Tumors of Uncertain Differentiation 12

Although numerous soft tissue neoplasms resemble various connective tissues in the body, some have no identifiable histologic counterpart. Like other diagnostic groups, the behavior of tumors of uncertain differentiation varies from benign to highly malignant. Repetitive genetic aberrations are frequent among these neoplasms and can be used for diagnostic purposes.

12.1 Intramuscular Myxoma

Intramuscular myxoma is a benign neoplasm that most frequently occurs as a well-delineated and deeply situated mass in the thigh. It arises in adults in the fifth to seventh decade of life, and some patients note symptoms of pain or tenderness [1, 2]. Patients with Mazabraud syndrome have a combination of multiple intramuscular myxomas and fibrous dysplasia of the bone [3].

Pathology
Microscopically, these tumors show abundant background myxoid substance that contains scattered stellate cells with small, bland nuclei (Figs. 12.1 and 12.2). Macrophages containing mucinous material can sometimes be seen [4].

Ancillary Studies

- The diagnosis is primarily based on histologic features.
- The majority of intramuscular myxomas contain mutations in the *GNAS1* gene [5].

Differential Diagnosis

- Myxoid liposarcoma
- Myxofibrosarcoma
- Low-grade fibromyxoid sarcoma

K. Perry, *Soft Tissue Pathology for Clinicians*, Pathology for Clinicians,
DOI 10.1007/978-3-319-55654-3_12

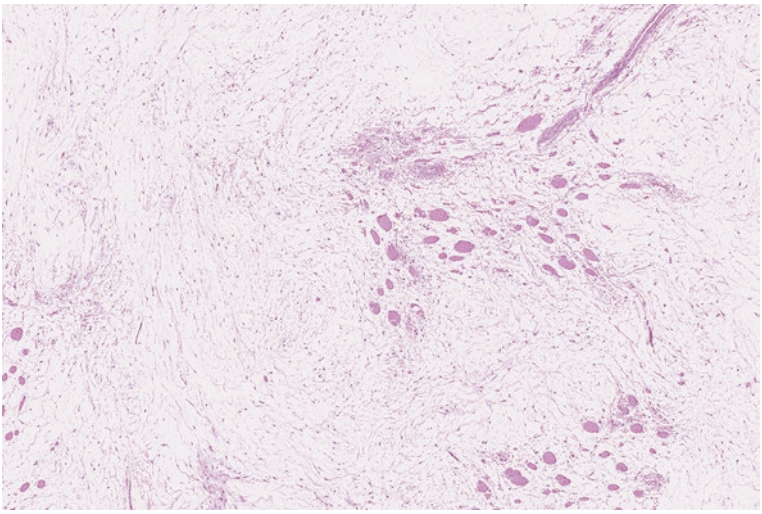

Fig. 12.1 Skeletal muscle fibers surrounded and dissected by intramuscular myxoma

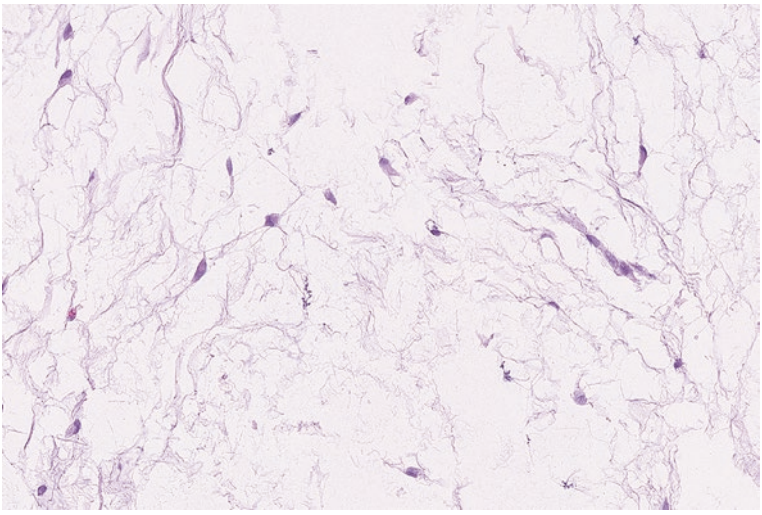

Fig. 12.2 Intramuscular myxoma with occasional cells with small and stellate nuclei

Comment

1. Intramuscular myxomas can have similar features with other myxoid tumors, such as myxofibrosarcoma, myxoid liposarcoma, and low-grade fibromyxoid sarcoma.
2. Myxoid liposarcoma has a more conspicuous interconnecting "chicken wire" capillary network with scattered lipoblasts.

3. Myxofibrosarcoma contains more atypical mesenchymal cells with nuclear hyperchromasia that are associated with curvilinear vessels.
4. Low-grade fibromyxoid sarcoma shows a more organized pattern of alternating fibrous and myxoid stroma and is positive for a MUC4 immunohistochemical stain.
5. Given limited material, the diagnosis of intramuscular myxoma on a needle core biopsy can be difficult. A descriptive interpretation of "low-grade myxoid neoplasm" is sometimes made.
6. Intramuscular myxoma is a benign neoplasm. Surgical excision is generally curative [4].

12.2 Superficial Angiomyxoma

Superficial angiomyxomas present as polypoid or nodular lesions in the dermis of the head and neck, trunk, or lower limbs in children and adults [6]. The majority of these lesions measure from 1 to 5 cm in greatest dimension [7]. They are morphologically identical to the myxomas in Carney syndrome, a condition associated with endocrine overactivity, spotty pigmentation, and multiple myxomas [8].

Pathology
Superficial angiomyxomas often have a multinodular architecture and contain a myxoid background with bland-appearing stromal cells (Fig. 12.3). Small to medium delicate blood vessels course through the lesion, and scattered associated neutrophils and lymphocytes can be seen (Fig. 12.4). Some angiomyxomas are associated with an epidermoid cyst [7].

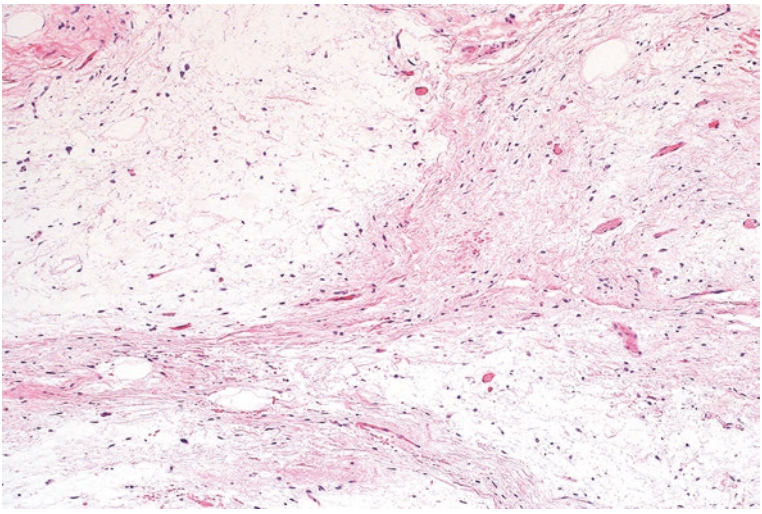

Fig. 12.3 Superficial angiomyxoma with conspicuous blood vessels in the background of myxoid material

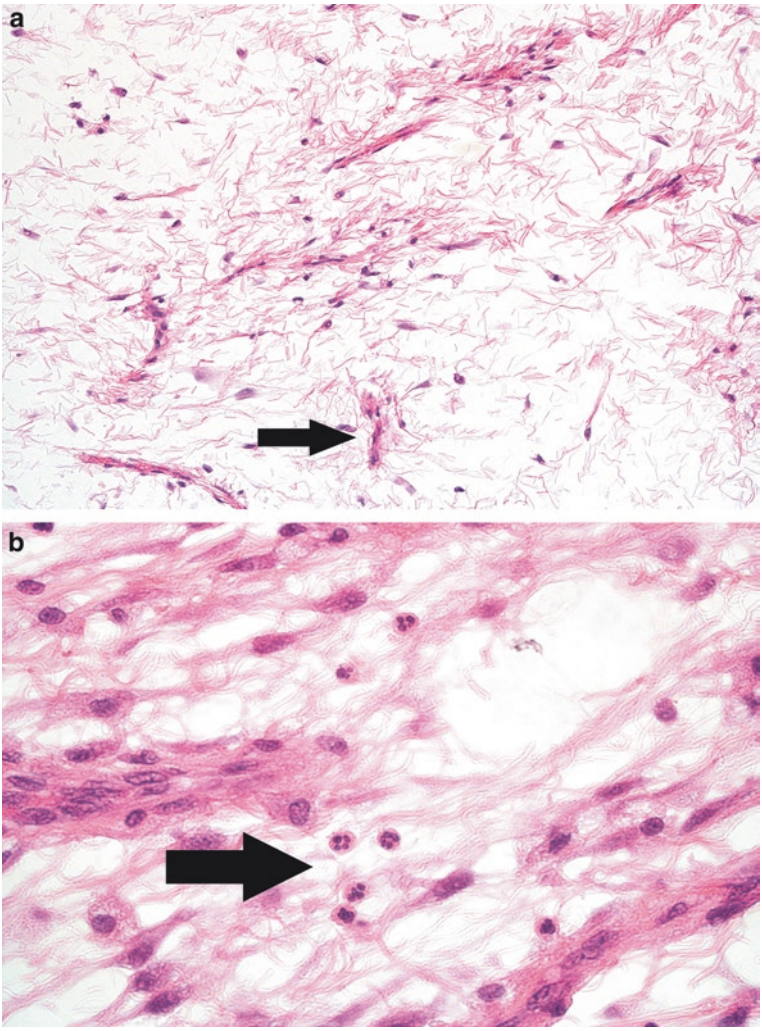

Fig. 12.4 (**a**) Superficial angiomyxoma with small blood vessels (*arrow)* (**b**) Higher power examination of these vessels reveals associated scattered neutrophils (*arrow*)

Differential Diagnosis

- Superficial acral fibromxyoma
- Myxofibrosarcoma
- Myxoid liposarcoma

Comment

1. Superficial angiomyxoma should be distinguished from other myxomatous neoplasms that occur in the extremities, such as myxoid liposarcoma, superficial acral fibromyxoma, and myxofibrosarcoma.

2. Superficial acral fibromyxomas are confined to the distal extremities and lack the associated inflammatory infiltrate of superficial angiomyxoma.
3. Myxofibrosarcoma contains mesenchymal cells with more nuclear atypia.
4. Myxoid liposarcoma arises in the deep soft tissue of the extremities, has scattered lipoblasts, and manifests highly specific translocations involving the *DDIT3* gene.
5. Superficial angiomyxomas are benign tumors, but can recur if incompletely excised [7, 9].

12.3 Hemosiderotic Fibrolipomatous Tumor

Hemosiderotic fibrolipomatous tumor (HFLT) is a lesion that often arises in the subcutaneous tissue around the ankles of adult women, most commonly in the fifth decade of life. Prior to pathologic examination, these can be mistaken for lipomas or ganglion cysts [10–12].

Pathology

Under the microscope, HFLT shows background adipocytic tissue that is traversed by fibrous septa containing bland-appearing spindle cells (Fig. 12.5). Associated lymphocytes, mast cells, and hemosiderin deposition are typically seen (Fig. 12.6). Small to medium sized blood vessels with thickened walls typically course through the fat as well.

Ancillary Studies

- The spindle cells are positive for a CD34 immunohistochemical stain.
- Genetic translocations involving *TGFBR3* and *MGEA5* have been identified in these tumors [13].

