

Chapter 2

Lesions of the Vulva and Vagina

Keywords Vulva • Vagina • Dysplasia • Carcinoma • Melanoma

with benign angiomyofibroblastoma and deep aggressive angiomyxoma primarily involving these areas.

2.1 General Classification of Tumors or Tumor-Like Conditions of Vulva and Vagina

Tumors of vulva and vagina are generally classified into squamous, glandular, melanocytic, and mesenchymal neoplasms. Squamous carcinoma is by far the most common primary malignancy involving both organs. Squamous intraepithelial neoplasia is the most common preinvasive condition of squamous cell carcinoma (SCC). Lichen sclerosus is also considered as a preneoplastic condition of vulvar SCC (Fig. 2.1). Condyloma acuminatum is the most common squamous disorder, caused by low-risk HPV subtypes (HPV 6 and 11), and does not progress to malignancy, except in rare cases where high-risk HPV is a causal factor. Conventional mullerian adenocarcinomas are rare in vulva and vagina. Extramammary Paget's disease represents a special form of glandular malignancy outside of the breast and is generally not associated with an invasive component. Primary clear cell carcinoma of the vagina is famous for its association with intrauterine DES exposure in the past, but is very rare nowadays. Melanoma represents 5% of vulvar cancers and is capable of widespread metastasis. A variety of benign and malignant mesenchymal tumors can be seen in the vulvar and vaginal regions,

2.2 Benign, Preneoplastic, and In Situ Neoplastic Squamous Lesions

Squamous cell hyperplasia of the vulva is a thickened plaque-like lesion consisting of maturing squamous proliferation with hyperkeratosis and/or parakeratosis. No cytologic atypia is present (Fig. 2.2). The diagnosis requires the exclusion of other squamous proliferative disorders, particularly a condyloma.

Squamous papilloma of the vulva may be multiple and consists of simple papillary proliferation of squamous epithelium without complex branching (Fig. 2.3). The absence of definite HPV koilocytosis distinguishes it from a condyloma.

Seborrheic keratosis involves hair-bearing squamous epithelium of the vulva. Multiple lesions may be associated with Leser–Trelat syndrome. The lesion is characterized by symmetric squamous acanthosis, papillomatosis, and hyperkeratosis with keratin horn cysts (Fig. 2.4). Cytologic atypia and HPV-related koilocytosis are absent.

Condyloma acuminatum is a common, sexually transmitted, papillomatous squamous proliferation related to HVP 6 and 11, and is not

Fig. 2.1 Vulvar lichen sclerosis. Note the blunting of the rete pegs and the presence of homogenous collagen deposition in the upper dermis (H.E. $\times 40$)

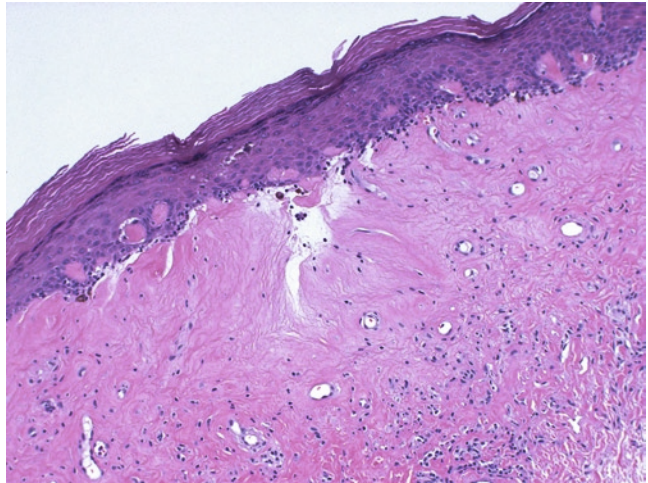


Fig. 2.2 Vulvar squamous hyperplasia. Note the presence of acanthosis and hyperkeratosis, and the absence of HPV-related koilocytosis and epithelial cell dysplasia (H.E. $\times 200$)

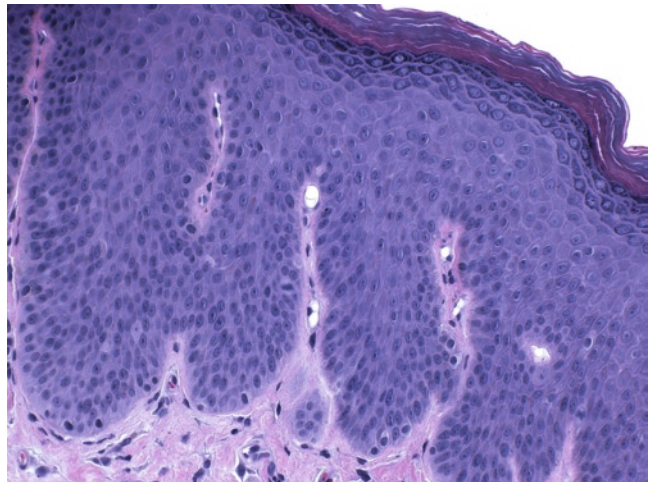


Fig. 2.3 Vulvar squamous papilloma. Note the papillomatosis and the absence of HPV-related koilocytopathic effect (H.E. $\times 40$)

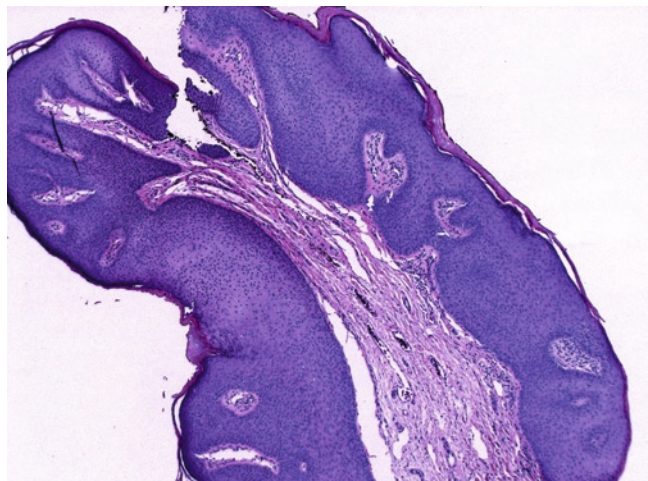
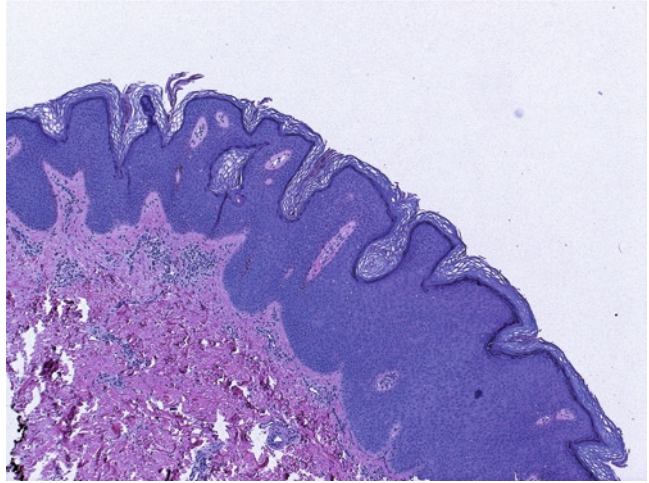


Fig. 2.4 Seborrheic keratosis. Note the symmetric squamous acanthosis, papillomatosis, and hyperkeratosis with keratin horn cysts (H.E. $\times 40$)



considered progressive toward invasive cancer. Its appearance is clinically distinct with a verrucous growth and is frequently multifocal, and even confluent, involving large areas. Histologically, the lesion consists of papillomatous squamous proliferation with fibrous stroma (Fig. 2.5a). Marked acanthosis, parakeratosis, and hyperkeratosis are common. The hallmark of condyloma is the presence of koilocytes. Koilocytosis frequently involves superficial areas of the lesion with nuclear enlargement, multinucleation, hyperchromasia, irregular or raisinoid nuclear membrane, and perinuclear halo (Fig. 2.5b). Koilocytosis may be focal and involves clusters of superficial squamous cells. Prominent granulocytic layer is also characteristic. Distinguishing from a squamous papilloma requires the presence of koilocytes, and when in doubt, the presence of Ki-67 positive nuclei in the upper half of the epithelium favors a diagnosis of condyloma.

