CHAPTER 2
UNCOMMON AND RELATIVELY UNCOMMON LESIONS OF THE FEMALE REPRODUCTIVE SYSTEM

Michael G. Conner, M.D.*

1. INTRODUCTION

This chapter will be devoted to infrequently encountered lesions of the female reproductive tract. Some of these will be lesions that are rarely seen, while others will be lesions that you may anticipate seeing from time to time, although certainly not every day.

2. UTERINE SARCOMAS

Malignant mesenchymal tumors of the uterus as a group comprise less than 5% of all malignant uterine neoplasms. Three groups of sarcoma account for the vast majority of the malignant mesenchymal tumors of the uterus (see Table 1). These are leiomyosarcomas, endometrial stromal sarcomas, and malignant mixed Müllerian tumors (MMMT). Leiomyosarcomas are considerably more common than the others.

Table 1. Classification of uterine mesenchymal lesions

	Smooth muscle lesions	Endometrial stromal lesions	Biphasic müllerian lesions
Benign	Leiomyoma	Stromal nodule	Adenofibroma
Uncertain malignant potential	Smooth muscle tumor of uncertain malignant potential	None recognized	Biphasic Müllerian tumor of uncertain malignant potential
Malignant	Leiomyosarcoma	Endometrial stromal sarcoma	MMMT[a] Adenosarcoma

[a] Malignant mixed Müllerian tumors.

* Associate Professor, Department of Pathology, University of Alabama, Birmingham, AL.

These three groups of uterine sarcomas are probably best considered as individual subsets of three distinct groups of uterine mesenchymal tumors, each of which demonstrates a spectrum of histopathologic changes ranging from obviously benign at the lower end to obviously malignant at the upper end. Some of these exhibit lesions of uncertain malignant potential between the two extremes.

Other extremely rare uterine sarcomas have been described including Ewing's sarcoma, rhabdomyosarcoma, malignant fibrous histiocytoma, osteosarcoma, angiosarcoma, liposarcoma, granulocytic sarcoma, and alveolar soft-part sarcoma. Some of these may represent pure monophasic MMMTs with sarcomatous overgrowth. Exceedingly rare are "mixed" sarcomas containing two or more sarcomatous components but no epithelial component.

3. UTERINE ADENOSARCOMA

Adenosarcoma is by definition a biphasic Müllerian neoplasm which consists of a benign epithelial component and a malignant sarcomatous component. The epithelial component may be somewhat atypical but never malignant. The sarcomatous component is usually low-grade. These lesions may be thought of as being part of a spectrum of lesions that range from benign adenofibromas on the lower end to malignant mixed Müllerian tumors (carcinosarcoma) on the higher end.

These lesions generally occur in post-menopausal women (70%) but have been described in virtually all age groups (14 to 89 years with a median age of 58 years in one study). They usually present with abnormal vaginal bleeding and may be associated with pelvic pain and an enlarged uterus. In approximately one-half of the cases the lesion protrudes through the external cervical os where it may be confused with endocervical polyps clinically.

The typical gross appearance of the lesion is similar to a malignant mixed Müllerian tumor. It usually is present within the endometrial cavity or endocervical canal as a large polypoid mass. Ninety percent are endometrial in origin while ten percent are endocervical. In rare instances there may be two separate primary lesions involving both the endometrium and the endocervix. Adenosarcomas are almost always stage I lesions at presentation.

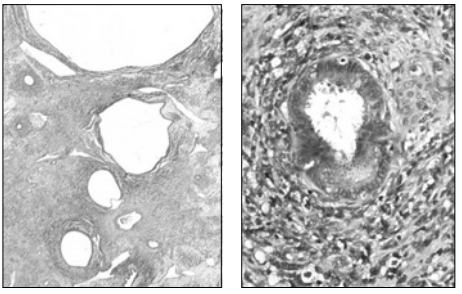

Figure 1. Adenosarcoma. The lesion exhibits a benign glandular component and a malignant sarcomatous component. (Left: H&E x100) High magnification showing concentric concentration of spindle cells surrounding a benign gland in a 'cambium' layer. (Right: H&E x 400)

Histologically, the lesion exhibits a benign glandular component and a malignant sarcomatous component (see Figure 1A). The glandular component may exhibit dilated glands and occasionally shows architectural and cytologic atypia. The glands are usually lined by proliferative-type endometrium but may also show endocervical epithelium, tubal metaplasia, squamous metaplasia, or hobnail metaplasia. The sarcomatous component is predominant and usually low-grade, consisting of round to

spindled cells. The spindled cells are present in whorls while the round cells are somewhat loosely dispersed. The appearance is usually that of an endometrial stromal sarcoma, fibrosarcoma, or a combination of the two. Smooth muscle differentiation is uncommon. A characteristic finding is a concentric concentration of spindled cells surrounding benign glands in a type of "cambium" layer (see Figure 1B). Mitotic activity is highest in these areas where 4 or more mitotic figures per ten HPFs are found in 80% of the cases. Heterologous elements such as small foci of fat, cartilage, or rhabdomyoblasts may be found in 20% of the cases. Myometrial invasion is present in only about 15% of these lesions.