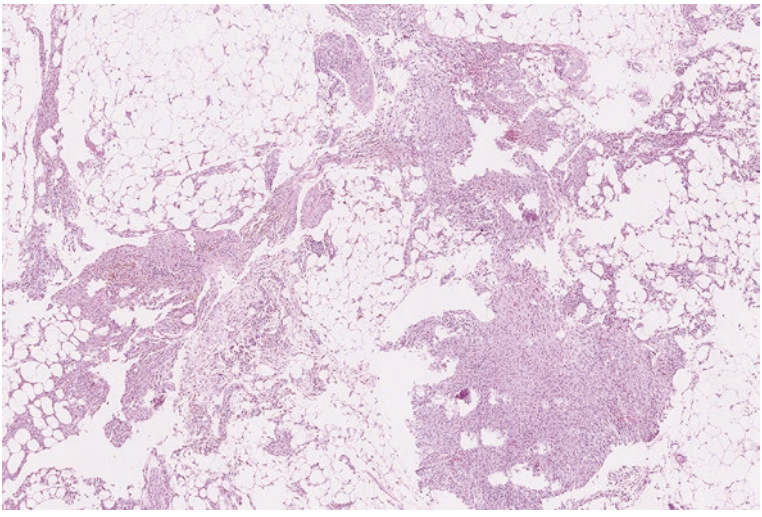

Fig. 12.5 Hemosiderotic fibrolipomatous tumor with adipose tissue that is traversed by bands of fibrous tissue

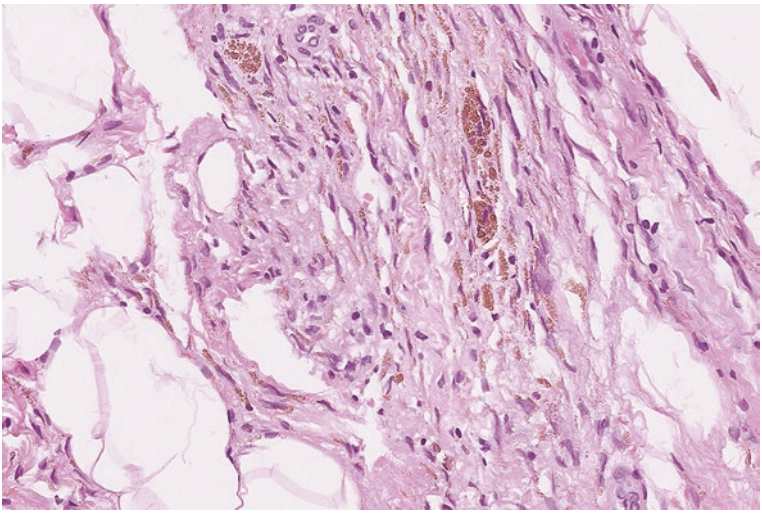

Fig. 12.6 High-power examination of this hemosiderotic fibrolipomatous tumor shows deposition of *golden-brown* hemosiderin pigment

Differential Diagnosis

- Dermatofibrosarcoma protuberans
- Fibrous histiocytoma
- Pleomorphic hyalinizing angiectatic tumor

Comment

1. Hemosiderotic fibrolipomatous tumor can resemble fibrous and fibrohistiocytic tumors such as dermatofibrosarcoma protuberans, fibrous histiocytoma, and pleomorphic hyalinizing angiectatic tumor.
2. The spindle cells in dermatofibrosarcoma exhibit a whorling pattern and entrap the surrounding adipose tissue in a "honeycomb" pattern.
3. Fibrous histiocytoma does not demonstrate the septated pattern of hemosiderotic fibrolipomatous tumor.
4. Hemosiderotic fibrolipomatous tumors share morphologic and cytogenetic features with pleomorphic hyalinizing angiectatic tumor and are suspected to be related lesions [14].
5. Approximately 25–50% of hemosiderotic fibrolipomatous tumors recur [10, 15]. Treatment consists of complete excision [12].

12.4 Myoepithelioma of Soft Tissue

Myoepitheliomas of the soft tissue occur in children and adults over a broad age range. They often arise in the extremities or the head and neck area. These can be infiltrative or well circumscribed and measure up to 20 cm in size [16, 17].

Pathology
Myoepitheliomas display a wide variety of morphologic appearances. The myoepithelial cells can appear as epithelioid, ovoid, or spindle cells that are arranged in sheets, clusters, cords, or interconnected strands (Fig. 12.7a, b). Benign myoepitheliomas

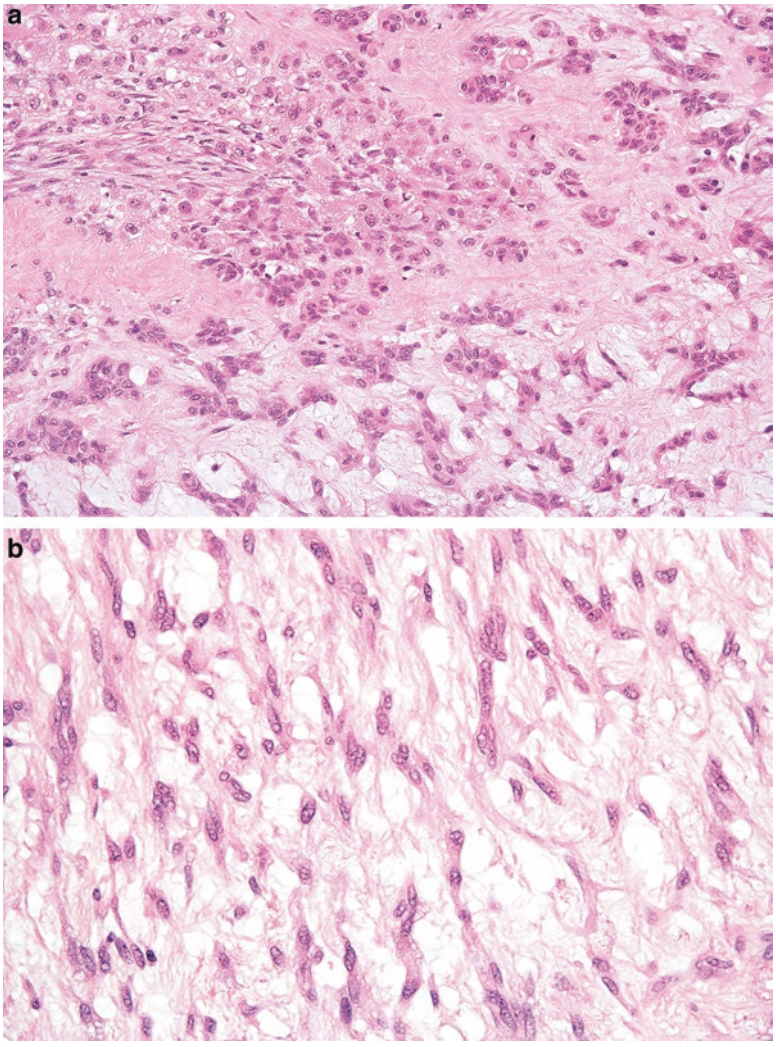

Fig. 12.7 (**a**) Myoepithelioma of soft tissue with epithelioid cells. (**b**) Myoepithelioma with an interconnected network of more spindled cells

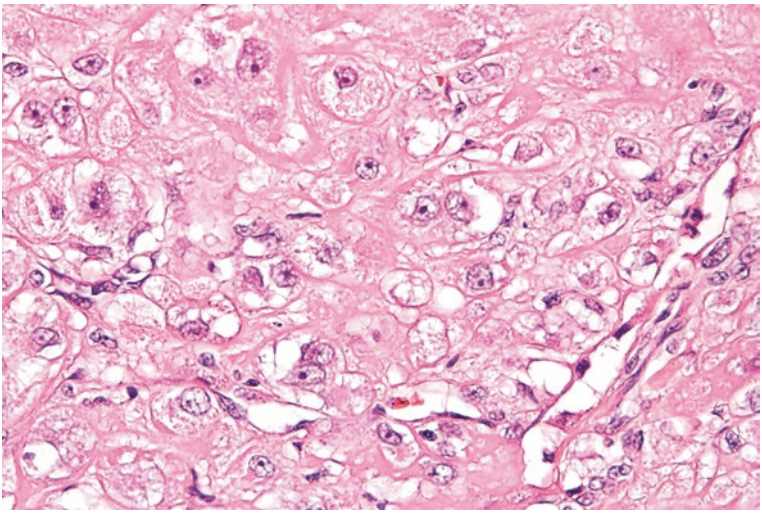

Fig. 12.8 Malignant myoepithelioma of soft tissue with vesicular nuclei and prominent nucleoli

contain bland appearing nuclei while malignant ones contain either hyperchromatic or vesicular nuclei and prominent nucleoli (Fig. 12.8).

Ancillary Studies

- Myoepithelial cells are positive for S100, calponin, pancytokeratin, and sometimes GFAP [18].
- Translocations involving the *EWSR1* gene are detected in approximately half of cases. Partner genes include *POU5F1*, *ZNF444*, and *PBX1* [19].

Differential Diagnosis

- Ossifying fibromyxoid tumor
- Extraskeletal chordoma
- Extraskeletal myxoid chondrosarcoma

Comments

1. Given their highly variable appearance, myoepitheliomas can mimic many types of neoplasms. Common considerations include extraskeletal myxoid chondrosarcoma, extraskeletal chordoma, and ossifying fibromyxoid tumor.
2. Ossifying fibromyxoid tumor has ovoid cells but usually has at least a partial peripheral shell of bone surrounding the lesion.
3. Cells in a chordoma can have a similar appearance to some myoepithelial tumors. Unlike soft tissue myoepithelioma, chordomas rarely arise in the peripheral soft tissue and are positive for a brachyury immunohistochemical stain.

4. Extraskeletal myxoid chondrosarcoma also demonstrates rearrangements involving the *EWSR1* gene; however, these tumors have different partner genes (e.g. *NR4A3*) than myoepithelioma.
5. The behavior of soft tissue myoepithelioma is difficult to predict.
6. Of myoepithelial tumors that appeared histologically benign, 18% recurred locally and none metastasized [17].
7. Of myoepithelial tumors that had histologically malignant features, 42% recurred locally and 32% metastasized [17].
8. Complete surgical excision is the primary treatment for these tumors [12].

12.5 Ossifying Fibromyxoid Tumor

Ossifying fibromyxoid tumors arise in the subcutaneous tissue or muscle in the upper and lower extremities and head and neck region. These occur in adults with a median age of presentation of 50 years. They are typically painless and develop slowly [20].

Pathology

Ossifying fibromyxoid tumors are composed of round to oval cells with vesicular nuclei that are arranged in a linear or reticular pattern (Fig. 12.9a). On closer examination, the tumor cells contain bland nuclei and are in the background of a fine collagenous or myxoid stroma (Fig. 12.9b). A partial shell of mature bone often surrounds the lesion (Fig. 12.10).

Ancillary Studies

- The cells in this tumor usually express S100 and can be positive for desmin [21].
- Ossifying fibromyxoid tumors frequently have translocations involving the *PHF1* gene [22].

Differential Diagnosis

- Myoepithelioma of soft tissue
- Chondroid syringoma
- Extraskeletal myxoid chondrosarcoma

Comment

1. The cord-like arrangement of cells in ossifying fibromyxoid tumor can resemble patterns seen in extraskeletal myxoid chondrosarcoma, chondroid syringoma, or myoepithelioma of soft tissue.
2. Unlike chondroid syringoma and myoepithelioma of soft tissue, ossifying fibromyxoid tumor only rarely expresses cytokeratins and usually has at least focal peripheral osteoid deposition.

