Fibrous/Myofibroblastic Proliferations of the Vulva

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Introduction

Fibrous and myofibroblastic vulvar proliferations are some of the most common mesenchymal tumors of the vulva (Table 13.1). They are usually benign and composed of spindle and stellate-shaped cells with a stroma that contains collagen and a supportive vascular tree. Many of these tumors tend to be restricted to the lower gynecological anatomic region and are less frequently identified in analogous regions in men. As they are uncommon and have distinctive and often overlapping features, their accurate diagnosis can be challenging to the surgical pathologist. Ancillary studies such as immunohistochemistry may be helpful in their recognition; however, they are usually not pathognomonic because of similar antigen expression profiles by fibroblasts and myofibroblasts. Accordingly, morphology is the mainstay for diagnosis.

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Fibroepithelial Stromal Polyp

Clinical Features

Fibroepithelial stromal polyps often present as an incidental lesions that arise in the vulvovaginal region. Clinically, they may produce a mass sensation, bleeding, or discharge [1, 2].

They occur in premenopausal women and are hormone related; therefore, their development in postmenopausal women has been shown to be associated with hormone replacement therapy [3, 4]. The lesions are pedunculated, variable in size, and usually do not exceed 5 cm; rare examples of tumors as large as 20 cm have been described [5]. Fibroepithelial polyps are usually solitary lesions; however, multiple lesions can be seen during pregnancy [6, 7]. Treatment is simple excision and the risk of local recurrence is very low.

Histopathology

The gross appearance is that of a flesh-colored soft solid mass that is covered by squamous mucosa or skin (Fig. 13.1). The lesion has a fibrovascular core that contains spindled fibroblasts and scattered multinucleated stellate stromal cells that are often distributed close to the overlying epithelium without a grenz zone (Figs. 13.2 and 13.3). The stroma is usually hypocellular and edematous, but there can be areas of hypercellularity and limited nuclear pleomorphism. Importantly, a minority of

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Table 13.1 Fibrous/myofibroblastic lesions

	Age	Location	Clinical presentation	Gross	Microscopic features	Ancillary tests
Fibroepithelial stromal polyp	Reproductive age	Vulvovaginal region	Single mass Multiple in pregnancy	Flesh-colored mass covered with skin	Fibrous tissue and blood vessels Scattered multinucleated giant cells	Positive immunohistochemistry for desmin, ER, PR
Massive vulvar edema	Mean age: 46.5	Vulva, penis or scrotum	Usually in morbidly obese generalized genital enlargement present from 6 months to 6 years	Massive pedunculated masses	Edematous fibrous tissue with dilated lymphatics Verrucous hyperplasia or papillomatosis of epidermis	
Prepubertal vulvar fibroma	Prepubertal	Labia majora	Unilateral submucosal or subcutaneous mass	Tan-gray and ill delineated	Hypocellular fibrous tissue with bland fibroblast Thick and wavy collagen fibers in stroma	Positive immunohistochemistry for CD34
Cellular angiofibroma	Mean age: 54	Labia majora and perineal region	Small, painless mass in the superficial soft tissues	Yellow to white firm mass	Well-circumscribed hypercellular spindle cell lesion Hyalinized branching blood vessels	Positive immunohistochemistry for CD34, ER, PR
Angiomyofibroblastoma	Middle-aged women	Vulvovaginal region/labia majora	Painful mass that is usually misdiagnosed as Bartholin gland cyst or inguinal hernia	Gray to white, soft to rubbery, well-circumscribed mass	Well demarcated with hypo- and hypercellular areas Wavy collagen fibers with spindle or stellate neoplastic cells	Positive immunohistochemistry for desmin
Aggressive angiomyxoma	Mean age: 40	Pelvis, perineum or vulva	Large asymptomatic lesion sometimes confused with a lipoma or leiomyoma	Tan-gray with rubbery consistence and gelatinous cut surface	Paucicellular tumor with myxoid stroma Bland spindle and stellate cells Medium-sized blood vessels	Positive immunohistochemistry for desmin, SMA, ER, PR, and HMGIC t(8;12) (p12:q15)
Superficial myofibroblastoma	Three to nine decades	Vulvovaginal region	Solitary nodular lesion<3 cm	Tan-pink to white firm lesion covered by vulvar skin	Vague fascicles with lacelike collagen fibers Bland spindle to ovoid cells	Positive immunohistochemistry for desmin, CD34, CD99 Variable ER, PR
Reactive fibroblastic and myofibroblastic proliferation of the vulva	55	Labia majora	Painful nodule perineal nodule exacerbated with physical activity (cycling, horseback riding)	Firm and fibrous with overlying skin	Adipose tissue with mildly cellular hyalinized stroma Haphazardly arranged vessels and nerves	Positive immunohistochemistry for ER, SMA
Postoperative spindle cell nodule	Middle age	Lower genitourinary tract	Three to seven weeks after a surgical procedure	Poorly defined polypoid nodule with reddish-gray appearance	Plump spindle cells in intersecting fascicles Numerous mitosis	Positive immunohistochemistry for SMA, focally desmin Trisomy 7

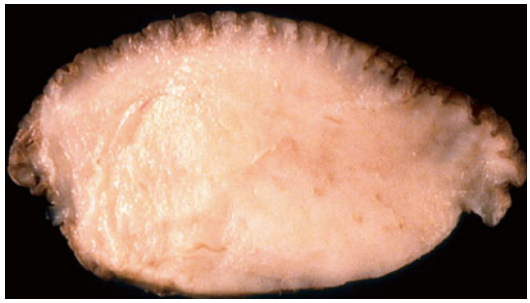

Fig. 13.1 Fibroepithelial polyp is solid, unencapsulated, and tan-white

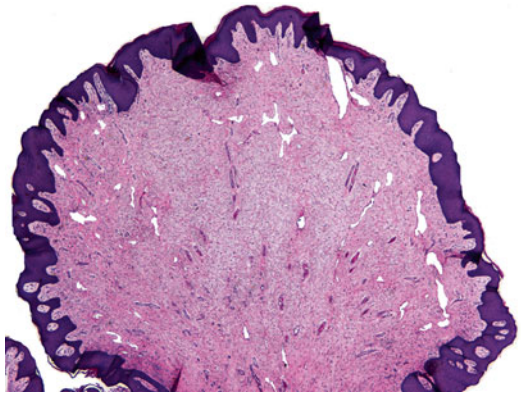

Fig. 13.2 Core of fibroepithelial polyp is composed of fibrous tissue and blood vessels

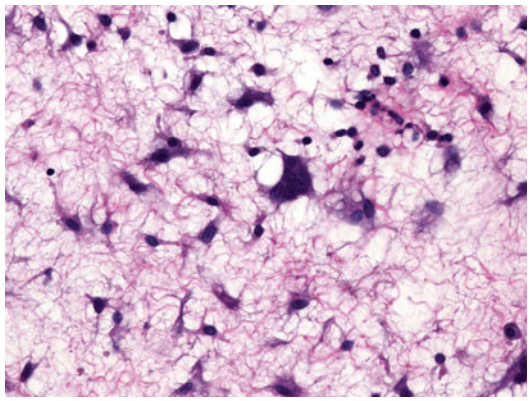

Fig. 13.3 The fibroepithelial polyp contains scattered multinucleated giant cells

polyps during pregnancy may show increased stromal cellularity, nuclear atypia, and numerous mitotic figures (Fig. 13.4) [8]. The overlying epithelium may demonstrate varying degrees of hyperplasia [4, 9, 10]. The stromal cells are often

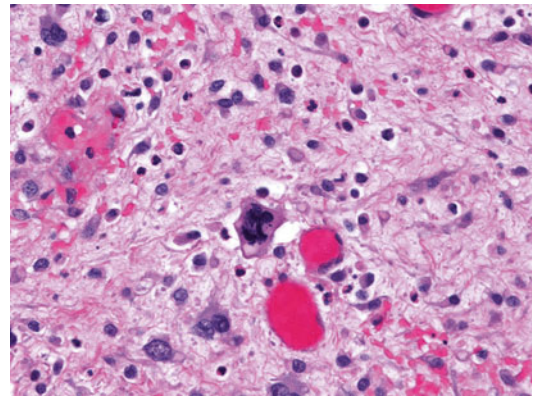

Fig. 13.4 Pseudosarcomatous fibroepithelial polyp is hypercellular and contains cells with enlarged pleomorphic nuclei that are mitotically active

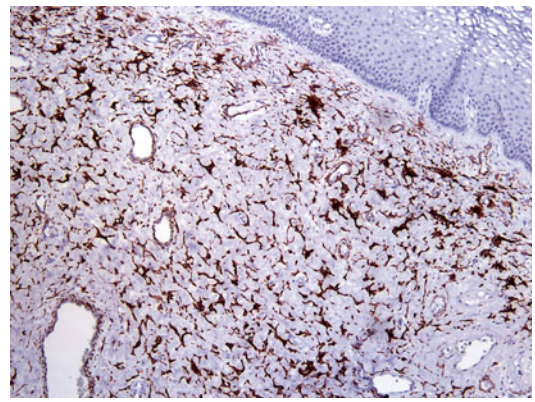

Fig. 13.5 The spindle and stellate cells of fibroepithelial polyps express desmin

positive for desmin, estrogen receptor (ER), and progesterone receptor (PR), and in some cases they express CD34 and smooth muscle actin (SMA) (Fig. 13.5). The lesional cells are negative for keratin, S100, myogenin, and MyoD-1 [8].