Approximately 10% of the cases are associated with sarcomatous overgrowth which by definition means that 25% of the lesion consists of a pure sarcoma. The sarcoma in the area of the overgrowth is usually higher grade and exhibits more mitotic activity than that in the adenosarcomatous portion of the lesion.

Adenosarcomas of the uterus are in general much less aggressive than their carcinosarcomatous cousins. Approximately 25% of women with this tumor eventually die of their disease, often after prolonged intervals of 5 years or more. Factors that adversely affect the prognosis are sarcomatous overgrowth and myometrial invasion.

4. MALIGNANT MIXED MÜLLERIAN TUMOR ("CARCINOSARCOMA")

Malignant mixed Müllerian tumors (MMMTs) are defined as malignant neoplasms which contain both a carcinomatous and a sarcomatous component and account for roughly 2% to 5% of all uterine corpus malignancies. They are further subdivided into types depending on the nature of the sarcomatous component. The homologous type is characterized by a sarcomatous component composed of tissue types native to the uterus, that is, endometrial stroma (endometrial stromal sarcoma), fibrous tissue (fibrosarcoma), and smooth muscle (leiomyosarcoma) (see Figure 2). The heterologous type contains a sarcomatous component composed of tissue types not native to the uterus, that is, cartilage (chrondrosarcoma), skeletal muscle (rhabdomyosarcoma), and less commonly bone (osteosarcoma) (see Figure 3). The carcinomatous and sarcomatous components usually demonstrate an intimate admixture, but it is not unusual to find focal areas of pure carcinoma or pure sarcoma. Less commonly, one component may predominate to the

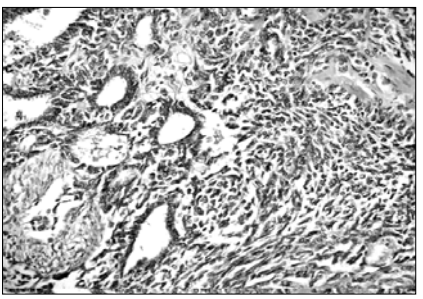

Figure 2. Malignant mixed Müllerian tumors with homologous type. The sarcomatous component resembles that of endometrial stromal sarcoma. (H&E, x 200)

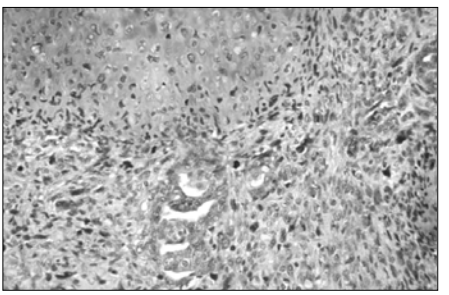

Figure 3. Malignant mixed Müllerian tumors with heterologous type. The sarcomatous component demonstrates cartilagenous differentiation which is foreign to the uterus. (H&E, x 200)

extent that it is difficult to find the other component. Grossly, the lesion typically presents as a broad-based polypoid mass which fills and distends the endometrial cavity and may extend distally into the endocervical canal. Some extend through the external cervical os and may present as a "polyp." Occasionally the uterus is greatly enlarged. Myometrial invasion deeper than the inner third is very frequent (80%) and extension into the outer half occurs in approximately 40% of cases.

MMMTs occur predominantly in postmenopausal women with a median age of about 66 years. Unusual cases have been found in younger women and rarely in children. Some of the risk factors for developing an MMMT are similar (but weaker) to those of routine endometrial adenocarcinoma and include obesity, exogenous estrogenic stimulation, and nulliparity. Some studies have linked tamoxifen therapy to an increased risk for developing an MMMT. There is also a positive relationship with previous pelvic irradiation and the subsequent development of MMMTs. Various studies have shown that between 7% and 37% of women who develop MMMTs have a history of previous pelvic irradiation. Pelvic irradiation was used for benign conditions in the past such as abnormal uterine bleeding. Today the most common situation is a history of pelvic irradiation for carcinoma of the cervix. Postradiation MMMTs develop between 10 and 20 years after the irradiation therapy. Some studies have reported that postradiation MMMTs develop at a younger age than in those women without a history of pelvic irradiation and that the lesion is more widespread at the time of diagnosis in those women. It has also been reported that women with a history of radiation exposure who develop MMMTs are more likely to exhibit heterologous elements in the sarcomatous component.