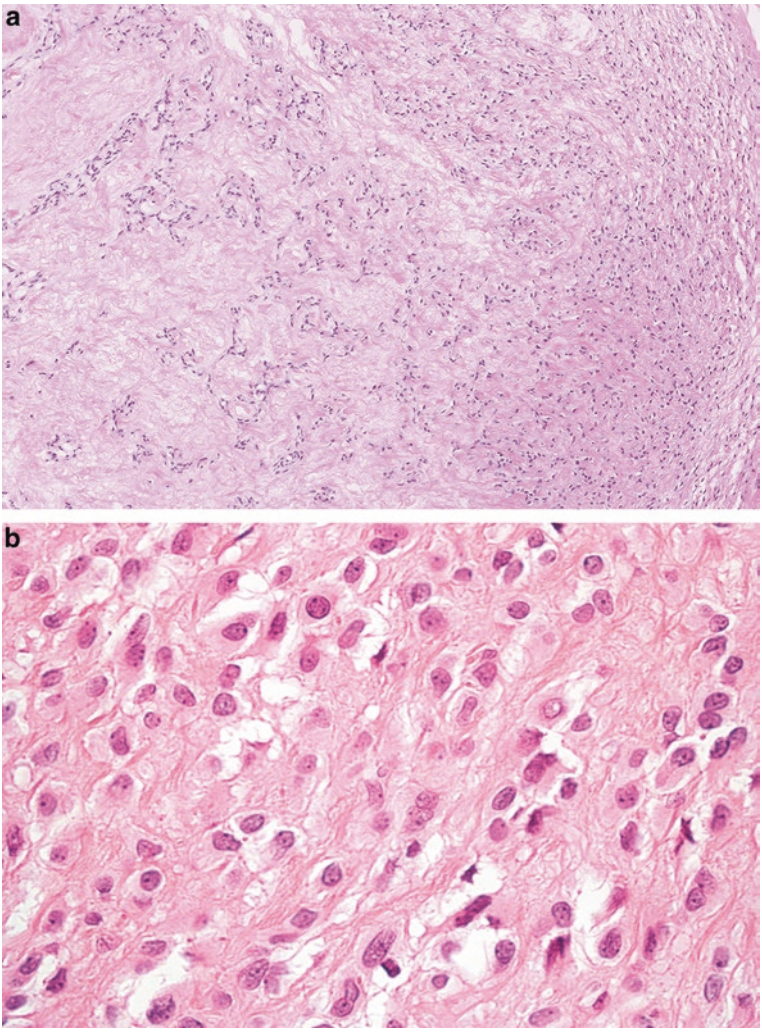

Fig. 12.9 (**a**) Ossifying fibromyxoid tumor with a cord-like and reticular arrangement of ovoid cells. (**b**) Neoplastic cells of ossifying fibromyxoid tumor with bland nuclei and fine collagen background

3. Extraskeletal myxoid chondrosarcoma typically has translocations involving the *EWSR1* gene.
4. Typical ossifying fibromyxoid tumor has a recurrence rate of 17% and a metastatic rate of 5% [23].
5. Histologically malignant ossifying fibromyxoid tumors demonstrate high cellularity, increased mitoses (over 2 per 10 high power fields), and high nuclear grade [23].
6. Malignant ossifying fibromyxoid tumors have a metastatic rate of 22% [21].

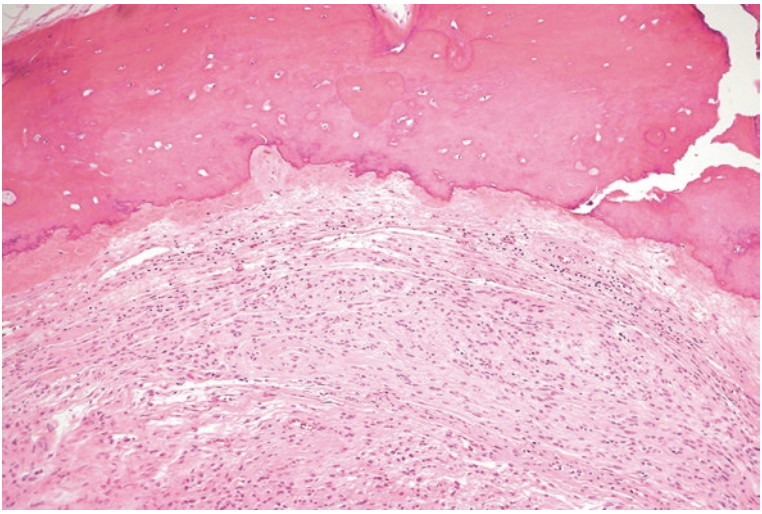

Fig. 12.10 Peripheral bone of an ossifying fibromyxoid tumor

12.6 Alveolar Soft Part Sarcoma

Alveolar soft part sarcomais a malignant tumor that primarily arises in adolescents and young adults (median age of 22 years). The most common sites of occurrence include the buttock, leg, and trunk [24]. In younger patients, these can arise in the head and neck [25]. A subset of patients have metastasis at the time of diagnosis.

Pathology
Microscopically, these tumors are composed of nests of neoplastic cells with eosinophilic and granular cytoplasm. The central cells in these nests drop out, giving the tumor an alveolar appearance similar to lung tissue (Fig. 12.11). The nuclei of the tumor cells are enlarged and prominent nucleoli can be seen (Fig. 12.12).

Ancillary Studies

- The neoplastic cells are positive for a TFE3 immunohistochemical stain [26].
- These tumors exhibit an *ASPSCR1-TFE3* fusion transcript that can be used to confirm the diagnosis by molecular studies [26].

Differential Diagnosis

- Granular cell tumor
- Renal cell carcinoma

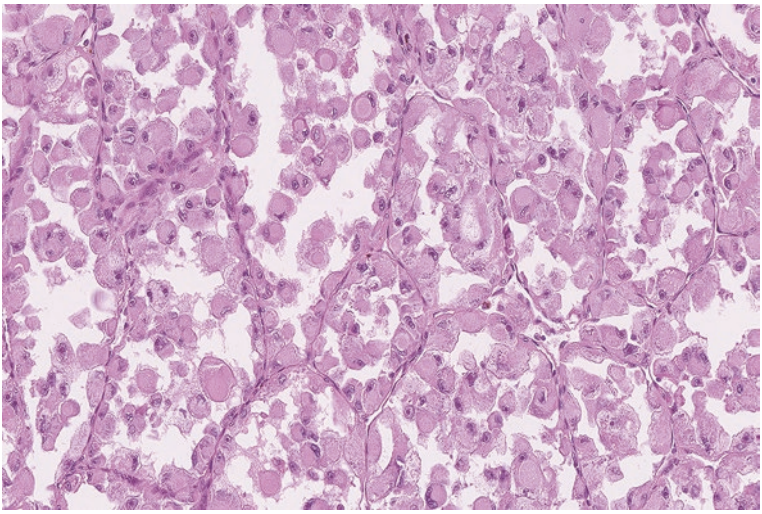

Fig. 12.11 Nests of eosinophilic cells forming an alveolar architecture in this alveolar soft part sarcoma

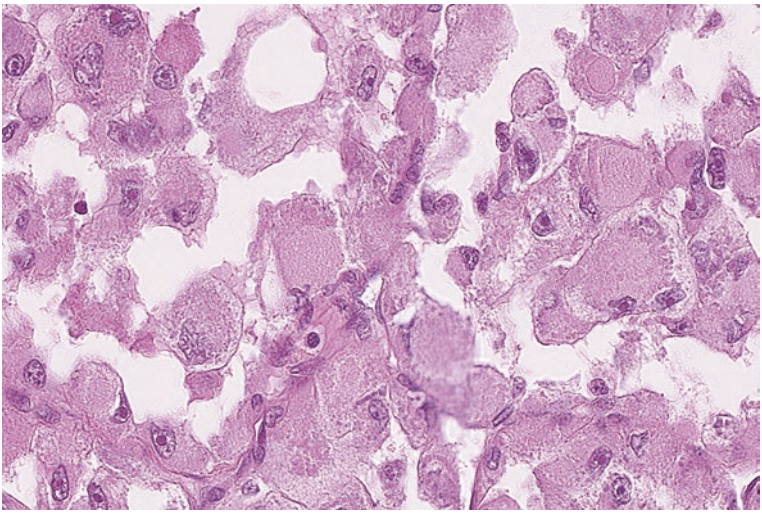

Fig. 12.12 Neoplastic cells of an alveolar soft part sarcoma with enlarged nuclei and prominent nucleoli

Comments

1. Alveolar soft part sarcoma can be confused for other tumors with eosinophilic cytoplasm, such as granular cell tumor and renal cell carcinoma.
2. Alveolar soft part sarcoma lacks the S100 staining seen in granular cell tumor and cytokeratin or PAX-8 staining seen in renal cell carcinoma.

3. These tumors are aggressive from a long-term perspective. While the 5-year overall survival is 87%, the 20-year survival is 15%.
4. The 5-year overall survival for patients with metastatic disease is only 20% [24, 27].
5. Treatment consists of radical surgical excision and possible radiotherapy and chemotherapy [9].

12.7 Clear Cell Sarcoma of Soft Tissue

Clear cell sarcoma is a malignant soft tissue tumor that arises in young adults at a median age of 30 years. These typically occur as slow-growing nodules in the foot, ankle, or hands and are intimately associated with a tendon [28, 29].

Pathology
Microscopically, these tumors are composed of bundles of spindle cells with eosinophilic to clear cytoplasm in the background of fibrotic stroma (Fig. 12.13). The cells contain enlarged vesicular nuclei and prominent nucleoli (Fig. 12.14). Scattered associated giant cells and melanin pigment can occasionally be seen.

Ancillary Studies

- Tumor cells are positive for S100, HMB-45, and Melan-A immunohistochemical stains [30].
- Clear cell sarcoma of soft tissue has been found to have *EWSR1-ATF1* or *EWSR1-CREB1* fusion transcripts [31, 32].

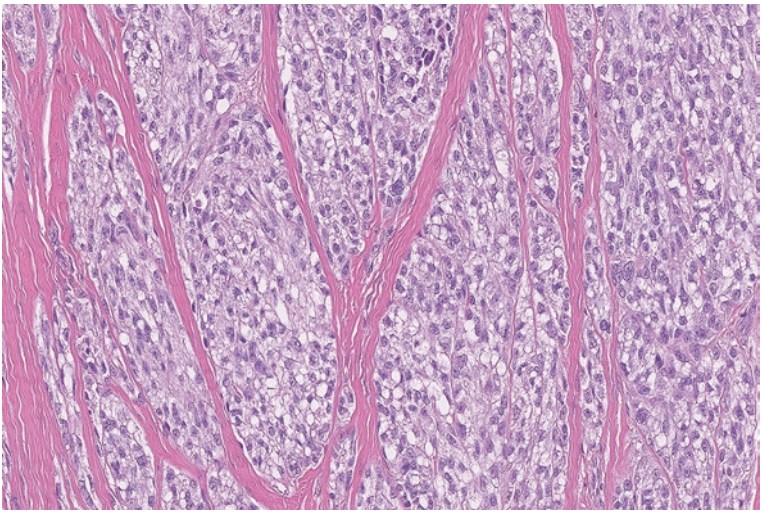

Fig. 12.13 Clear cell sarcoma of soft tissue with vaguely spindle cells containing clear and eosinophilic cytoplasm

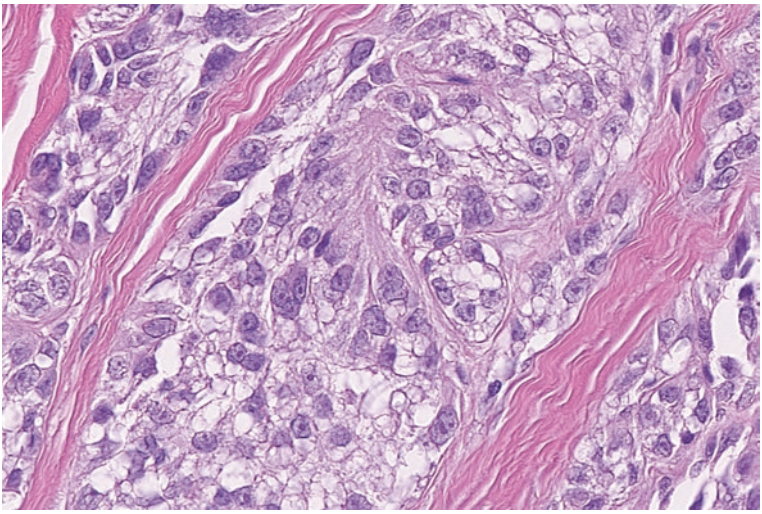

Fig. 12.14 The cells in this clear cell sarcoma contain large nuclei and prominent nucleoli

Differential Diagnosis

- Spindle cell or desmoplastic melanoma
- Malignant peripheral nerve sheath tumor
- Leiomyosarcoma

Comments

1. Clear cell sarcoma of the soft tissue can be confused for other spindle cell neoplasms such as desmoplastic melanoma, leiomyosarcoma, or malignant peripheral nerve sheath tumor.
2. The absence of an overlying skin lesion helps differentiate this lesion from a melanoma. Melanoma typically lacks mutations involving the *EWSR1* gene.
3. Malignant peripheral nerve sheath tumor demonstrates only focal (if any) S100 staining.
4. Leiomyosarcoma lacks S100 staining and is positive for desmin and smooth muscle actin.
5. Clear cell sarcoma is an aggressive tumor. Approximately 14% recur and 63% metastasize [29].
6. The 5-year survival rate is approximately 66%. Complete surgical excision is the primary treatment, and radiation therapy has been used if the surgical margins are positive [28].