Differential Diagnosis

The degree of hypercellularity and nuclear pleomorphism may mimic a malignant process, particularly embryonal rhabdomyosarcoma, and this explains why some lesions have been termed pseudosarcoma botryoides. In distinction from the botryoides variant of rhabdomyosarcoma, a cellular fibroepithelial polyp does

not have a distinct cambium layer, nor does it demonstrate skeletal muscle differentiation by light microscopy or immunohistochemically [3]. (See Vignette 3 at the end of this chapter) The epithelial hyperplasia and fingerlike projections can mimic a condyloma acuminatum. The absence of viral changes such as koilocytes supports the diagnosis of fibroepithelial stromal polyp rather than human papillomavirus (HPV)-derived infection.

The tip of deep-seated aggressive angiomyxoma may present as a polypoid mass; however, it can be distinguished from fibroepithelial stromal polyp by virtue of its infiltrative growth pattern, deep location, presence of a prominent undulating vascular tree, and the hypocellular and myxoid nature of the tumor.

Summary

Clinical Presentation

- Present in premenopausal women
- Hormone related
- Single mass, may be multiple in pregnancy

Histopathologic Features

- Solid, unencapsulated, and tan-white.
- Core composed of fibrous tissue and blood vessels.
- Scattered multinucleated giant cells are characteristic.

Differential Diagnosis

- Embryonal rhabdomyosarcoma
- Condyloma acuminatum

Takeaway Essentials

Clinical Relevant Pearls

- Lesions are hormone related and have been associated with hormone replacement therapy.
- Should be considered in the differential diagnosis of vulvar polyps in premenopausal women.

Pathology Interpretation Pearls

- Hypocellular and edematous stroma without a grenz zone, but can be hypercellular and with nuclear pleomorphism in pregnancy.
- Squamous mucosa may demonstrate reactive hyperplasia that should not be confused with squamous cell carcinoma or viral changes.

Massive Vulvar Edema

Clinical Features

The lesion presents as enlargement of the vulva, most often bilateral, that may be massive and appear as confluent verrucous lesions. It usually affects morbidly obese individuals, and some patients may have a history of immobility, pregnancy, and hypothyroidism [11–13]. The mean age at presentation is 46.5 years [14]. The enlargement is slowly progressive and the overlying skin may ulcerate.

Histopathology

Grossly the lesion is tan-gray and poorly defined and ranges from a few to greater than 20 cm in dimension (Fig. 13.6). The epidermis may show verrucous hyperplasia or papillomatosis [14]. The accompanying adipose tissue shows thickening of the connective tissue septae that contain increased amounts of fibroblasts, collagen, myxoid stroma, lymphatics, and small- to medium-sized blood vessels (Figs. 13.7 and 13.8). The fibroblasts are spindle and stellate shaped and contain eosinophilic cytoplasm and nuclei that have fine chromatin. The fat may show foci of necrosis associated with macrophages, and the blood vessels can have a perivascular chronic inflammatory infiltrate.

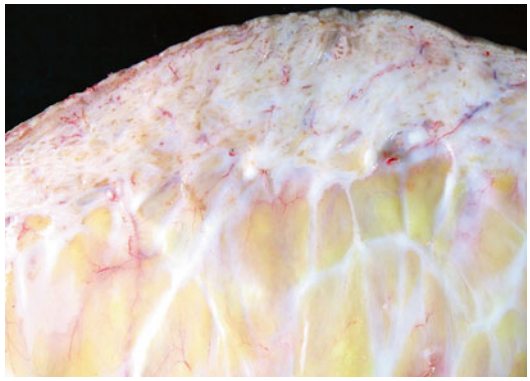

Fig. 13.6 The dermis and fat septae are expanded by *tan-gray* tissue in massive lymphedema

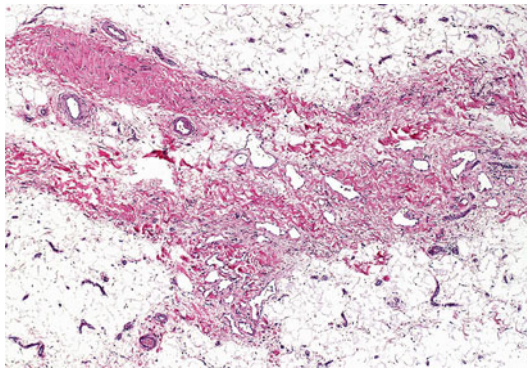

Fig. 13.7 The septae in the fat in massive lymphedema are expanded by edematous fibrous tissue that contains increased numbers of dilated lymphatics

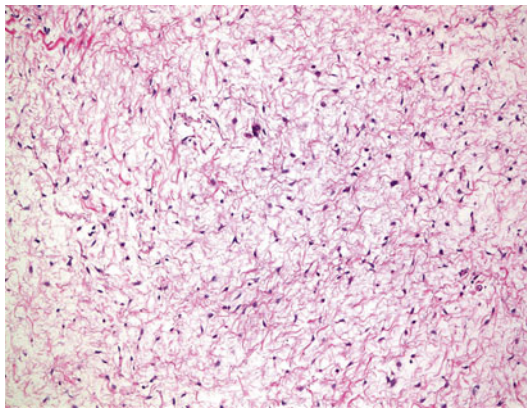

Fig. 13.8 In massive lymph edema, the subcutaneous tissue is replaced by bland fibro-myxoid tissue

Differential Diagnosis

The main lesion in the differential diagnosis is aggressive angiomyxoma. Distinguishing features are the presence of the tortuous and dilated lymphatics present in massive vulvar edema and the absence of broad fibromyxoid tissue. Because of the secondary changes that occur in the fat liposarcoma may be a consideration; however, lipoblasts and cells with enlarged hyperchromatic nuclei characteristic of liposarcoma are absent.

Summary

Clinical Presentation

- Bilateral vulvar enlargement, may be massive
- Slowly progressing, can lead to skin ulceration

Histopathologic Features

- The septae of the subcutis are expanded by fibrous tissue.
- Edematous fibrous tissue contains increased numbers of dilated lymphatics.

Differential Diagnosis

- Aggressive angiomyxoma

Takeaway Essentials

Clinical Relevant Pearls

- Bilateral lesion usually associated with morbid obesity and/or immobility, hyperthyroidism, and pregnancy

Pathology Interpretation Pearls

- Pathologic findings are centered in the subcutis, an unusual location for liposarcoma.
- Dilated lymphatics should not be confused with a primary lymphatic tumor.

Prepubertal Vulvar Fibroma

Clinical Features

The lesion presents as painless progressive swelling that causes enlargement of the labia majora in prepubertal females. It usually appears as a unilateral submucosal or subcutaneous mass with ill-defined borders. Treatment is complete excision as the lesion can recur locally.

Histopathology

Grossly the lesion is tan-gray and poorly delineated from the surrounding tissues. Microscopically, it is hypocellular and composed of scattered spindle cells that are cytologically bland; there is no pleomorphism and mitoses are rare (Fig. 13.9). The stroma consists of collagen fibers that are thick and wavy and contains medium-sized blood vessels (Fig. 13.10). Histologically the lesion is poorly demarcated and infiltrates into the surrounding tissues. The spindle cells are strongly positive for CD34.