There is some debate with respect to the nomenclature of this lesion. "Malignant mixed Müllerian tumor" is an older term but one that exerts a strong "hold" on gynecologic oncologists. At one time the term "carcinosarcoma" was reserved for those lesions in which the sarcomatous component was homologous. The terms "malignant mixed Müllerian tumor" or "mixed mesodermal tumor" were reserved for those lesions in which the sarcomatous component was heterologous. At one time it was felt that the heterologous lesions had a worse prognosis, but this is no longer felt to be true. It is now recommended that all these lesions be called "carcinosarcoma" and subdivided into homologous and heterologous types. The term "malignant mixed Müllerian tumor" is deeply ingrained in the clinical gynecologic literature and therefore will not soon disappear.

The histogenesis of this lesion is interesting and in some ways reflects the nomenclature controversy. In an attempt to explain the histogenesis of this lesion three theories have been proposed, that is, the "collision" theory, the "composition" theory, and the "combination" theory (see Table 2).

Table 2. Theoretical developmental schemes for malignant mixed Müllerian tumors

Theory	Mechanism of action
Collision	Epithelial and mesenchymal neoplastic components arise independently and collide giving the appearance of a single mixed tumor.
Composition	The tumor is an adenocarcinoma which provokes the stroma to a degree that results in the development of reactive stromal atypia.
Combination	The tumor develops from a single pluripotential stem cell which retains the ability to differentiate along both epithelial and mesenchymal lines.

"Collision" tumors do occur but they are usually easily recognized. Such tumors are not true MMMTs and should result in little if any diagnostic difficulty.

The "combination" theory is probably the most widely accepted theory at present. Several studies have shown that most (but not all) MMMTs are monoclonal, that is, derived from a single cell line. During embryological development the uterine fundus is formed by fusion of a portion of the Müllerian ducts. The Müllerian epithelium (derived from coelomic epithelium) then differentiates into endometium and stroma. It is thought that MMMTs develop in a similar fashion, that is, from a primitive pluripotential stem cell that gives rise to a monoclonal population which differentiates into both epithelial and stromal components. The development of primary peritoneal carcinomas ("ovarian carcinoma of extraovarian origin") is theoretically related to this same process.

There is evidence that the "combination" theory may not apply in all cases of MMMTs. The "composition" theory explains some of the observations in MMMTs better than does the "combination" theory. Not all MMMTs are monoclonal. The epithelial portion of MMMTs is generally the most aggressive component. Lymphovascular invasion almost always involves the epithelial component. Distant metastasis is almost always of the epithelial component. The sarcomatous component seems to have little metastatic ability. The biological behavior of MMMTs does not seem to be related to the grade, mitotic index, or type of sarcomatous elements present but is much more reflective of the type and grade of epithelial elements present. These findings offer support to the "composition" theory in which the "sarcomatous" component may be only an atypical bystander. However, when MMMTs and pure carcinomas of the endometrium are compared, matching the epithelial components by type and grade and the patients by stage, MMMTs have a poorer prognosis.

Women with stage I disease have about a 50% five-year survival. In general, the overall five-year survival rate with MMMTs is less than 20%.

5. UTERINE LEIOMYOSARCOMA

Leiomyosarcoma is the most common "pure" sarcoma that occurs in the uterus. They account for approximately 45% of uterine sarcomas. If malignant mixed Müllerian tumors are excluded from the category of uterine sarcomas (as some believe they should be) then leiomyosarcomas account for approximately 80% of all uterine sarcomas. The proportion of smooth muscle tumors of the uterus that are malignant reportedly ranges from 0.13% to 6%. That is a 50-fold variation which reflects the various diagnostic criteria used by different pathologists in making that diagnosis.

Leiomyosarcomas occur during the third to ninth decade of life. Most women are over the age of 40 years when diagnosed. This is about 10 years older than the typical patient with benign leiomyomata. Leiomyosarcomas may be more common in black women (similar to leiomyomata) and there has been some indication of increased frequency in women taking tamoxifen for breast cancer (a similar observation has been made in uterine adenosarcomas as well). These lesions usually present with abnormal vaginal bleeding, pelvic pain, and an enlarged uterus.