Squamous intraepithelial neoplasia of vulva (VIN) or vagina (VAIN) is, by analogy to cervical intraepithelial lesions, divided into grades 1, 2, and 3, based on the presence of neoplastic/dysplastic squamous cells limited to the lower one-third, middle one-third, or the full thickness of the epithelium, respectively. The lesions clinically present as erythematous patches, or verruciform or even pigmented plaques. They may be multiple and involve large areas including the

perineum. VIN and VAIN can be subclassified into (1) the so-called warty type when koilocytes are present, (2) bowenoid type when the lesion consists of smaller, basaloid yet cellular dysplastic cells without koilocytosis (Fig. 2.6), and (3) “differentiated” or simplex type, in which deceptive benign squamous papillomatosis is seen in association with paradoxical parakeratosis (cytoplasmic eosinophilia) in the lower half of the epithelium and dysplastic cells are limited to the basal layer. P53 immunostain may show a diffuse nuclear positivity throughout the entire epithelium.

Invasive squamous cell carcinoma is most commonly seen in patients over 60 years of age and may be preceded by VIN or VAIN. Most well-differentiated SCCs (Fig. 2.7) arise from a background of dermatosis or lichen sclerosus, however. Warty and basaloid carcinomas can occur along with their corresponding intraepithelial neoplasia (Figs. 2.8 and 2.9). The well-differentiated verrucous carcinoma shows no significant cytologic atypia and obvious stromal invasion. The diagnosis can be extremely difficult and relies on the overall pushing growth pattern into the underlying stroma (Fig. 2.10), usually requiring large, well-oriented excision or vulvectomy for its separation from condyloma, squamous papilloma, and pseudoepitheliomatous hyperplasia. Poorly differentiated SCCs are not uncommon in vulva and vagina. Anaplastic, acantholytic,

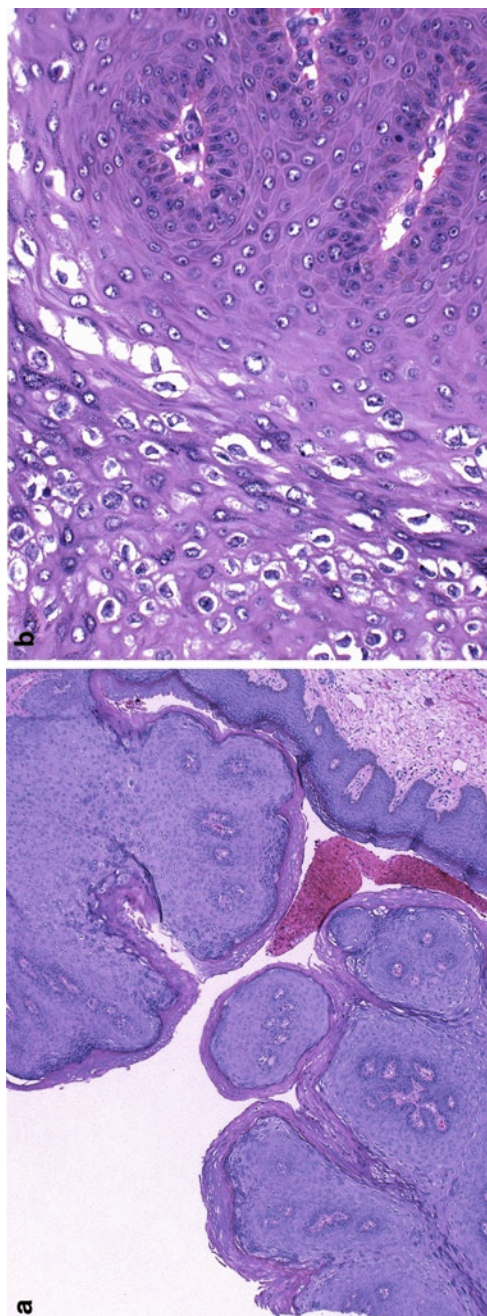


Fig. 2.5 Condyloma acuminatum. Note the marked papillomatosis, acanthosis, parakeratosis, and hyperkeratosis (a) (H.E. x200). The hallmark of condyloma is the presence of koilocytes (b) (H.E. x40).

Fig. 2.6 Vulvar intraepithelial neoplasia 2 (H.E. $\times 100$)

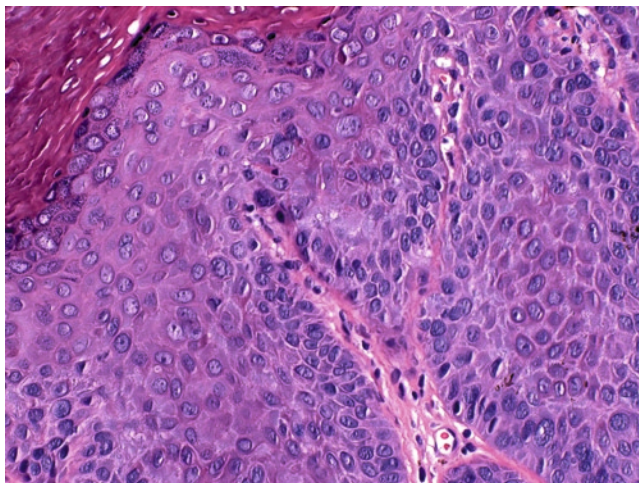


Fig. 2.7 Vulvar well-differentiated keratinizing squamous cell carcinoma (H.E. $\times 40$)

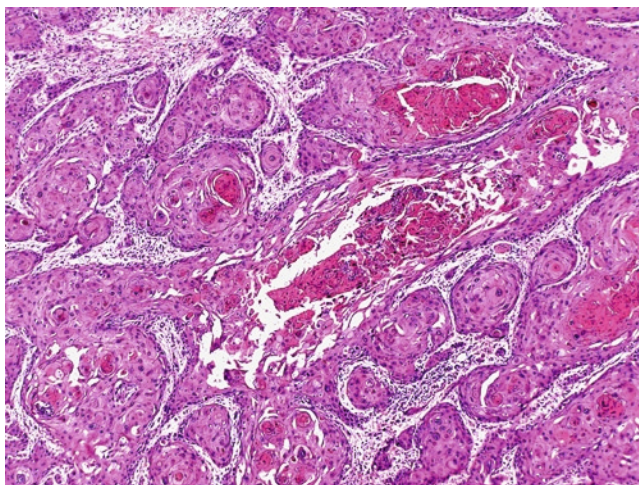


Fig. 2.8 Warty squamous cell carcinoma. Note the condylomatous and koilocytoid carcinomatous nests (H.E. $\times 40$)