Differential Diagnosis

The infiltrative borders and hypocellularity can suggest the possibility of aggressive angiomyxoma; however, the collagenous stroma in aggressive angiomyxoma is composed of delicate fibrils, different from the thick, wavy fibers present in this entity, and the vessels in aggressive angiomyxoma are larger, more numerous, and undulating. Immunohistochemistry can also be helpful in the distinction in that the tumor cells in angiomyxoma express desmin, whereas the cells in prepubertal vulvar fibroma are typically negative for this antigen. Cytogenetics is also useful in separating these tumors from one another; however, the histological and immunohistochemical findings should allow for accurate identification [15].

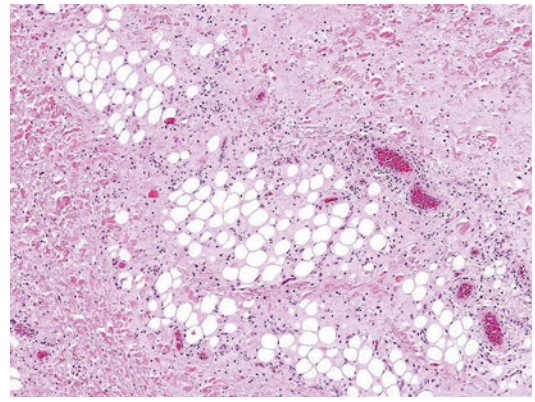

Fig. 13.9 Hypocellular fibrous tissue replacing fat in prepubertal fibroma

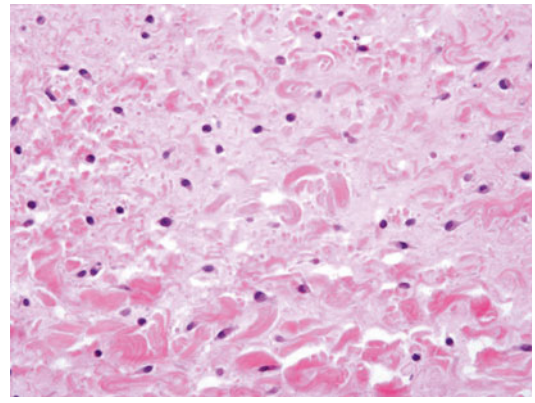

Fig. 13.10 The fibroblasts in prepubertal fibroma have bland nuclei and are associated with varying amounts of collagen

Angiomyofibroblastoma should also be distinguished from prepubertal vulvar fibroma; however, the former is usually well circumscribed and shows a greater degree of cellularity. Additionally, the tumor cells are desmin positive. Fibroepithelial polyps can be included in the differential, as well, but they protrude from the surface and are more cytologically heterogeneous with multinucleation, nuclear pleomorphism, and mitotic activity [16].

Summary

Clinical Presentation

- Occurs in prepubertal females
- Unilateral submucosal or subcutaneous mass in labia majora

Histopathologic Features

- Hypocellular fibrous tissue with bland fibroblasts replacing fat.
- Stroma has thick and wavy collagen fibers.

Differential Diagnosis

- Aggressive angiomyxoma
- Angiomyofibroblastoma
- Fibroepithelial stromal polyp

Takeaway Essentials

Clinical Relevant Pearls

- Mass in labia majora of prepubertal females with painless progressive swelling
- Can cause emotional distress and should be addressed promptly

Pathology Interpretation Pearls

- Bland fibroblasts admixed with variable amounts of thick and wavy collagen are good clues of the benign nature of the lesion.
- Infiltrative growth into the surrounding tissues can cause confusion with more aggressive soft tissue tumors.
- CD34 reactivity can be also seen in vulvar prepubertal fibromas and cellular angiofibroma; however, vulvar fibroma lacks hyalinized vessels and is not well circumscribed.

Cellular Angiofibroma

Clinical Features

The tumor arises in the vulva, particularly the labia majora and perineal regions of women who are middle aged (mean age, 54 years). Cellular angiofibroma is painless, relatively small (mean, 3.7 cm),

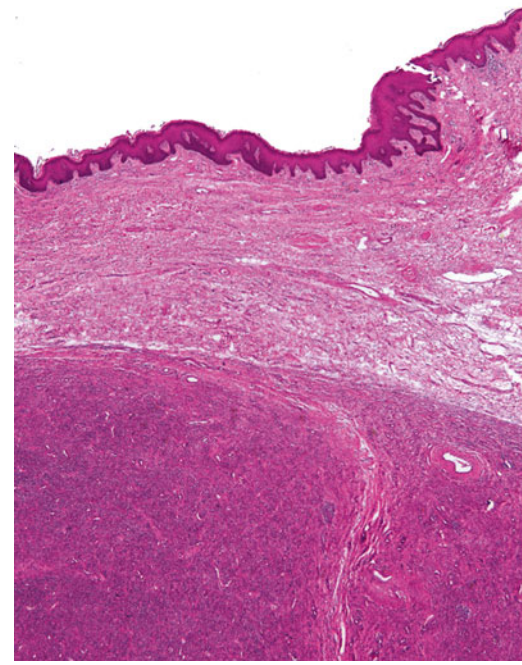

Fig. 13.11 Cellular angiofibroma has well-delineated margins

and sometimes exophytic, that is, well circumscribed, and is centered in the superficial soft tissues [17–19]. Biologically, it is benign, rarely undergoes malignant transformation, and treatment is complete excision; recurrence rates are very low [20]. It harbors a monoallelic deletion of *RB1* and *FOXO1* located on 13q14 that also occurs in spindle cell lipoma and myofibroblastoma, and this finding suggests that these are very closely related to one another [21].

Histopathology

Grossly, cellular angiofibromas are yellow to white firm masses that are sometimes polypoid and infrequently gelatinous or cystic. They tend to be partially encapsulated but can have focally infiltrative borders [21] (Fig. 13.11).

Histologically the tumor is hypercellular and composed of haphazardly arranged spindle cells with fusiform or ovoid bland nuclei and pale indistinct eosinophilic cytoplasm. Interspersed in the tumor there are multiple small- to medium-sized blood vessels that usually have hyalinized

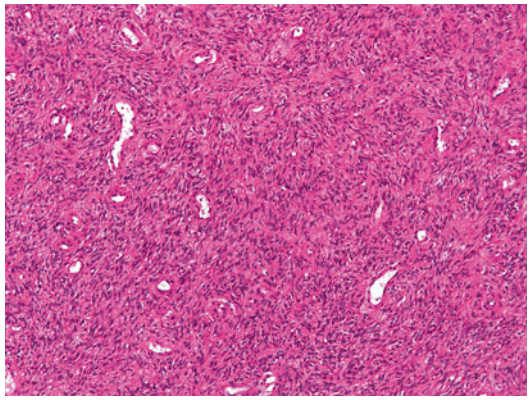

Fig. 13.12 Cellular angiofibroma is hypercellular and contains a staghorn-like vascular tree

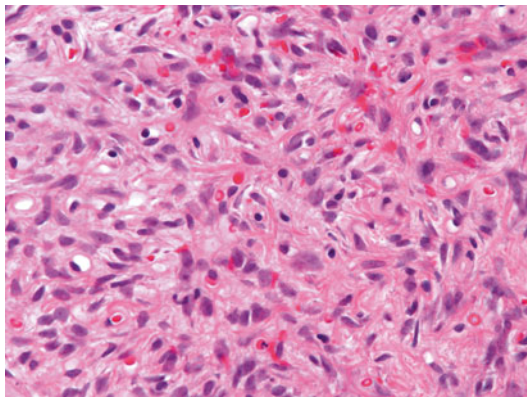

Fig. 13.13 The tumor cells in cellular angiofibroma are spindled with bland nuclei. The stroma contains wirelike bundles of collagen

walls and are arranged in a staghorn-like branching pattern (Fig. 13.12). The stroma contains wirelike collagen fibers, and scattered adipocytes and mast cells may be present (Fig. 13.13). The lesional cells are positive for CD34 and exhibit nuclear positivity staining for estrogen and androgen receptor and are often negative for all smooth muscle markers including SMA, desmin and h-caldesmon [22].