12.8 Extraskeletal Ewing Sarcoma

Ewing sarcoma is a malignancy that is usually associated with the bone; however, approximately 20% of these tumors will arise in extraskeletal locations such as the pelvis, thigh, paraspinal area, or foot [33, 34]. Most patients with Ewing sarcoma are between 5 and 20 years old, and the median occurrence is at 14 years of age [35].

Pathology

This tumor is a classic example of a "small round cell sarcoma." Compared to other aggressive mesenchymal tumors, the cells are smaller in size and have a high nuclear to cytoplasmic ratio (Fig. 12.15). Sometimes this limited cytoplasm can have a clear appearance due to increased glycogen (Fig. 12.16). The cells are usually arranged in sheets but sometimes can be seen in a circular arrangement, termed a Homer-Wright rosettes [36].

Ancillary Studies

- The tumor cells are strongly positive for CD99, but this is not in itself diagnostic [37].
- Ewing sarcoma often exhibits a fusion between the *EWSR1* and *FLI-1* genes. It can also have alternative genetic translocations, resulting in fusion transcripts such as *EWSR1-ERG* [38].

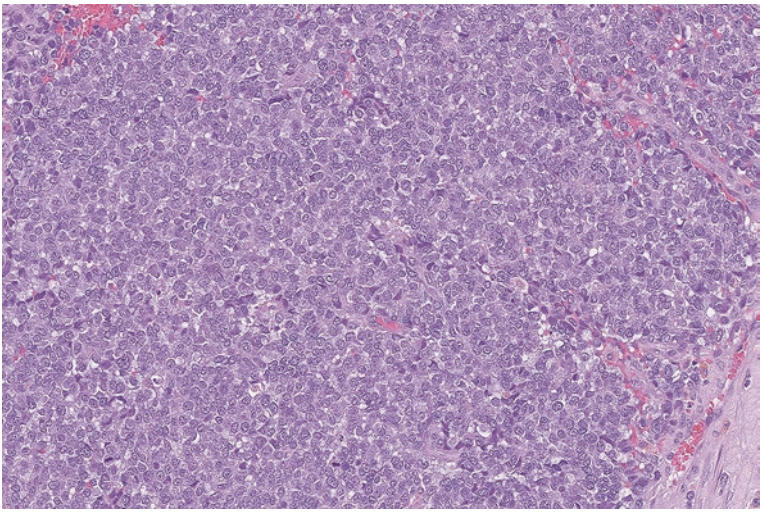

Fig. 12.15 The high nuclear to cytoplasmic ratio of the tumor cells of this Ewing sarcoma can be confused for other malignancies, such as lymphoma

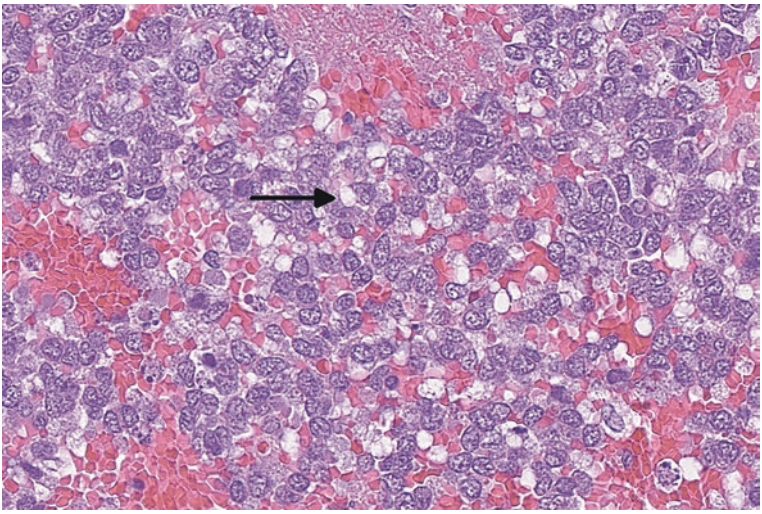

Fig. 12.16 The tumor cells of this Ewing sarcoma contain scattered clear cytoplasmic vacuolizations consistent with increased glycogen content (*arrow*)

Differential Diagnosis

- Rhabdomyosarcoma
- Desmoplastic round cell tumor
- Poorly differentiated synovial sarcoma

Comment

1. Ewing sarcoma must be differentiated from other tumors that are composed of similar undifferentiated "small round cells," such as rhabdomyosarcoma, desmoplastic synovial sarcoma, and poorly differentiated synovial sarcoma.
2. Rhabdomyosarcoma typically expresses MyoD1 and myogenin, which is usually not seen in Ewing sarcoma.
3. Desmoplastic round cell tumor contains a similar "small round cell" population, but these are usually positive for desmin.
4. Unlike Ewing sarcoma, synovial sarcoma frequently expresses TLE-1 and has distinct translocations involving the *SYT* gene.
5. Modern treatment consists of surgical resection and either radiotherapy or chemotherapy. Survival for localized tumors is approximately 75%. However, approximately 25% of patients have clinically identifiable metastasis at diagnosis [12, 39].

12.9 Desmoplastic Small Round Cell Tumor

Desmoplastic small round cell tumor is a rare sarcoma that occurs in the abdomen or pelvic peritoneum of adolescent or young adult males. The average age of occurrence is 22 years [40]. Patients can present with abdominal pain, weight loss, increased abdominal girth, ascites, and constipation and are usually found to have a primary tumor mass with multiple associated peritoneal implants [41].

Pathology

The name of this tumor accurately describes its microscopic appearance. Similar to Ewing sarcoma, the tumor cells contain minimal cytoplasm and are arranged in scattered sheets, nests, and cords. However, in desmoplastic round cell tumor, these cells are typically seen in the background of dense fibrous tissue (Fig. 12.17). Scattered areas of coagulative necrosis are frequently identified.

Ancillary Studies

- Desmoplastic round cell tumors are positive for epithelial (cytokeratin), myogenic (desmin staining in a dot-like pattern), and neurogenic (S100) immunohistochemical stains [40].
- These tumors contain a unique genetic translocation that forms an *EWSR1-WT1* fusion transcript [42].

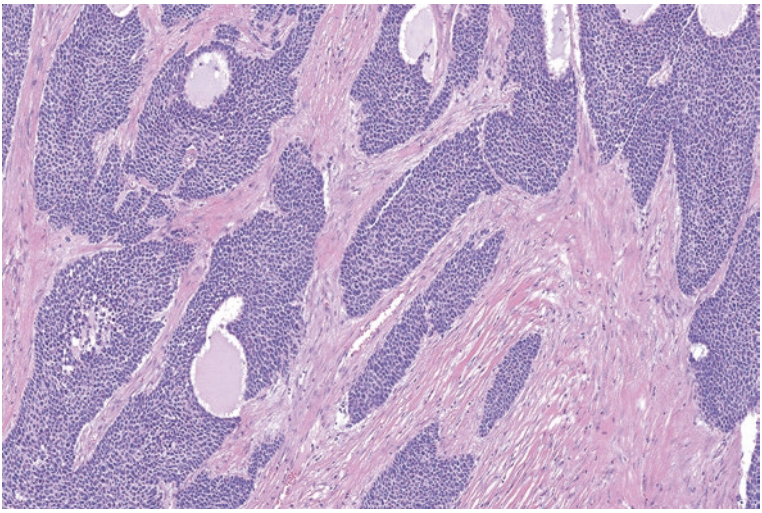

Fig. 12.17 Desmoplastic small round cell tumor with nests of tumor cells in the background of fibrotic stroma

Differential Diagnosis

- Ewing sarcoma
- Poorly differentiated carcinoma
- Rhabdomyosarcoma
- Mesothelioma

Comment

1. Desmoplastic round cell tumor can be confused with other tumors that demonstrate "round cell" morphology. These include Ewing sarcoma and rhabdomyosarcoma. They also must be distinguished from other tumors such as poorly differentiated carcinoma and mesothelioma.
2. Ewing sarcoma has morphologic similarities but does not display desmin positivity or contain the *EWSR1-WT1* fusion transcript seen in desmoplastic round cell tumor.
3. Poorly differentiated carcinomas, rhabdomyosarcomas, and mesotheliomas do not exhibit coexpression of mesenchymal, epithelial, and neural antigens [9].
4. Desmoplastic round cell tumor is a highly malignant sarcoma. Only approximately 28% of affected patients survive [43].
5. Treatment approaches include total surgical resection, external beam radiation therapy, and hyperthermic intraperitoneal chemotherapy [44].

12.10 PEComa (and Similar Neoplasms)

Perivascular epithelioid cell neoplasms (PEComas) are tumors that arise in middle-aged females, most often in the fourth decade. Common sites include the gynecologic tract, omentum, pelvis, retroperitoneum, and falciform ligament [45]. These tumors are part of a larger perivascular epithelioid cell family of neoplasms, which includes angiomyolipoma, lymphangiomyoma, and pulmonary clear cell sugar tumor [9, 46].

Pathology
Microscopically, PEComas are composed of eosinophilic and clear cells that are both spindled and epithelioid in appearance. They are arranged in nests and sheets around blood vessels (Fig. 12.18).

Ancillary Tests

- PEComas usually show expression of both smooth muscle actin and melanocytic markers (HMB-45, and MART-1) [9].

