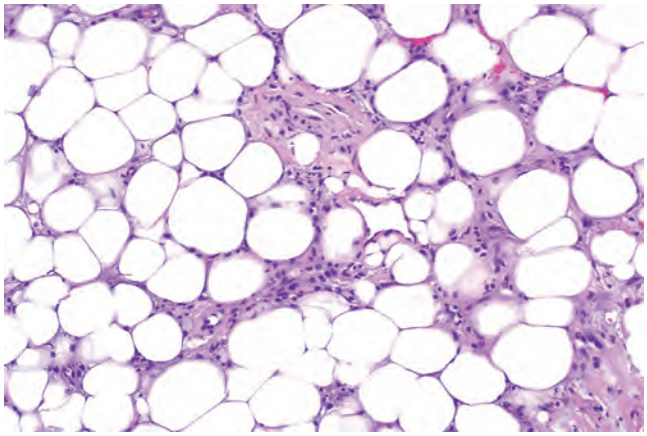

Fig. 6. **Fat necrosis of the morbidly obese.** Histiocytes infiltrate the adipose tissue. Note the arteriolosclerosis.

NEVUS LIPOMATOSUS SUPERFICIALIS

Definition
- A rare cutaneous hamartomatous lesion characterized by multiple small collections of adipocytes within the dermis

Clinical features
Epidemiology
- Affected individuals are children or adolescents
- Adults present with solitary variant
- No sex predilection

Presentation
- Multiple painless papules
- Size ranges from few millimeters up to 2 cm
- Most commonly affect the gluteal area, upper thighs, and lower back

Prognosis and treatment
- Cured by simple excision

Pathology
Histology
- Nonencapsulated lesion composed of variable number of fatty lobules deposited in the upper portion of the dermis
- The lobules condense around blood vessels and are interspersed by loose fibrous tissue
- Secondary changes include perifollicular fibrosis, follicular hyperkeratosis, and epidermal atrophy

Immunohistochemistry/special stains
- The mature adipocytes strongly express S100 protein

Main differential diagnoses
- Lipofibroma
- Fibroepithelial polyp

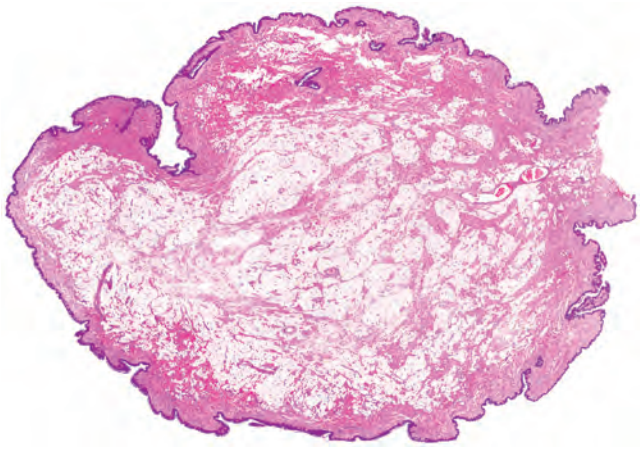

Fig. 1. **Nevus lipomatosus superficialis.** A lesion in the upper dermis composed of variably sized lobules of mature adipocytes.

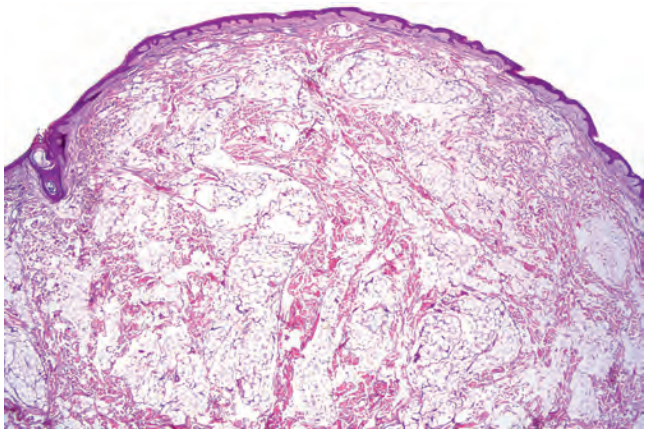

Fig. 2. **Nevus lipomatosus superficialis.** The overlying epidermis is slightly atrophic.

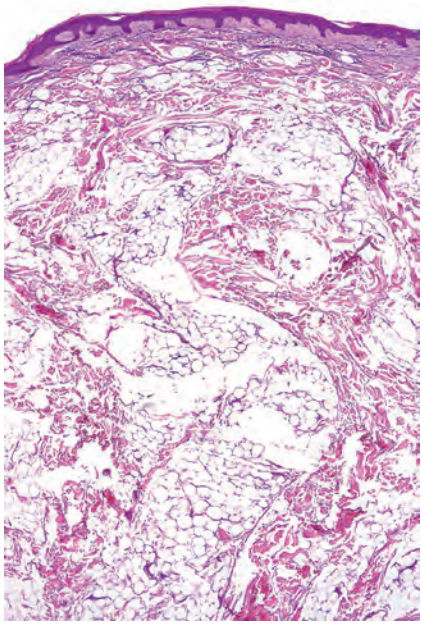

Fig. 3. **Nevus lipomatosus superficialis.** The adipocytic lobules are separated by fibrous septa.

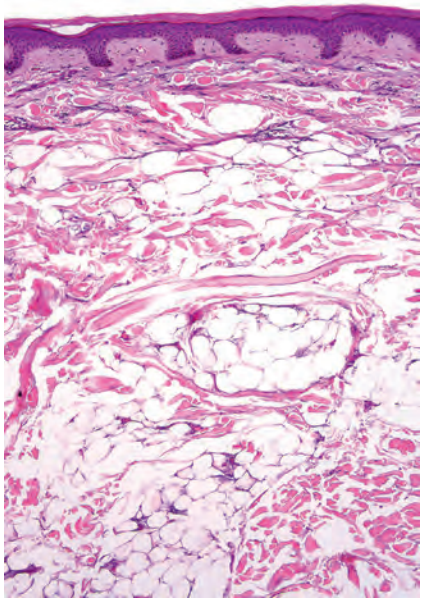

Fig. 4. **Nevus lipomatosus superficialis.** High-power view demonstrates mature adipocytes with small, eccentric nuclei. Note the interspersed collagen fibers.

FIBROHISTIOCYTIC LIPOMA

Definition
- A rare variant of lipoma characterized by the presence of fibrohistiocytic proliferation in addition to the conventional lipomatous component

Clinical features
Epidemiology
- Strong predilection for young adult males
- Anterior aspect of trunk is most commonly affected

Presentation
- Small, painless, subcutaneous lesions
- Usually solitary

Prognosis and treatment
- Cured by local excision
- No reports of recurrence or metastasis

Pathology
Histology
- Well-circumscribed subcutaneous lipomas with fibrohistiocytic foci
- Fibrohistiocytic foci depict slightly plump, bland-looking spindle cells arranged in fascicles in a collagenous stroma
- May exhibit minimal inflammation and/or hemosiderin deposition

Immunohistochemistry/special stains
- Tumor cells express CD34 and calponin
- Fibrohistiocytic component lacks S100 protein expression

Main differential diagnoses
- Benign fibrous histiocytoma
- Spindle cell lipoma
- Atypical lipomatous tumor
- Dermatofibrosarcoma protuberans

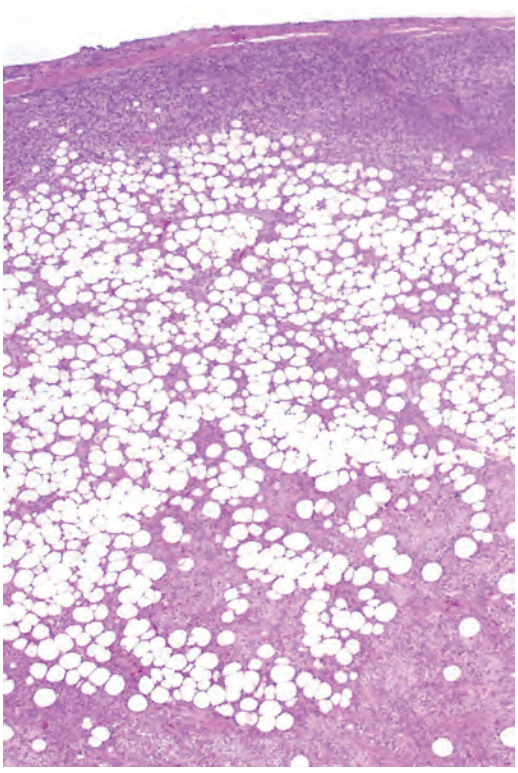

Fig. 1. **Fibrohistiocytic lipoma.** A circumscribed neoplasm admixing mature lipomatous cells and a spindle cell component. (Courtesy of Julie Fanburg-Smith, Washington, DC, USA.)

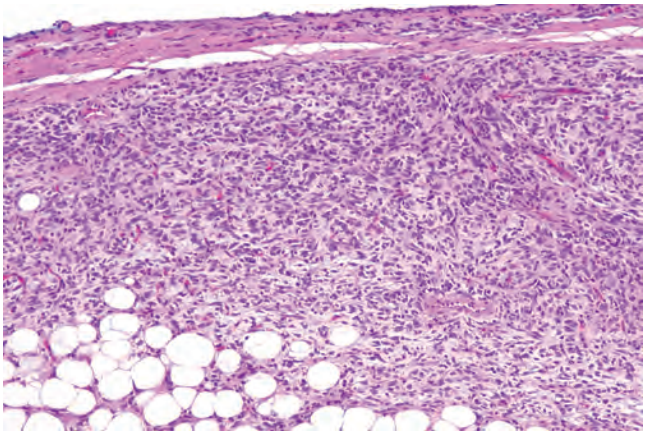

Fig. 2. **Fibrohistiocytic lipoma.** The spindle cells have a fibrohistiocytic pattern. (Courtesy of Julie Fanburg-Smith, Washington, DC, USA.)

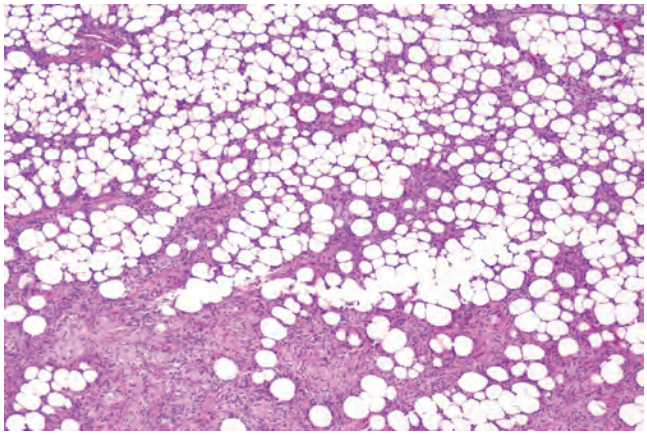

Fig. 3. **Fibrohistiocytic lipoma.** The adipose tissue and spindle cells can be admixed. (Courtesy of Julie Fanburg-Smith, Washington, DC, USA.)

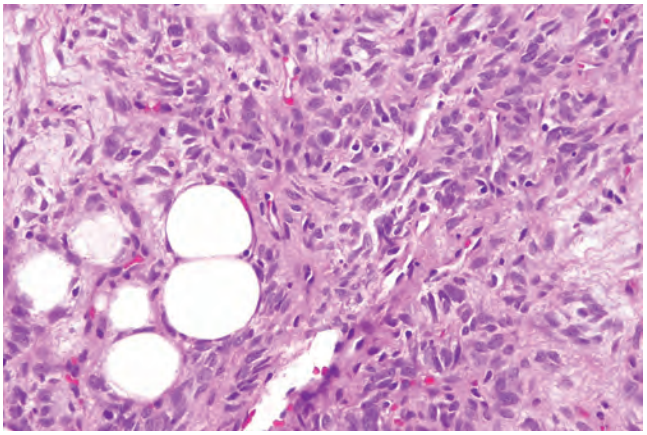

Fig. 5. **Fibrohistiocytic lipoma.** Intimate juxtaposition of mature adipocytic cells and fibrohistiocytic cells. (Courtesy of Julie Fanburg-Smith, Washington, DC, USA.)

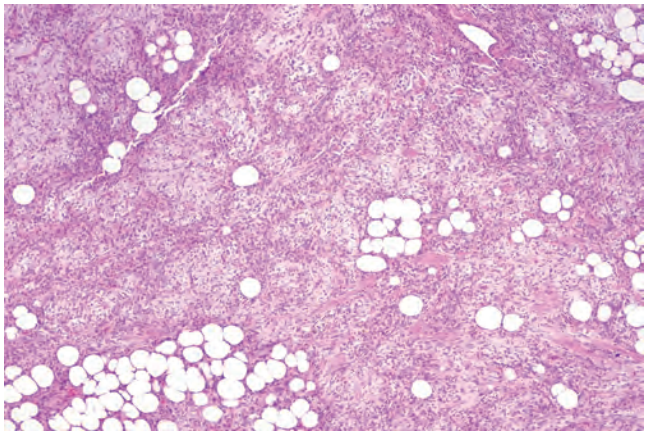

Fig. 4. **Fibrohistiocytic lipoma.** The non-adipocytic component can be predominant in areas. (Courtesy of Julie Fanburg-Smith, Washington, DC, USA.)

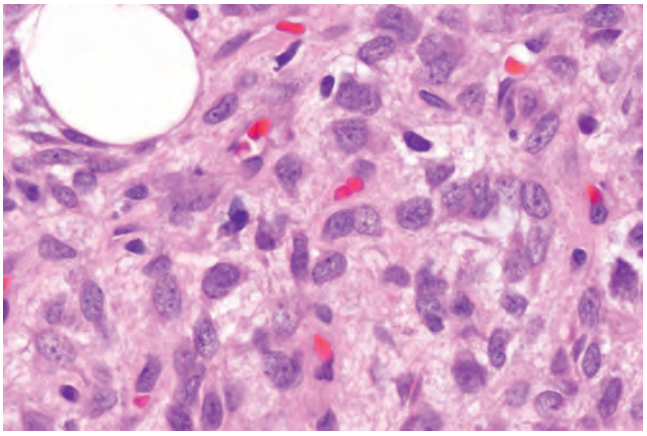

Fig. 6. **Fibrohistiocytic lipoma.** The nuclei are banal, and the cytoplasm is somewhat amphophilic. (Courtesy of Julie Fanburg-Smith, Washington, DC, USA.)

LIPOFIBROMATOSIS

Definition
- A benign fibrofatty neoplasm presenting in childhood

Clinical features
Epidemiology
- More common in males
- Develops in infancy and childhood (mean age 1 year)
- Already present at birth in a substantial number of cases (about 15%)

Presentation
- Slowly growing and ill-defined painless mass
- Size of the lesion usually between 2 and 5 cm
- Wide anatomical distribution with predilection for hands and feet

Prognosis and treatment
- Benign proliferation, associated with high rate of nondestructive recurrence(s) (about 70%)
- Diffuse involvement of the limbs can result in deformities of the underlying bone
- Risk factors for local recurrence(s) include congenital onset, male gender, incomplete excision, and increased mitotic rate
- Complete surgical excision generally curative, but may be difficult to achieve

Pathology
Histology
- Poorly delineated proliferation in the subcutis and/or deep soft tissues
- Two main components are mature fat and fibroblastic spindle-shaped cells
- Adipose tissue component
  - Integral part of the tumor
  - Usually the predominant component
  - Composed of mature adipocytes
  - Variably sized and poorly demarcated lobules
- Fibroblastic spindle cell component
  - Formation of fascicles, typically growing along the fat septa
  - Mild cytological atypia
  - Mitoses absent or rare in the majority of cases
  - Increased mitotic rate associated with increased likelihood of local recurrence
  - Small to moderate amounts of collagen
  - Focal myxoid change occasionally present
- Univacuolated cells
  - Usually encountered at the interface between the fibroblastic and adipocytic component
  - Characterized by a single vacuole in the cytoplasm
  - Likely represent degenerating adipocytes, lipid-rich fibroblasts, or transitional cells between fibroblast and adipocyte
  - Seen in the majority of lesions
- Entrapment of normal structures, including vessels, nerves, skin adnexa, and skeletal muscle within the tumor
- Pigmented melanocytic spindled or dendritic cells (similar to the ones found in Bednar tumor) exceptionally seen among the lesional cells

Immunohistochemistry/special stains
- Not contributory
- Focal S100 protein positivity in the spindle cell component occasionally detected
- β-catenin negative

Main differential diagnoses
- Juvenile hyaline fibromatosis
- Fibrous hamartoma of infancy
- Calcifying aponeurotic fibroma
- Lipoblastoma

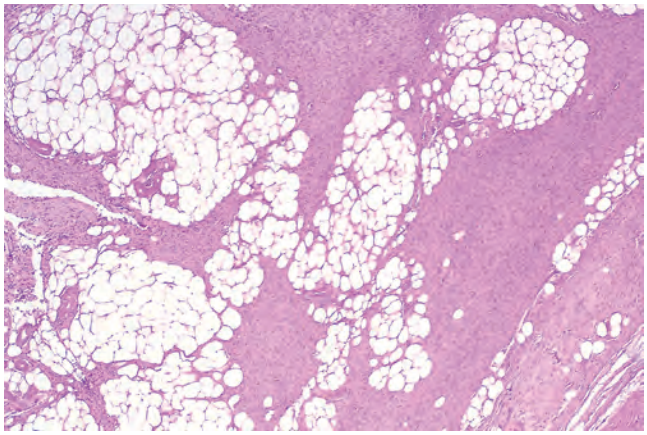

Fig. 1. **Lipofibromatosis.** An ill-defined neoplasm composed of proliferative fibrous tissue with islands of adipose tissue.

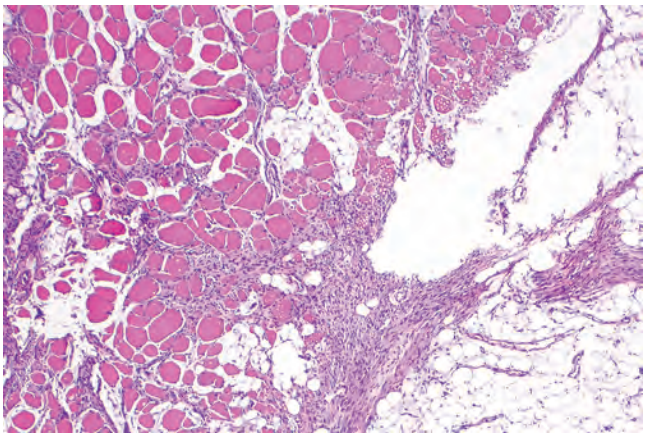

Fig. 4. **Lipofibromatosis.** The process infiltrates the underlying skeletal muscle.