In a minority of cases the tumor may contain scattered cells with enlarged hyperchromatic nuclei that are reminiscent of those in symplastic leiomyoma and ancient schwannoma [19]. The mitotic rate for these tumors is usually low (<1 mitosis per 10 high-power fields). Another very uncommon variant are cellular angiofibromas that have discrete areas of sarcomatous transformation. The sarcomatous component may exhibit the features of pleomorphic liposarcoma, atypical lipomatous tumor, or an undifferentiated pleomorphic spindle cell sarcoma. Immunohistochemistry has shown that the malignant component expresses p16, whereas the benign component is negative for this antigen. Despite the sarcomatous components, the affected patients have done well with no recurrences or metastases [19].

Differential Diagnosis

There are morphological and genetic similarities between cellular angiofibroma, spindle cell lipoma and myofibroblastoma, and these tumors likely represent a family of related lesions [21]. Myofibroblastoma has a fascicular arrangement of the tumor cells in contrast to the haphazard arrangement of cells in angiofibroma. Spindle cell lipoma has characteristic thick ropey collagen fibers that are typically absent in angiofibroma, and it also usually has a more prominent fatty component. Additionally, the hyalinized vessels are distinctive of cellular angiofibroma and not a feature of spindle cell lipoma [21].

Summary

Clinical Presentation

- Arises in labia majora of the vulva and perineum
- Unilateral subcutaneous mass

Histopathologic Features

- Well-circumscribed hypercellular spindle cell lesion with fusiform or ovoid nuclei
- Multiple hyalinized branching blood vessels
- Wirelike collagen fibers in the stroma
- Positive for CD34, nuclear positivity for ER and PR
- Negative for muscle markers

Differential Diagnosis

- Spindle cell lipoma
- Myofibroblastoma

Takeaway Essentials

Clinical Relevant Pearls

- Painless unilateral vulvar and perineal lesion, relatively small
- Monoallelic deletion of *RB1* and *FOXO1* on 13q14-same derangement as spindle cell lipoma and myofibroblastoma

Pathology Interpretation Pearls

- Well-delineated margins support benign nature of the tumor.
- Hypercellularity can cause confusion with more aggressive neoplasms.

Angiomyofibroblastoma

Clinical Features

This is an uncommon lesion that arises in the vulvovaginal area of middle-aged women, particularly in the labia majora [23]. It is often misdiagnosed clinically as a Bartholin gland cyst or inguinal hernia. Sometimes it presents as a pedunculated or painful mass. The treatment of choice is complete excision and local recurrence is infrequent [17, 18].

Histopathology

Angiomyofibroblastoma is a well-circumscribed tumor that has a soft to rubbery and gray-white to yellowish appearance (Fig. 13.14). Sometimes it can be shiny and gelatinous and rarely is cystic and hemorrhagic. They are usually small as they are usually less than 5 cm in greatest dimension.

Microscopically, angiomyofibroblastoma is well demarcated and has hypo- and hypercellular areas (Fig. 13.15). The stroma is edematous and contains wavy collagen fibers. The neoplastic cells are variable in appearance with spindle, stellate, plasmacytoid, or epithelioid shapes. They are randomly arranged and can be isolated or oriented in cords or nests around small- to medium-sized blood vessels (Figs. 13.16 and 13.17).

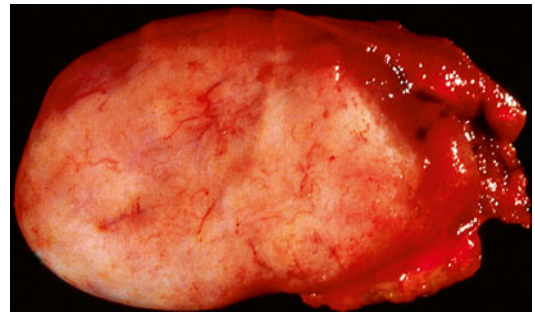

Fig. 13.14 Angiomyofibroblastoma is *tan*, *pale yellow* and well circumscribed

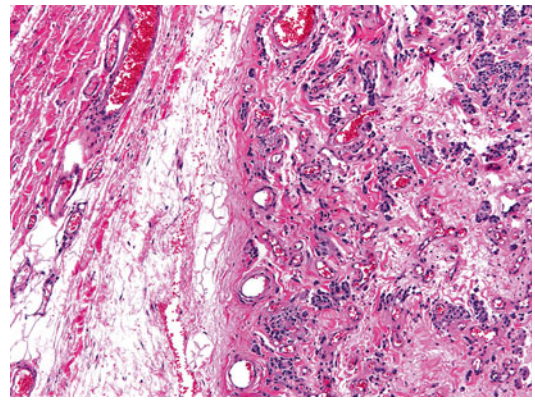

Fig. 13.15 Angiomyofibroblastoma has well-demarcated margins from the adjacent soft tissue

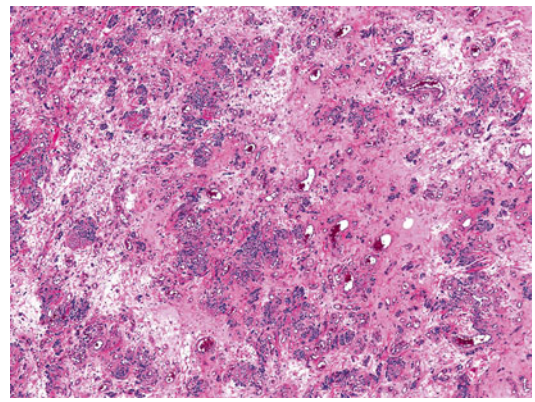

Fig. 13.16 Angiomyofibroblastoma contains scattered blood vessels with tumor cells growing in cords around blood vessels

Mitotic activity is limited (0–7 mitoses per 50 high-power fields). Adipocytes may be scattered throughout the mass. Immunohistochemically, the cells express desmin and are typically

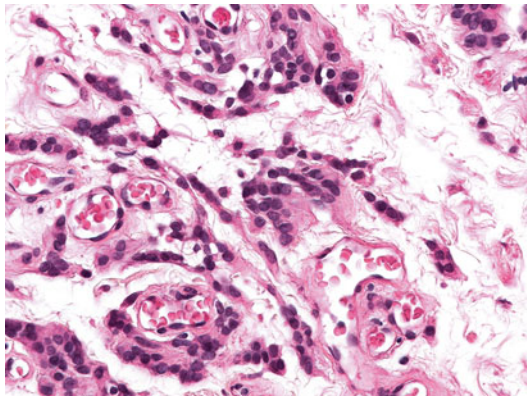

Fig. 13.17 The tumor cells in angiomyofibroblastoma have round bland nuclei and eosinophilic cytoplasm

negative for CD34 [17, 23, 24]. Extremely rare examples have been reported in which a typical angiomyofibroblastoma merged with sarcomatous areas that have the appearance of myxofibrosarcoma [23].

Differential Diagnosis

Aggressive angiomyxoma is an entity that should be considered in the differential diagnosis, as both contain spindle cells that are desmin positive. However, aggressive angiomyxoma is infiltrative, has larger undulating vessels, and lacks the hypercellularity [25].

Summary

Clinical Presentation

- Vulvovaginal lesion of middle-aged women
- Presents as painful mass

Histopathologic Features

- Well-demarcated lesion with hypo- and hypercellular areas
- Edematous stroma with wavy collagen
- Positive for desmin and negative for CD34

Differential Diagnosis

- Aggressive angiomyxoma

Takeaway Essentials

Clinical Relevant Pearls

- Painful mass that can be mistaken for a Bartholin gland cyst

Pathology Interpretation Pearls

- Clear demarcation from the surrounding tissue
- Tumor cells growing in cords around scattered blood vessels

Aggressive Angiomyxoma

Clinical Features

Aggressive angiomyxoma is a locally aggressive neoplasm that arises in the pelvis, perineum, or vulva region of middle-aged women (mean age, 40 years) and rarely in older men (mean age, 50–60) [26–29] (Fig. 13.18). The tumors can be asymptomatic but tend to be large (>10 cm) and are clinically confused with a Bartholin cyst, vaginal cyst, leiomyoma, or lipoma [30, 31]. This attests to the fact that their true size is often underestimated by clinical examination alone. Treatment is a wide (1 cm margin) excision; however, this may be difficult to attain which explains why the local recurrence rate is as high as 47 % [32, 33]. Rare cases of metastases have been reported [34]. Molecular analyses of a limited number of cases have revealed structural abnormalities of 12q13–15 that result in aberrant expression of the *HMGA2* gene. The structural aberrations include t(8;12)(p12;q15), and the expression of *HMGA2* can be detected by immunohistochemistry and used as a marker of microscopic residual disease [35]. Expression of HMGA2 is not limited to aggressive angiomyxoma as it is also present in other benign mesenchymal neoplasms including lipomas, leiomyomas, and pulmonary hamartomas [15, 36, 37].