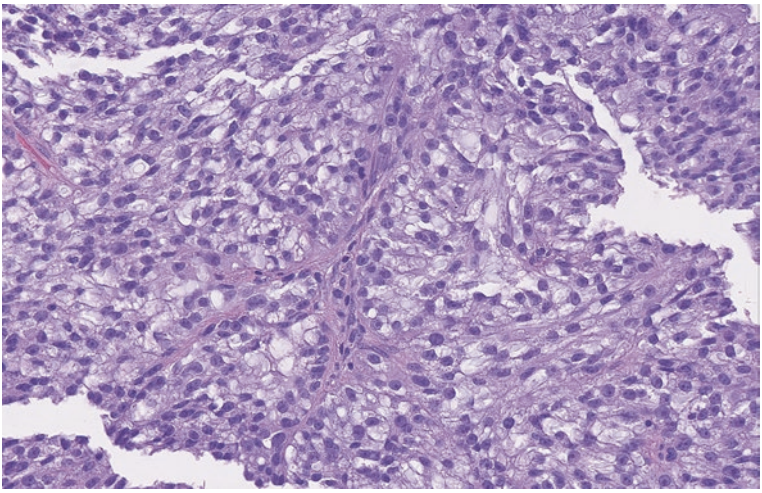

Fig. 12.18 PEComa with epithelioid cells with clear and eosinophilic cytoplasm

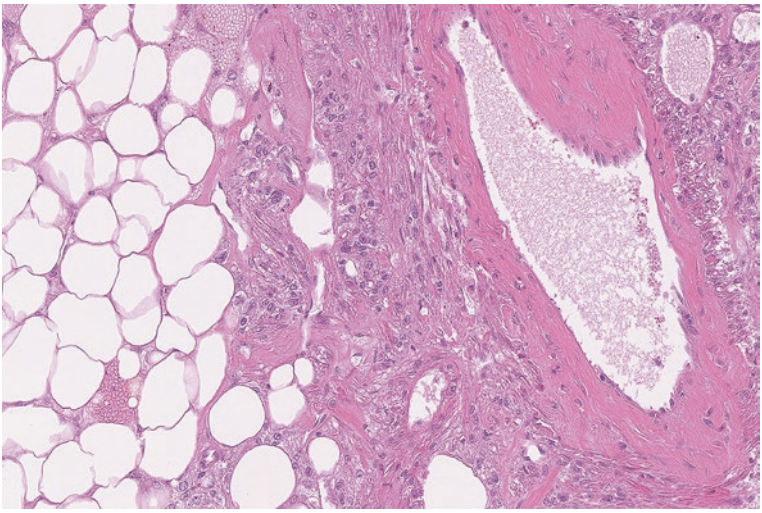

Fig. 12.19 Angiomyolipoma with adipocytes, vessels, and clear epithelioid-like cells

Related Neoplasms

- Angiomyolipoma
  - Angiomyolipomas arise in the kidney in women around the fifth decade of life. They are composed of a combination of adipose tissue, thick-walled blood vessels, and epithelioid cells arranged around vascular spaces (Fig. 12.19) [47].
- Lymphangiomyoma
  - Lymphangiomyoma presents in women as multiple nodules or cysts around the lymph nodes and lymphatics of the mediastinum and pulmonary insterstitium. Microscopic sections show lymphatic or vascular spaces surrounded by epithelioid-like cells with clear cytoplasm [48].

Differential Diagnosis

- Clear cell sarcoma
- Melanoma
- Leiomyosarcoma

Comments

1. The combined expression of smooth muscle actin and melanocytic markers (HMB-45, MART-1) differentiates PEComas from other similar appearing neoplasms such as clear cell sarcoma and melanoma. Leiomyosarcomas typically lack the numerous small vessels seen in PEComa and do not usually express MART-1.
2. Approximately 13% of PEComas recur and 21% will metastasize [45].
3. Concerning clinical or histologic features in a PEComa include a tumor size greater than 5 cm, infiltrative border, highly atypical nuclei, increased cellularity, greater than one mitosis per 50 high power field (hpf), coagulative necrosis, or vascular invasion.
4. Tumors that have two or more of these findings are considered malignant.
5. In addition to complete resection, some patients have been treated with adjuvant therapies such as mTOR inhibitors [49].

12.11 Epithelioid Sarcoma

Epithelioid sarcoma is a soft tissue neoplasm that arises in adolescents and young adults as a nodule in the hand, forearm, or pretibial region. These dermal, subcutaneous, or soft tissue lesions can be solitary or multiple and grow slowly [9, 50, 51]. Proximal-type epithelioid sarcoma, a particularly aggressive form of this tumor, often arises as a deep-seated mass in the pelvis, perineum, axilla, pubis, or buttocks [52].

Pathology

The conventional type of epithelioid sarcoma shows cells arranged around areas of degeneration or necrosis which can be mistaken for granulomatous inflammation (Fig. 12.20a). Closer inspection, however, will reveal ovoid and vesicular nuclei with atypical features such as multiple nucleoli and irregular borders (Fig. 12.20b). Although predominantly epithelioid, the tumor cells can transition into areas of a more spindled appearance (Fig. 12.20c).

The proximal type of epithelioid sarcoma demonstrates larger tumor cells with vesicular nuclei. These cells contain eosinophilic cytoplasmic inclusions that are typically described as "rhabdoid," given the vague similarity to immature skeletal muscle (Fig. 12.21).

Ancillary Tests

- The tumor cells are usually positive for EMA or various cytokeratin stains. A CD34 stain is positive in approximately half of cases [53].
- The tumors show loss of nuclear INI-1 expression.

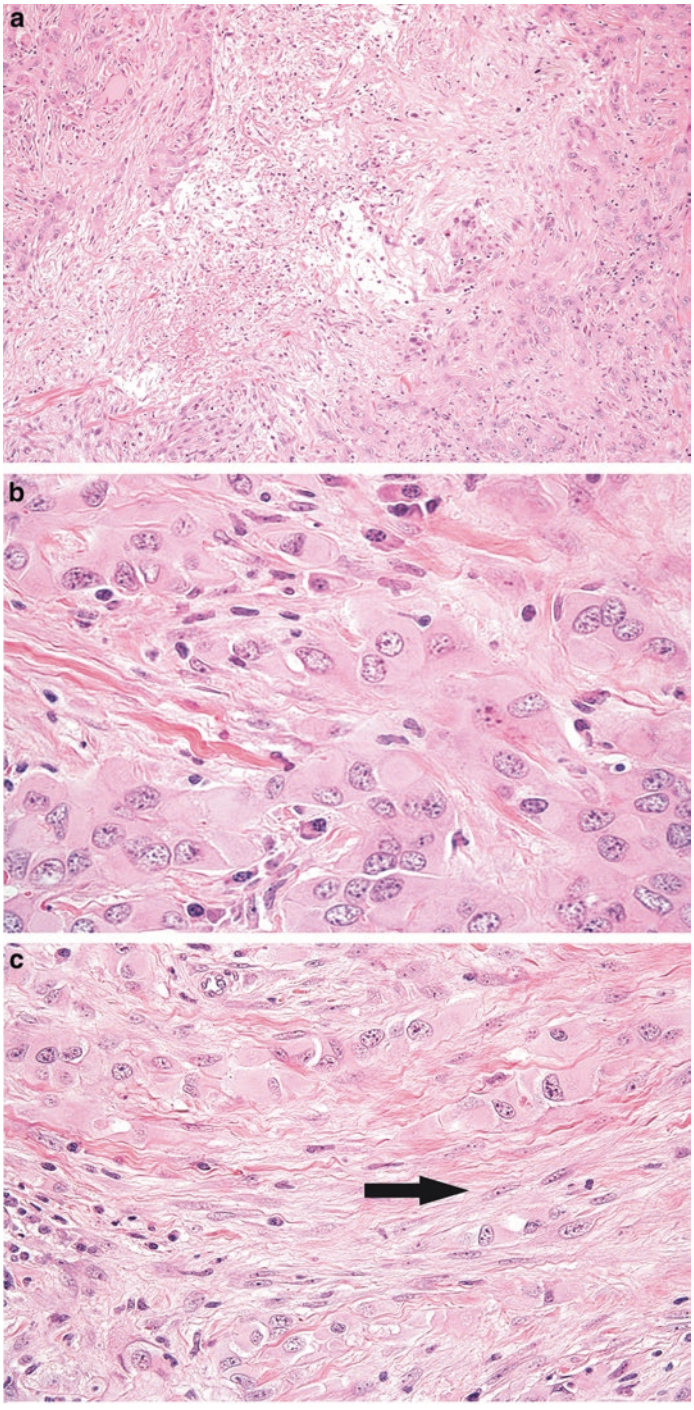

Fig. 12.20 (**a**) Epithelioid sarcoma with cells arranged around central area of necrosis. (**b**) High-power examination shows epithelioid-like cells with multiple nucleoli and nuclei of varying shape and size. (**c**) Other areas of epithelioid sarcoma show occasional cells which have a more spindled appearance (*arrow*)

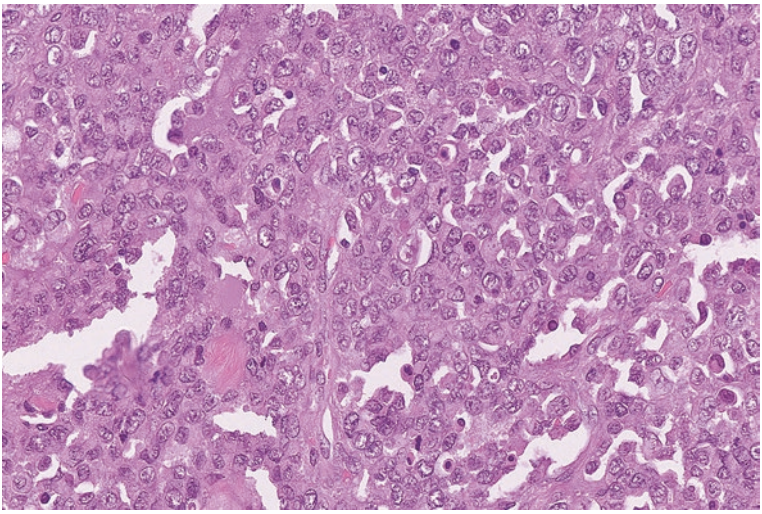

Fig. 12.21 Proximal variant of epithelioid sarcoma with larger tumor cells that contain eosinophilic cytoplasm

Differential Diagnosis

- Epithelioid angiosarcoma
- Carcinoma
- Malignant extrarenal rhabdoid tumor

Comments

1. Epithelioid sarcoma must be distinguished from other tumors with an epithelioid morphology such as epithelioid angiosarcoma, carcinoma, or malignant extrarenal rhabdoid tumor.
2. Although epithelioid sarcoma can be positive for CD34, this tumor lacks the staining for CD31 or ERG seen in epithelioid angiosarcoma.
3. Both epithelioid sarcoma and carcinoma are positive for cytokeratins; however, carcinomas typically have intact INI-1 nuclear expression and usually do not express CD34.
4. Malignant extrarenal rhabdoid tumor has similar morphologic and immunohistochemical features as the proximal variant of epithelioid sarcoma. However, malignant extrarenal rhabdoid tumors typically occur in the pediatric population and are negative for CD34.
5. Epithelioid sarcomas can metastasize to the lymph nodes as well as the lungs.
6. In one study 77% of tumors were found to recur and 45% metastasized. Tumors that are more proximal and larger and have vascular invasion, mitosis, or necrosis are associated with more aggressive behavior [54].
7. Treatment primarily consists of radical excision or amputation and regional lymph node dissection [9].

12.12 Extrarenal Rhabdoid Tumor

Malignant extrarenal rhabdoid tumors are highly malignant soft tissue tumors that are analogous to the rhabdoid tumors of the kidney or atypical teratoid/rhabdoid tumors of the central nervous system [55]. These occur in the pediatric population, particularly in the second decade of life, and often arise in the abdomen, pelvis, retroperitoneum, and neck [12, 56]. Rarely, an affected patient can have a family history or present with multiple rhabdoid tumors [57].

Pathology
Microscopically, the cells in this neoplasm have eosinophilic cytoplasmic globules that have been described as having a "rhabdoid" appearance (Fig. 12.22). The tumor cell nuclei are enlarged and vacuolated and contain prominent nucleoli.

Ancillary Studies

- Extrarenal rhabdoid tumors are positive for epithelial markers such as EMA and cytokeratins.
- The cells consistently lose nuclear expression of INI-1 protein due to mutations or deletions of the corresponding *SMARCB1* gene [58].