Grossly, these lesions typically present as a solitary mass that may or may not be accompanied by one or more benign leiomyoma. If several smooth muscle lesions are present the leiomyosarcoma is usually the largest of the group. Two-thirds of the leiomyosarcomas are intramural in location while the remaining are submucosal or subserosal. Gross examination may be helpful in making a diagnosis. Leiomyosarcomas

often exhibit an infiltrative border grossly, which is markedly different in appearance from the sharply circumscribed border of a leiomyoma (see Figure 4). The cut surface of a leiomyosarcoma often lacks the "bulging" appearance of a leiomyoma and the typical whorled appearance of the leiomyoma is absent. The consistency of leiomyosarcomas differs from that of leiomyomata. The typical leiomyoma has a firm, rubbery consistency, whereas a leiomyosarcoma typically has a softer "fleshy" consistency.

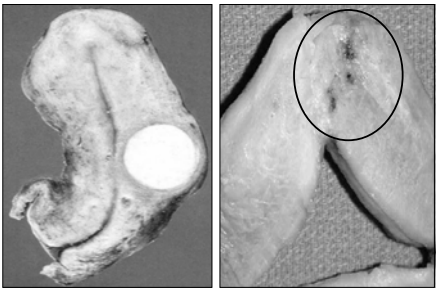

Figure 4. Right: Leiomyoma exhibits a sharply circumscribed border. Left: Leimyosarcoma exhibits an infiltrative border (circled area).

The variation in the percentage of malignant smooth muscle tumors noted above reflects the variation in diagnostic histopathologic criteria used in making a diagnosis of leiomyosarcoma. There is a wide range of histologic appearances that fall within the scope of leiomyosarcomas of the uterus, depending on the grade of the lesion and whether or not any of the less typical varieties are present. The typical features of a leiomyosarcoma include hypercellularity, diffuse cytologic (nuclear) atypia, and increased mitotic activity (usually ten or more mitotic figures per 10 HPFs) (see Figure 5). Other factors of importance include the presence of coagulative tumor cell necrosis, atypical mitotic figures, and an infiltrative tumor border.

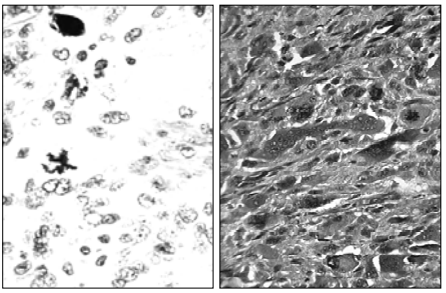

Figure 5. Leiomyosarcoma. The tumor is hypercellular and individual cells show marked nuclear atypia and increased mitotic activity. (H&E, x400)

Survival rates obviously depend upon the grade and extent of the lesion at the time of diagnosis. Survival rates have been variously quoted ranging from 15% to 30% with a mean survival ranging from 13 to 43 months. Most tumor-related deaths are due to distant metastasis often associated with local recurrence. Tumor size of less than 5 cm has been noted to be a relatively good prognostic indicator while a tumor size larger than 8 cm, vascular invasion, and infiltrative margins have been cited as adverse prognostic indicators.

6. PAGET'S DISEASE OF THE VULVA

Extramammary Paget's disease remains a mystery with respect to the cell of origin and its pathogenesis. Origin from intraepithelial stem cells or cells from sweat ducts has been postulated but never proven. Unlike Paget's disease of the breast there is almost never an underlying malignancy in extramammary Paget's disease. However, it has been stated that about 30% of the patients with extramammary Paget's disease will have a

synchronous internal carcinoma, usually involving the breast, uterine cervix, or urinary bladder unrelated to the Paget's disease.

Extramammary Paget's disease accounts for 1% to 5% of all vulvar malignancies. The patients are older, usually in the seventh decade of life although the disease may occur in late reproductive life. The disease may be present for years prior to diagnosis as a result of either the patient neglecting the disease or its being treated as some type of inflammatory reaction which it may resemble. The disease presents as a moist, weeping, erythematous, raised plaque associated with intense pruritis and burning. The erythematous weeping patches may be interspersed with areas of "leukoplakia" (hyperkeratosis) or ulceration. The lesion may initially be confined to the labia but later may extend to involve the clitoris, mons pubis, urethra, perianal area, and medial areas of the thighs.