Histopathology

The neoplasm is grossly circumscribed but histologically has infiltrative margins and invades the surrounding soft tissues. It is tan-gray to pink in

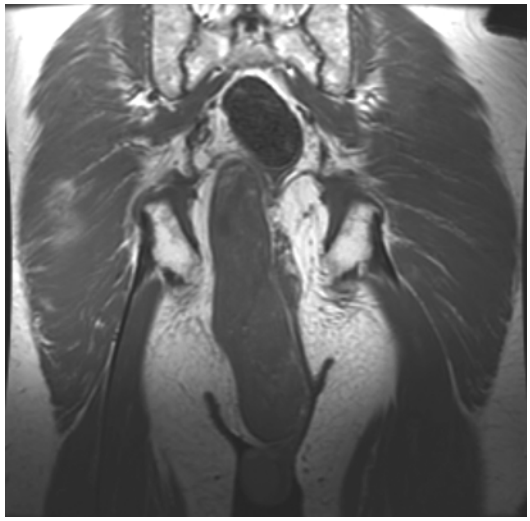

Fig. 13.18 Coronal T1-weighted MR of aggressive angiomyxoma shows a vertically oriented oblong dark mass in the pelvis

appearance, has a rubbery consistency, and has a gelatinous cut surface with foci of hemorrhage [27] (Fig. 13.19). Histologically, the tumor is paucicellular with the tumor cells enmeshed in a pale myxoid stroma that contains haphazardly arranged, linear, medium- to large-sized blood vessels that may have hyalinized walls (Fig. 13.20). The tumor cells are round to spindle and stellate with bland nuclei and ill-defined eosinophilic cytoplasm (Figs. 13.21 and 13.22). Delicate collagen fibrils and smooth muscle cells are associated with the blood vessels [8]. Immunohistochemically, the tumor cells express desmin, smooth muscle actin, and estrogen and progesterone receptors [31, 38].

Differential Diagnosis

Tumors that can be confused with aggressive angiomyxoma include angiomyofibroblastoma, superficial angiomyxoma, fibroepithelial stromal polyp, and fibromatosis. Findings supporting aggressive angiomyxoma are the classic infiltrative borders, involvement of deep tissues, paucicellularity, and the distinctive vasculature [32]. Fibromatosis can be deep seated, large, and infiltrative; however, the uniform neoplastic fibroblasts are arranged in broad sweeping fascicles, and the tumor does not contain the large blood vessels characteristic of aggressive angiomyxoma. (See Vignette 1 at the end of this chapter.) Superficial angiomyxoma may involve the vulva and attain a large size. However, this lesion is limited to the superficial soft tissues; the stroma is more myxoid and lacks large blood vessels, and the tumor cells do not express ER, PR, and desmin [39].

Summary

Clinical Presentation

- Neoplasm of middle-aged women in the pelvis, perineum, and vulva
- Usually large and has a high rate of local recurrence (up to 47 %)

Histopathologic Features

- Paucicellular with myxoid stroma and entrapped fat
- Bland spindle and stellate cells with medium to large vessels
- Expresses desmin, SMA, ER, and PR

Differential Diagnosis

- Angiomyofibroblastoma
- Superficial angiomyxoma
- Fibroepithelial stromal polyp
- Fibromatosis
- Superficial angiomyxoma

Takeaway Essentials

Clinical Relevant Pearls

- Asymptomatic tumor that is often greater than 10 cm in size.
- Deep location, infiltrative, and requires wide excision to prevent recurrence.
- Long-term follow-up is recommended due to the presence of late recurrences.

Pathology Interpretation Pearls

- Hypocellular myxocollagenous stroma with large vessels that infiltrate surrounding tissue
- Deceptively bland spindle and stellate cells that can lead to underdiagnosis
- Expression of HMGA2 can be detected by immunohistochemistry and used as a marker of microscopic residual disease

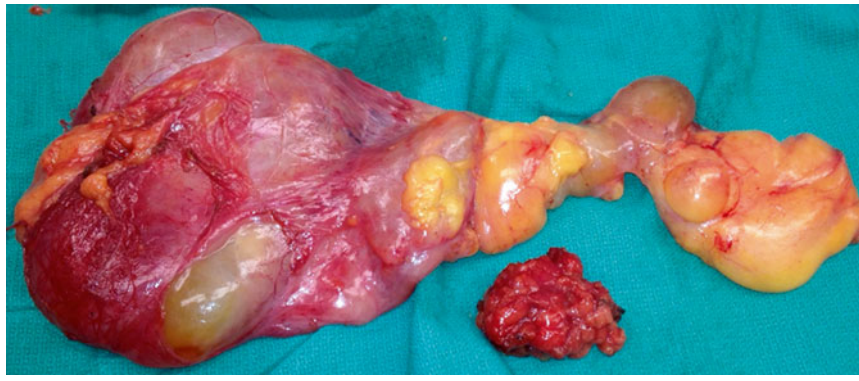

Fig. 13.19 Large polypoid *tan*, *red*, *gray* aggressive angiomyxoma with attached fat

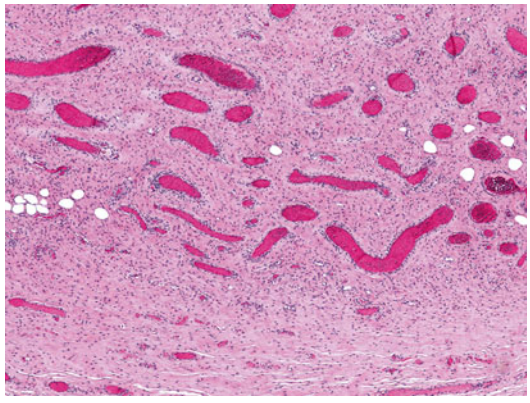

Fig. 13.20 Large undulating vessels with entrapped fat in aggressive angiomyxoma

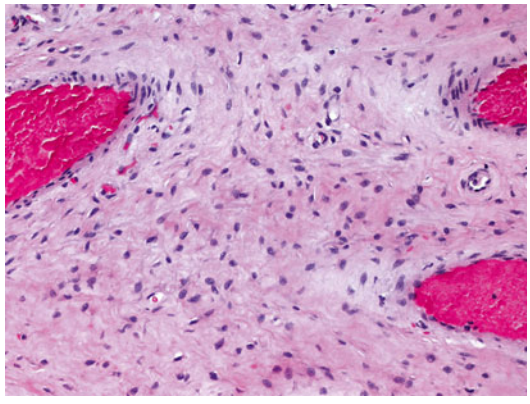

Fig. 13.21 Aggressive angiomyxoma with large vessels surrounded by spindle and stellate cells and the stroma is myxocollagenous

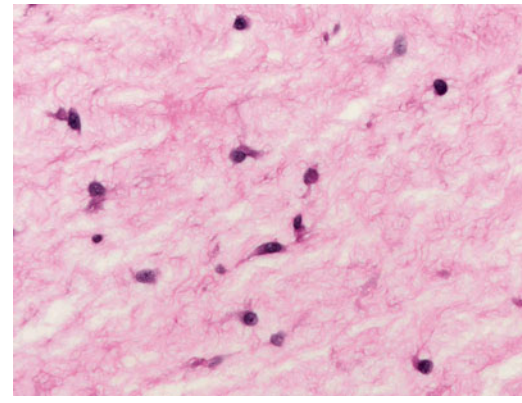

Fig. 13.22 The tumor cells in aggressive angiomyxoma have fine chromatin and indistinct cytoplasm

Superficial Myofibroblastoma

Clinical Features

As the name implies, the lesion is a superficial vulvovaginal polypoid or nodular mass that arises in females. The patients range in age from the third to the ninth decade (mean, 55 years) and presents as a solitary lesion that is usually less than 3 cm [40]. There is no proven hormonal influence although some reports have associated the lesion with tamoxifen therapy [41]. Adequate management is simple local excision; the tumor rarely recurs [42]. This lesion and spindle cell lipoma and cellular angiofibroma share alterations in the 13q14 region with loss of *RB1*.