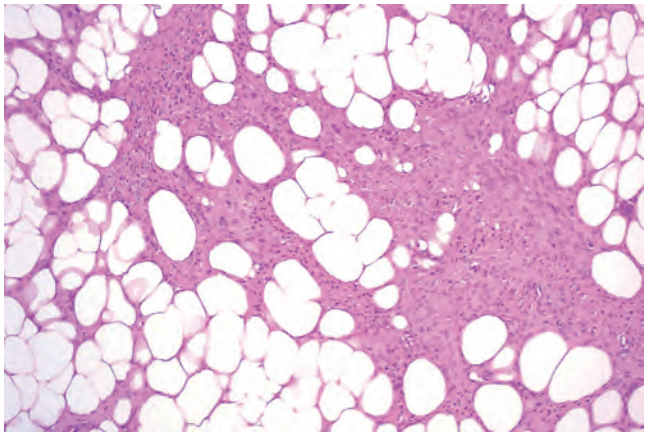

Fig. 2. **Lipofibromatosis.** Adipocytic and fibroblastic components are intimately admixed.

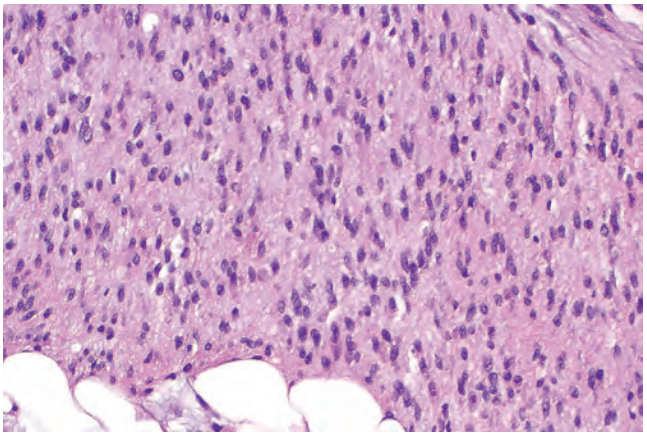

Fig. 5. **Lipofibromatosis.** The spindle cell fibroblasts reveal bland nuclear features.

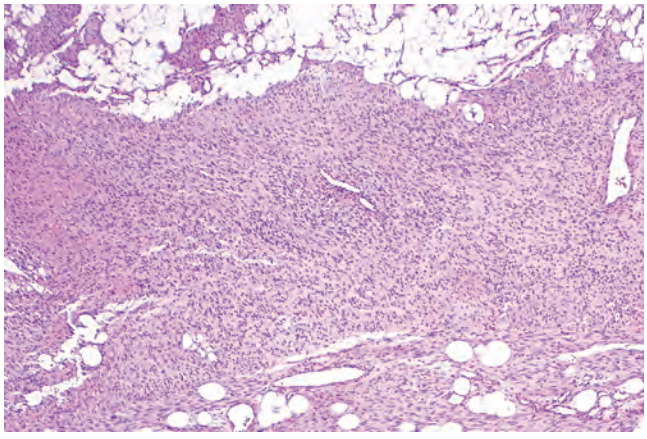

Fig. 3. **Lipofibromatosis.** Area with marked spindle cell fibroblastic proliferation with interspersed adipose tissue, somewhat resembling desmoid fibromatosis.

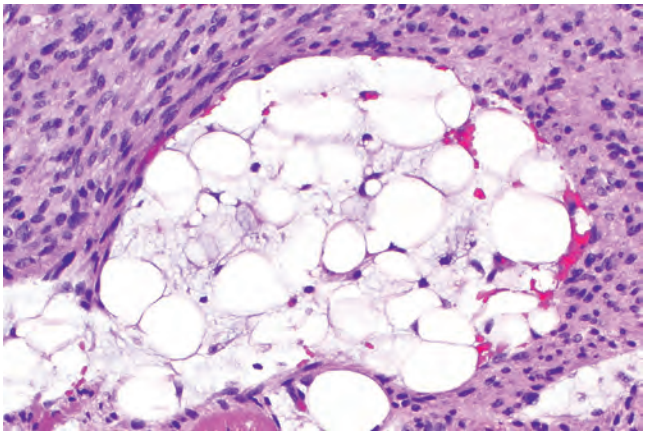

Fig. 6. **Lipofibromatosis.** The adipocytic component also demonstrates benign cytology.

LIPOBLASTOMA/LIPOBLASTOMATOSIS

Definition

- Lipoblastoma and lipoblastomatosis are lesions characterized by the presence of lobules of fetal-type adipose tissue
- Lipoblastoma is localized while lipoblastomatosis is the diffuse form of the disease

Clinical features

Epidemiology

- Lipoblastoma/lipoblastomatosis are considered the fetal counterpart of the adult lipoma and lipomatosis, respectively
- Most patients are infants or young children less than 3 years of age
- Boys are much more commonly affected than girls
- The extremities are the most common location followed by the mediastinum, the trunk, the retroperitoneum, and the head and neck

Presentation

- Discrete or diffuse superficial, painless masses of fatty tissue
- Small lesions, usually measure 2 to 5 cm

Prognosis and treatment

- Benign condition
- Localized form of disease is readily cured by total resection
- Lipoblastomatosis may recur on some occasions mainly due to inability to completely excise the lesion
- Untreated cases may undergo maturation into an adult-type lipoma/lipomatosis

Pathology

Histology

- Lobules of mature adipocytes admixed with lipoblasts in varying stages of development
- Number of lipoblasts present in the tumor tends to decrease as the patient age increases
- Lipoblastomatosis is less lobulated and may infiltrate skeletal muscle tissue
- May have prominent fibrous septa and myxoid matrix

Genetic profile

- 8q11~13 rearrangements resulting in *HAS2-PLAG1* or *COL1A2-PLAG1* fusion genes is common
- Gain of chromosome 8 seen in some cases

Main differential diagnoses

- Atypical lipomatous tumor
- Myxoid liposarcoma
- Lipofibromatosis

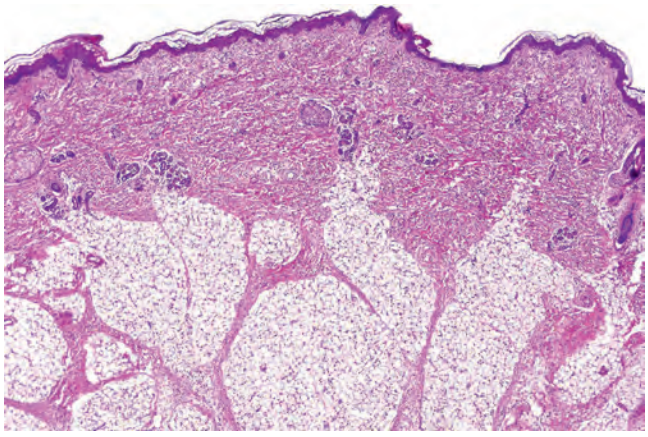

Fig. 1. **Lipoblastoma.** A discrete dermal neoplasm composed of lobules of adipose tissue separated by fibrous septa.

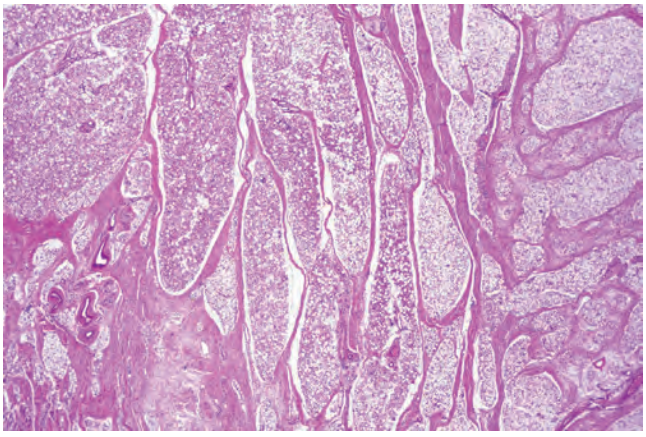

Fig. 2. **Lipoblastoma.** The neoplastic lobules are composed of adult- and fetal-type adipocytic components.

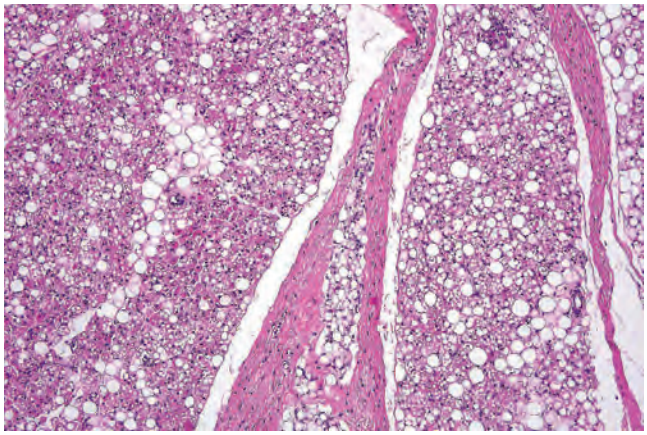

Fig. 3. **Lipoblastoma.** Fetal-type adipocytes at various stages of development admixed with mature adipocytes.

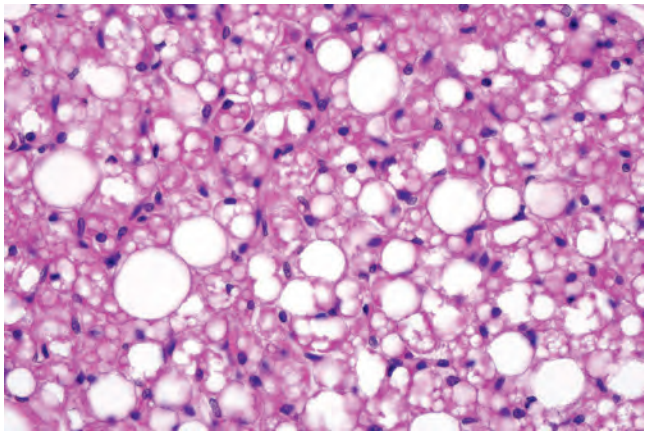

Fig. 4. **Lipoblastoma.** Numerous lipoblasts are seen with scattered mature adipocytes.

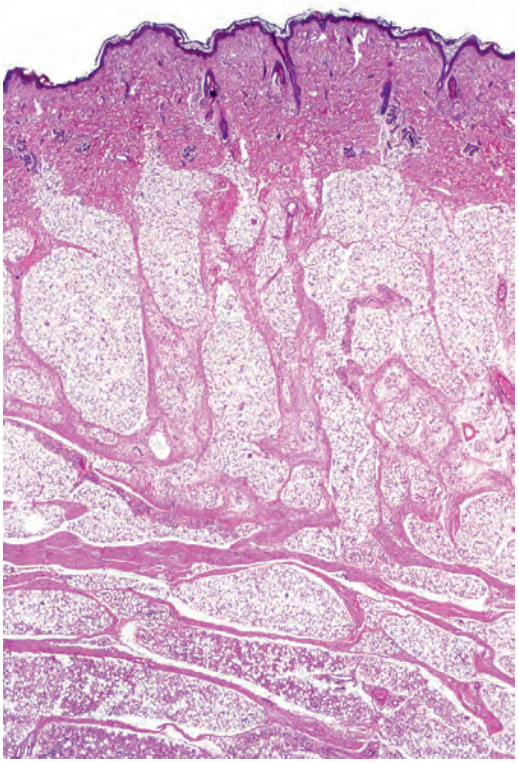

Fig. 5. **Lipoblastomatosis.** A diffuse dermal neoplasm composed of lobules of adult- and fetal-type adipose tissue, identical to isolated lipoblastoma.

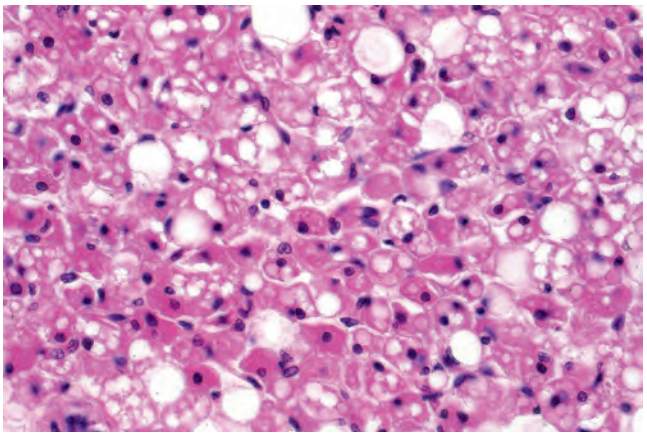

Fig. 6. **Lipoblastomatosis.** High-power view demonstrating numerous lipoblasts with occasional mature adipocytes.

LIPOBLASTOMA-LIKE TUMOR OF THE VULVA

Definition
- An extremely rare mesenchymal neoplasm characterized by adipocytic differentiation

Clinical features
Epidemiology
- Adolescent and young adult females

Presentation
- Superficial, painless vulvar masses
- Can be cystic
- Can have mucoid consistency

Prognosis and treatment
- Cured with surgical resection
- Recurrences and metastases have not been reported

Pathology
Histology
- Well-circumscribed and lobulated
- Lobules are composed of uniform spindle cells showing slightly eosinophilic cytoplasm and elongated nuclei and variable number of lipoblasts separated by thin fibrous septa
- Lacks nuclear atypia and hyperchromasia
- Plexiform, "chicken-wire" vascular networks are commonly seen

Immunohistochemistry/special stains
- Fat cells express S100 protein
- No CD34 expression

Main differential diagnoses
- Lipoblastoma
- Myxoid liposarcoma
- Spindle cell lipoma
- Aggressive angiomyxoma
- Angiomyofibroblastoma

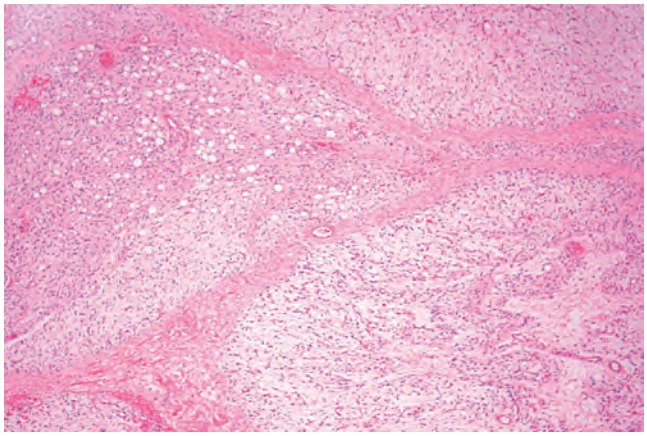

Fig. 1. **Lipoblastoma-like tumor of the vulva.** Somewhat lobulated neoplasm with myxoid areas separated by fibrous stroma. (Courtesy of Antonio Nascimento, São Paulo, Brazil.)

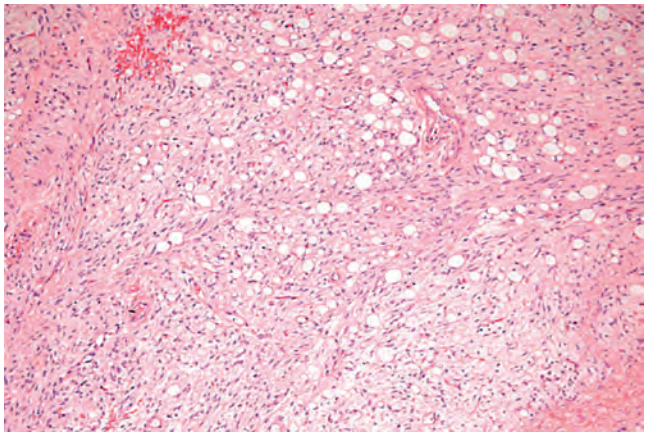

Fig. 2. **Lipoblastoma-like tumor of the vulva.** Scattered univacuolar lipoblast-like cells are noted. (Courtesy of Antonio Nascimento, São Paulo, Brazil.)

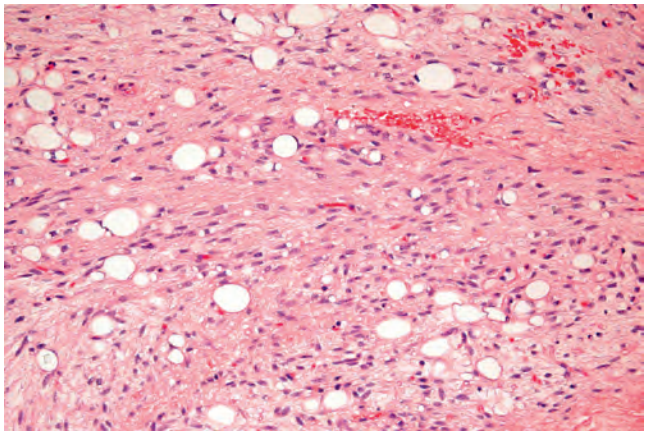

Fig. 3. **Lipoblastoma-like tumor of the vulva.** Higher power view reveals bivacuolated lipoblast-like cells as well. (Courtesy of Antonio Nascimento, São Paulo, Brazil.)

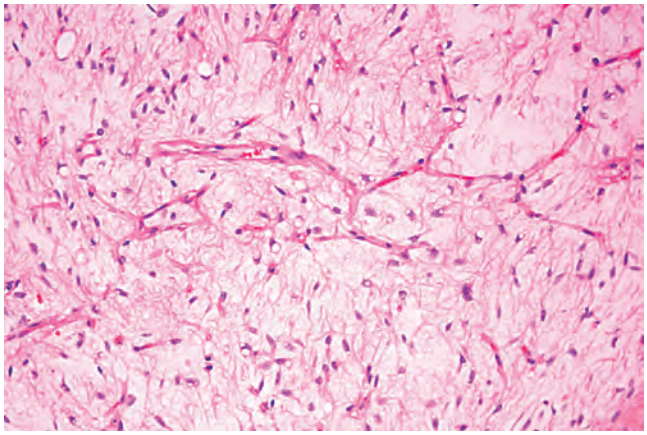

Fig. 4. **Lipoblastoma-like tumor of the vulva.** Hypocellular myxoid areas can be seen. (Courtesy of Antonio Nascimento, São Paulo, Brazil.)

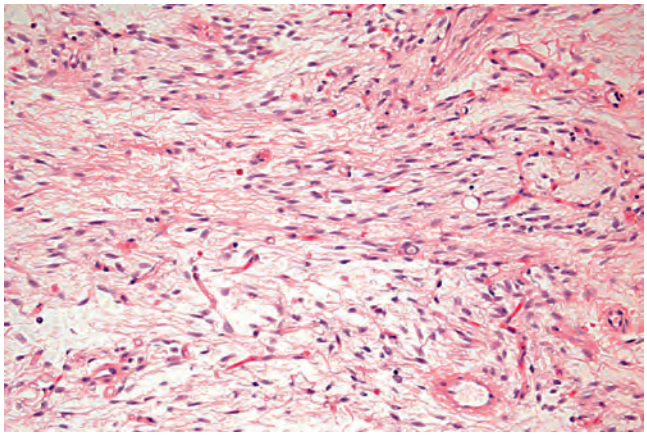

Fig. 5. **Lipoblastoma-like tumor of the vulva.** More cellular areas are highlighted in this picture. (Courtesy of Antonio Nascimento, São Paulo, Brazil.)