Differential Diagnosis

- Proximal variant of epithelioid sarcoma
- Pleomorphic rhabdomyosarcoma
- Carcinoma with rhabdoid features

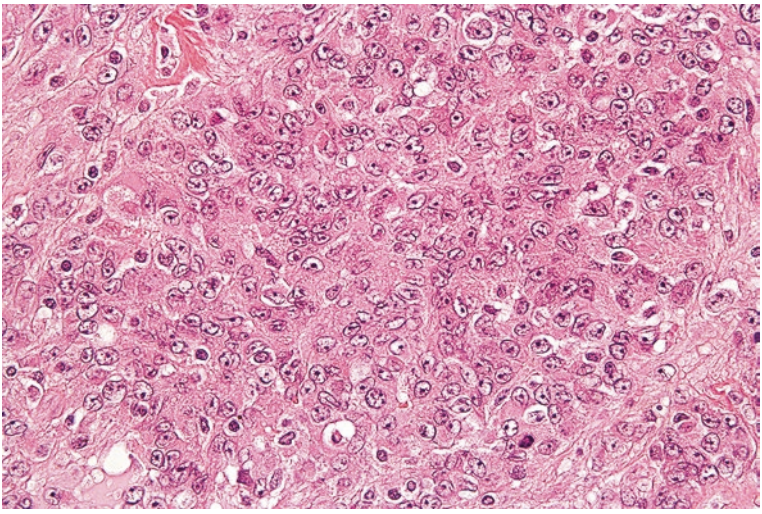

Fig. 12.22 The cells of this extrarenal rhabdoid tumor have eosinophilic cytoplasm and large vesicular nuclei with prominent nucleoli

Comment

1. Extrarenal rhabdoid tumors must be distinguished from other soft tissue and epithelial neoplasms which can have cells with a "rhabdoid appearance," including pleomorphic rhabdomyosarcoma, proximal variant of epithelioid sarcoma, and various types of carcinoma with rhabdoid features.
2. Proximal variant of epithelioid sarcoma usually arises in young adults and can express CD34 in about half of cases.
3. Pleomorphic rhabdomyosarcoma has highly anaplastic tumor cells with eosinophilic cytoplasm, but these cells show myogenic differentiation by desmin.
4. Carcinomas, such as renal cell carcinoma, can have rhabdoid features. However, there is often a more apparent residual epithelial element in a portion of the tumor. Also, carcinomas usually retain nuclear expression of INI-1.
5. Extrarenal rhabdoid tumors are highly aggressive. Approximately 82% of patients experience metastasis and 64% pass away after 19 months [56].
6. Treatment involves combinations of multiagent radiation and chemotherapy. Unfortunately, the response to chemotherapy tends to be temporary [12].

12.13 Synovial Sarcoma

Synovial sarcoma is a malignant soft tissue neoplasm that can arise in younger and older patients, with an average age of presentation of 35 years. Despite the name, the tumor does not originate from the synovium but is frequently found adjacent to major joint spaces in the proximal or distal extremities [59]. Numerous other anatomic sites have been documented, including the head and neck, chest wall, and abdominal, and thoracic cavity [60]. These tumors can grow at a deceivingly slow rate, sometimes delaying appropriate diagnosis and treatment for years [60, 61].

Pathology

Synovial sarcomas are known to have three distinct morphologic patterns. The biphasic type contains intersecting bundles of spindle cells and a second component of epithelioid-like cells that can be arranged in a glandular-like architecture (Fig. 12.23). The monophasic type contains only bundles of spindle cells (Fig. 12.24). Poorly-differentiated synovial sarcoma manifests as sheets of cells that lack a glandular or spindle cell arrangement (Fig. 12.25).

Ancillary Studies

- Synovial sarcomas are at least focally positive pancytokeratin or EMA, particularly in the epithelioid-like areas, but also in the spindled component [62].
- TLE-1, a stain that highlights expression of a transcriptional corepressor protein, is positive in synovial sarcoma [63].
- Synovial sarcoma exhibits one of two highly specific translocations resulting in the creation of a *SYT-SSX1* or *SYT-SSX2* fusion transcript [64].

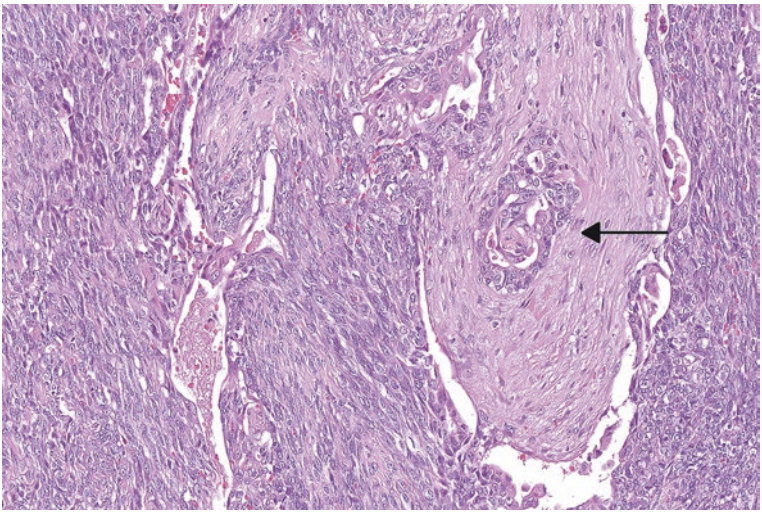

Fig. 12.23 Synovial sarcoma with a biphasic appearance. The spindle cells merge with epithelioid cells with a glandular appearance (*arrow*)

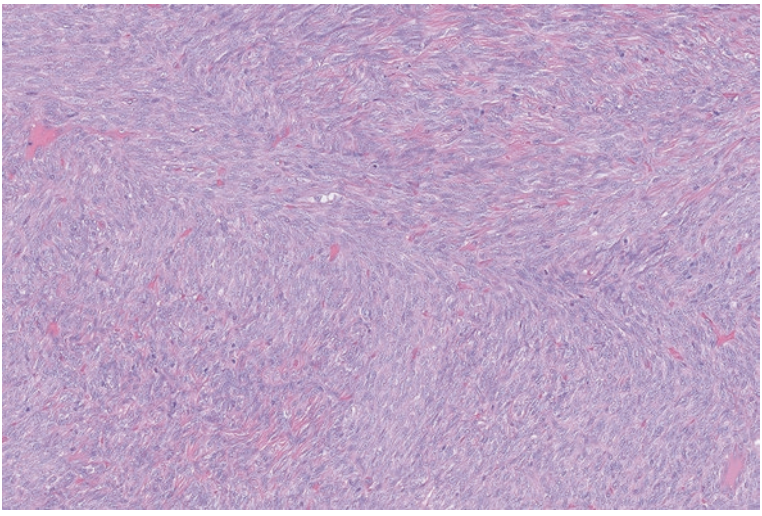

Fig. 12.24 Monophasic synovial sarcoma. This morphologic type is composed exclusively of intersecting bundles of spindle cells

Differential Diagnosis

- The differential diagnosis of synovial sarcoma depends on the morphology type.
- Biphasic tumors with an epithelioid component must be distinguished from sarcomatoid carcinoma or mesothelioma.

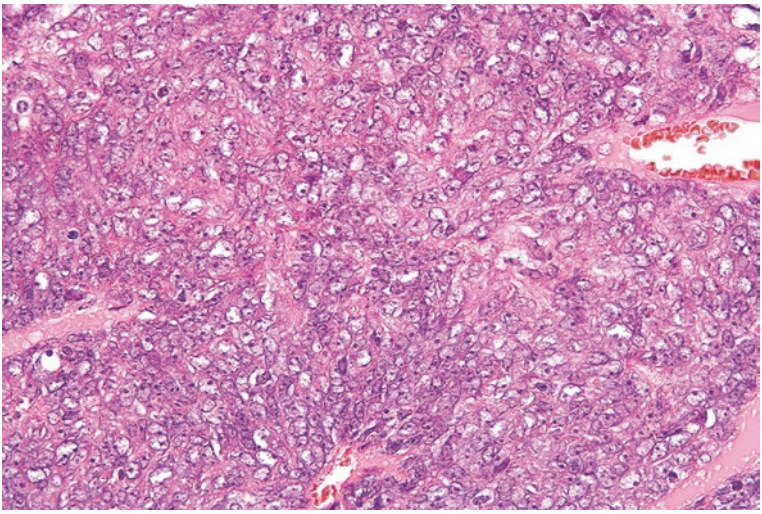

Fig. 12.25 Poorly differentiated synovial sarcoma. The tumor cells lack either a glandular or spindled architecture

- Monophasic tumors need to be separated from other tumors with a "spindled and fascicular pattern," such as malignant peripheral nerve sheath tumor, leiomyosarcoma, solitary fibrous tumor, or fibrosarcoma.
- Poorly differentiated synovial sarcoma should be distinguished from other small round blue cell neoplasms such as Ewing sarcoma.

Comments

1. Although the differential of synovial sarcoma is broad, the finding of a *SYT-SSX1* or *SYT-SSX2* fusion transcript differentiates synovial sarcoma from these histologic mimics.
2. The 5-, 10-, and 15-year event-free survival of synovial sarcoma is 60%, 50%, and 45%, respectively. Occurrence at an adult age, larger tumor size, and poorly differentiated tumors have a worse prognosis [65, 66].
3. Synovial sarcomas are often treated with radical local excision and adjuvant chemotherapy and/or radiotherapy [9].

12.14 Extraskeletal Myxoid Chondrosarcoma

Extraskeletal myxoid chondrosarcoma is a vaguely chondroid-like neoplasm that occurs as a slow-growing deep subcutaneous or soft tissue mass in adults. It occurs in the proximal extremities or trunk and most frequently arises in the sixth decade of life. Males tend to be affected twice as often as females [67, 68].

Pathology

Grossly, these tumors appear as multicystic lesions with substantial associated gelatinous material. Microscopically, there is abundant background myxoid matrix with strands and cords of neoplastic cells with characteristically eosinophilic cytoplasm (Fig. 12.26a, b).

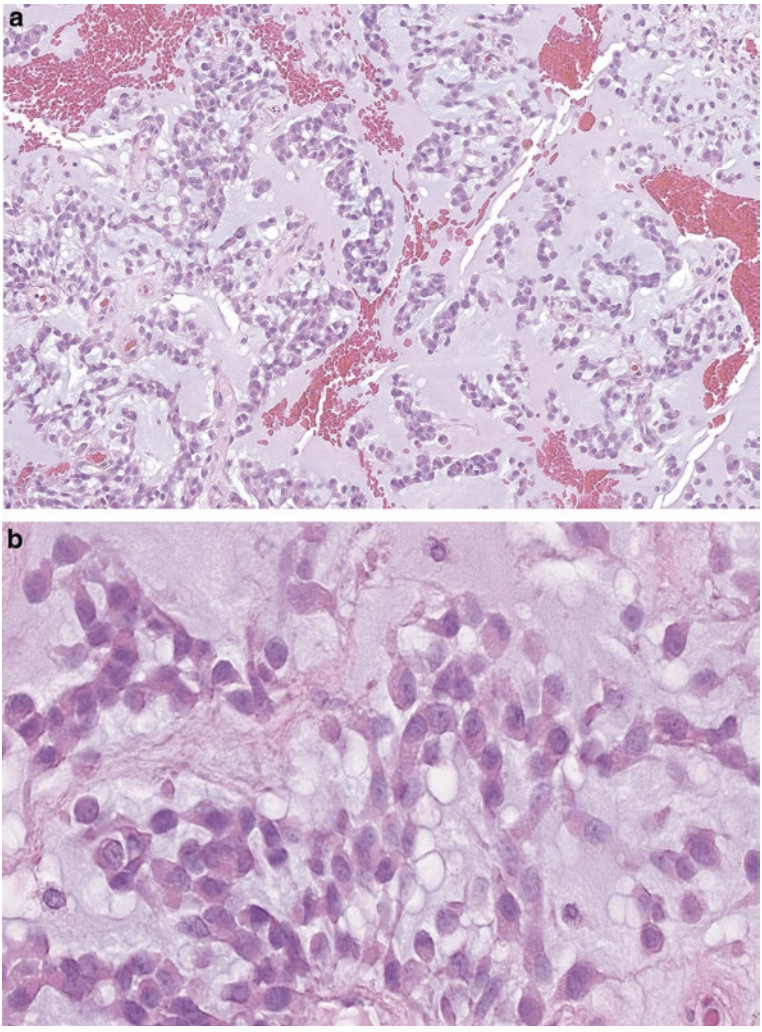

Fig. 12.26 (**a**) Extraskeletal myxoid chondrosarcoma with strands and cords of cells in a myxoid background. (**b**) The cells of this extraskeletal myxoid chondrosarcomas have a prominently eosinophilic cytoplasm

Ancillary Studies

- Extraskeletal myxoid chondrosarcoma typically demonstrates a translocation involving the *NR4A3* gene.
- Fusion transcripts include *NR4A3-EWSR1*, *NR4A3-TAF15*, or *NR4A3-TCF12* [9, 69].