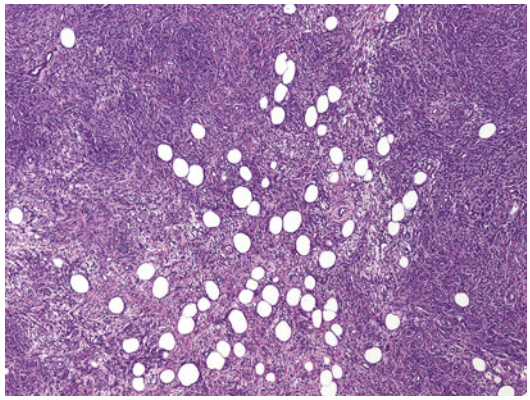

Fig. 13.23 Superficial myofibroblastoma is hypercellular and may contain fat

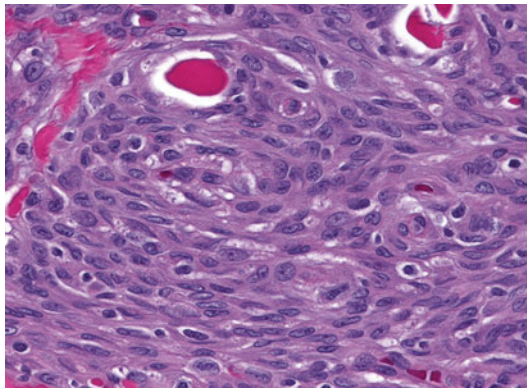

Fig. 13.24 The tumor cells in superficial myofibroblastoma have fine chromatin, and the stroma contains a wire-like collagen

Histopathology

The mass is well circumscribed, is firm and white to tan-pink, and has a smooth glistening to fleshy cut surface [41, 43].

Histologically, the tumor is composed of bland spindle to ovoid or stellate cells that have scant eosinophilic cytoplasm (Fig. 13.23). A minority of cells is multinucleated, and entrapped adipocytes are often present. The tumor cells are arranged in a variety of architectural patterns including vague fascicles with dense collagen fibers (Fig. 13.24) and a lacelike or sievelike pattern with myxoid stroma. Commonly, there is a grenz zone between the tumor and the overlying epithelium [8, 40, 41, 43].

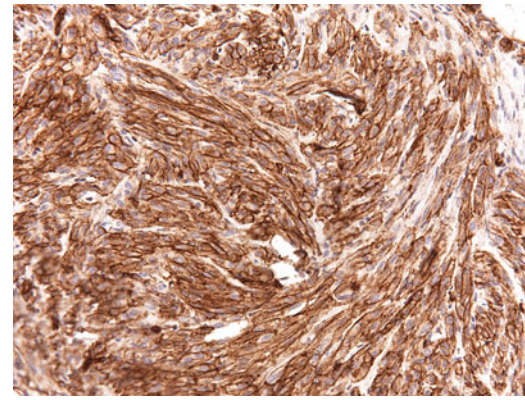

Fig. 13.25 The tumor cells in superficial myofibroblastoma are strongly positive for CD34

Immunohistochemically, the tumor cells are diffusely positive for desmin, CD34, CD99 and variably express estrogen and androgen receptors, and Bcl-2 (Fig. 13.25).

Differential Diagnosis

The differential diagnosis includes angiomyofibroblastoma and aggressive angiomyxoma. Angiomyofibroblastoma contains round to epithelioid cells with a perivascular arrangement, a characteristic that is not present in superficial myofibroblastoma. Aggressive angiomyxoma is a deep, poorly circumscribed infiltrative lesion, which helps in making the correct diagnosis [40].

Summary

Clinical Presentation

- Polypoid superficial vulvovaginal mass
- Solitary lesion usually less than 3 cm
- Rarely recurs

Histopathologic Features

- Bland spindle to ovoid cells
- Vague fascicles with dense collagen fibers or lacelike with myxoid stroma
- Positive for CD34 and CD99 and variable expression of ER, PR, and Bcl-2

Differential Diagnosis

- Angiomyofibroblastoma
- Aggressive angiomyxoma

Takeaway Essentials

Clinical Relevant Pearls

- Reports associating it with tamoxifen therapy
- Shares the loss of *RB1*-like spindle cell lipoma and cellular angiofibroma

Pathology Interpretation Pearls

- Well circumscribed with grenz zone
- Hypercellular with wirelike collagen fibers

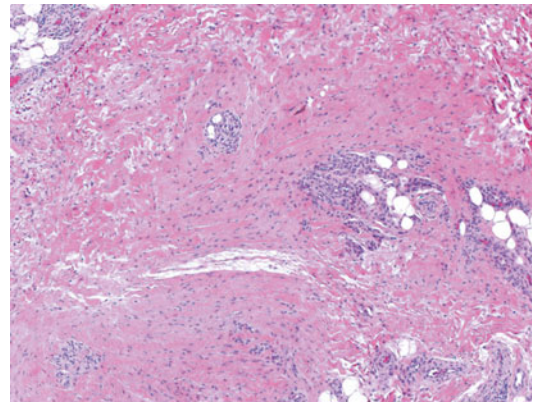

Fig. 13.26 Reactive fibroblastic and myofibroblastic lesion containing hyalinized fibrous tissue associated with blood vessels

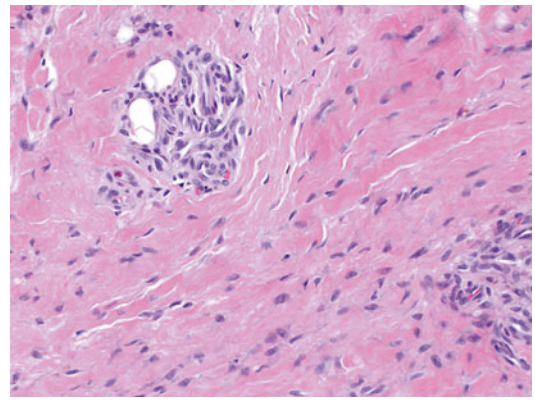

Fig. 13.27 The fibroblasts in reactive fibroblastic and myofibroblastic lesion have spindle nuclei with fine chromatin

Reactive Fibroblastic and Myofibroblastic Proliferation of the Vulva

Clinical Features

Also described as cyclist's nodule, it presents as a superficial nodule arising in the labia majora in competitive female cyclers, and similar lesions have been described in a horseback rider and a male cyclist [44, 45]. It is likely due to repeated microtrauma with a reparative response of fibroblasts and myofibroblasts. It measures from 1 to 4 cm. Although a benign nonneoplastic lesion, some cases have recurred, requiring re-excision.

Histopathology

Grossly the lesion is firm and fibrous, with no clear circumscription from the surrounding tissues. The overlying skin may show mild acanthosis or be unremarkable.

Histologically, the lesion is composed of adipose tissue admixed with mildly cellular hyalinized stroma composed of bland fibroblasts with small- to medium-sized vessels and nerves arranged haphazardly throughout the lesion (Figs. 13.26 and 13.27). Some of the lesional cells are ganglion-like, epithelioid, or plasmacytoid in appearance.

Immunohistochemistry is nonspecific, with the cells expressing ER and smooth muscle actin, and is negative for desmin, S100, and CD34.

Differential Diagnosis

It is limited, but the presence of fat may suggest infiltration as seen in aggressive angiomyxoma, but this lesion is not myxoid and cytologically different. The presence of fibrous tissue, adipose tissue, nerves, and blood vessels is similar to a prepubertal fibroma, but the age and specific association with repetitive trauma as well as the ganglion-like cells help to differentiate these two lesions [46].

Summary

Clinical Presentation

- Described as cyclist nodule
- Present as small nodule in labia majora of competitive female cyclists
- Rarely recurs

Histopathologic Features

- Adipose tissue with mildly cellular hyalinized stroma
- Haphazardly arranged small to medium vessels and nerves

Differential Diagnosis

- Aggressive angiomyxoma
- Prepubertal fibroma

Takeaway Essentials

Clinical Relevant Pearls

- A thorough clinical history is necessary to elicit the association of this tumor with repetitive trauma like in professional cyclists.

Pathology Interpretation Pearls

- Hyalinized fibrous tissue may be prominent in these lesions.
- These lesions show a wide range of proliferative cells, from spindled to ganglion-like, epithelioid or plasmacytoid in appearance.

Postoperative Spindle Cell Nodule

Clinical Features

The lesion develops within the lower genitourinary tract during a period of 3–7 weeks following a surgical procedure. Specific sites of involvement include the vulva, vagina, urethra, endometrium, bladder, and oral cavity [47]. It has benign behavior and rarely recurs after surgical excision [48].