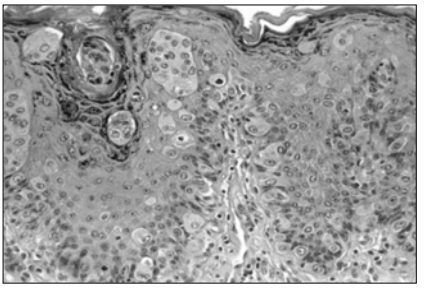

Figure 6. Paget disease of the vulva. The lesion is characterized by the presence of large, pale-staining epithelioid cells in the epidermis. (H& E, x200)

Histologically, the lesion is characterized by the presence of large, pale-staining epithelioid cells which are larger than the surrounding keratinocytes (see Figure 6). These cells are present within the epidermis as single cell, in small clusters, and occasionally in glandular formation. A characteristic finding is clustering of tumor cells in the basal areas of the epithelium but epidermotrophic infiltration of the upper areas of the epidermis is usually present. The cells may infiltrate into the pilosebaceous units and sweat ducts. Rarely, the tumor cells will exhibit superficial invasion into the underlying dermis. Regional metastasis to local lymph nodes is a rare occurrence. The individual tumor cells are large, contain a vesicular nucleus, prominent nucleolus, and abundant pale amphophic cytoplasm.

The differential diagnosis includes superficial spreading malignant melanoma and pagetoid vulvar intraepithelial neoplasia. Diagnosis may be facilitated by histochemical stains for mucin and immunohistochemical stains for S-100, HMB-45, CEA, and CK7 (see Table 3).

Table 3. Differential immunophenotype

Entities	Mucin	S-100	HMB-45	CEA	CK7
Paget's disease	Positive	Negative	Negative	Positive	Positive
Pagetoid VIN[†]	Negative	Negative	Negative	Negative	Negative
Melanoma	Negative	Positive	Positive	Negative	Negative

Recurrence is extremely common following excision of the lesion. In fact, the margins of excision on resected lesions are more often positive for tumor cells than not. This, plus the fact that the tumor cells spread down into pilosebaceous units and sweat ducts, account for a very high rate of recurrence. Multiple recurrences are common over a

[†] VIN: vulval intraepithelial neoplasia.

period of many years. Progression to invasive disease rarely occurs. Invasion to a depth of greater than 1.0 mm, when it does occur, is associated with a worse prognosis with increased risk of regional lymph node metastasis, distant metastasis, and potential death from the disease.

7. ADENOID BASAL CARCINOMA OF THE CERVIX

Adenoid basal carcinoma is a rare and frequently asymptomatic tumor of the cervix which occurs in older postmenopausal females, especially Afro-American females. The median age of these patients is 60 years. The lesion is often associated with high-grade CIN and frequently is diagnosed incidentally during evaluation of hysterectomy or cervical cold knife cone specimens for HGSIL following an abnormal Pap smear. An association with HPV (typically HPV-16) has been observed as the neoplastic cells exhibit immunoreactivity with HPV-16 antibodies. Occasionally, the lesion is a completely incidental finding in hysterectomy specimens done for other unrelated conditions such as endometrial hyperplasia in patients with a normal cytology history. Grossly, the cervix is usually unremarkable or at most may demonstrate a slight degree of nodularity.

Microscopically, the tumor resembles basosquamous cell carcinoma of the skin with nests of relatively bland small tumor cells which exhibit peripheral palisading. The individual tumor cells are oval and hyperchromatic with an increased N/C ratio and occur in small nests and cords which may exhibit branching. These nests may be widely spaced. A stromal response may or may not be present. The edges of the neoplastic nests and cords are smooth rather than irregular and jagged (as seen in typical invasive squamous cell carcinoma). The centers of the nests may demonstrate focal areas of glandular differentiation with small acini lined by a single layer of cuboidal to columnar epithelium sometimes producing mucin. Squamous differentiation is also encountered. Nests containing areas of squamous differentiation usually retain peripheral palisading of small oval cells. The lesion is frequently associated with areas of high-grade squamous dysplasia and rarely may be found merging with areas which demonstrate microinvasive or invasive squamous cell carcinoma. The lesion is thought to arise from pluripotential reserve cells of the endocervix. It is usually found deep to the endocervical glands and for that reason may not be seen in routine cervical biopsy or superficial LEEP cone specimens. This lesion must be distinguished from the more aggressive adenoid cystic carcinoma of the cervix which is similar in appearance to an adenoid cystic carcinoma of the salivary glands.