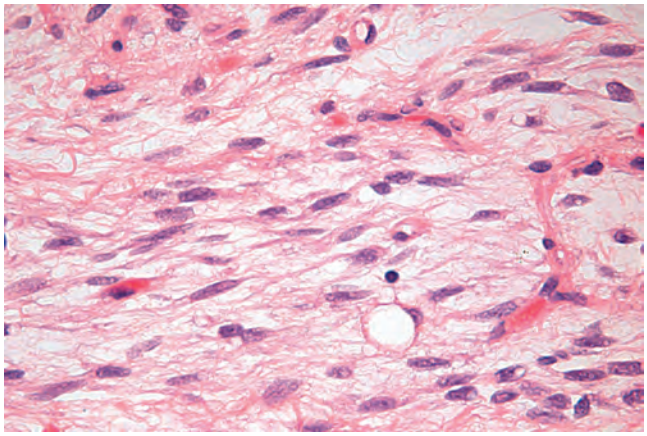

Fig. 6. **Lipoblastoma-like tumor of the vulva.** The spindle cells have bland nuclear features. (Courtesy of Antonio Nascimento, São Paulo, Brazil.)

ANGIOLIPOMA

Definition
- A benign dermal or subcutaneous encapsulated mesenchymal tumor composed of mature adult-type adipose tissue and thin-walled small blood vessels

Clinical features
Epidemiology
- Mainly affects adolescents and young adults
- Predilection for females
- Familial in 5% of cases and shows autosomal-dominant mode of transmission
- Most commonly encountered in the upper limbs, trunk, and distal extremities

Presentation
- Many are painful
- Commonly multiple
- Size ranges from a few millimeters to 2 cm

Prognosis and treatment
- Cured by conservative, complete surgical excision
- No recurrence or metastasis reported

Pathology
Histology
- Encapsulated tumors composed of adipocytes and variable number of thin-walled small blood vessels
- Blood capillary vessels commonly show microthrombi
- No atypia, pleomorphism, mitoses, or hyperchromasia
- A rare cellular variant is recognized
- Older lesions can show increased fibrosis

Immunohistochemistry/special stains
- The adipocytes express S100 protein
- The endothelial cells are highlighted by CD34, CD31, and ERG

Genetic profile
- Low-level mutations of protein kinase D_2 have been demonstrated in 80% of cases

Main differential diagnoses
- Lipoma
- Hemangioma
- Kaposiform hemangioendothelioma
- Kaposi sarcoma
- Angiosarcoma

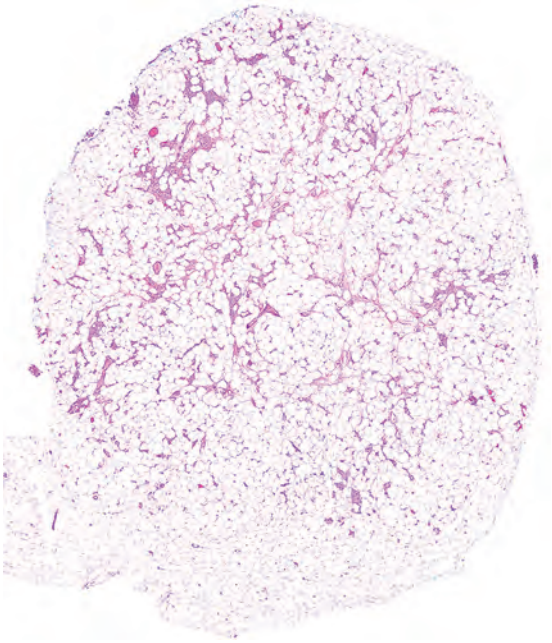

Fig. 1. **Angiolipoma.** A well-circumscribed neoplasm composed of predominantly adipose tissue with interspersed capillary blood vessels.

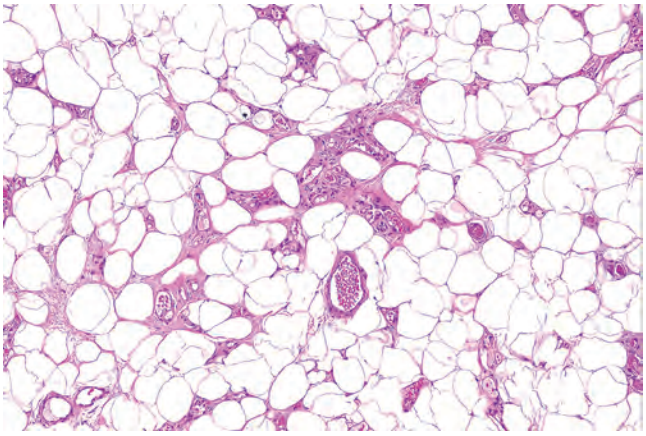

Fig. 2. **Angiolipoma.** Capillary blood vessels are variably prominent.

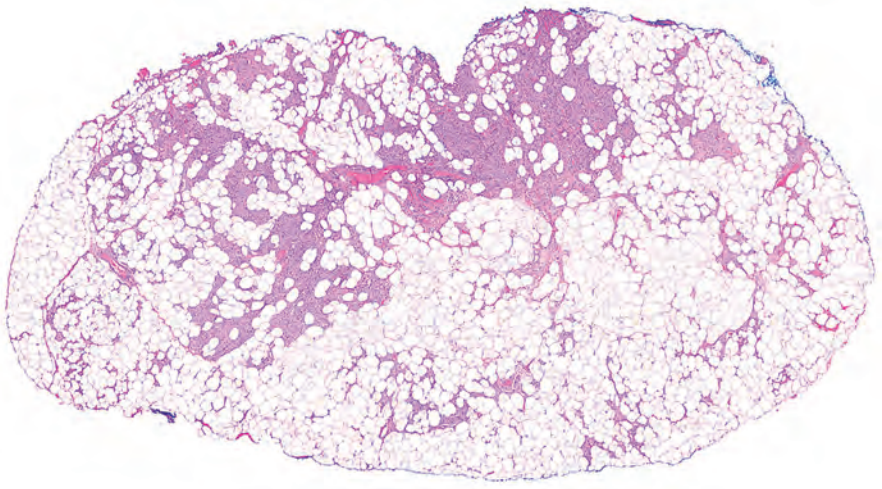

Fig. 3. **Angiolipoma.** This case shows a more abundant vascular component.

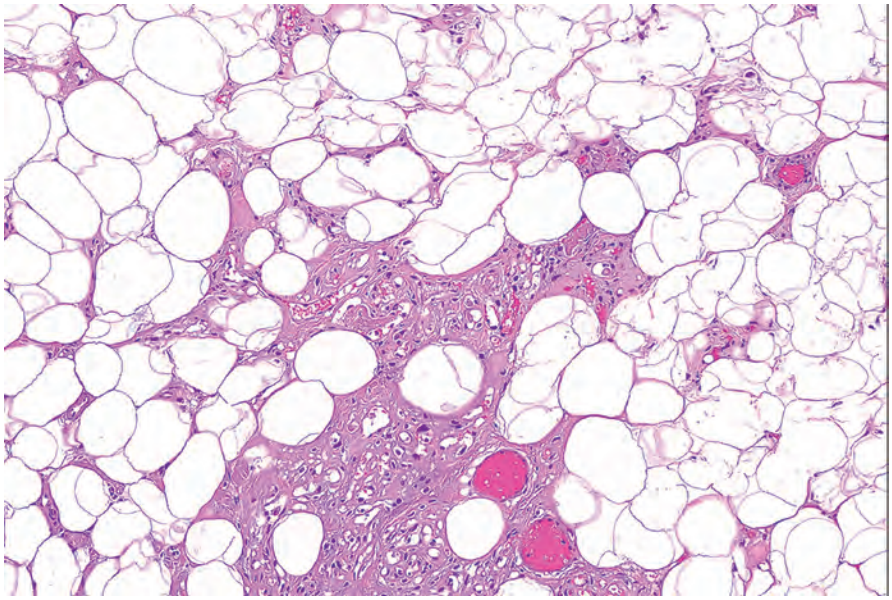

Fig. 4. **Angiolipoma.** Focal microthrombi involvement of capillaries is characteristic.

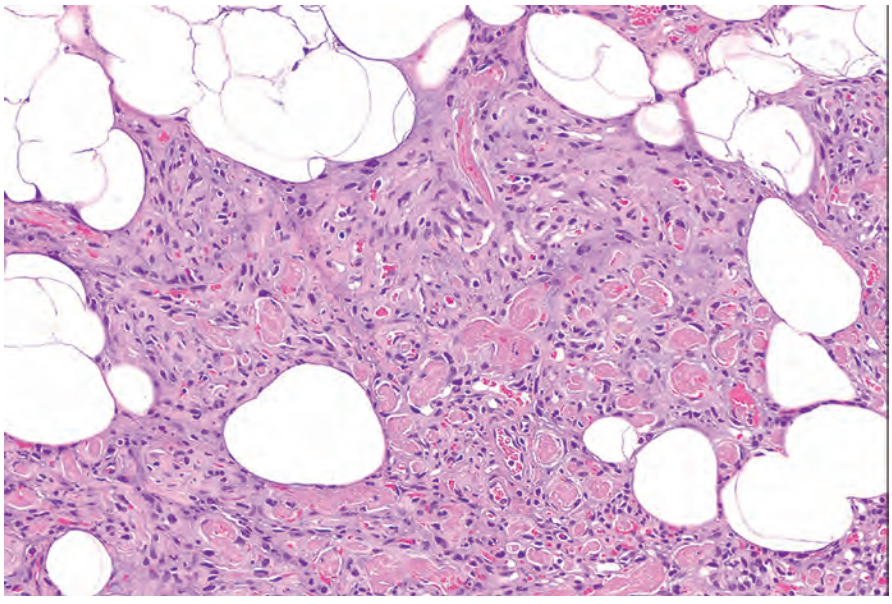

Fig. 5. **Angiolipoma.** Area with marked proliferation of small blood vessels, some of which show intravascular microthrombi.

MYOLIPOMA OF SOFT TISSUE

Definition
- A benign neoplasm characterized by the admixture of mature smooth muscle and mature adipose tissue

Clinical features
Epidemiology
- Exceptionally rare
- Affected patients are usually adults
- Female predilection
- Subcutaneous examples generally involve abdominal wall and extremities

Presentation
- Commonly present as asymptomatic masses
- Size is variable; subcutaneous tumors tend to be smaller than their deeply situated counterpart

Prognosis and treatment
- Cured by complete excision
- Benign tumor with no reports of recurrence or metastasis

Pathology
Histology
- A biphasic tumor composed of smooth muscle intimately admixed with mature adipose tissue
- Generally smooth muscle component predominates
- Smooth muscle fibers arranged in fascicles, resembling leiomyoma; scattered mast cells may be seen
- Smooth muscle cells show no atypia or mitoses; however, degenerative atypia is occasionally noted
- Mature adipocytes comprising the adipocytic component do not show atypia
- Edematous or hyalinized stroma can be present
- Lipoblasts are not seen
- Necrosis is absent

Immunohistochemistry/special stains
- The smooth muscle cells express smooth muscle actin, desmin, and often estrogen receptors
- Nuclear HMGA2 expression is commonly encountered in both the smooth muscle cells and the adipocytes
- CDK4 and MDM2 are usually negative

Genetic profile
- *HMGA2* rearrangement has been reported in a single case

Main differential diagnoses
- Spindle cell lipoma
- Myofibroblastoma
- Leiomyoma
- Angiomyolipoma
- Leiomyosarcoma

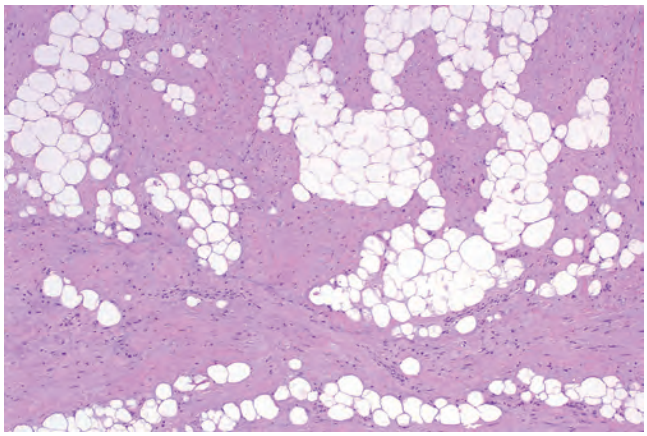

Fig. 1. **Myolipoma.** The neoplasm is predominantly composed of smooth muscle admixed with a lesser component of mature adipose tissue.

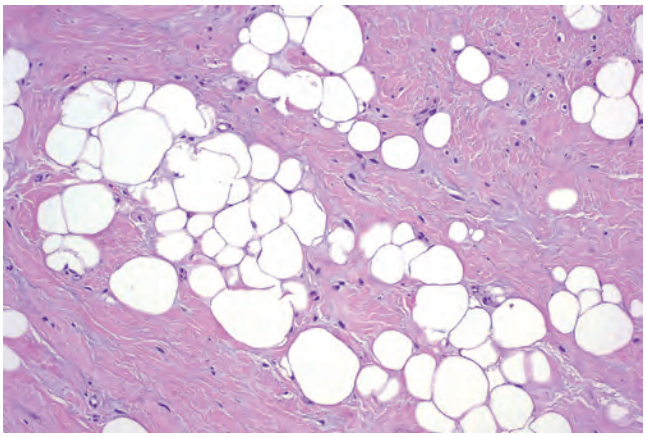

Fig. 2. **Myolipoma.** There is an intimate admixture of smooth muscle and adipose tissue.

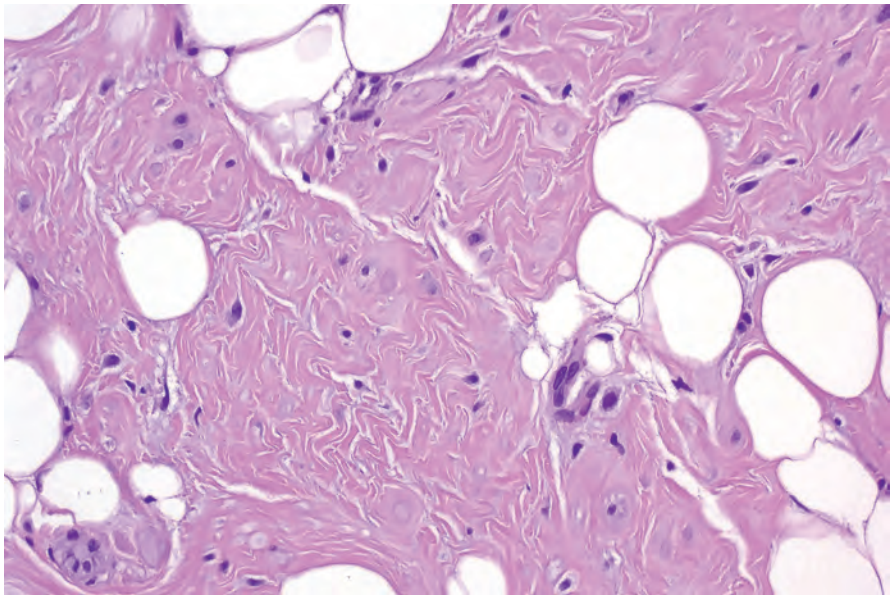

Fig. 3. **Myolipoma.** Note the bland morphology of both the smooth muscle and the adipocytic components. There is no hyperchromasia, atypia, or mitoses.

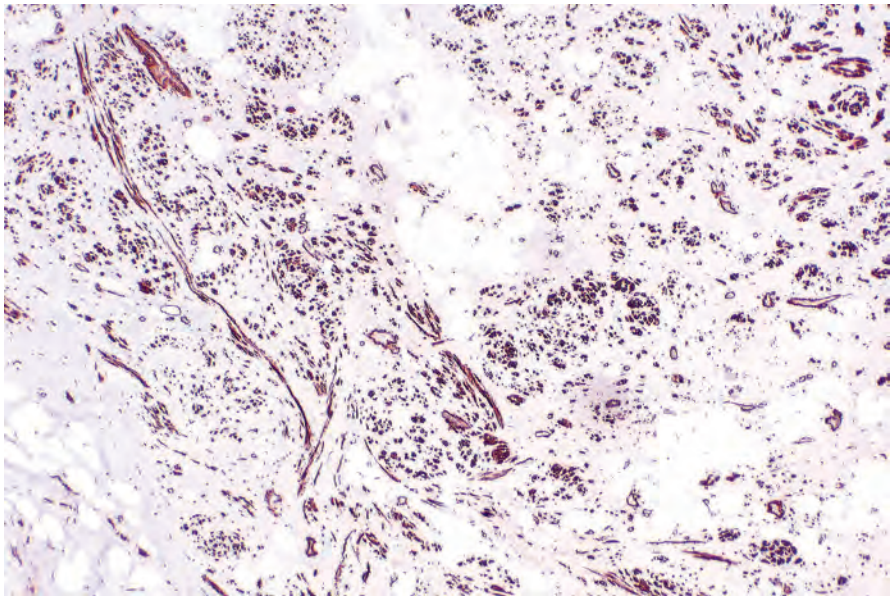

Fig. 4. **Myolipoma.** The smooth muscle cells diffusely express smooth muscle actin (SMA) on immunohistochemistry.

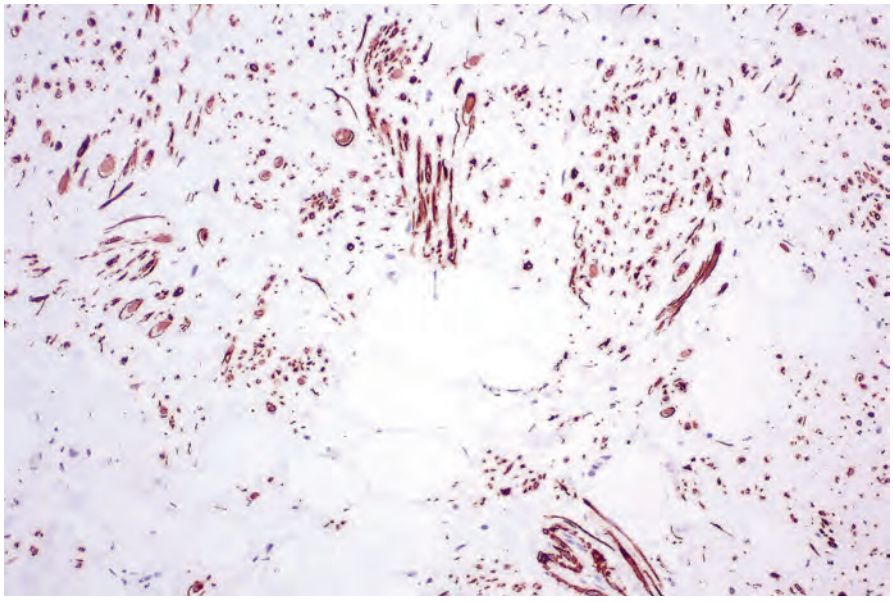

Fig. 5. **Myolipoma.** Diffuse coexpression of desmin is characteristic.