Histopathology

The lesion is characterized as a poorly defined polypoid nodule with a reddish-gray appearance

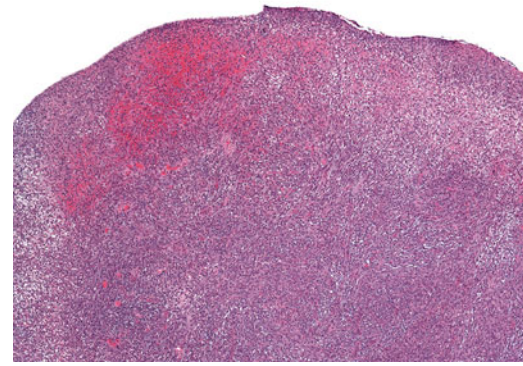

Fig. 13.28 Surface of postoperative spindle cell nodule that has ulcerated the overlying mucosa

that usually measures 2–3 cm (Fig. 13.28). Sometimes the nodule causes ulceration of the overlying mucosa.

Microscopically, the tumor is composed of intersecting fascicles of plump, spindle-shaped cells with moderate amounts of eosinophilic cytoplasm, and the nuclei have fine chromatin and small nucleoli. Mitotic figures are frequent and no atypical forms are present. The stroma is inconspicuous and contains an intervening network of small caliber blood vessels and scattered chronic inflammatory cells (Fig. 13.29a, b). The lesion can exhibit focal irregular infiltration into the adjacent soft tissues.

Immunohistochemistry shows that the spindle cells are positive for smooth muscle actin and focally for desmin. S100 and keratin are negative [48]. Cytogenetic abnormalities include trisomy 7 [49], although this is a controversial aberration in cancer cytogenetics because it has been described in a variety of neoplasms, nonneoplastic lesions, and normal tissues.

Differential Diagnosis

The differential diagnosis includes spindle cell sarcomas, spindle cell carcinoma, and benign entities such as nodular fasciitis. The latter shows more edema, the arrangement of cells is less compact, and a myxoid stroma is more prominent. (See Vignette 2 at the end of the chapter.) The spindle cell sarcomas, particularly leiomyosarcoma, are the most important in the differential

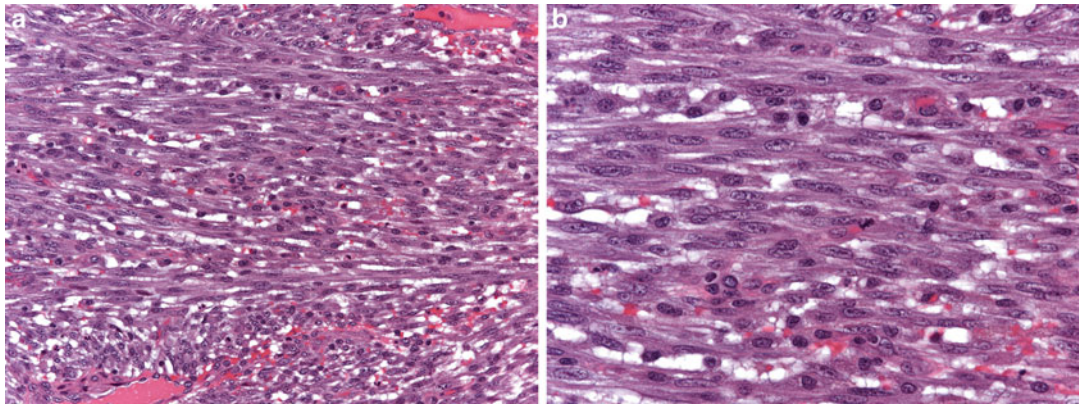

Fig. 13.29 (**a**, **b**) The densely cellular postoperative spindle cell nodule is composed of spindle cells that are mitotically active with scattered inflammatory cells

diagnosis, and useful distinguishing features include the benign-appearing nuclei of the postoperative spindle cell nodule, the contrasting atypia manifest in sarcomas, and the presence of atypical mitoses. Keratin immunohistochemistry and cytological features can help differentiate this entity from spindle cell carcinoma [48].

Summary

Clinical Presentation

- Lesion associated with recent (3–7 weeks) surgical procedure.
- Rapid growth with benign behavior.
- Rare recurrences have been reported.

Histopathologic Features

- Hypercellular, composed of plump spindle cells (fibroblasts and myofibroblasts) arranged in intersecting fascicles.
- Numerous mitoses, with no atypical forms.
- Cells express SMA and desmin (focal), and they are negative for S100 and keratin.

Differential Diagnosis

- Leiomyosarcoma
- Spindle cell carcinoma
- Nodular fasciitis

Takeaway Essentials

Clinical Relevant Pearls

- The rapid growth of the lesion is not associated with aggressive behavior.
- Has trisomy of chromosome 7, although this has been reported in benign lesions.

Pathology Interpretation Pearls

- Awareness of its increased mitotic activity should help avoid overdiagnosing this benign lesion.

Case Vignettes

Vignette 1

Clinical history: A 31-year-old woman noted a slowly enlarging mass in the vulvar region. On examination the lesion is firm, measures 6 cm on palpation, and is painless.

Microscopic description: The excised mass is leathery and tan-white in appearance and has poorly defined margins (Fig. 13.30). The tumor is moderately cellular and composed of a uniform population of fibroblasts arranged in broad sweeping fascicles. (Fig. 13.31) The tumor cells are spindle shaped, with an undulating configuration and have fine chromatin and small nucleoli (Fig. 13.32). Immunohistochemistry shows that the tumor cells are negative for CD 34 and desmin, but the nuclei express beta-catenin (Fig. 13.33).

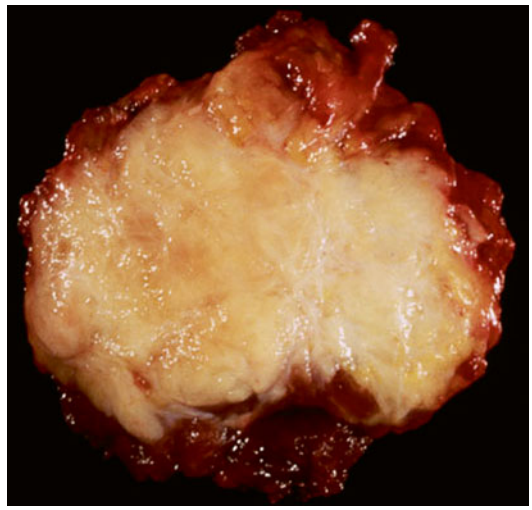

Fig. 13.30 Vignette 1. leathery, *tan-white*, and poorly defined mass

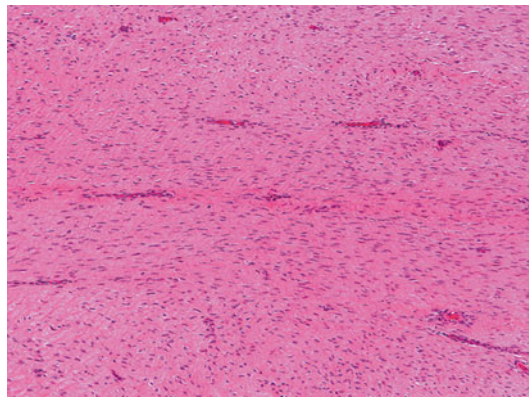

Fig. 13.31 Vignette 1. The tumor cells are arranged in broad sweeping fascicles

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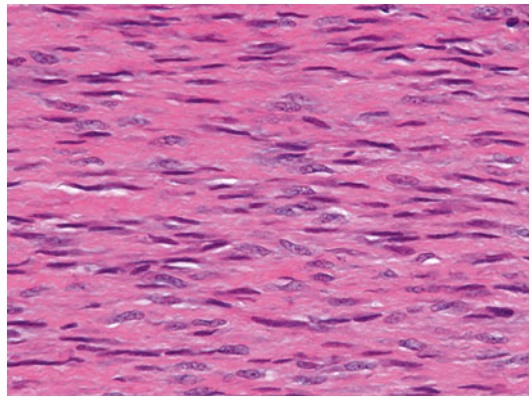

Fig. 13.32 Vignette 1. The tumor cells are spindle shaped and have undulating nuclei that follow the contours of the neighboring collagen fibers