Differential Diagnosis

- Myxoid liposarcoma
- Myxofibrosarcoma
- Conventional chondrosarcoma

Comment

1. Extraskeletal myxoid chondrosarcoma lacks the delicate thin-walled capillaries or aberrations of the *DDIT3* gene found in myxoid liposarcoma.
2. Extraskeletal myxoid chondrosarcoma does not exhibit the curvilinear vessels or hyperchromatic cells noted in myxofibrosarcoma.
3. Correlation with the radiologic findings is necessary to exclude soft tissue extension of a conventional chondrosarcoma.
4. This is a malignant tumor. Approximately 35–50% of patients experience local recurrence, and 25–50% encounter distant metastasis.
5. The 10-year overall survival rate is 70% [12].
6. Larger tumor size (greater than 10 cm), increased mitotic activity (greater than 2 per 10 hpf), high cellularity, and anaplasia or rhabdoid features are associated with more aggressive behavior.
7. Extraskeletal myxoid chondrosarcoma is treated with wide excision and possible adjuvant radiation therapy [70].

12.15 Undifferentiated High-Grade Pleomorphic Sarcoma

Previously designated as "malignant fibrous histiocytoma (MFH)," undifferentiated high-grade pleomorphic sarcoma is common among soft tissue malignancies. This classification likely encompasses multiple entities in which the current lack of specific morphologic, immunohistochemical, or genetic findings precludes a more definitive diagnosis. They often arise in older adults as a large painless mass in the thigh or upper extremity.

Pathology
Microscopically, these tumors demonstrate a wide range of appearances. Highly pleomorphic cells are arranged in varying patterns with numerous mitoses and areas of necrosis (Figs. 12.27 and 12.28). Bizarre giant cells, background myxoid stroma, or inflammation can be present.

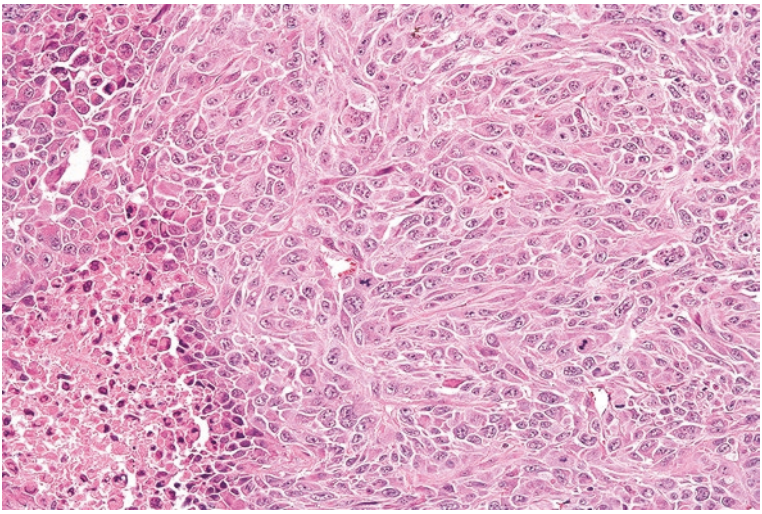

Fig. 12.27 Undifferentiated high-grade pleomorphic sarcoma with sheets of poorly differentiated cells

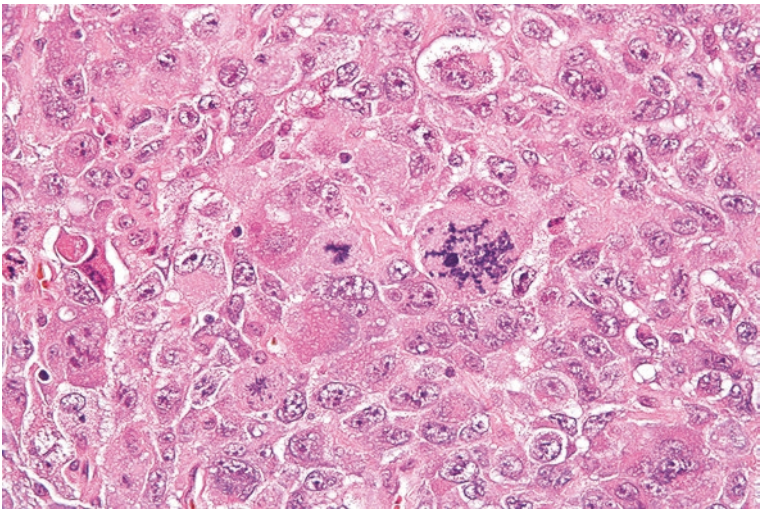

Fig. 12.28 Undifferentiated high-grade pleomorphic sarcoma with bizarre-appearing tumor cells with both epithelioid and spindled appearances

Ancillary Studies

- By definition, these tumors do not have a defining immunohistochemical or genetic finding which allows for classification as another soft tissue neoplasm.

Differential Diagnosis

- Dedifferentiated liposarcoma
- Pleomorphic leiomyosarcoma or rhabdomyosarcoma
- Pleomorphic liposarcoma
- High-grade myxofibrosarcoma
- Poorly differentiated carcinoma
- Anaplastic lymphoma
- Melanoma

Comment

1. Undifferentiated high-grade pleomorphic sarcoma must be distinguished from other tumors that have bizarre tumor cells, such as melanoma, carcinoma, or lymphoma.
2. In the retroperitoneum, dedifferentiated liposarcoma can mimic an undifferentiated high-grade pleomorphic sarcoma. However, undifferentiated high-grade pleomorphic sarcoma lacks the *MDM2* gene amplification found in dedifferentiated liposarcoma.
3. The lack of myogenic staining (e.g. desmin) helps exclude pleomorphic myogenic tumors.
4. Pleomorphic liposarcoma can be excluded by the lack of lipoblasts.
5. Over a 5-year period, a third of undifferentiated high-grade pleomorphic sarcomas will recur or metastasize.
6. Given the aggressive nature of these tumors, wide excision with adjuvant radiation therapy is administered.
7. The 5-year event-free survival is approximately 70% [71].

References

1. Enzinger FM. Intramuscular myxoma; a review and follow-up study of 34 cases. Am J Clin Pathol. 1965;43:104–13.
2. Kindblom LG, Stener B, Angervall L. Intramuscular myxoma. Cancer. 1974;34(5):1737–44.
3. Zoccali C, Teori G, Prencipe U, Erba F. Mazabraud's syndrome: a new case and review of the literature. Int Orthop. 2009;33(3):605–10.
4. Nielsen GP, O'Connell JX, Rosenberg AE. Intramuscular myxoma: a clinicopathologic study of 51 cases with emphasis on hypercellular and hypervascular variants. Am J Surg Pathol. 1998;22(10):1222–7.
5. Delaney D, Diss TC, Presneau N, Hing S, Berisha F, Idowu BD, et al. GNAS1 mutations occur more commonly than previously thought in intramuscular myxoma. Mod Pathol. 2009;22(5):718–24.
6. Calonje E, Guerin D, McCormick D, Fletcher CD. Superficial angiomyxoma: clinicopathologic analysis of a series of distinctive but poorly recognized cutaneous tumors with tendency for recurrence. Am J Surg Pathol. 1999;23(8):910–7.
7. Allen PW, Dymock RB, MacCormac LB. Superficial angiomyxomas with and without epithelial components. Report of 30 tumors in 28 patients. Am J Surg Pathol. 1988;12(7):519–30.

8. Ferreiro JA, Carney JA. Myxomas of the external ear and their significance. Am J Surg Pathol. 1994;18(3):274–80.
9. Goldblum J, Weiss S, Folpe AL, editors. Enzinger and Weiss's soft tissue tumors. 6th ed. Philadelphia: Elsevier; 2013.
10. Browne TJ, Fletcher CD. Haemosiderotic fibrolipomatous tumour (so-called haemosiderotic fibrohistiocytic lipomatous tumour): analysis of 13 new cases in support of a distinct entity. Histopathology. 2006;48(4):453–61.
11. Kazakov DV, Sima R, Michal M. Hemosiderotic fibrohistiocytic lipomatous lesion: clinical correlation with venous stasis. Virchows Arch. 2005;447(1):103–6.
12. Hornick JL, editor. Practical soft tissue pathology: a diagnostic approach. Philadelphia: Saunders; 2013.
13. Antonescu CR, Zhang L, Nielsen GP, Rosenberg AE, Dal Cin P, Fletcher CD. Consistent t(1;10) with rearrangements of TGFBR3 and MGEA5 in both myxoinflammatory fibroblastic sarcoma and hemosiderotic fibrolipomatous tumor. Genes Chromosom Cancer. 2011;50(10):757–64.
14. Carter JM, Sukov WR, Montgomery E, Goldblum JR, Billings SD, Fritchie KJ, et al. TGFBR3 and MGEA5 rearrangements in pleomorphic hyalinizing angiectatic tumors and the spectrum of related neoplasms. Am J Surg Pathol. 2014;38(9):1182–992.
15. Marshall-Taylor C, Fanburg-Smith JC. Hemosiderotic fibrohistiocytic lipomatous lesion: ten cases of a previously undescribed fatty lesion of the foot/ankle. Mod Pathol. 2000;13(11):1192–9.
16. Kilpatrick SE, Hitchcock MG, Kraus MD, Calonje E, Fletcher CD. Mixed tumors and myoepitheliomas of soft tissue: a clinicopathologic study of 19 cases with a unifying concept. Am J Surg Pathol. 1997;21(1):13–22.
17. Hornick JL, Fletcher CDM. Myoepithelial tumors of soft tissue: a clinicopathologic and immunohistochemical study of 101 cases with evaluation of prognostic parameters. Am J Surg Pathol. 2003;27(9):1183–96.
18. Hornick JL, Fletcher CDM. Cutaneous myoepithelioma: a clinicopathologic and immunohistochemical study of 14 cases. Hum Pathol. 2004;35(1):14–24.
19. Antonescu CR, Zhang L, Chang NE, Pawel BR, Travis W, Katabi N, et al. EWSR1-POU5F1 fusion in soft tissue myoepithelial tumors. A molecular analysis of sixty-six cases, including soft tissue, bone, and visceral lesions, showing common involvement of the EWSR1 gene. Genes Chromosom Cancer. 2010;49(12):1114–24.
20. Enzinger FM, Weiss SW, Liang CY. Ossifying fibromyxoid tumor of soft parts. A clinicopathological analysis of 59 cases. Am J Surg Pathol. 1989;13(10):817–27.
21. Graham RP, Dry S, Li X, Binder S, Bahrami A, Raimondi SC, et al. Ossifying fibromyxoid tumor of soft parts: a clinicopathologic, proteomic, and genomic study. Am J Surg Pathol. 2011;35(11):1615–25.
22. Gebre-Medhin S, Nord KH, Moller E, Mandahl N, Magnusson L, Nilsson J, et al. Recurrent rearrangement of the PHF1 gene in ossifying fibromyxoid tumors. Am J Pathol. 2012;181(3):1069–77.
23. Folpe AL, Weiss SW. Ossifying fibromyxoid tumor of soft parts: a clinicopathologic study of 70 cases with emphasis on atypical and malignant variants. Am J Surg Pathol. 2003;27(4):421–31.
24. Lieberman PH, Brennan MF, Kimmel M, Erlandson RA, Garin-Chesa P, Flehinger BY. Alveolar soft-part sarcoma. A clinico-pathologic study of half a century. Cancer. 1989;63(1):1–13.
25. Fanburg-Smith JC, Miettinen M, Folpe AL, Weiss SW, Childers EL. Lingual alveolar soft part sarcoma; 14 cases: novel clinical and morphological observations. Histopathology. 2004;45(5):526–37.
26. Tsuji K, Ishikawa Y, Imamura T. Technique for differentiating alveolar soft part sarcoma from other tumors in paraffin-embedded tissue: comparison of immunohistochemistry for TFE3 and CD147 and of reverse transcription polymerase chain reaction for ASPSCR1-TFE3 fusion transcript. Hum Pathol. 2012;43(3):356–63.
27. Portera Jr CA, Ho V, Patel SR, Hunt KK, Feig BW, Respondek PM, et al. Alveolar soft part sarcoma: clinical course and patterns of metastasis in 70 patients treated at a single institution. Cancer. 2001;91(3):585–91.