MYELOLIPOMA

Definition
- A rare neoplasm characterized by the presence of mature adipose tissue admixed with a variable proportion of hematopoietic elements

Clinical features
Epidemiology
- Affected patients are usually adults
- Extraadrenal examples have been described in mediastinum, kidney, retroperitoneum, liver, and other sites
- Cutaneous cases are exceptionally rare

Presentation
- Asymptomatic solitary mass
- Usually well circumscribed or pseudoencapsulated

Prognosis and treatment
- Conservative surgical excision is curative
- No reports of recurrence or metastasis

Pathology
Histology
- Mature adipose tissue resembling conventional lipoma
- Varying proportions of hematopoietic component
- Osseous metaplasia may be present

Immunohistochemistry/special stains
- Adipocytes express S100 protein

Genetic profile
- t(3;21)(q25;p11) has been reported in some cases

Main differential diagnoses
- Lipoma

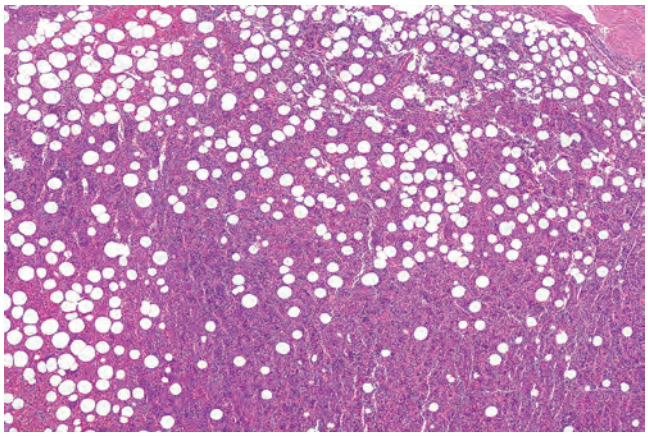

Fig. 1. **Myelolipoma.** Admixture of mature adipose tissue, resembling conventional lipoma, and a varying amount of hematopoietic component are characteristic.

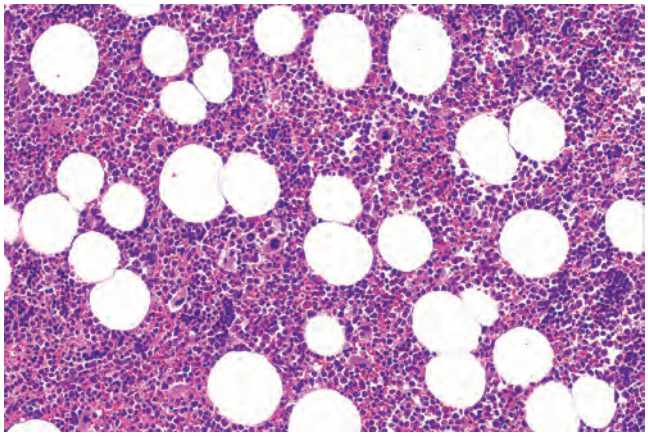

Fig. 2. **Myelolipoma.** This example exhibits predominantly hematopoietic tissue with interspersed adipocytes.

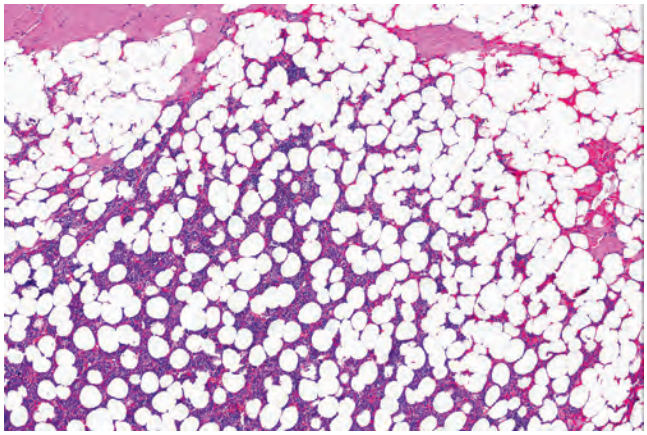

Fig. 3. **Myelolipoma.** A myelolipoma with a predominantly lipomatous component. The more limited hematopoietic element infiltrates amidst the adipocytes.

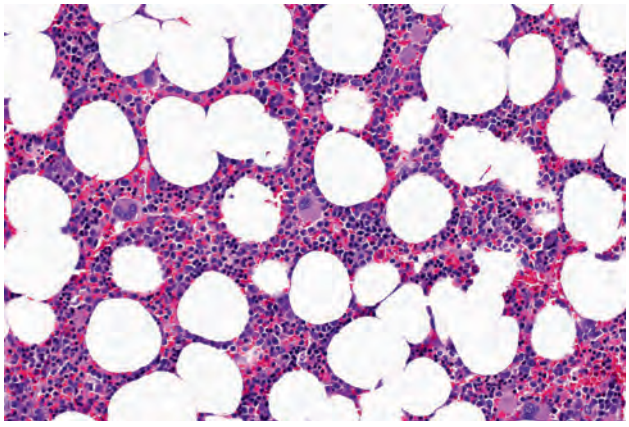

Fig. 4. **Myelolipoma.** Mature adipocytes are intermingled with trilineage hematopoietic cells.

CHONDROID LIPOMA

Definition
- A rare benign neoplasm composed of mature adipose tissue and a variable number of lipoblasts in a myxochondroid matrix

Clinical features
Epidemiology
- Vast majority of affected patients are adult females

Presentation
- Rare type of lipoma
- Painless, slow-growing, small tumors
- Subcutaneously located, but can be intramuscular
- Most tumors are located at the proximal extremities

Prognosis and treatment
- Benign course
- Cured by surgical excision
- Rarely recur and do not metastasize

Pathology
Histology
- Well circumscribed or pseudoencapsulated
- Nests of lipoblasts, mature adipocytes, and/or brown adipocytes
- Prominent myxochondroid matrix and vasculature
- No atypia or pleomorphism
- No or rare mitoses

Immunohistochemistry/special stains
- The mature adipocytes strongly express S100 protein
- Weak S100 protein expression is found in the lipoblasts
- Cyclin D1 is strongly expressed
- Cytokeratin is rarely expressed

Genetic profile
- t(11;16)(q13;p13) has been detected, resulting in *C11orf95* and *MLK2* fusion

Main differential diagnoses
- Lipoma with chondroid metaplasia
- Myxoid liposarcoma
- Extraskeletal myxoid chondrosarcoma
- Extraskeletal chondroma

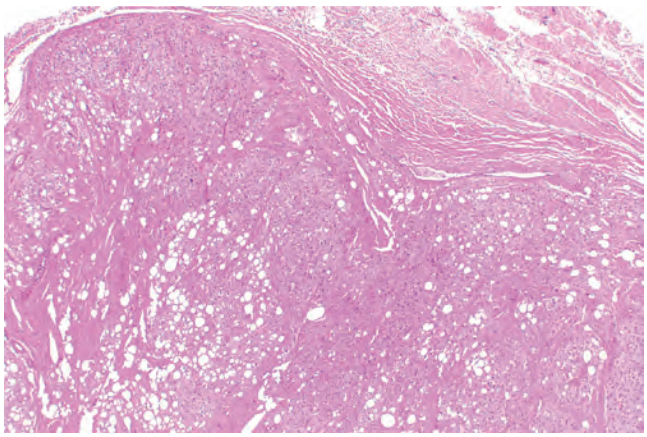

Fig. 1. **Chondroid lipoma.** A fibrous pseudocapsule surrounds this dermal neoplasm.

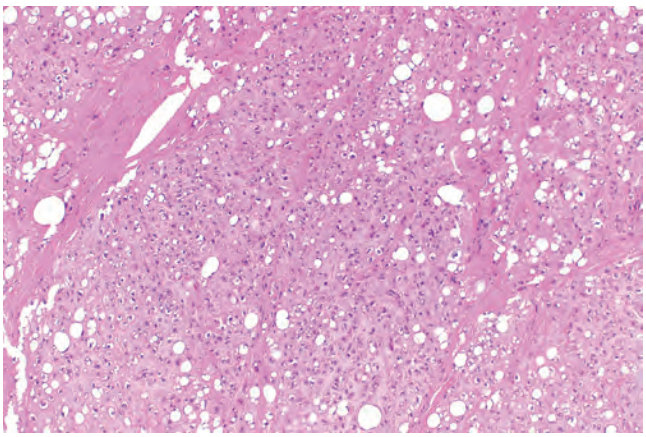

Fig. 2. **Chondroid lipoma.** Note the fibrous septa and the prominent chondromyxoid matrix.

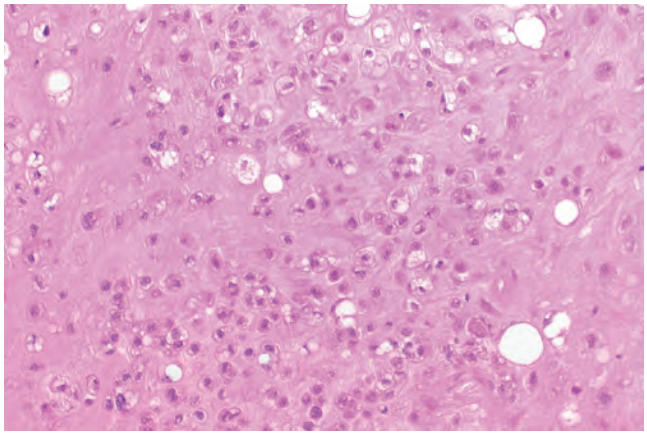

Fig. 3. **Chondroid lipoma.** Abundant chondromyxoid component with scattered mature adipocytes.

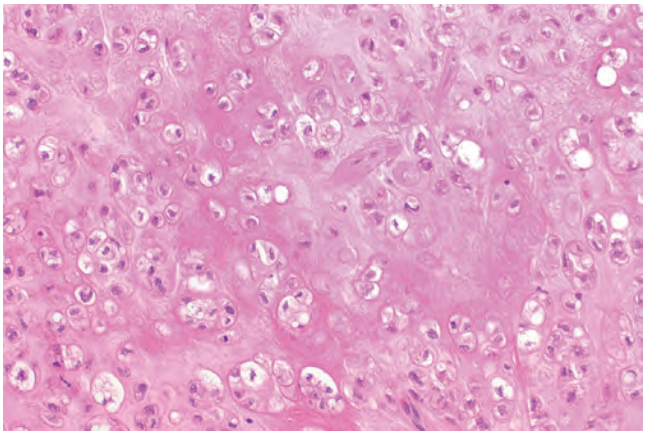

Fig. 6. **Chondroid lipoma.** Note the bland nuclear morphology of the chondromyxoid element.

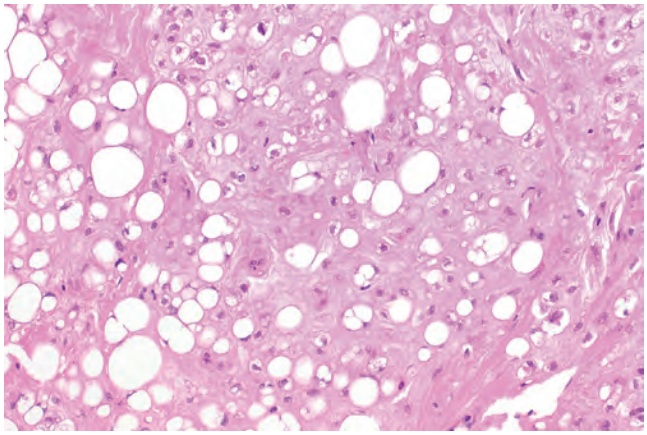

Fig. 4. **Chondroid lipoma.** Mature adipocytes along with a variable number of lipoblasts embedded in a chondromyxoid matrix is typical of this rare entity.

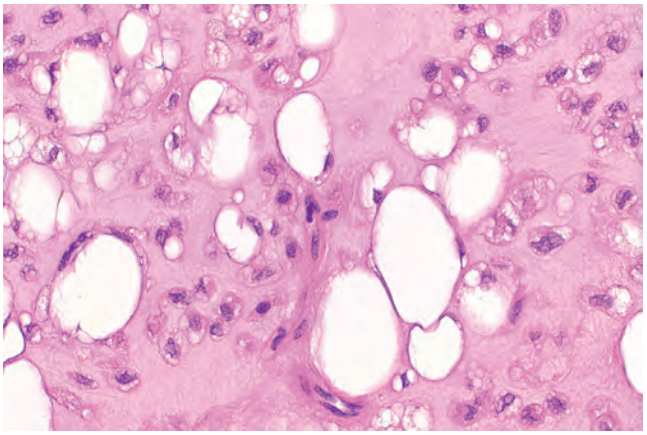

Fig. 7. **Chondroid lipoma.** Mature adipocytes embedded in a chondromyxoid matrix.

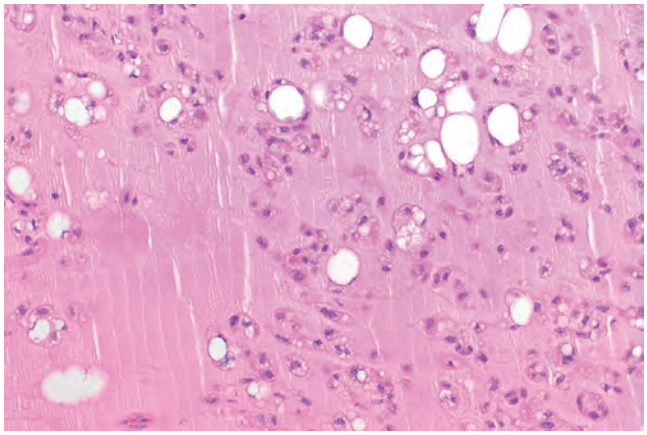

Fig. 5. **Chondroid lipoma.** This example demonstrates the predominant matrix with acellular areas.

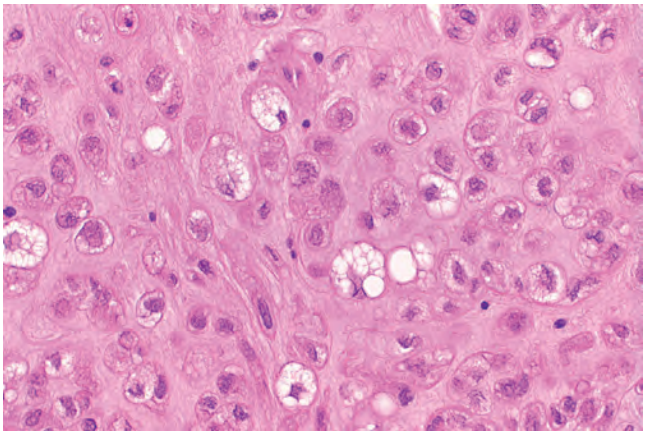

Fig. 8. **Chondroid lipoma.** Lipoblasts are characteristic of chondroid lipoma.

SPINDLE CELL LIPOMA

Definition
- An uncommon variant of lipoma that exhibits prominent spindle cell morphology
- It represents one end of a spectrum of the spindle cell lipoma–pleomorphic lipoma continuum
- Some tumors show a mixture of both entities

Clinical features
Epidemiology
- The majority of cases are subcutaneous in the shoulders and posterior aspect of the neck
- Commonly affects elderly males
- Familial and multiple lesions are rare
- Dermal lesions show female predilection and primarily facial location

Presentation
- Small, well-circumscribed tumors
- Slowly growing and solitary
- Consistency is firmer than with conventional lipomas

Prognosis and treatment
- Cured by complete surgical excision
- Rarely recur
- No reports of metastasis

Pathology
Histology
- A variable mixture of bland-appearing spindle cells, mature adipocytes, and giant floret cells in a collagenous ("ropey" collagen) or myxoid stroma
- The spindle cells show pale eosinophilic cytoplasm and small nuclei
- The floret cells are multinucleated giant cells with hyperchromatic nuclei arranged in a concentric wreathlike pattern
- Mitoses are rarely seen
- Lipoblasts can be seen occasionally

Immunohistochemistry/special stains
- The adipocytes express S100 protein
- The spindle cells are positive for CD34 but negative for S100 protein
- Loss of nuclear retinoblastoma protein (RB1) can be demonstrated by immunohistochemistry

Genetic profile
- Monosomy or partial loss of long arms of chromosomes 13 and 16, with the former containing *RB1* (13q14)
- Pleomorphic lipoma, mammary-type myofibroblastoma, cellular angiofibroma, and superficial acral fibromyxoma also show *RB1* loss

Main differential diagnoses
- Atypical lipomatous tumor
- Spindle cell liposarcoma

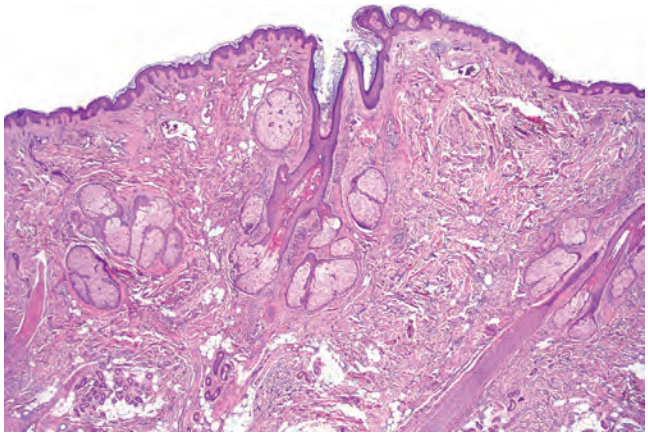

Fig. 1. **Spindle cell lipoma.** A superficial dermal case is composed of spindle cells and thick collagen fibers admixed with lobules of mature adipose tissue.

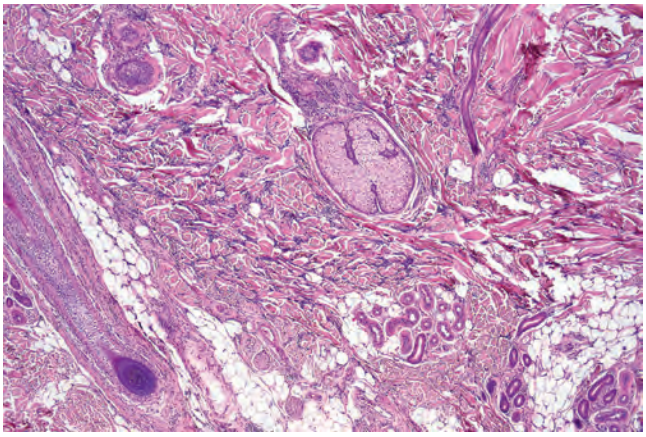

Fig. 2. **Spindle cell lipoma.** Neoplastic spindle cells and adipocytes surrounding skin adnexal structures.

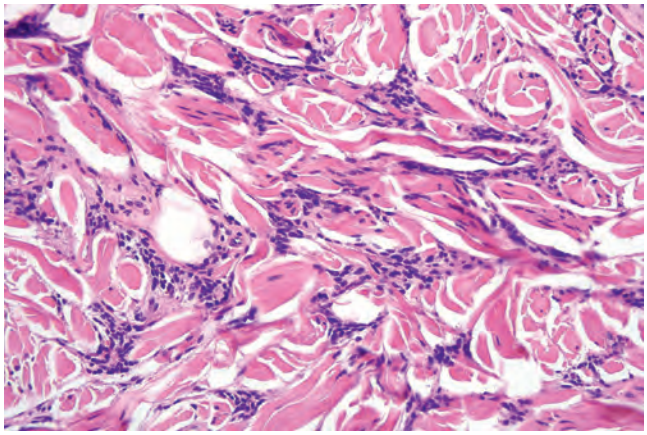

Fig. 3. **Spindle cell lipoma.** High-power view. Note the characteristic "ropey" collagen fibers.