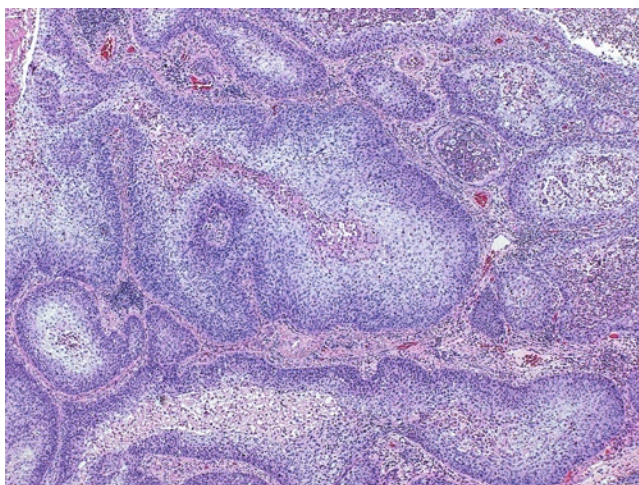
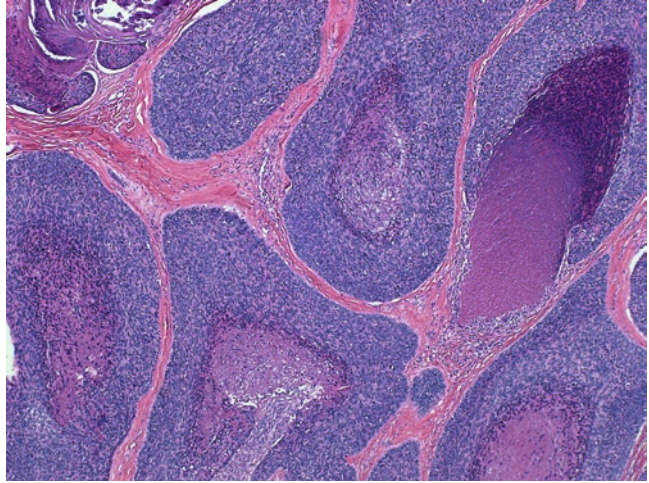


Fig. 2.9 Basaloid squamous cell carcinoma of the vulva. Note the hypercellularity and palisading of tumor cells at the periphery of the tumor nests (H.E. $\times 40$)



sarcomatoid, and lymphoepithelioma-like carcinomas are rare variants of SCC.

Microinvasive squamous cell carcinoma is diagnosed when early stromal invasion is less than 1 mm in depth. Its differential diagnosis from VIN or VAIN can be often difficult. Singles or irregular clusters of dysplastic epithelial cells extruding from the base of an in situ lesion are diagnostic. Isolated tumor nests with paradoxical maturation and haphazard arrangements of tumor cells are highly suggestive of early invasion (Fig. 2.11). A stromal response is almost always present, including desmoplasia, edema, and/or lymphoplasmacytic infiltration.

2.3 Glandular Lesions

2.3.1 Benign Glandular Lesions

Common tumor-like conditions include epidermal inclusion cyst, Bartholin cyst (location is important for diagnosis, Fig. 2.12), Bartholin gland hyperplasia (Fig. 2.13), mucinous cyst and ciliated cyst, ectopic breast tissue with associated benign conditions (adenosis and papilloma), and others. *Hidradenoma* (papilliferum or clear cell) is the most common vulvar benign glandular tumor. It is usually asymptomatic and

small (less than 1 cm), frequently involving the labia majora. Majority of cases of hidradenoma papilliferum are nodular and composed of compact glandular or tubular epithelial growth with papillary formations. The epithelium is, at least focally, double layered with inner tall columnar glandular cells and outer myoepithelial cells (Fig. 2.14a, b). The lobulated clear cell variant is solid and consists of tumor cells with clear cytoplasm and uniform nuclei (Fig. 2.15). The presence of hyalinized stroma is frequently found. The absence of infiltrative border and minimal cytologic atypia attest the benignancy of both subtypes of hidradenoma. The presence of mitosis in both variants, even frequent, does not necessarily indicate malignancy. Benign mixed tumor is essentially similar to that of the salivary glands. Vaginal benign glandular tumor or tumor-like lesions are less frequent and include DES-related adenosis (mucinous, tuboendometrial, and embryonic types), microglandular hyperplasia, and Mullerian papilloma of infancy.

2.3.2 Adenocarcinomas

Adenocarcinomas of the vulva and the vagina are rare, among which vulvar Paget's disease and vaginal clear cell carcinomas are of special concern.

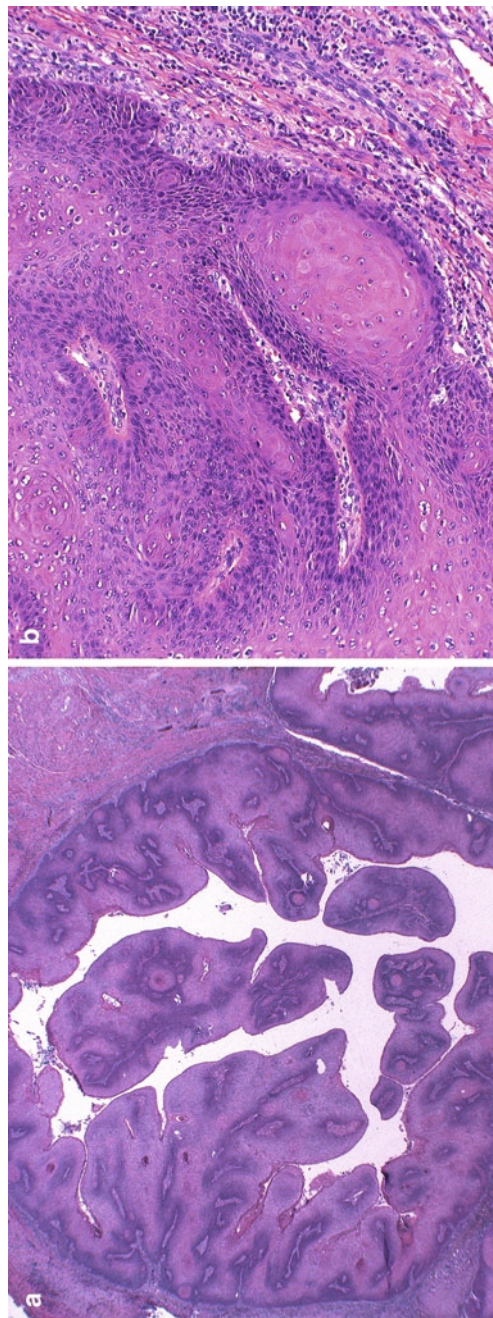


Fig. 2.10 (a, b) Verrucous squamous carcinoma. Note the deceptive well-differentiated squamous epithelium and the pushing invasion into the underlying stroma (H.E. x20 (a), x100 (b))

Fig. 2.11 Microinvasive squamous cell carcinoma. Note the isolated tumor nests with paradoxical maturation and haphazard arrangements of tumor cells (H.E. $\times 40$)

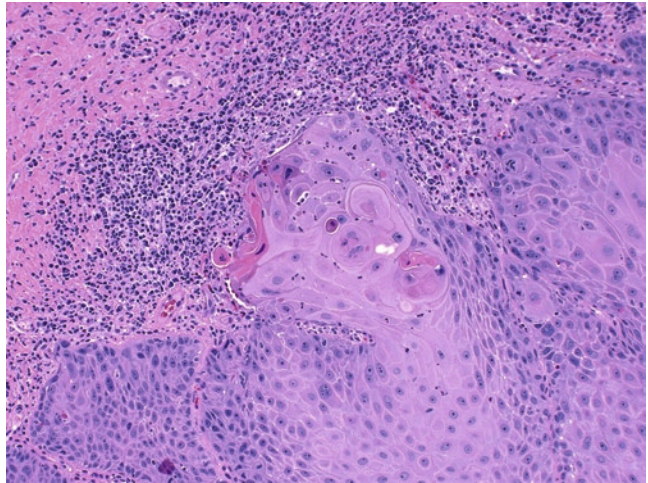


Fig. 2.12 Bartholin gland cyst. Note the presence of Bartholin gland hyperplasia (H.E. $\times 100$)