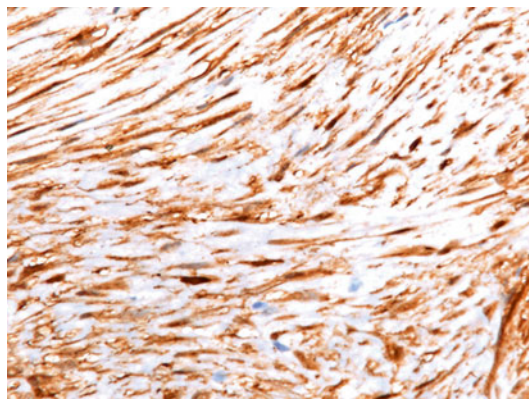

Fig. 13.33 Vignette 1. Beta-catenin stains the nuclei of scattered tumor cells. The cytoplasm also shows staining

Diagnosis: Musculoaponeurotic fibromatosis (desmoid tumor)

Discussion: Musculoaponeurotic fibromatosis is a benign but locally aggressive neoplasm that usually arises in the deep soft tissues [50]. The neoplastic cells are fibroblastic in phenotype and are arranged in broad sweeping fascicles that infiltrate the surrounding soft tissues. A minority of cases occur in the setting of syndromes including Gardner syndrome and adenomatous polyposis syndrome. Sporadic tumors are associated with mutations in the beta-catenin or *APC* genes. Treatment is medical therapy or surgical excision; resected tumors have a high rate of local recurrence.

Vignette 2

Clinical history: A 19-year-old woman presents to her physician with a rapidly growing mass on the left labia majora.

Microscopic description: The tumor is richly cellular and consists of plump, immature-appearing fibroblasts arranged in irregular short fascicles (Fig. 13.34). The cells vary in size and shape (spindle to stellate) and have discrete nucleoli and abundant mitotic figures which are not abnormal (Fig. 13.35). Aggregates of extravasated red blood cells and scattered mononuclear inflammatory cells are common.

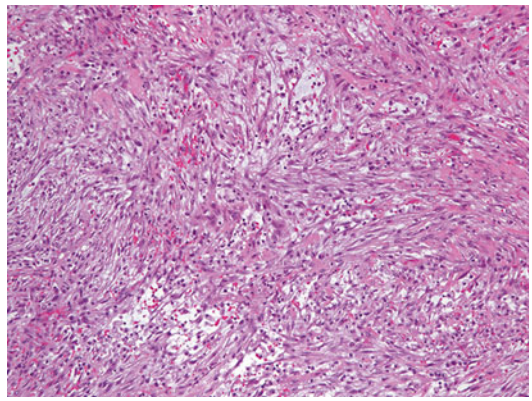

Fig. 13.34 Vignette 2. Sections show at the beginning of the phrase intersecting fascicles of spindle cells which are enmeshed in a myxocollagenous stroma

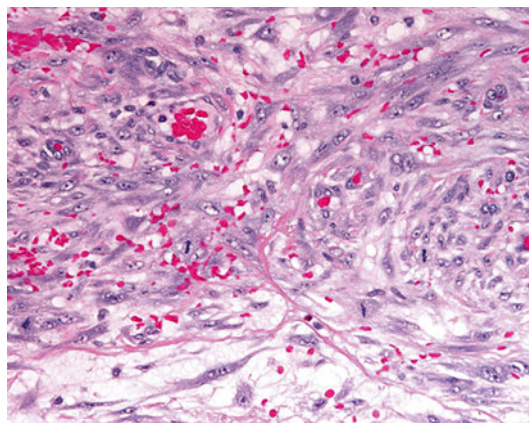

Fig. 13.35 Vignette 2. The plump spindle cells have vesicular nuclei and prominent nucleoli and foci of scattered extravasated red blood cells

Diagnosis: Nodular fasciitis

Discussion: Nodular fasciitis is a relatively common benign lesion that is associated with a consistent translocation involving *MYH9* and *USP6* [51]. Most patients present complaining of a several-week history of a solitary, rapidly growing, and sometimes painful mass. The patients range from infants

(continued)

to the elderly with the majority within the third and sixth decades of life. The lesions are most commonly located in the soft tissues of the volar aspect of the forearm followed in frequency by the chest and back. Most cases arise in the subcutis, but they may also originate in the dermis, deep fascia, and skeletal muscle. Treatment is simple excision and the recurrence rate is very low.

Vignette 3

Clinical history: A 10-year-old girl presents with a rapidly growing polypoid mass protruding from the vulva (Fig. 13.36).

Microscopic description: The tumor is cellular with a hypercellular zone beneath the squamous epithelium (Fig. 13.37). The tumor cells are composed of cytologically atypical round and spindle cells. Some of the spindle cells have abundant eccentric cytoplasm that contains fibrillar cytoplasm with cross striations evident (Fig. 13.38). Immunohistochemistry shows that the tumor cells are strongly positive for desmin and myogenin (Fig. 13.39).

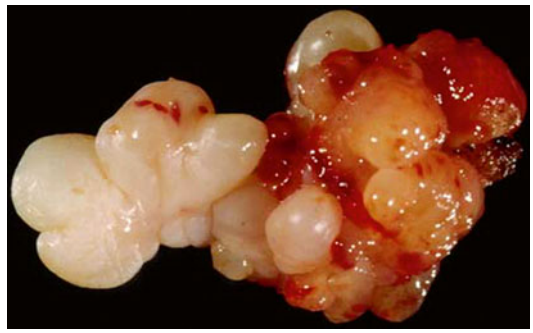

Fig. 13.36 Vignette 3. Glistening polypoid mass composed of multiple grapelike nodules of tumor

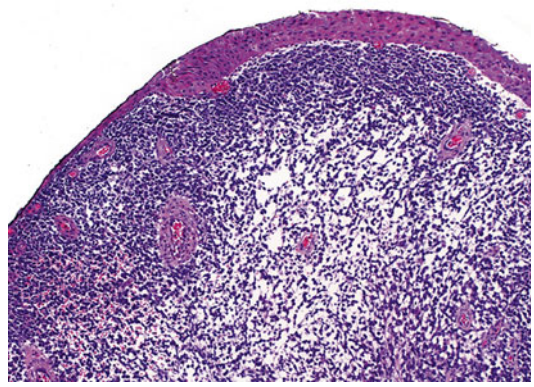

Fig. 13.37 Vignette 3. Hypercellular region beneath the squamous epithelium

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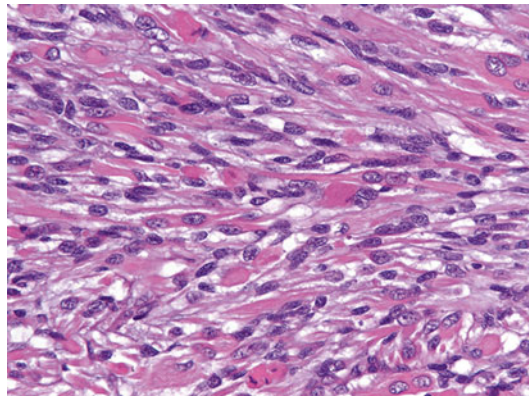

Fig. 13.38 Vignette 3. Some of the tumor cells have eccentric fibrillar eosinophilic cytoplasm and represent rhabdomyoblasts

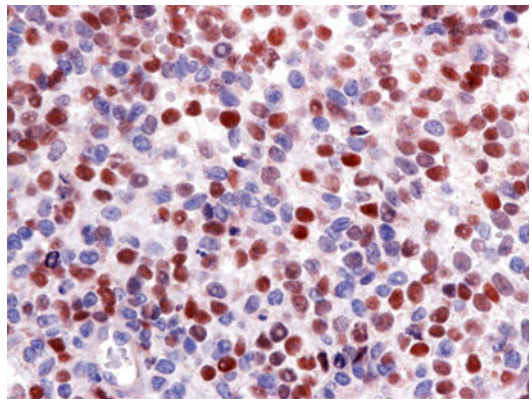

Fig. 13.39 Vignette 3. Scattered neoplastic cells show nuclear expression of myogenin

Diagnosis: Embryonal rhabdomyosarcoma

Discussion: Embryonal rhabdomyosarcoma often arises in the genital region of children and can present as a polypoid tumor that can be confused with benign lesions such as a fibroepithelial polyp. Histologically the tumor is cytologically malignant which helps distinguish it from the benign fibroblastic and myofibroblastic tumor of the vulva.

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