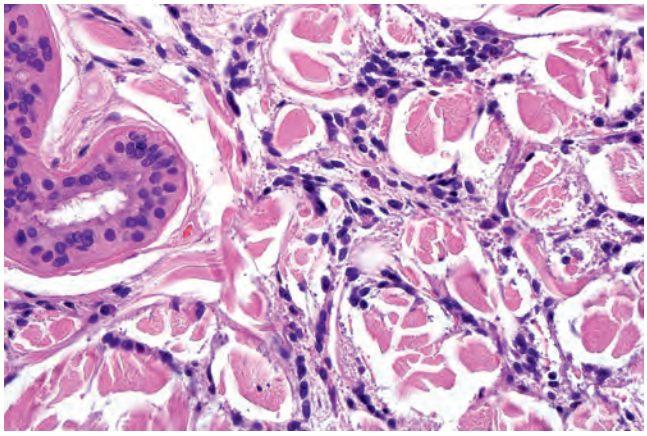

Fig. 4. **Spindle cell lipoma.** Spindle cells show banal cytology.

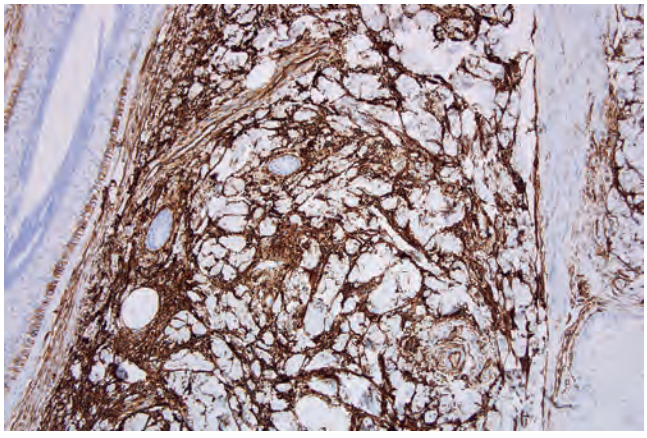

Fig. 5. **Spindle cell lipoma.** The spindle cells strongly express CD34.

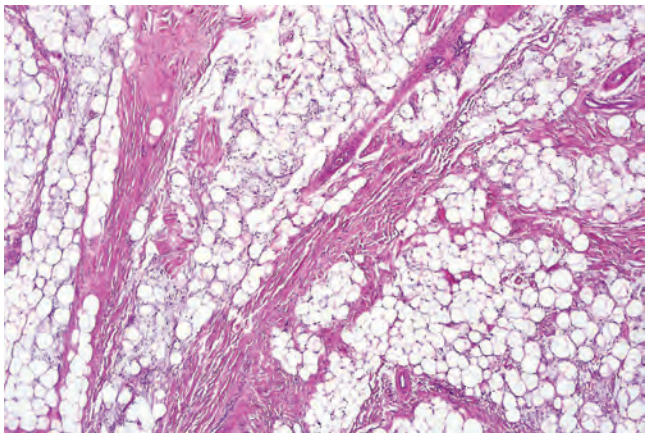

Fig. 6. **Spindle cell lipoma.** This example exhibits a more abundant adipocytic component.

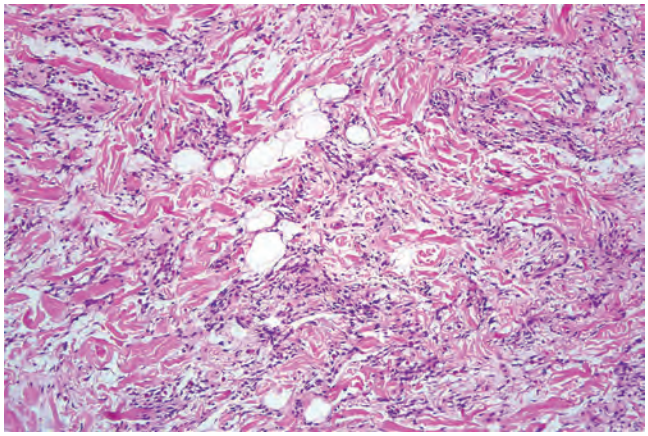

Fig. 7. **Spindle cell lipoma.** Area predominantly composed of spindle cells with interlaced thick collagen fibers.

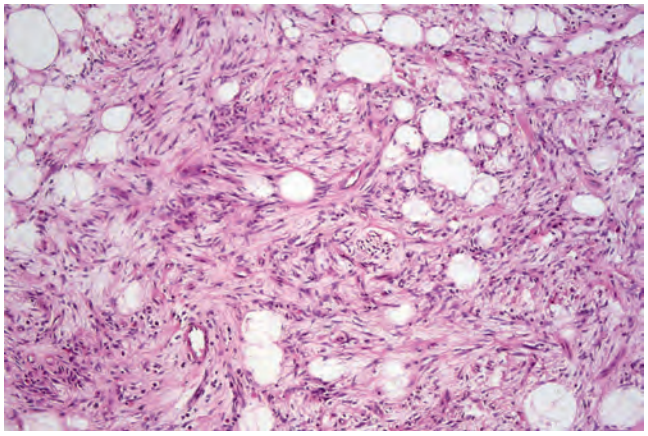

Fig. 8. **Spindle cell lipoma.** The spindle cells have pale eosinophilic cytoplasm and small nuclei.

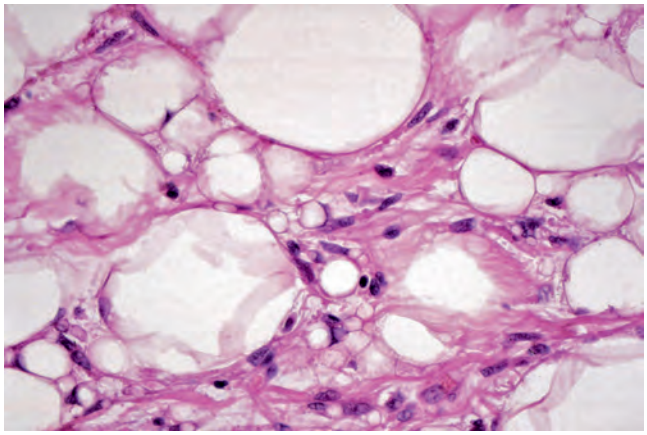

Fig. 9. **Spindle cell lipoma.** Lipoblasts can be seen.

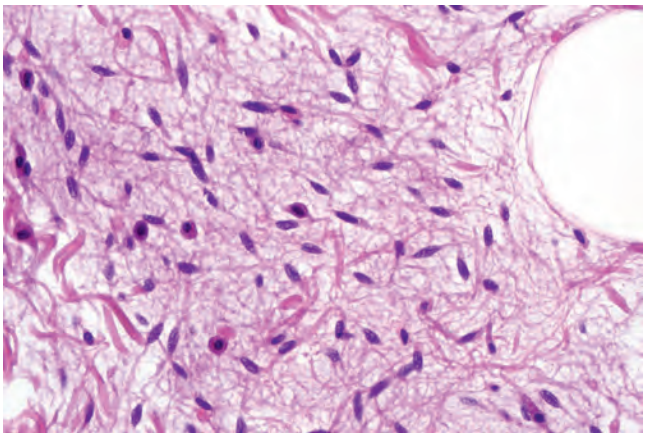

Fig. 11. **Spindle cell lipoma.** Bland-appearing spindle cells embedded in a myxoid stroma. This subtype of spindle cell lipoma must be differentiated from myxoid liposarcoma.

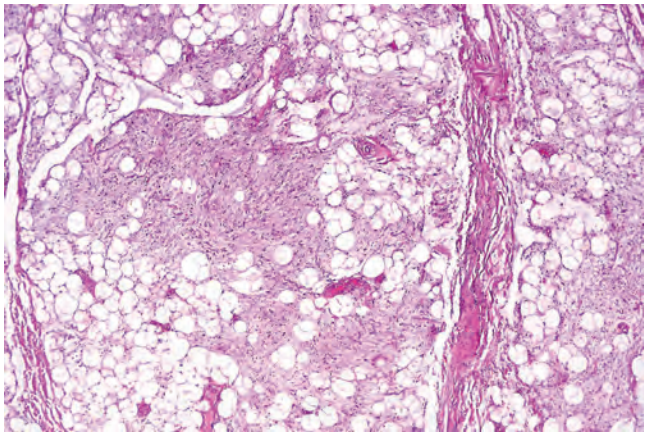

Fig. 10. **Spindle cell lipoma.** Abundant myxoid stroma is seen in some cases.

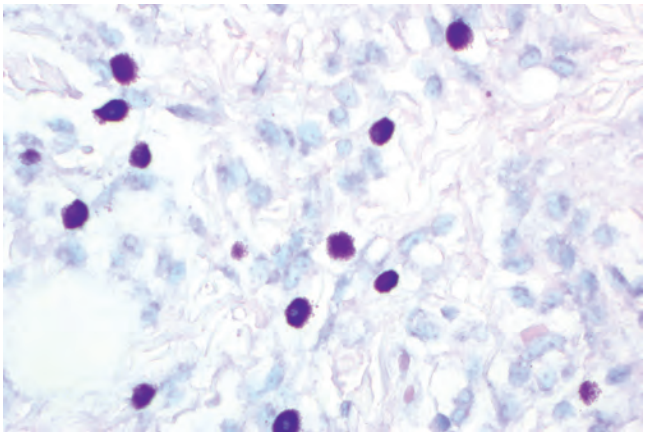

Fig. 12. **Spindle cell lipoma.** Mast cells within the myxoid areas are highlighted using Giemsa stain.

PLEOMORPHIC LIPOMA

Definition
- An uncommon variant of lipoma composed of a mixture of variably sized mature adipocytes, scattered pleomorphic forms, and giant floret cells
- It represents one end of a spectrum of the spindle cell lipoma–pleomorphic lipoma continuum
- Most tumors show mixture of features from both entities, at least focally

Clinical features
Epidemiology
- The majority of cases are located in the dermis of the shoulders and posterior aspect of the neck
- Affected patients are mainly elderly males
- Pure pleomorphic forms are much less common than spindle cell lipoma

Presentation
- Small, well-circumscribed tumors
- Slowly growing and solitary
- Consistency is firmer than with conventional lipomas

Prognosis and treatment
- Cured by complete surgical excision
- May rarely recur
- No reports of metastasis

Pathology
Histology
- Dermally located, well-circumscribed tumor
- Admixed and scattered pleomorphic forms are readily identified
- A mixture of variably sized mature adipocytes and giant floret cells in a collagenous fibrous stroma
- Mitoses are rarely seen
- Spindle-shaped cells can also be detected
- Lipoblasts can be rarely seen

Immunohistochemistry/special stains
- The adipocytes express S100 protein
- The other cells are positive for CD34

Genetic profile
- Similar to spindle cell lipoma, suggesting close relation between the two entities
- Monosomy or partial loss of long arms of chromosomes 13 and 16, with the former containing *RB1* (13q14)
- Spindle cell lipoma, mammary-type myofibroblastoma, cellular angiofibroma, and superficial acral fibromyxoma also show *RB1* loss

Main differential diagnoses
- Atypical lipomatous tumor
- Spindle cell liposarcoma

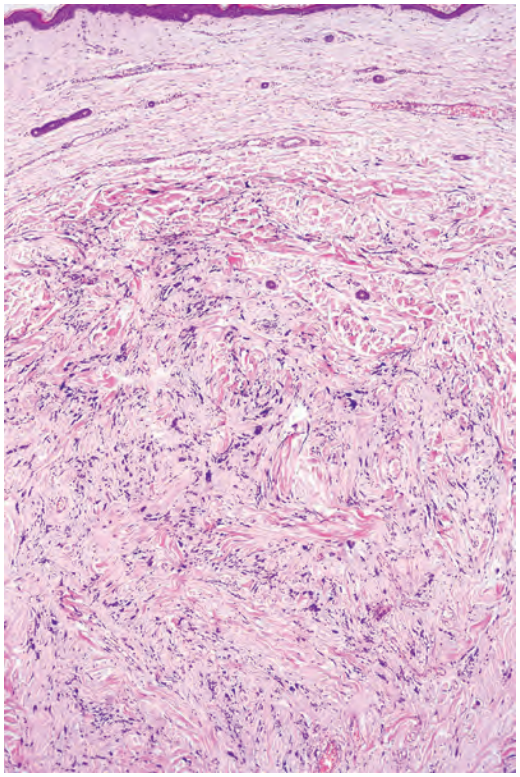

Fig. 1. **Pleomorphic lipoma.** This case is a discrete dermal neoplasm, composed of spindle cells and multinucleate giant cells.

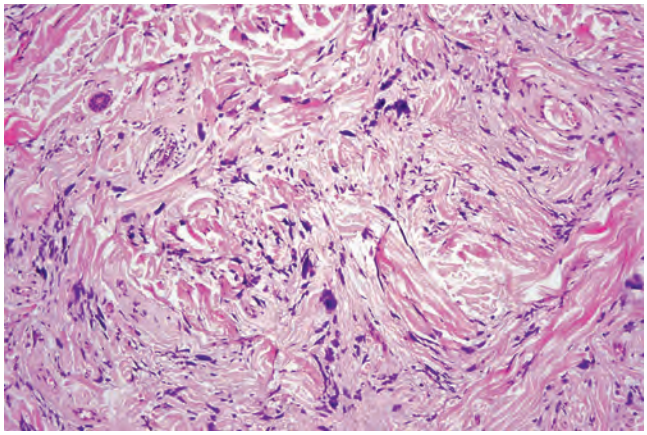

Fig. 2. **Pleomorphic lipoma.** Spindle cells, multinucleate giant cells, and thick "ropey" collagen fibers demonstrating morphological overlap with spindle cell lipoma.

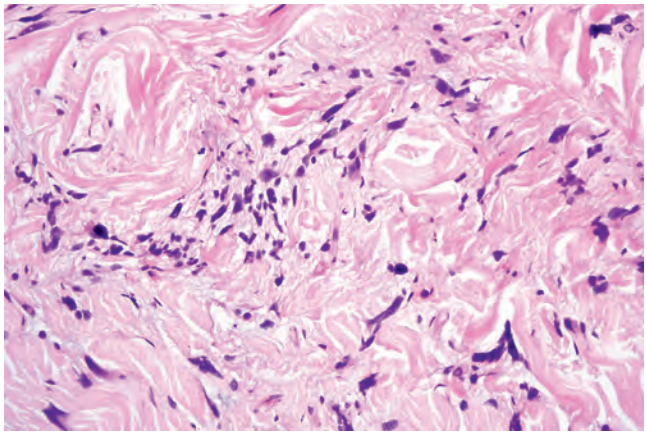

Fig. 3. **Pleomorphic lipoma.** The spindle cell component here demonstrates mild hyperchromasia and pleomorphism. Scattered multinucleate giant cells are also seen.

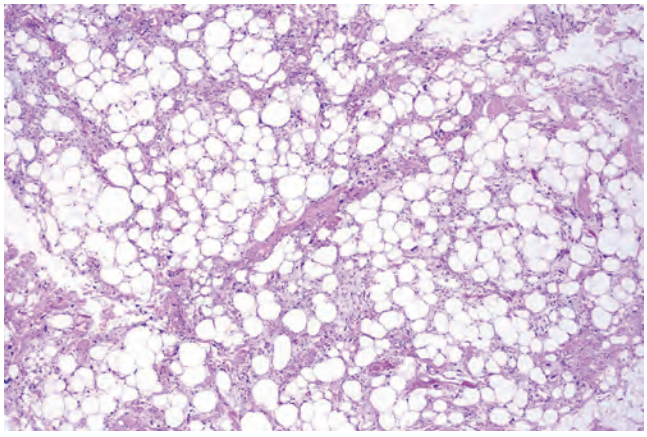

Fig. 4. **Pleomorphic lipoma.** Another example showing more conspicuous adipocytic component.

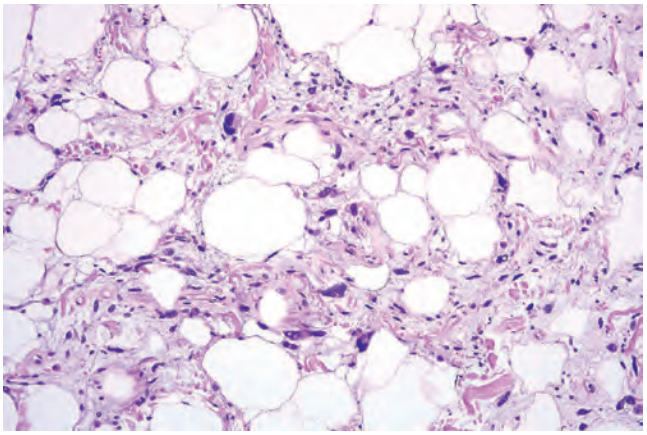

Fig. 5. **Pleomorphic lipoma.** Floret-type giant cells, spindle cells, and mature adipocytes are characteristic, but can be seen in varying degrees from case to case.

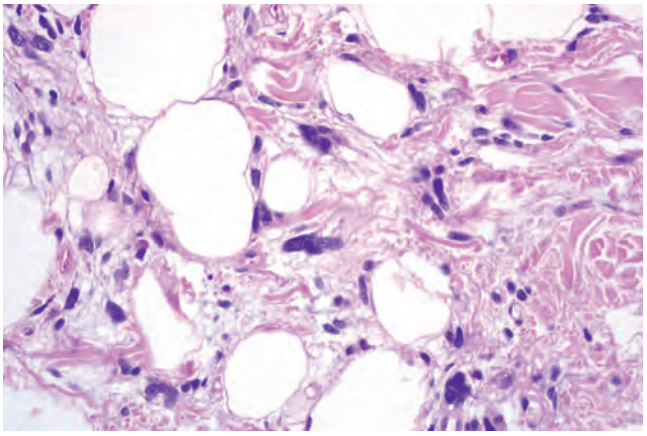

Fig. 6. **Pleomorphic lipoma.** Note the mild hyperchromasia and the pleomorphism of the floret-type giant cells.

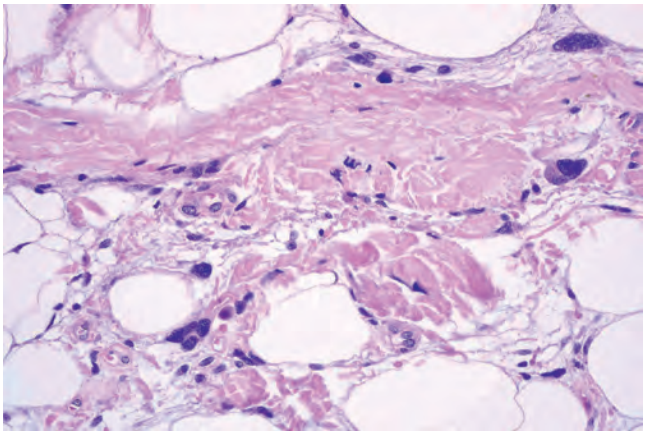

Fig. 7. **Pleomorphic lipoma.** Mature adipocytes have banal features.