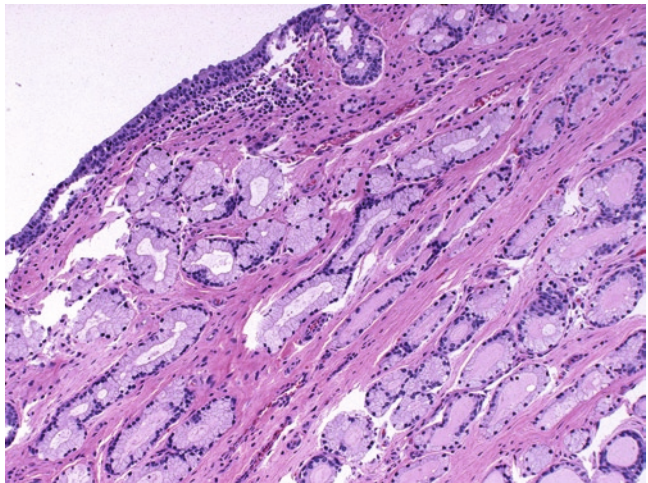
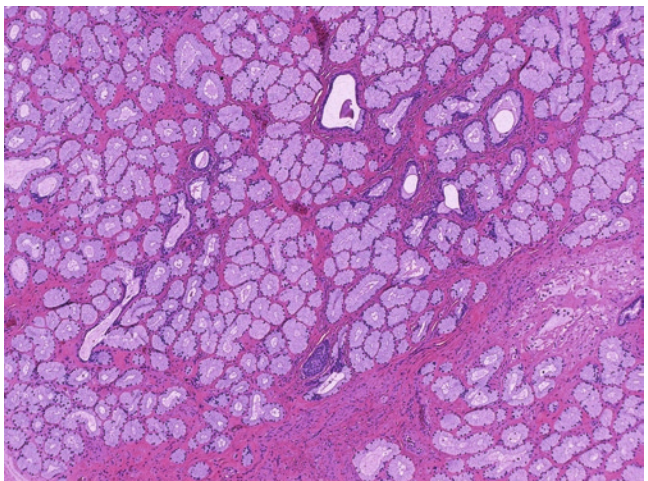


Fig. 2.13 Bartholin gland hyperplasia. Note the lobular hyperplasia of mucinous glands (H.E. $\times 40$)



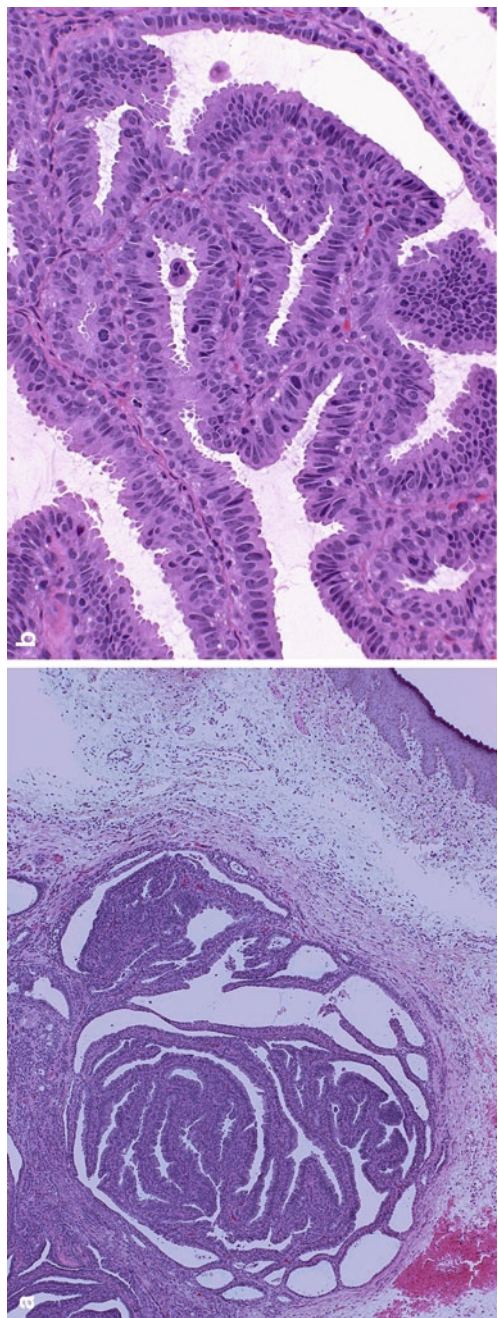


Fig. 2.14 (a, b) Hidradenoma papilliferum. Note the nodular proliferation of compact glandular or tubular epithelial growth with papillary formations (a, H.E., ×40), and the presence of double layers of inner tall columnar glandular cells and outer myoepithelial cells (b, H.E., ×200)

Fig. 2.15 Clear cell hidradenoma. The tumor consists of lobules of solid tumor cells with clear cytoplasm and uniform nuclei (H.E. $\times 40$)

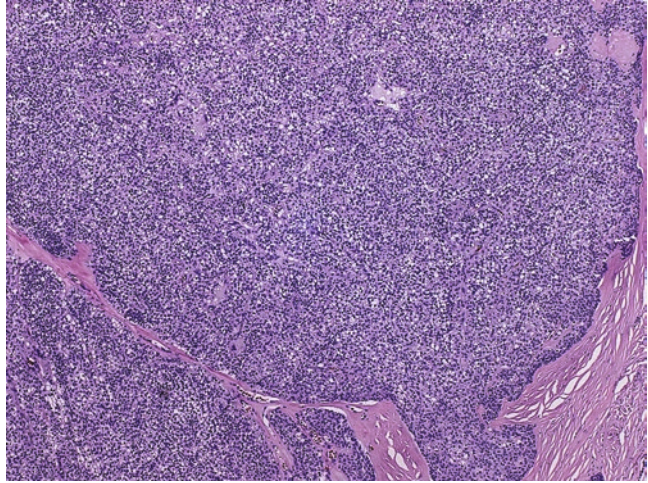
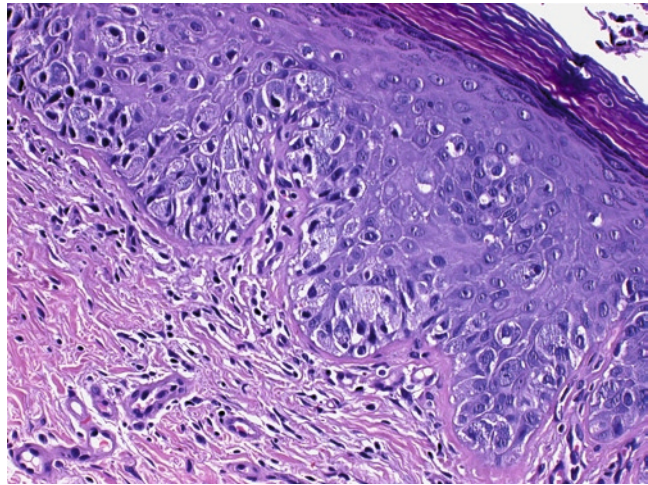


Fig. 2.16 Vulvar Paget's disease. Note the presence of scattered single or clusters of large mucin-containing cells involving the lower half of the squamous epithelium (H.E. $\times 200$)