28. Ferrari A, Casanova M, Bisogno G, Mattke A, Meazza C, Gandola L, et al. Clear cell sarcoma of tendons and aponeuroses in pediatric patients: a report from the Italian and German Soft Tissue Sarcoma Cooperative Group. Cancer. 2002;94(12):3269–76.
29. Lucas DR, Nascimento AG, Sim FH. Clear cell sarcoma of soft tissues. Mayo Clinic experience with 35 cases. Am J Surg Pathol. 1992;16(12):1197–204.
30. Hisaoka M, Ishida T, Kuo TT, Matsuyama A, Imamura T, Nishida K, et al. Clear cell sarcoma of soft tissue: a clinicopathologic, immunohistochemical, and molecular analysis of 33 cases. Am J Surg Pathol. 2008;32(3):452–60.
31. Antonescu CR, Tschernyavsky SJ, Woodruff JM, Jungbluth AA, Brennan MF, Ladanyi M. Molecular diagnosis of clear cell sarcoma: detection of EWS-ATF1 and MITF-M transcripts and histopathological and ultrastructural analysis of 12 cases. J Mol Diagn. 2002;4(1):44–52.
32. Wang WL, Mayordomo E, Zhang W, Hernandez VS, Tuvin D, Garcia L, et al. Detection and characterization of EWSR1/ATF1 and EWSR1/CREB1 chimeric transcripts in clear cell sarcoma (melanoma of soft parts). Mod Pathol. 2009;22(9):1201–9.
33. Rud NP, Reiman HM, Pritchard DJ, Frassica FJ, Smithson WA. Extraosseous Ewing's sarcoma. A study of 42 cases. Cancer. 1989;64(7):1548–53.
34. Fletcher CDM, Bridge JA, Hogendoorn PC, Mertens F, editors. Pathology and genetics of tumours of soft tissue and bone. 4th ed. Lyon: World Health Organization; 2013.
35. Khoury JD. Ewing sarcoma family of tumors. Adv Anat Pathol. 2005;12(4):212–20.
36. Goldblum JR, Folpe AL, Weiss SW, editors. Enzinger and Weiss's soft tissue tumors. 6th ed. Philadelphia: Saunders; 2013.
37. Devoe K, Weidner N. Immunohistochemistry of small round-cell tumors. Semin Diagn Pathol. 2000;17(3):216–24.
38. Shing DC, McMullan DJ, Roberts P, Smith K, Chin SF, Nicholson J, et al. FUS/ERG gene fusions in Ewing's tumors. Cancer Res. 2003;63(15):4568–76.
39. Balamuth NJ, Womer RB. Ewing's sarcoma. Lancet Oncol. 2010;11(2):184–92.
40. Gerald WL, Ladanyi M, de Alava E, Cuatrecasas M, Kushner BH, LaQuaglia MP, et al. Clinical, pathologic, and molecular spectrum of tumors associated with t(11;22)(p13;q12): desmoplastic small round-cell tumor and its variants. J Clin Oncol. 1998;16(9):3028–36.
41. Lae ME, Roche PC, Jin L, Lloyd RV, Nascimento AG. Desmoplastic small round cell tumor: a clinicopathologic, immunohistochemical, and molecular study of 32 tumors. Am J Surg Pathol. 2002;26(7):823–35.
42. Ladanyi M, Gerald W. Fusion of the EWS and WT1 genes in the desmoplastic small round cell tumor. Cancer Res. 1994;54(11):2837–40.
43. Ordonez NG. Desmoplastic small round cell tumor: I: a histopathologic study of 39 cases with emphasis on unusual histological patterns. Am J Surg Pathol. 1998;22(11):1303–13.
44. Hayes-Jordan A, Anderson PM. The diagnosis and management of desmoplastic small round cell tumor: a review. Curr Opin Oncol. 2011;23(4):385–9.
45. Folpe AL, Mentzel T, Lehr HA, Fisher C, Balzer BL, Weiss SW. Perivascular epithelioid cell neoplasms of soft tissue and gynecologic origin: a clinicopathologic study of 26 cases and review of the literature. Am J Surg Pathol. 2005;29(12):1558–75.
46. Martignoni G, Pea M, Reghellin D, Zamboni G, Bonetti F. PEComas: the past, the present and the future. Virchows Arch. 2008;452(2):119–32.
47. Eble JN. Angiomyolipoma of kidney. Semin Diagn Pathol. 1998;15(1):21–40.
48. Taylor JR, Ryu J, Colby TV, Raffin TA. Lymphangioleiomyomatosis. Clinical course in 32 patients. N Engl J Med. 1990;323(18):1254–60.
49. Wagner AJ, Malinowska-Kolodziej I, Morgan JA, Qin W, Fletcher CD, Vena N, et al. Clinical activity of mTOR inhibition with sirolimus in malignant perivascular epithelioid cell tumors: targeting the pathogenic activation of mTORC1 in tumors. J Clin Oncol. 2010;28(5):835–40.
50. Enzinger FM. Epitheloid sarcoma. A sarcoma simulating a granuloma or a carcinoma. Cancer. 1970;26(5):1029–41.
51. Chbani L, Guillou L, Terrier P, Decouvelaere AV, Gregoire F, Terrier-Lacombe MJ, et al. Epithelioid sarcoma: a clinicopathologic and immunohistochemical analysis of 106 cases from the French sarcoma group. Am J Clin Pathol. 2009;131(2):222–7.

52. Guillou L, Wadden C, Coindre JM, Krausz T, Fletcher CD. "Proximal-type" epithelioid sarcoma, a distinctive aggressive neoplasm showing rhabdoid features. Clinicopathologic, immunohistochemical, and ultrastructural study of a series. Am J Surg Pathol. 1997;21(2):130–46.
53. Miettinen M, Fanburg-Smith JC, Virolainen M, Shmookler BM, Fetsch JF. Epithelioid sarcoma: an immunohistochemical analysis of 112 classical and variant cases and a discussion of the differential diagnosis. Hum Pathol. 1999;30(8):934–42.
54. Chase DR, Enzinger FM. Epithelioid sarcoma. Diagnosis, prognostic indicators, and treatment. Am J Surg Pathol. 1985;9(4):241–63.
55. Weeks DA, Beckwith JB, Mierau GW, Luckey DW. Rhabdoid tumor of kidney. A report of 111 cases from the National Wilms' Tumor Study Pathology Center. Am J Surg Pathol. 1989;13(6):439–58.
56. Fanburg-Smith JC, Hengge M, Hengge UR, Smith Jr JS, Miettinen M. Extrarenal rhabdoid tumors of soft tissue: a clinicopathologic and immunohistochemical study of 18 cases. Ann Diagn Pathol. 1998;2(6):351–62.
57. Roberts CW. Genetic causes of familial risk in rhabdoid tumors. Pediatr Blood Cancer. 2006;47(3):235–7.
58. Sigauke E, Rakheja D, Maddox DL, Hladik CL, White CL, Timmons CF, et al. Absence of expression of SMARCB1/INI1 in malignant rhabdoid tumors of the central nervous system, kidneys and soft tissue: an immunohistochemical study with implications for diagnosis. Mod Pathol. 2006;19(5):717–25.
59. Ladanyi M, Antonescu CR, Leung DH, Woodruff JM, Kawai A, Healey JH, et al. Impact of SYT-SSX fusion type on the clinical behavior of synovial sarcoma: a multi-institutional retrospective study of 243 patients. Cancer Res. 2002;62(1):135–40.
60. Fisher C. Synovial sarcoma. Ann Diagn Pathol. 1998;2(6):401–21.
61. Ferrari A, Gronchi A, Casanova M, Meazza C, Gandola L, Collini P, et al. Synovial sarcoma: a retrospective analysis of 271 patients of all ages treated at a single institution. Cancer. 2004;101(3):627–34.
62. Smith TA, Machen SK, Fisher C, Goldblum JR. Usefulness of cytokeratin subsets for distinguishing monophasic synovial sarcoma from malignant peripheral nerve sheath tumor. Am J Clin Pathol. 1999;112(5):641–8.
63. Foo WC, Cruise MW, Wick MR, Hornick JL. Immunohistochemical staining for TLE1 distinguishes synovial sarcoma from histologic mimics. Am J Clin Pathol. 2011;135(6):839–44.
64. Brodin B, Haslam K, Yang K, Bartolazzi A, Xie Y, Starborg M, et al. Cloning and characterization of spliced fusion transcript variants of synovial sarcoma: SYT/SSX4, SYT/SSX4v, and SYT/SSX2v. Possible regulatory role of the fusion gene product in wild type SYT expression. Gene. 2001;268(1–2):173–82.
65. Palmerini E, Staals EL, Alberghini M, Zanella L, Ferrari C, Benassi MS, et al. Synovial sarcoma: retrospective analysis of 250 patients treated at a single institution. Cancer. 2009;115(13):2988–98.
66. Bergh P, Meis-Kindblom JM, Gherlinzoni F, Berlin O, Bacchini P, Bertoni F, et al. Synovial sarcoma: identification of low and high risk groups. Cancer. 1999;85(12):2596–607.
67. Meis-Kindblom JM, Bergh P, Gunterberg B, Kindblom L. Extraskeletal myxoid chondrosarcoma: a reappraisal of its morphologic spectrum and prognostic factors based on 117 cases. Am J Surg Pathol. 1999;23(6):636–50.
68. Enzinger FM, Shiraki M. Extraskeletal myxoid chondrosarcoma. An analysis of 34 cases. Hum Pathol. 1972;3(3):421–35.
69. Stenman G, Andersson H, Mandahl N, Meis-Kindblom JM, Kindblom LG. Translocation t(9;22)(q22;q12) is a primary cytogenetic abnormality in extraskeletal myxoid chondrosarcoma. Int J Cancer. 1995;62(4):398–402.
70. Oliveira AM, Sebo TJ, McGrory JE, Gaffey TA, Rock MG, Nascimento AG. Extraskeletal myxoid chondrosarcoma: a clinicopathologic, immunohistochemical, and ploidy analysis of 23 cases. Mod Pathol. 2000;13(8):900–8.
71. Le Doussal V, Coindre JM, Leroux A, Hacene K, Terrier P, Bui NB, et al. Prognostic factors for patients with localized primary malignant fibrous histiocytoma: a multicenter study of 216 patients with multivariate analysis. Cancer. 1996;77(9):1823–30.