HIBERNOMA

Definition
- A rare subcutaneous tumor composed of benign brown adipocytes

Clinical features
Epidemiology
- Rare neoplasms comprising only 1% of adipocytic tumors
- Most affected patients are young adults; uncommon in children
- Thighs are the most common location, followed by the trunk, upper extremities, and the head and neck

Presentation
- Slow-growing, painless, superficial lesions
- May be intramuscular
- Size is variable

Prognosis and treatment
- Benign; cured by local excision
- May recur if incompletely excised

Pathology
Histology
- Tumors composed of a variable mixture of brown and mature white adipocytes
- The brown fat cells are characterized by the presence of multivacuolated granular eosinophilic or pale cytoplasm and small, centrally located nuclei
- No atypia
- Histologically subclassified into four variants:
  - Typical
  - Myxoid
  - Lipoma-like
  - Spindle cell

Immunohistochemistry/special stains
- Tumor cells show vimentin and variable S100 protein expression
- Spindle cell variant exhibits CD34 positivity

Genetic profile
- 11q13-21 rearrangements are seen

Ultrastructure
- Hibernoma cells have multiple lipid droplets and abundant pleomorphic mitochondria
- Basal lamina surrounds individual tumor cells

Main differential diagnoses
- Granular cell tumor
- Other neoplasms with granular cell features

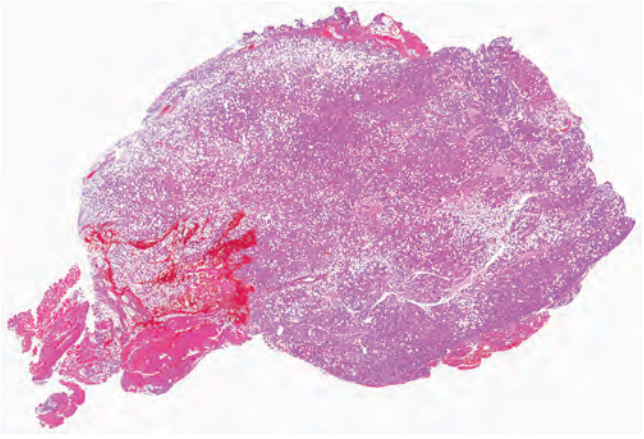

Fig. 1. **Hibernoma.** The neoplasm is composed of a mixture of adult/white and fetal/brown adipocytes.

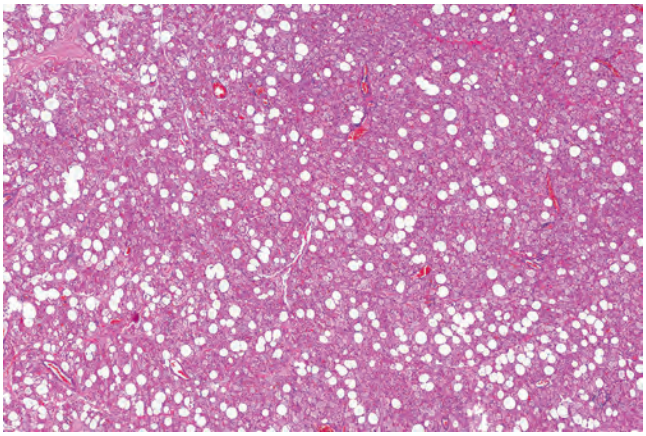

Fig. 2. **Hibernoma.** Varying proportions of adult/white and fetal/brown adipocytes can be encountered. Delicate vascularized fibrous septa traverse the neoplasm.

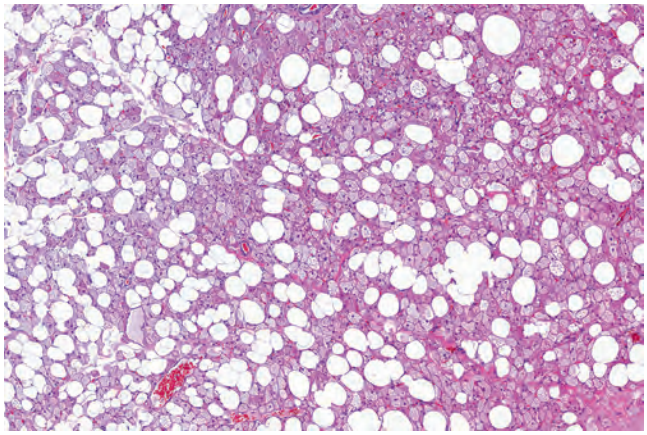

Fig. 3. **Hibernoma.** The adult/white and fetal/brown adipocytes can be quite mixed.

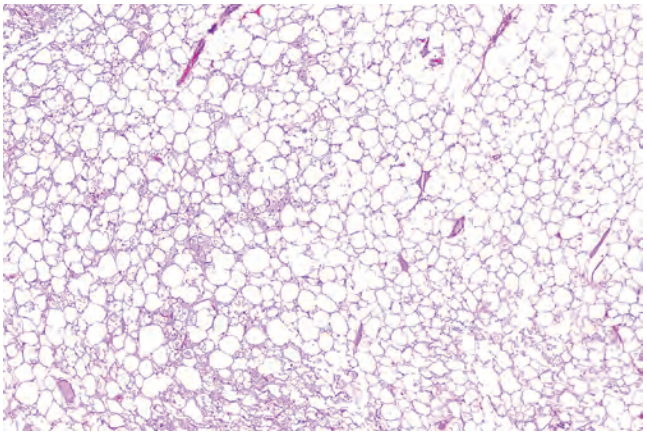

Fig. 6. **Hibernoma.** The adult-type adipocytes predominate in this example.

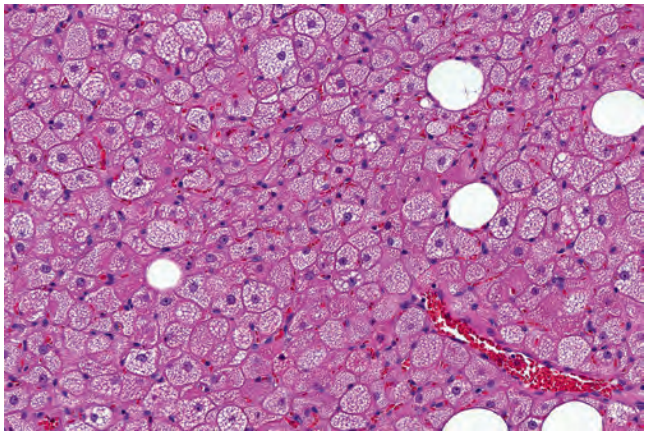

Fig. 4. **Hibernoma.** The fetal/brown adipocytes characteristically exhibit multivacuolated cytoplasm and centrally located small nuclei.

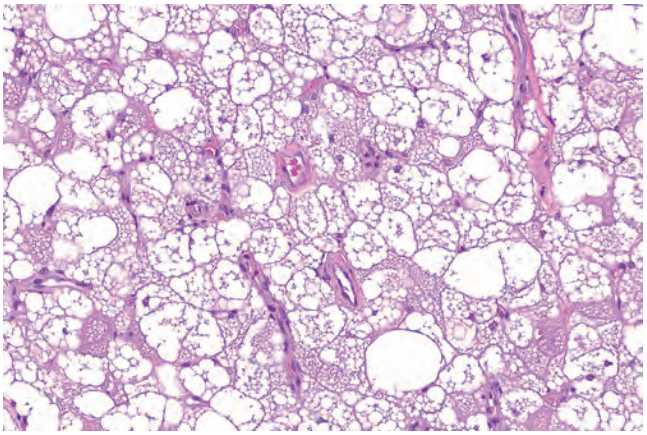

Fig. 7. **Hibernoma.** The multivacuolated brown fat can exhibit granular-appearing cytoplasm. Note the lack of atypia and mitoses.

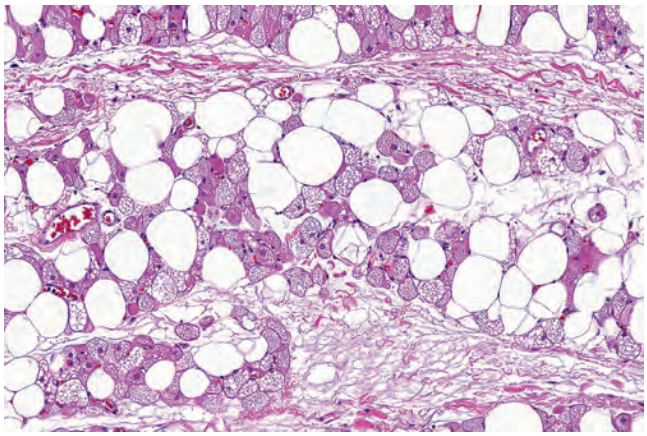

Fig. 5. **Hibernoma.** This example shows focal myxoid matrix.

ATYPICAL LIPOMATOUS TUMOR/ WELL-DIFFERENTIATED LIPOSARCOMA/ DEDIFFERENTIATED LIPOSARCOMA

Definition

- Atypical lipomatous tumor/well-differentiated liposarcoma is a locally aggressive neoplasm characterized by its gross and microscopical resemblance to mature adipose tissue
- Currently, the two names *well-differentiated liposarcoma (WDL)* and *atypical lipomatous tumor (ALT)* are being used synonymously
- Some use WDL terminology for deep areas such as the retroperitoneum where complete excision is often not possible and ALT for superficial and extremity tumors amenable to complete excision
- Dedifferentiation represents an abrupt transition to a nonadipocytic sarcomatous component with conspicuous mitotic activity

Clinical features

Epidemiology

- The most common type of sarcoma in adults
- Most patients are in their sixth to seventh decade of life
- The majority of tumors are deeply situated
- Subcutaneous tumors are rare and mostly affect the lower extremities
- Ninety percent of dedifferentiated liposarcomas arise de novo, and only 10% are diagnosed in recurrent ALT/WDL

Presentation

- Slowly enlarging, painless masses
- Variably sized but usually attain large size

Prognosis and treatment

- WDL/ALT tends to recur locally but does not metastasize unless it undergoes dedifferentiation
- The tendency to dedifferentiate depends largely on the location and the duration of the tumor
- Subcutaneous peripheral tumors have a more favorable outcome and are very unlikely to undergo dedifferentiation, but tend to locally recur due to incomplete resection

Pathology

Histology

- Neoplastic mature adipocytes that show marked pleomorphism and nuclear hyperchromasia
- Thick, fibrous septa with stromal spindle and multinucleate cells
- Variable number of lipoblasts, but their presence is not required for the diagnosis, nor are they pathognomonic
- The stroma may show a myxoid quality
- Three histological variants:
  - Adipocytic (lipoma-like)
  - Sclerosing
  - Inflammatory
- Dedifferentiated component often resembles undifferentiated pleomorphic or spindle cell sarcoma
- Dedifferentiated areas can sometimes show heterologous differentiation such as a rhabdomyosarcomatous or angiosarcomatous component
- Dedifferentiation is exceedingly rare in superficial atypical lipomatous tumor

Immunohistochemistry/special stains

- Neoplastic cells show positive reaction with S100 protein (mature adipocytic component), MDM2, and CDK4

Genetic profile

- Supernumerary giant rod or ring chromosome containing an amplified 12q13~15 region that encodes for MDM2 is constantly found
- *CDK4, CPM, SAS,* and *HMGA2* genes are also frequently amplified from the same genomic interval

Main differential diagnoses

- Lipoma
- Spindle cell or pleomorphic lipoma
- Myxoid liposarcoma
- Pleomorphic liposarcoma
- Undifferentiated pleomorphic sarcoma

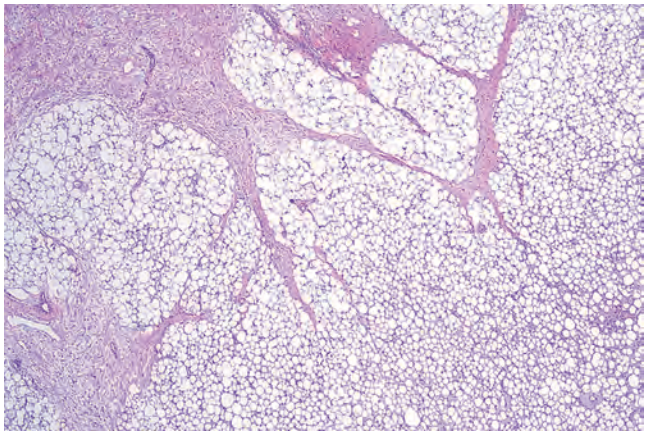

Fig. 1. **Atypical lipomatous tumor/well-differentiated liposarcoma.** Classic lipoma-like atypical lipomatous tumor/well-differentiated liposarcoma. The neoplasm is composed of lobules of variably sized adult-type adipocytes separated by thick, fibrous septa.

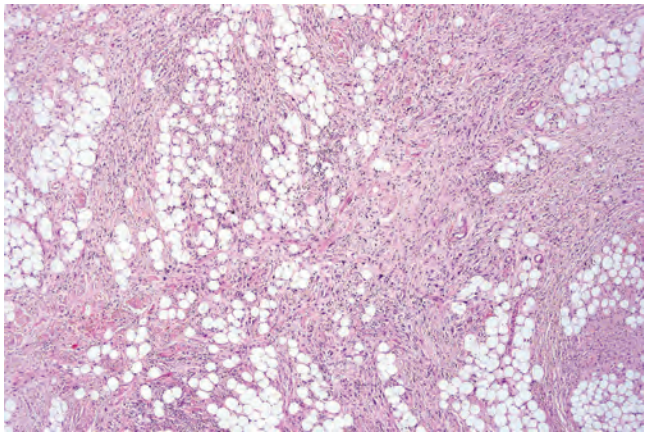

Fig. 2. **Atypical lipomatous tumor/well-differentiated liposarcoma.** Scattered cell nuclei within the fibrous septa exhibit hyperchromasia and pleomorphism.

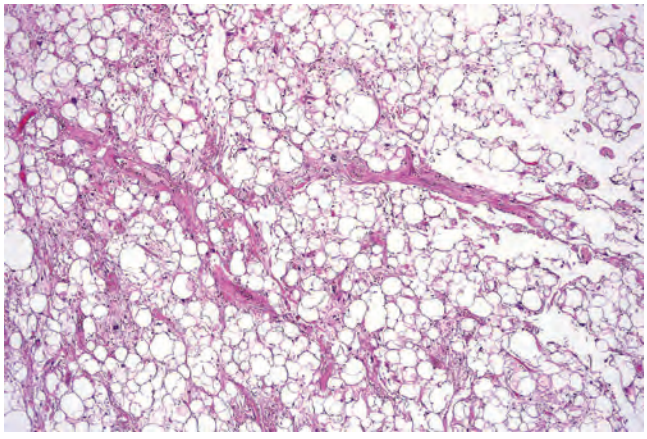

Fig. 3. **Atypical lipomatous tumor/well-differentiated liposarcoma.** Lipoma-like area composed of adult-type adipocytes demonstrating variably sized cells.

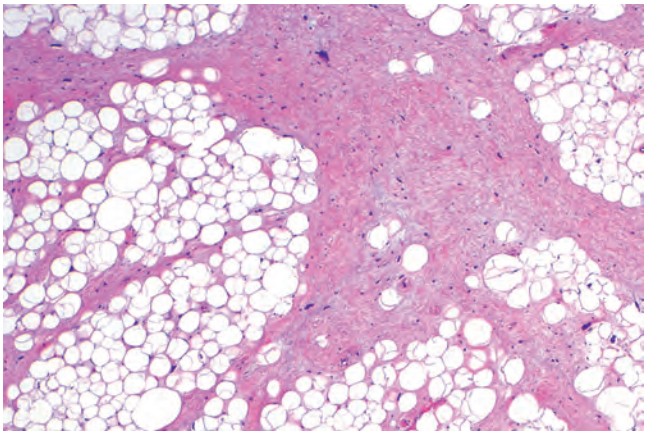

Fig. 4. **Atypical lipomatous tumor/well-differentiated liposarcoma.** Fibrous septa with scattered stromal cells exhibiting nuclear hyperchromasia. Occasional multinucleate giant cells are also seen.

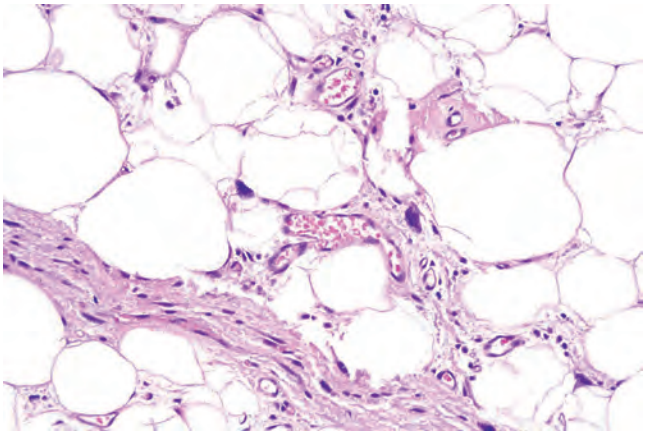

Fig. 5. **Atypical lipomatous tumor/well-differentiated liposarcoma.** Scattered adipocytes demonstrate nuclear atypia, hyperchromasia, and pleomorphism.

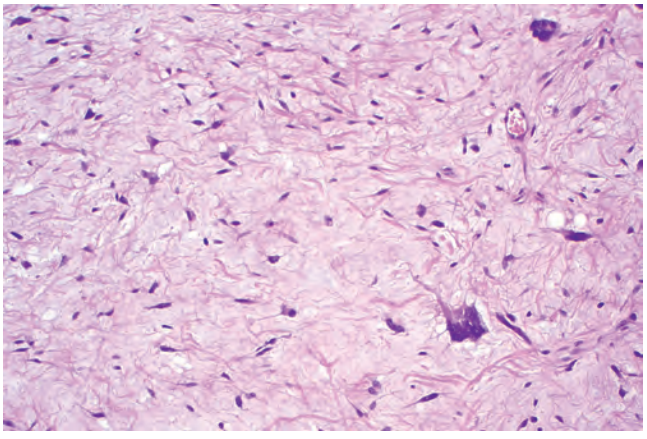

Fig. 6. **Atypical lipomatous tumor/well-differentiated liposarcoma.** Atypical stromal cells and the multinucleate giant cells can both show nuclear hyperchromasia and pleomorphism.

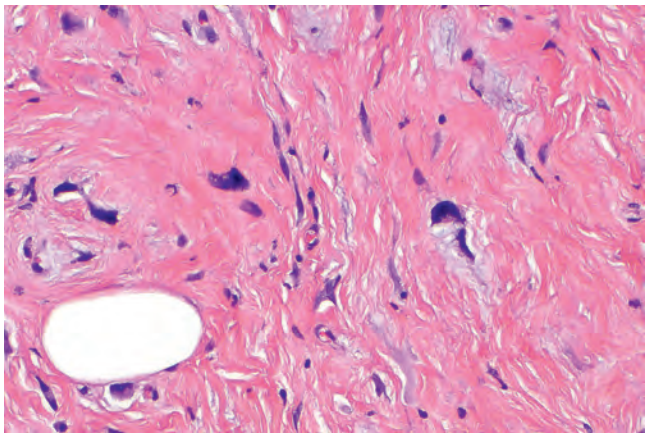

Fig. 7. **Atypical lipomatous tumor/well-differentiated liposarcoma.** High-power view of the fibrous septa.