Vulvar Paget's disease is a form of in situ adenocarcinoma of the extramammary Toker-like cell. It represents 5% of vulvar malignancy. Characteristically, the tumor demonstrates as red eczematous plaques in the agnogenital region of an older Caucasian woman. Her-2/neu protein overexpression and/or gene amplification are frequently seen (up to 50%). Histologically, the involved epidermis is disrupted by scattered single or clusters of large mucin-containing cells involving the lower half or entire epithelium. The tumor cells have abundant pale cytoplasm with central round nuclei (Fig. 2.16). Mitosis can be frequent. They may replace the entire epithelium

or spread into hair follicles or other skin adnexal structures. However, invasive vulvar Paget's disease is rare. The main differential diagnoses include malignant melanoma and colonization of the vulva by urothelial or anal carcinomas. Paget cells are characteristically stained for mucin (PAS, Alcian blue, and mucicarmine) and CAM5.2, CK7, GCDFP, MUDC5AC, and CEA, in contrast to melanocytic markers (HMB45 and Mel-A) expressed in melanomas. The presence of glandular structure within the tumor nests is highly suggestive of Paget's disease. Patients with Pagetoid spreading of an anal-rectal adenocarcinoma usually have a documented history

and the tumor cells are positive for CK20 but negative for CK7. Spreading of an urothelial carcinoma to the vulva likely demonstrates an immunohistochemical profile of CK7 and CK20 positivity and GCDFP negativity.

Vaginal clear cell carcinoma has become very rare as the population with possible DES exposure is in their postmenopausal age. The tumor typically occurs in adolescents and young adults with average age at diagnosis of 17 years. Vaginal bleeding or discharge is typical clinical presentation. Vaginal adenosis, cervical ectropion, or transverse septum or cervical ridges are commonly associated with clear cell carcinoma of the vagina. Most tumors are superficially invasive at presentation. Three major histologic growth patterns are seen: tubulocystic, solid, and papillary. The most common tubulocystic variant consists of round to oval cystic glands or tubules lined by flat, cuboidal, or columnar cells with abundant clear cytoplasm. Marked cytologic atypia and frequent mitotic activities are present in most tumors. Characteristically, hobnailing of the marked atypical cells can be found, at least focally (Fig. 2.17). Extracellular mucin production may be seen, whereas intracellular mucin production is extremely rare. The papillary variant consists of glands or cysts lined by hierarchical papillary proliferation of clear cells. Psammoma bodies may occasionally be seen. In the solid type, the tumor cells are polygonal

with abundant glycogenated clear cytoplasm and sharp demarcated borders (simulating vegetable cells), and grow in solid sheets.

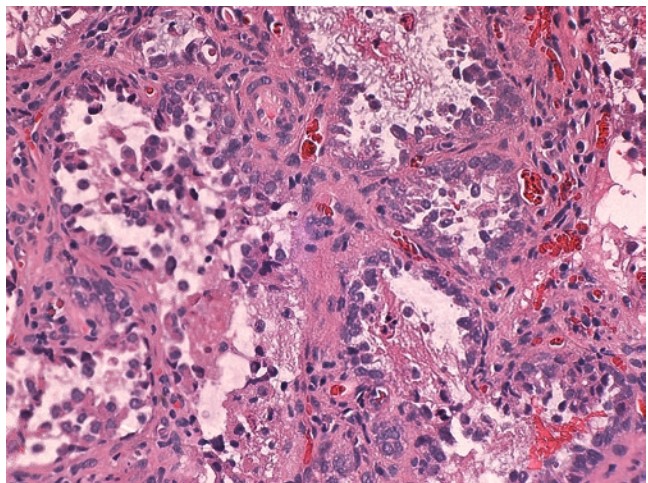
2.4 Other Epithelial or Epithelioid Lesions

Carcinomas of the Bartholin gland represent 5% of vulvar cancers with diagnostic qualifiers including tumor involving Bartholin gland area, histologic transition between normal and carcinoma components, and no primary tumor elsewhere. Histologic variants of Bartholin gland carcinomas include squamous cell carcinoma (40%), adenocarcinoma (25%), adenocystic carcinoma (12%), and other types (mucinous of the intestinal type, adenosquamous, transitional cell, and undifferentiated including small cell neuroendocrine carcinomas). Of the patients with Bartholin gland carcinomas, 40% present with nodal metastasis. The overall 10-year survival is 60%.

Adenocarcinoma of the mammary type is rare and likely arises from the ectopic breast tissue. These tumors resemble conventional breast ductal and lobular carcinomas. Metastatic breast lesions must be ruled out before such diagnosis is made.

Basal cell carcinomas account for 3% of vulvar cancers, and are typically seen in elderly

Fig. 2.17 Vaginal clear cell carcinoma. Note the tubulocystic spaces lined by flat, cuboidal, or columnar cells with abundant clear cytoplasm. Marked cytologic atypia and frequent mitotic activities are present. (H.E. ×200)



patients and frequently with extravulvar basal cell carcinoma.

Vaginal primary yolk sac tumor affects children less than 3 years of age and accounts for 90% of extragonadal yolk sac tumor. Vaginal polypoid lesion with bleeding is common and AFP is typically elevated at presentation. The histologic features are similar to those of the gonadal counterpart with reticular growth patterns, the presence of Schiller–Duval bodies and eosinophilic globular bodies. A cure can be achieved by combined chemotherapy with or without surgery in most cases.

2.5 Melanocytic Lesions

Malignancy melanoma represents 5–10% of vulvar or vaginal cancers, typically seen in elderly patients with atypical extravulvar melanocytic lesions. Pigmented irregular plaques or nodules are seen in most cases, although amelanotic melanoma is not uncommon. The majority of the cases are of mucosal lentiginous type with spindle invasive cells and prominent perineural invasion. The main differential diagnoses include vulvar Paget's disease (see above) and poorly differentiated carcinomas.

2.6 Mesenchymal and Lymphoid Neoplasms

Although rare, a variety of benign and malignant soft tissue tumors involve vulva and vagina. Relatively common benign soft tissue tumors or tumor-like lesions include fibroepithelial polyp, angiomyofibroblastoma, postoperative spindle cell nodule, nodular fasciitis, dermatofibroma, leiomyoma, rhabdomyoma, granular cell tumor (Fig. 2.18), and others. Aggressive angiomyoma, leiomyosarcoma, proximal epithelioid sarcoma, rhabdomyosarcoma, and others are among malignant soft tissue tumors. Diffuse large B-cell lymphoma is the most common lymphoproliferative disorder.

Fibroepithelial polyp is a common polypoid lesion covered by simple, mature squamous epithelium (Fig. 2.19a). Frequently, the stromal myofibroblasts are multinucleated and bizarre in appearance. A cellular pseudosarcomatous fibroepithelial polyp may show hypercellular stromal cells with marked pleomorphism, nuclear hyperchromasia, mitotic activity of more than 10 mitosis/10 high-power fields (HPF), and even atypical mitoses (Fig. 2.19b).

Postoperative spindle cell nodule is a polypoid or nodular reactive spindle cell proliferation that develops a few months after hysterectomy.

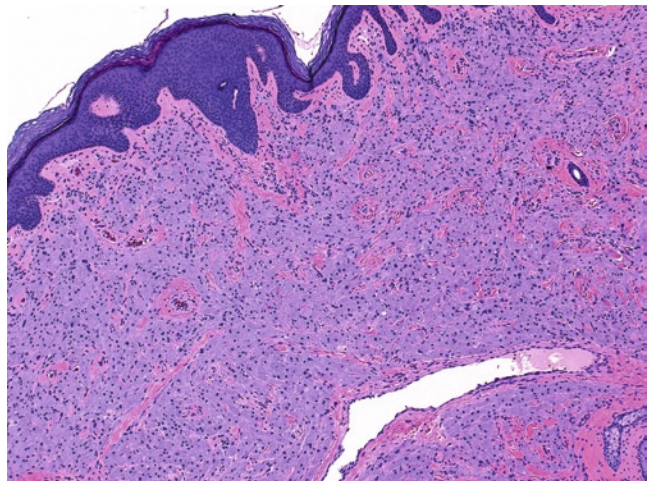


Fig. 2.18 Vulvar granular cell tumor (H.E. ×100)

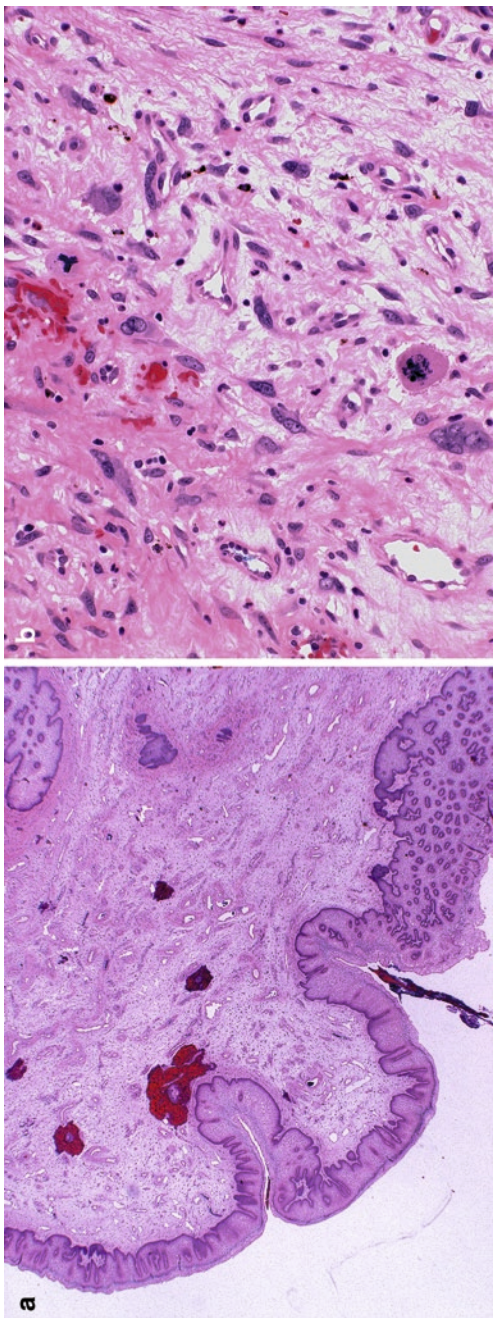
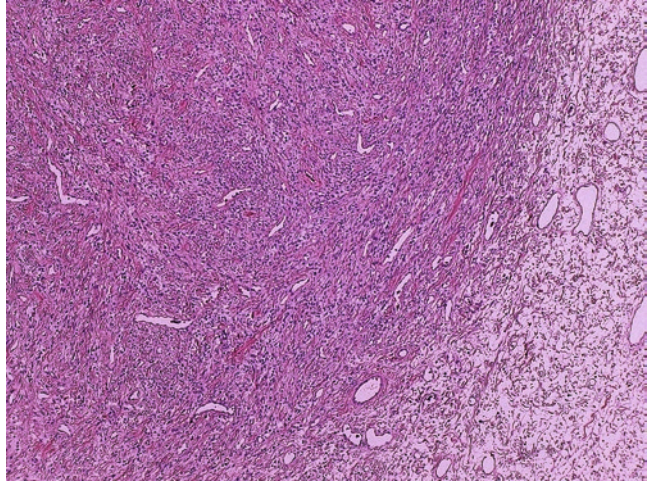


Fig. 2.19 (a, b) Vaginal fibroepithelial polyp. Pseudosarcomatous stroma is present in the particular vaginal polyp (H.E. x40 (a), x200 (b))

Fig. 2.20 Angiomyofibroblastoma of the vulva. Note the nodules of alternating cellular to hypocellular proliferations of small round to spindle cells with eosinophilic cytoplasm, embedded in an edematous to collagenous matrix. Hemangiopericytoma-like vasculature is present (H.E. $\times 40$)



The lesion consists of fascicles of spindle myofibroblasts in a background of delicate capillaries and inflammatory cells. Mitoses are numerous.

Angiomyofibroblastoma involves almost exclusively vulvovaginal soft tissue. Usually, the lesion is less than 5 cm in size with a sharply defined margin. Histologically, the tumor consists of alternating cellular to hypocellular proliferations of small, round to spindle cells with eosinophilic cytoplasm, embedded in an edematous to collagenous matrix. Somewhat epithelioid tumor cells are typically clustered around capillaries (Fig. 2.20). The spindle cells are immunoreactive for desmin.

Aggressive angiomyxoma is a locally recurrent, deep-seated, soft tissue tumor involving mainly pelvicoperineal soft tissue of women in their reproductive age. The tumor is often more than 10 cm in size and poorly circumscribed. The lesion is grossly gelatinous and imperceptively infiltrates into adjacent structures. Histologically, the tumor is usually hypocellular with abundant edematous to myxoid matrix (Fig. 2.21a). The tumor consists of uniformly bland, short spindle cells with round nuclei and eosinophilic cytoplasm with cytoplasmic processes. Clusters of vasculatures of various calibers, including medium to large arterials, are characteristically present, and some of the vessels may be cuffed by eosinophilic collagen (Fig. 2.21b). The tumor cells are reactive for desmin, SMA, ER, and PR. The deep location, infiltrative margin, uniform

paucicellularity, and typical vascular clustering with collagen cuffing separate the tumor from superficial angiomyxoma, angiomyofibroblastoma, and fibroepithelial polyp. Adequate resection with generous margins cures most of the tumor without further recurrence.

Leiomyoma and leiomyosarcoma of vulva and vagina are rare smooth muscle tumors. Leiomyomas are much more common than leiomyosarcomas. Most leiomyomas are conventional mature smooth muscle tumors (Fig. 2.22). Epithelioid and myxoid leiomyomas can also occur. A diagnosis of malignancy follows the criteria similar to those of a soft tissue leiomyosarcoma, including the presence of two of the following: tumor more than 5 cm in size, more than 2–5 mitotic figures per 10 HPF, and moderate or severe cytologic atypia.

Botryoid rhabdomyosarcoma (sarcoma botryoides) is a rare sarcoma of patients under 5 years of age. Polypoid or lobulated tumor with myxoid stroma containing primitive round to spindle cells are characteristic. The presence of cambium layer (condensed tumor cells underneath the tumor surface) and the finding of rhabdomyoblasts are diagnostic clues.

Proximal epithelioid sarcoma involves principally the genital area, with more aggressive behavior than those of the distal counterpart. A multinodular growth with large eosinophilic, epithelioid tumor cells is characteristic (Fig. 2.23). The tumor cells are strongly reactive for cytokeratin, EMA, and CD34 immunohistochemistry.