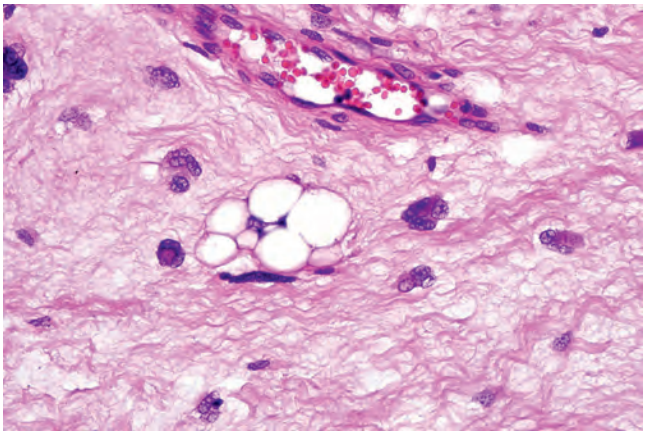

Fig. 10. **Atypical lipomatous tumor/well-differentiated liposarcoma.** High-power view of classic lipoblast showing multivacuolated cytoplasm. Multinucleate stromal cells are also seen.

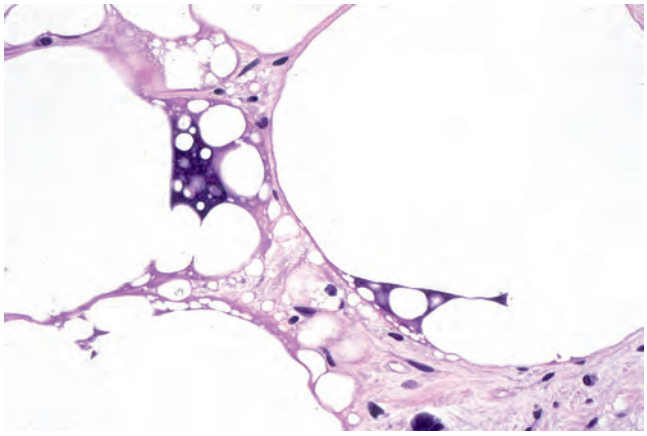

Fig. 8. **Atypical lipomatous tumor/well-differentiated liposarcoma.** High-power view of lipoblasts.

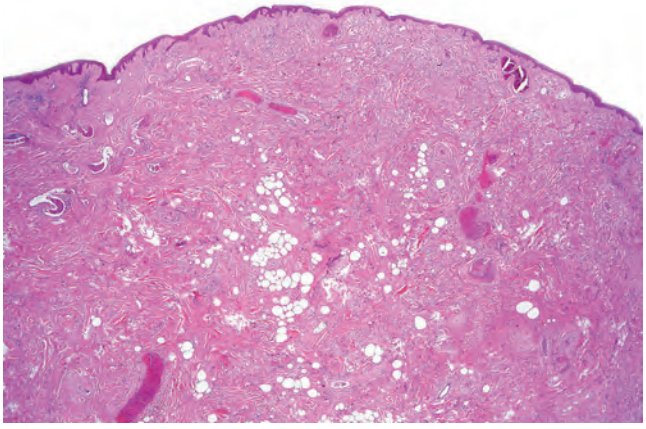

Fig. 11. **Atypical lipomatous tumor/well-differentiated liposarcoma.** This dermal example is primarily sclerotic.

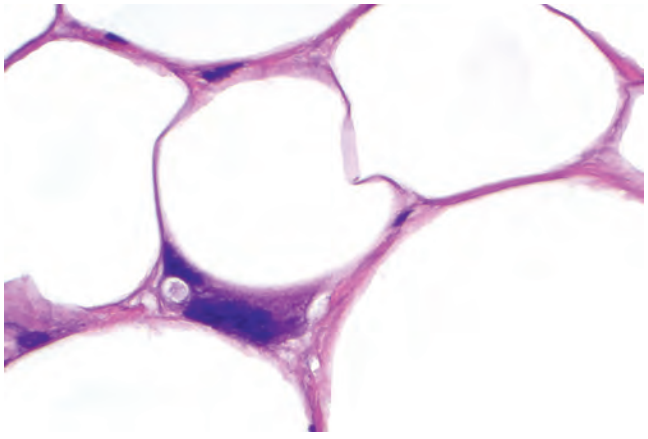

Fig. 9. **Atypical lipomatous tumor/well-differentiated liposarcoma.** High-power view of atypical adipocytes depicting marked nuclear atypia. Lipoblasts are also seen.

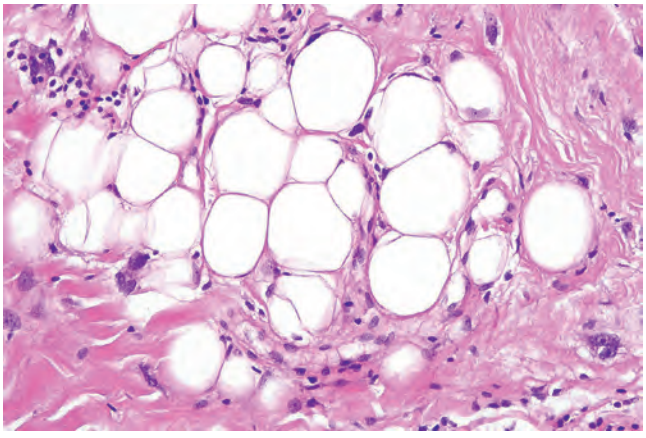

Fig. 12. **Atypical lipomatous tumor/well-differentiated liposarcoma.** Dermal case with adipocytic atypia.

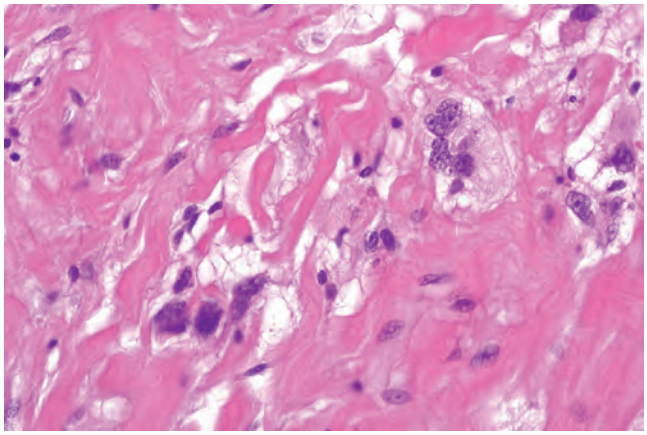

Fig. 13. **Atypical lipomatous tumor/well-differentiated liposarcoma.** Dermal case with area of overt atypia in the stromal/sclerotic component.

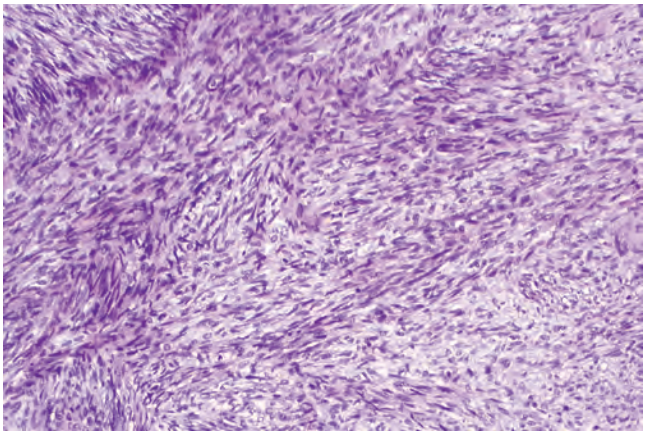

Fig. 16. **Atypical lipomatous tumor/well-differentiated liposarcoma.** Dedifferentiation presenting as spindle cells arranged in herringbone-like pattern, resembling fibrosarcoma. Mitoses are readily identified.

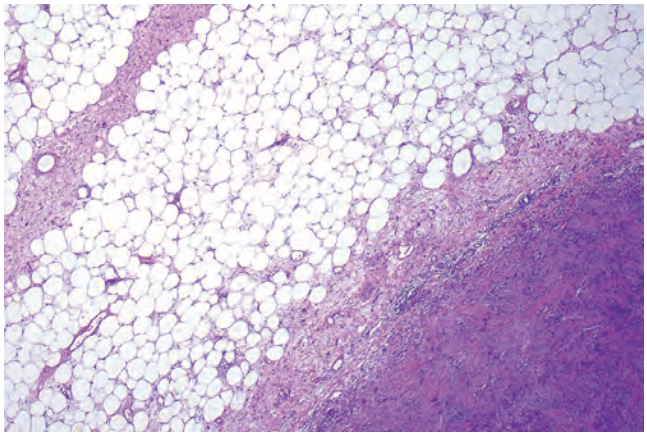

Fig. 14. **Atypical lipomatous tumor/well-differentiated liposarcoma.** Demarcation is usually stark between the atypical lipomatous tumor/well-differentiated liposarcoma component and the hypercellular, dedifferentiated spindle cell component.

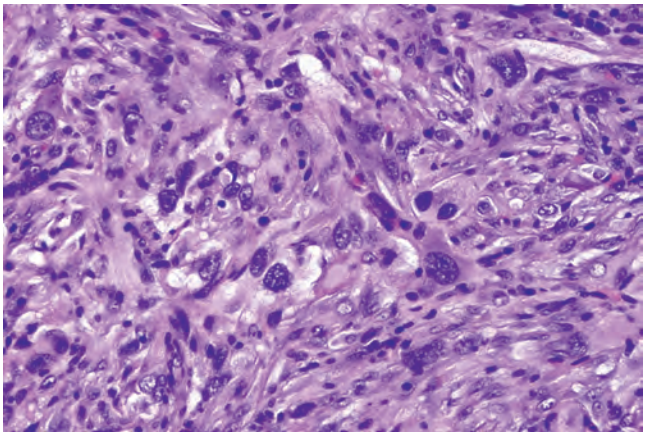

Fig. 17. **Atypical lipomatous tumor/well-differentiated liposarcoma, dedifferentiated.** Case demonstrating dedifferentiated pleomorphic sarcomatous area.

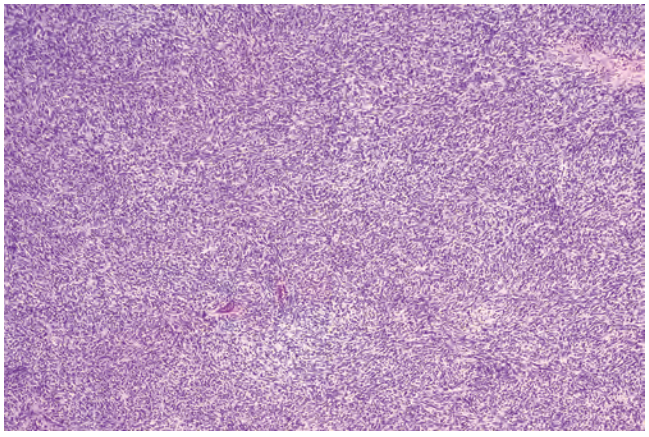

Fig. 15. **Atypical lipomatous tumor/well-differentiated liposarcoma.** Dedifferentiated spindle cell sarcoma area.

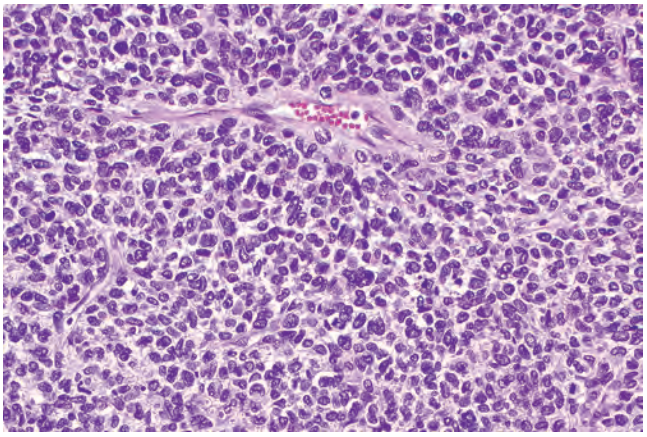

Fig. 18. **Atypical lipomatous tumor/well-differentiated liposarcoma.** Dedifferentiation presenting as a small cell sarcomatous area resembling Ewing sarcoma in this unusual case.

SPINDLE CELL LIPOSARCOMA

Definition
- A liposarcoma that is composed primarily of spindle cells
- It has been considered in the past a variant of ALT/WDL, myxoid liposarcoma and a malignant counterpart of spindle cell lipoma
- Recently recognized as an exceedingly rare distinct type of liposarcoma with unique clinicopathological and molecular features that does not belong to the spectrum of atypical lipomatous tumor
- The term *fibrosarcoma-like lipomatous neoplasm* has been proposed to distinguish it from spindle cell morphological variants of other liposarcomas

Clinical features
Epidemiology
- Rare liposarcoma subtype
- Affected individuals are usually adults
- Slight male predilection is noted
- Tumors tend to occur in the subcutaneous tissues of extremities, trunk, and head and neck
- Commonly seen in thighs and chest walls

Presentation
- Painless, slow-growing masses
- Size is variable

Prognosis and treatment
- Usually managed by surgical excision, occasionally combined with adjuvant radiotherapy
- Limited follow-up reports show favorable prognosis with rare recurrences and no metastases
- Generally considered a low-grade sarcoma but biological behavior needs to be assessed further

Pathology
Histology
- Vaguely nodular neoplasms with thin, fibrous bands that are usually confined to subcutis but can invade underlying skeletal muscles
- Tumors composed of fibroblast-like spindle cells embedded in variably myxoid stroma
- Multivacuolated and signet-ring lipoblasts are easily identified, as well as more primitive mesenchymal cells
- The tumor recapitulates early stages of embryonic fat development
- Networks of thin-walled capillaries resembling those seen in myxoid liposarcoma can be recognized

Immunohistochemistry/special stains
- S100 protein is commonly seen, and CD34 is occasionally expressed
- No MDM2, HMGA2, or CDK4 expression

Genetic profile
- No *MDM2*/*CDK4* amplification (12q13–15)
- No *DDIT3* gene rearrangement (12q13)
- *RB1* deletion was detected in some cases (13q14)

Main differential diagnoses
- Spindle cell variant of ALT/WDL
- Spindle cell lipoma
- Spindle cell sarcoma involving adipose tissue

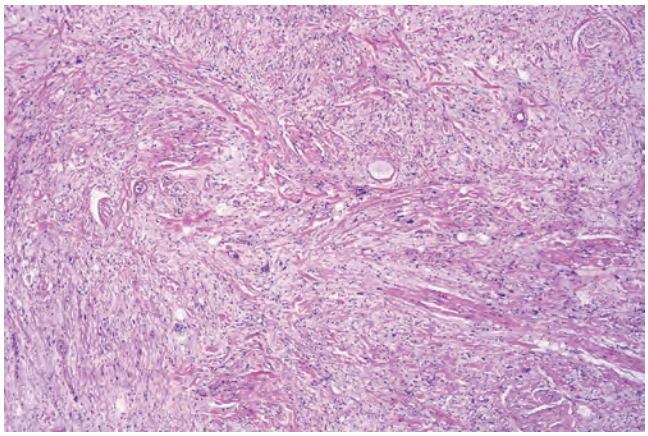

Fig. 1. **Spindle cell liposarcoma.** A vaguely nodular neoplasm composed of predominantly spindle cells.

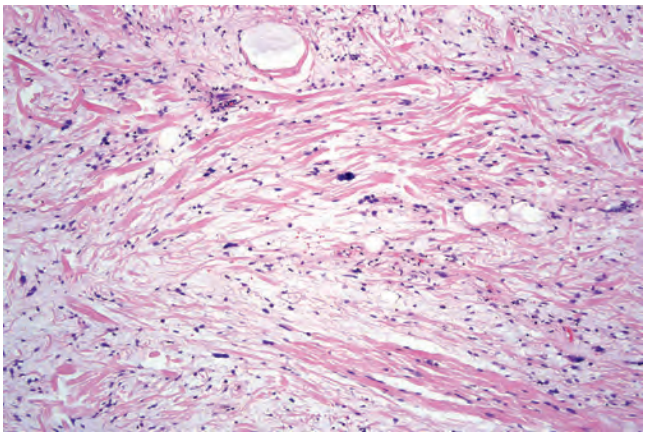

Fig. 2. **Spindle cell liposarcoma.** Fibrous bands and fibroblast-like spindle cells with myxoid stroma constitute this neoplasm. Spindle cells with hyperchromatic nuclei are seen.

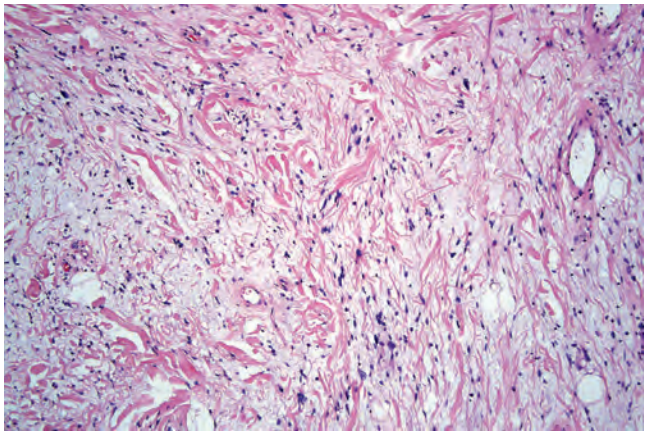

Fig. 3. **Spindle cell liposarcoma.** The presence of a variable amount of myxoid stroma is a typical feature of spindle cell liposarcoma.

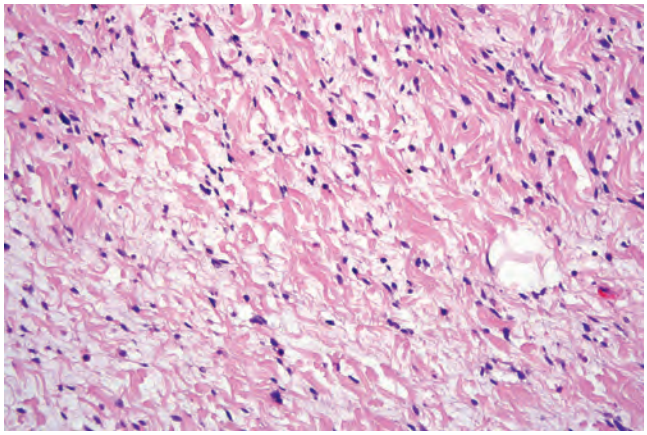

Fig. 4. **Spindle cell liposarcoma.** Spindle cells in a background of collagenous and myxoid matrix. This example can be difficult to distinguish from benign spindle cell lipoma.