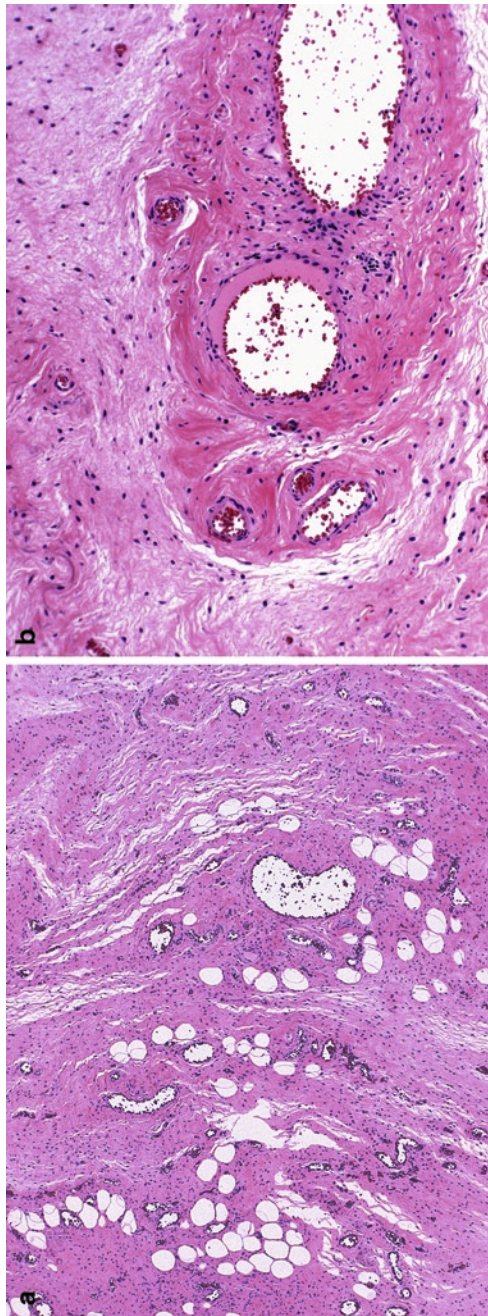


Fig. 2.21 (a, b) Aggressive angiomyxoma. The tumor is hypocellular with abundant edematous to myxoid matrix with invasion into adjacent adipose tissue (a, H.E., $\times 40$). Clusters of vasculatures of various calibers, including medium to large arterials, are characteristically present, and some of the vessels may be cuffed by eosinophilic collagen (b, H.E., $\times 100$)

Fig. 2.22 Vulvar leiomyoma
(H.E. $\times 40$)

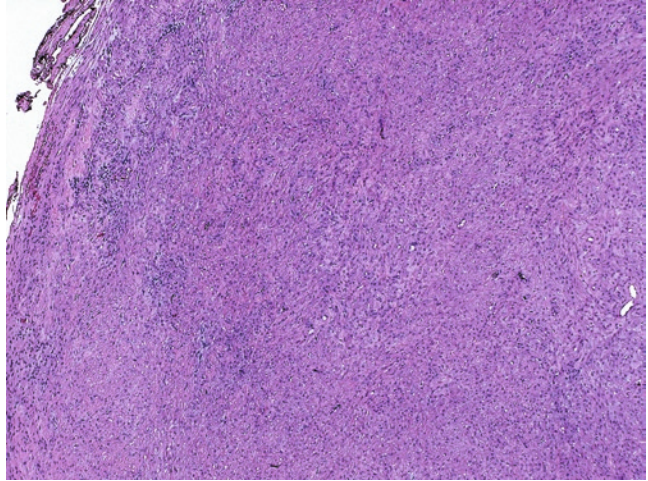
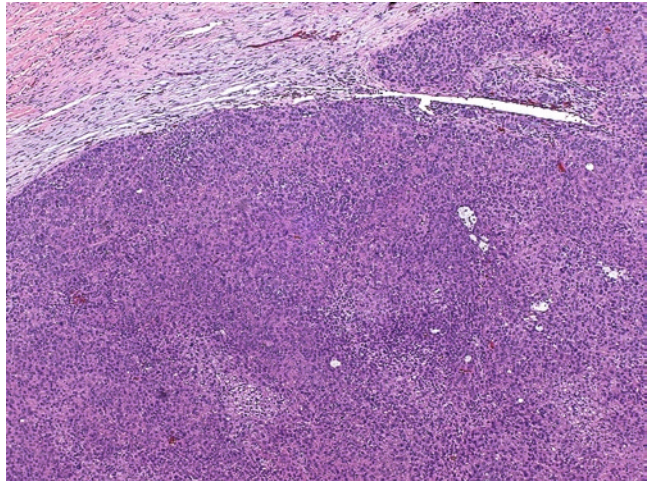


Fig. 2.23 Proximal
epithelioid sarcoma. Note the
nodular growth with large
eosinophilic, epithelioid
tumor cells and vague
granulomatous configuration
(H.E. $\times 40$)



Expression of desmin and SMA can also been demonstrated. The differential diagnoses include poorly differentiate carcinomas and melanoma, which can be resolved by typical immunohistochemical phenotypes of each tumors. The presence of in situ melanocytic lesion favors malignant melanoma.

Vulvar and vaginal lymphomas are mostly secondary. Primary lymphomas account for roughly one-third. Although there is a wide range of histologic subtypes, diffuse large B-cell lymphoma is the single most common subtype. Misdiagnosis of vulvar and vaginal lymphomas is common and a diagnosis of “lymphoma-like lesion” should be used with caution. Consultation

with a hematopathologist should be made when in doubt.

2.7 Secondary Tumors

Secondary tumors of the vagina are at least four times more common than primary lesions. Most are direct extension from a cervical or an endometrial cancer (50%). Metastatic tumors from breast, colorectum, ovary, and even left kidney can occur. Similar metastatic tumor types can involve the vulva, half of which are gynecologic primaries.

2.8 Cytology of Vulva

For nonulcerated lesions, vigorous scraping of the area with sampling devices such as the scalpel blade or spatula is necessary for obtaining cellular materials which can then be smeared on the slides. Placing a warm, moist towel or cloth over the lesion helps softens the superficial keratinizing layers and increases the cellular yield. For ulcerated lesions, sampling can be achieved by swabbing the edge of the ulcer or directly touching the lesion with a glass slide. The slides should be fixed immediately by immersing in 95% ethanol or using a spray fixative. Pigmented lesions should be best sampled by biopsy.

2.8.1 Dysplasia (Vulvar Intraepithelial Neoplasia)

Similar to their cervical counterpart, a two-tier classification system is used in vulvar cytology; low-grade vulvar lesions encompass VIN 1 and HPV cytopathic changes and high-grade vulvar lesions encompass VIN 2 and 3. Although the cytologic findings are similar to those of their cervical counterparts, hyperkeratosis and perkeratosis are frequent and often obscure any rare dysplastic cells that may be present. This may explain a recent report of a lack of correlation between vulvar cytologic findings and histologic degree of VIN.

2.8.2 Squamous Cell Carcinoma

For most instances, the cytologic findings of vulvar SCC are similar to those of their cervical counterparts. However, there are a few variants that deserve special attention. Verrucous carcinoma is characterized by sheets of anucleated and parakeratotic squamous cells. Nuclear atypia is often minimal; therefore, a definitive cytologic diagnosis of malignancy is often impossible. Basal cell carcinoma presents with small and

uniform neoplastic cells with scant cytoplasm and hyperchromatic nucleoli.

2.8.3 Paget's Disease

The neoplastic cells are large with a variable amount of cytoplasm, large eccentrically placed nuclei, and prominent nucleoli. Occasional large cytoplasmic vacuoles or signet ring-like cells can be seen. The cells arrange either singly or in small groups. Cells-in-cells arrangement is thought to be typical of Paget's disease. The differential diagnosis includes nonkeratinizing SCC and malignant melanoma. Biopsy and ancillary studies are necessary to arrive at the right diagnosis.

2.8.4 Mimics of Neoplastic Diseases

Pemphigus vulgaris is a noninfectious inflammatory disease that may sometimes involve the vulva. Diagnostic material can be obtained by scraping the base of the lesion and consists of isolated and loosely cohesive aggregates of acantholytic squamous cells. The latter is characterized by round to oval, large nuclei with vesicular chromatin and prominent nucleoli and may be mistaken as malignant cells (Fig. 2.24). Biopsy and immunofluorescence studies are required for a definitive diagnosis.

Lichen sclerosis and other dermatoses characterized by squamous cell hyperplasia demonstrate similar cytologic findings, showing a mixture of nucleated and anucleated squamous cells as well as parakeratotic squamous cells (Fig. 2.25). Reactive atypia may be evident and should not be confused with dysplastic changes.

2.9 Cytology of Vagina

Collection methods for exfoliative vaginal cytology are similar to those for cervical cytology. To avoid contamination, vaginal cytology samples should be obtained before sampling the cervix.

Fig. 2.24 Pemphigus vulgaris. Loosely cohesive groups of squamous cells with large, round nuclei and prominent nucleoli (conventional preparation, Papanicolaou, $\times 400$)

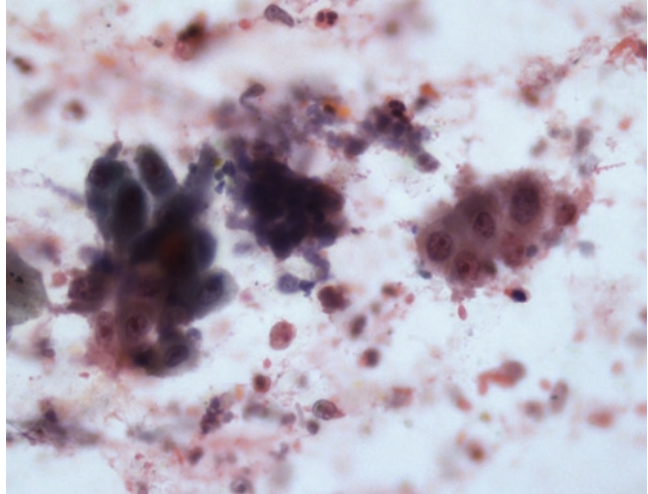
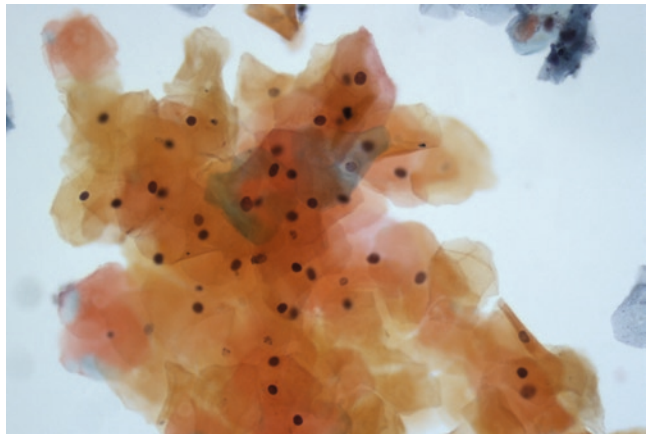


Fig. 2.25 Lichen sclerosis. Predominantly anucleated squamous cells consistent with hyperkeratosis. (ThinPrep, Papanicolaou, $\times 400$)



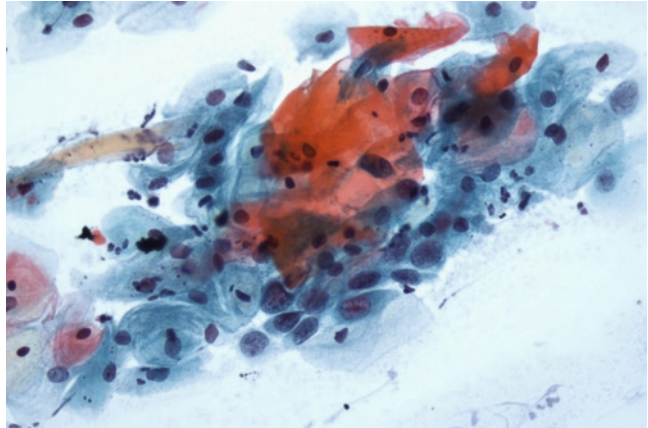
2.9.1 Diethylstilbestrol-Related Abnormalities

The incidence of DES-related vaginal adenosis varies widely. Cytologically, the glandular cells of vaginal adenosis resemble endocervical cells with or without accompanying metaplastic squamous cells. The tumor cells derived from DES-related clear cell adenocarcinoma appear singly or in small aggregates. Individual cells have finely vacuolated cytoplasm, enlarged nuclei, and macronucleoli. There is little variation in nuclear size and shape.

2.9.2 Vaginal Intraepithelial Neoplasia

TBS is used for reporting vaginal cytology; LSIL encompasses VAIN 1 and HPV cytopathic changes and HSIL encompasses VAIN 2 and 3. The cytologic findings are similar to those of their cervical counterparts (Fig. 2.26). For most patients with an abnormal Pap test and a cervix in situ, the lesion is usually confined to the cervix. Occasionally, the dysplasia may extend from the cervix to the vagina. In very rare instances, when colposcopic examination and

Fig. 2.26 Vaginal intraepithelial neoplasia III (VAIN III). Parabasal squamous cells with high N:C ratio, nuclear enlargement, and hyperchromasia (conventional preparation, Papanicolaou, $\times 400$)



biopsy fail to identify any lesion in the cervix in the presence of a positive cervical cytology, the vagina should be carefully examined to rule out any VAIN.

2.9.3 Squamous Cell Carcinoma

Cytologically, SCC of the vagina cannot be distinguished from those that arise from other parts of the female genital tract.

2.9.4 Embryonal Rhabdomyosarcoma

The typical presentation is the finding of isolated and cohesive aggregates of small cells with eccentrically located, round to oval or elongated nuclei and a variable amount of cytoplasm. Tail-like or broad band-like cytoplasmic projections are frequently present. The clinical presentation is also helpful; most patients are usually aged 5 years or younger and present with a grape-like mass expanding the vagina.

2.9.5 Mimics of Neoplastic Diseases

Atrophic vaginitis may be noted in postmenopausal women and other women who lack estrogen stimulation. Cytology of atrophic vaginitis has

been previously described. Microorganisms such as candida, trichomonas, and bacteria can be seen in vaginal samples. The finding of benign glandular cells in vaginal cytology samples in patient status post-hysterectomy is of little clinical significance and not indicative of adenocarcinoma; this also applies to patients with a history of uterine adenocarcinoma.

2.9.6 Role of Vaginal Cytology Screening After Total Hysterectomy

Until recently, routine annual Pap test has been the standard practice for women who have had a hysterectomy for both benign and neoplastic diseases. However, this practice has come under discussion. Although patients with hysterectomy for benign conditions can occasionally develop primary vaginal neoplasia, it may not be cost effective to offer screening to these patients because of the very low incidence of primary vaginal neoplasia. Even for patients who had undergone hysterectomy for malignant diseases such as uterine endometrial adenocarcinoma, the incidence of asymptomatic vaginal recurrence of uterine cancer is less than 1%. Therefore, current guidelines suggest reducing or eliminating routine annual Pap test surveillance for patient status post-hysterectomy for both benign and malignant conditions. For symptomatic patients, appropriate examination and testing procedures should be performed promptly.

Suggested Reading

- Cooper AL, Dornfeld-Finke JM, Banks HW, Davey DD, Modesitt SC. Is cytologic screening an effective surveillance method for detection of vaginal recurrence of uterine cancer? *Obstet Gynecol.* 2006;107:71–6.
- EJ Wilkinson. Premalignant and malignant tumors of the vulva. In Kurman RJ, ed. *Blaustein's Pathology of the Female Genital Tract*. 5th Edition. Springer, Berlin. 2002.

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