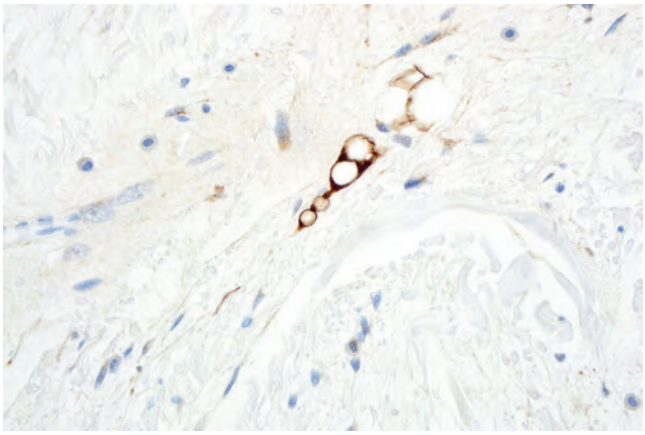

Fig. 5. **Spindle cell liposarcoma.** The adipocytic differentiation of neoplastic cells is supported by S100 protein expression.

MYXOID LIPOSARCOMA

Definition
- A malignant mesenchymal neoplasm characterized by the presence of a variable number of small, round, primitive mesenchymal cells; lipoblasts; and myxoid stroma with a characteristic delicate, chicken-wire–like vasculature and *DDIT3–FUS* fusion
- Increased confluent cellularity suggests more aggressive behavior, but is no longer termed *round cell liposarcoma*

Clinical features
Epidemiology
- The second most common type of liposarcoma after ALT/WDL
- Most patients are diagnosed during the fourth to fifth decade of life
- The most common liposarcoma in patients under the age of 20 years
- No sex predilection
- Majority of tumors are located in the thighs
- Subcutaneous localization is rare

Presentation
- Painless, slowly growing, large masses

Prognosis and treatment
- Increased confluent cellularity in more than 5% of tumor adversely affects survival
- Managed by wide surgical excision with or without chemoradiation
- Tend to metastasize to bones (particularly spine) and unusual locations such as fat-bearing areas before the lungs

Pathology
Histology
- Nodular tumors composed of a variable amount of hypocellular myxoid areas and cellular round cell areas
- The myxoid areas represent lower-grade component and the hypercellular areas represent the higher-grade component of tumor
- The myxoid areas are composed of uniform, bland-looking, round cells and small signet ring lipoblasts embedded in an abundant myxoid stroma that have a delicate chicken-wire vascular network
- The hypercellular areas are formed by solid sheets of primitive mesenchymal round cells with conspicuous nucleoli and high nuclear-to-cytoplasmic ratio
- Generally, no conspicuous pleomorphism, giant tumor cells, or significant mitosis

Immunohistochemistry/special stains
- S100 protein is variably expressed

Genetic profile
- Virtually all cases show t(12;16)(q13;p11) leading to fusion of *DDIT3* (previously known as *CHOP*) located at 12q13, and *FUS* (also known as *TLS*) located at 16p11, to form *FUS-DDIT3* (or *TLS-CHOP*) fusion gene
- t(12;22)(q13;q12) where the *EWSR1* gene (related to *FUS*) fuses with *DDIT3* is encountered rarely
- Thirty percent of cases show *TP53* mutations

Main differential diagnoses
- Atypical lipomatous tumor/well-differentiated liposarcoma
- Extraskeletal myxoid chondrosarcoma
- Myxofibrosarcoma

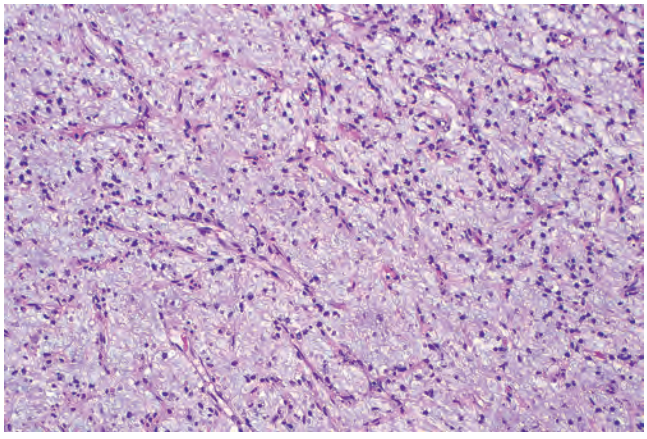

Fig. 1. **Myxoid liposarcoma.** Classic morphology depicting a hypocellular myxoid neoplasm composed of small, round cells with bland-appearing nuclei. Note the delicate "chicken-wire" vasculature.

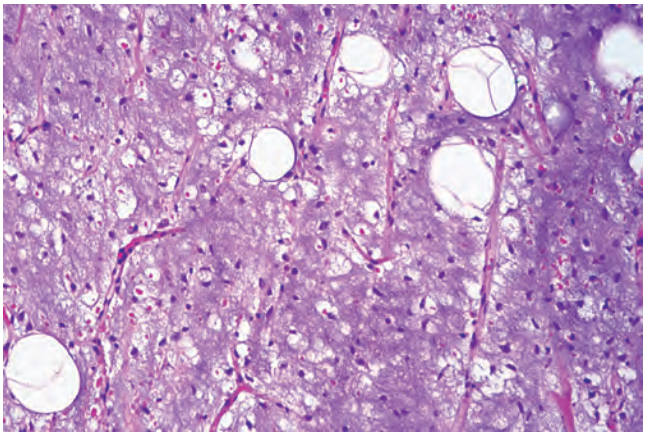

Fig. 2. **Myxoid liposarcoma.** Strikingly myxoid stroma and delicate blood vessels.

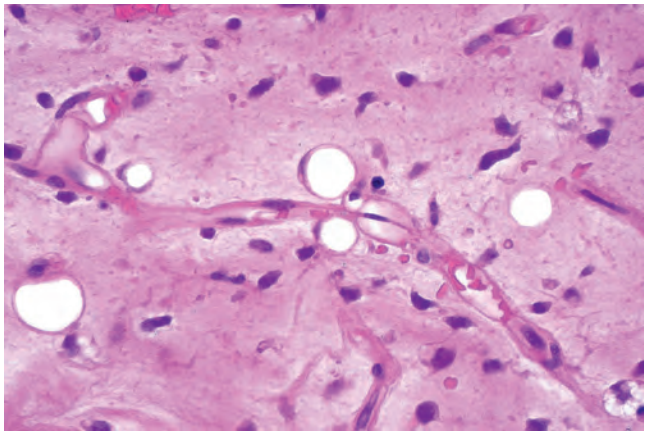

Fig. 3. **Myxoid liposarcoma.** High-power view showing signet ring cells representing univacuolated lipoblasts.

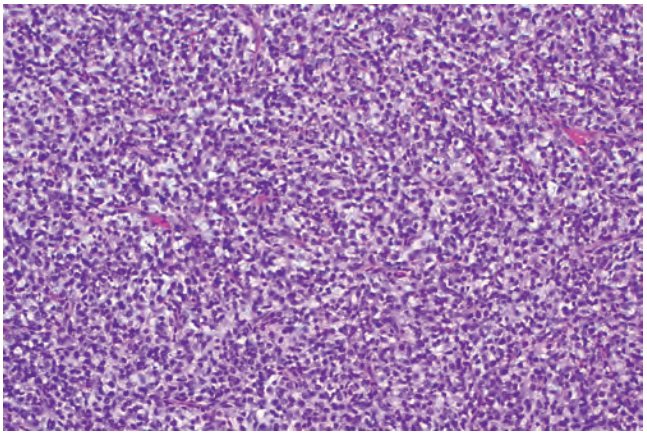

Fig. 5. **Myxoid liposarcoma.** Hypercellular component composed of sheets of monomorphic primitive mesenchymal round cells representing progression to a higher-grade neoplasm.

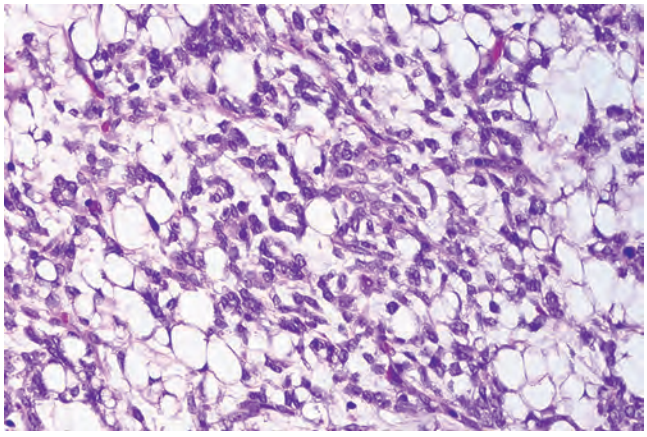

Fig. 4. **Myxoid liposarcoma.** Round cells admixed with signet ring–like lipoblast cells with no intervening stroma.

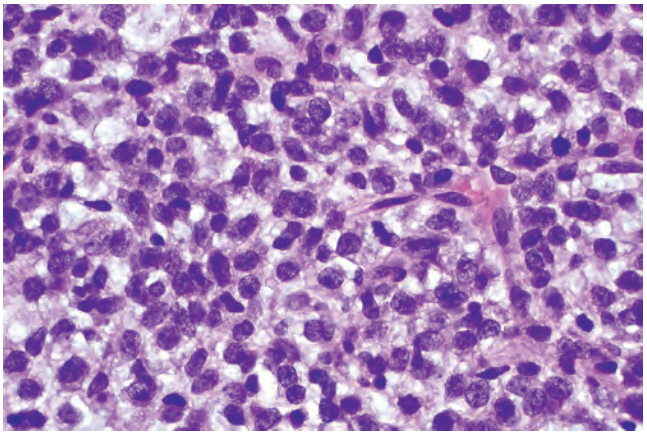

Fig. 6. **Myxoid liposarcoma.** The hypercellular component demonstrates high nuclear-to-cytoplasmic ratio, minimal pleomorphism, and infrequent mitoses.

PLEOMORPHIC LIPOSARCOMA

Definition
- A high-grade pleomorphic sarcoma characterized by the presence of a variable number of pleomorphic lipoblasts

Clinical features
Epidemiology
- Rare subtype of liposarcomas but perhaps the most common to arise in dermis
- The extremities are the most common site
- Subcutaneous localization is rare

Presentation
- Painless, often large masses

Prognosis and treatment
- The most aggressive type of liposarcoma with high rate of metastasis
- Managed by wide excision, often combined with chemoradiation

Pathology
Histology
- Either well-circumscribed or infiltrative tumors with a variable number of characteristic pleomorphic lipoblasts
- Background of a high-grade pleomorphic sarcoma (similar to undifferentiated pleomorphic sarcoma) with the presence of spindle cells, inflammatory cells, and giant cells
- Brisk mitosis is usual
- The presence of lipoblasts is required to make the diagnosis
- Lack areas of typical ALT/WDL or heterologous differentiation
- An epithelioid variant is recognized

Immunohistochemistry/special stains
- S100 protein is expressed in less than 50% of cases
- Smooth muscle actin expression is common

Genetic profile
- Complex chromosomal structural rearrangements
- High rate of *TP53* mutation

Main differential diagnoses
- Undifferentiated pleomorphic sarcoma
- Dedifferentiated liposarcoma
- Pleomorphic variant of other sarcomas such as leiomyosarcoma or rhabdomyosarcoma

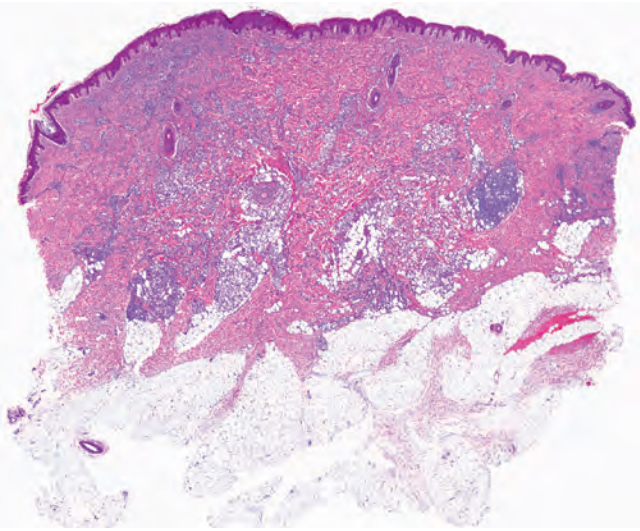

Fig. 1. **Pleomorphic liposarcoma.** This case is an infiltrative dermal neoplasm. (Courtesy of Sate Hamza, Winnipeg, Manitoba, Canada.)

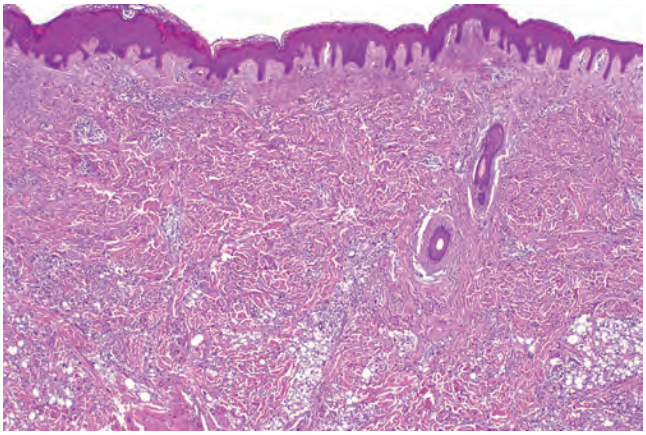

Fig. 2. **Pleomorphic liposarcoma.** Dermal neoplasm composed of cells demonstrating adipocytic differentiation. (Courtesy of Sate Hamza, Winnipeg, Manitoba, Canada.)

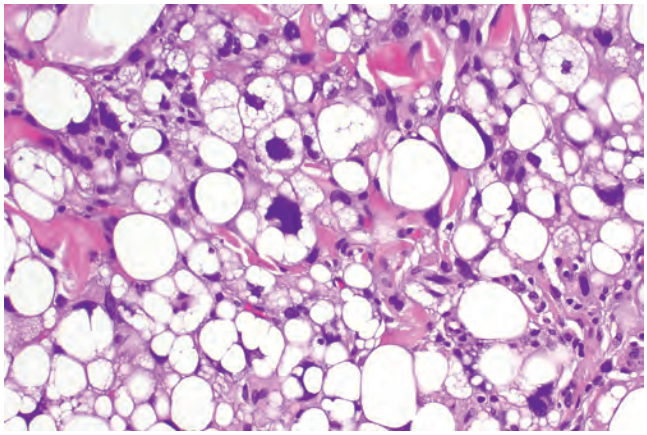

Fig. 3. **Pleomorphic liposarcoma.** High-power view showing variably sized adipocytes and prominent multivacuolated lipoblasts exhibiting marked nuclear atypia. (Courtesy of Sate Hamza, Winnipeg, Manitoba, Canada.)

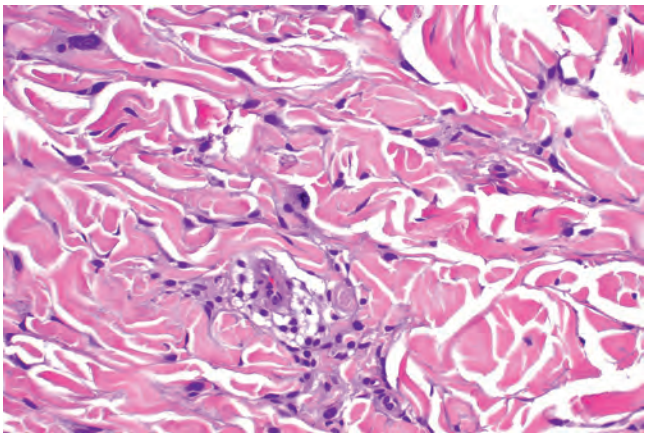

Fig. 4. **Pleomorphic liposarcoma.** Small round cells, lipoblasts, and larger cells with atypical, hyperchromatic nuclei infiltrating the dermal collagenous tissue. (Courtesy of Sate Hamza, Winnipeg, Manitoba, Canada.)

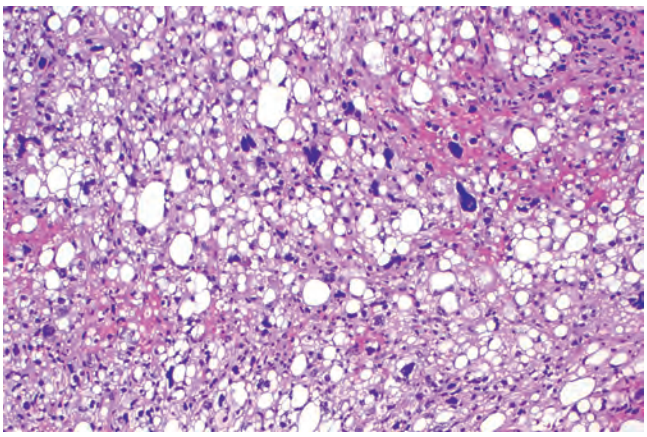

Fig. 5. **Pleomorphic liposarcoma.** Markedly pleomorphic adipocytes, some of which exhibit bizarre-appearing nuclei.

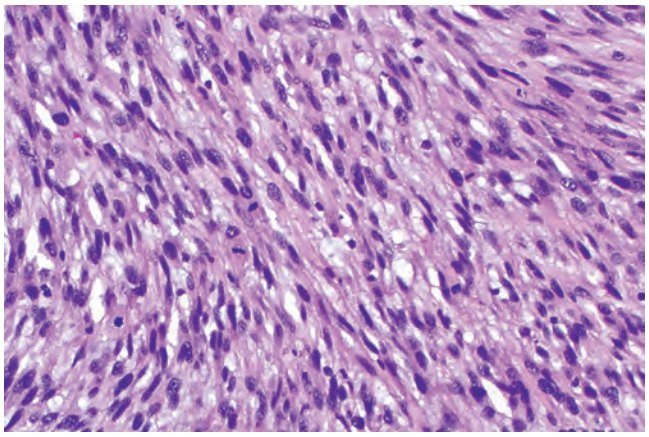

Fig. 6. **Pleomorphic liposarcoma.** Spindle cell sarcomatous area with brisk mitotic activity.

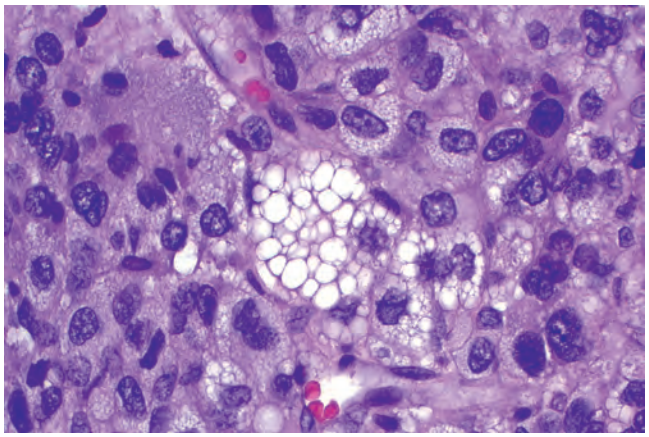

Fig. 7. **Pleomorphic liposarcoma.** Lipoblasts with characteristic multivacuolated cytoplasm.

Further Reading

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