No pure case of adenoid basal carcinoma of the cervix has ever been reported to have metastasized or to have caused the death of the patient. For that reason some have argued that this is not a malignant lesion and have proposed the term “adenoid basal epithelioma” for it. Others argue that the lesion should retain its malignant classification based on the fact that it can be deeply infiltrative, occasionally extends to the lower uterine segment, and has occasionally presented as a grossly ulcerated symptomatic mass.

8. SMALL-CELL NEUROENDOCRINE CARCINOMA OF THE CERVIX

This highly aggressive tumor is basically an “oat” cell carcinoma similar to those seen in the lung and other organs. Small-cell neuroendocrine carcinomas, carcinoid

tumors, atypical carcinoid tumors, and large-cell neuroendocrine carcinomas of the cervix are generally placed into a heterogeneous group referred to as “endocrine tumors” by some investigators. Small-cell neuroendocrine carcinomas are the most frequently encountered lesion among those within this group, accounting for about 2% of all cervical carcinomas. They are thought to arise from agyrophilic cells found within endocervical and ectocervical epithelium in normal females. Molecular studies have demonstrated that these tumors share features with both small-cell carcinomas of the lung and typical squamous cell carcinoma of the cervix. These tumors are found within a wide range of age from the third to the ninth decades of life. The median and mean is in the fifth decade. These lesions usually present with vaginal bleeding. Rarely, there is evidence of hormonal production (ACTH, insulin, serotonin, or vasopressin), either biochemical or clinical. A history of abnormal Pap smear may or may not be present in these women. Pelvic examination generally reveals a cervical mass that is often ulcerated and deeply infiltrative.

Histologically, these tumors are very similar to their counterparts in the lung. They consist of sheets, nests, and cords of small hyperchromatic cells associated with areas of necrosis. Pseudo-rosette or acinar structures may be present. The nuclear features are those classically found in neuroendocrine differentiation, that is, a finely dispersed granular “salt-and-pepper” pattern and may exhibit smudging and “molding.” Nucleoli generally are not prominent. Mitotic activity may be brisk. The tumor may exhibit crush artifact. Occasionally, a tumor will exhibit so-called “intermediate type cells” which have larger round to oval more uniform nuclei with coarser chromatin and prominent nucleoli. These cells are often admixed with the more classical “small-cells.” Small-cell neuroendocrine carcinoma of the cervix may be present in a “pure” form but frequently it is admixed with a typical squamous cell carcinoma or endocervical adenocarcinoma. I have seen one case in which an endometrial small-cell neuroendocrine carcinoma was present in association with an endometrial adenocarcinoma.

The histopathological features on routinely stained sections of small-cell neuroendocrine carcinoma usually suggest the possibility of that diagnosis. However, the differential diagnosis includes poorly differentiated nonkeratinizing squamous cell carcinoma of the small-cell type, malignant lymphoma, and less commonly other lesions such as endometrial stromal sarcoma. The diagnosis is confirmed immunohistochemically with neuroendocrine markers (NSE, synaptophysin, and chromogranin). A negative leukocyte common antigen (CD45) effectively excludes malignant lymphoma.

About 75% of these women present as clinical stage I or II, but over 50% of them are found to be surgical stage III or IV, attesting to the aggressive nature of this lesion and its propensity for early and widespread metastasis. Frequent sites of metastasis are distant lymph nodes, lung, bone, brain, and liver. The overall five-year survival is less than 25% and most patients die within the first two years. The prognosis is better in surgical stage I or II patients who as a group exhibit a five-year survival of about 70%.

9. SCLEROSING STROMAL TUMOR OF THE OVARY

Sclerosing stromal tumors are benign unilateral ovarian tumors 80% of which usually present within the first three decades of life (mean age is 27 years). All reported cases have been clinically benign. They usually present as a pelvic mass but rare cases

have been associated with estrogen or androgen production. Grossly, the tumor is present as a discrete mass that is well circumscribed. The cut surface is usually white but may show yellowish areas, edema, and cystic changes. Rarely, the tumor presents as a cystic mass.

The typical low-power microscopic feature of this lesion is the presence of a distinctive pseudolobular pattern with cellular neoplastic islands separated by a paucicellular fibrous, collagenous, or edematous connective tissue stroma. Another distinctive low-power feature of this lesion is the presence of a prominent vascular pattern. The blood vessels are thin-walled and may be dilated, resembling a hemangiopericytoma.

Higher-powered microscopic examination reveals the cellular islands to be predominantly composed of relatively large rounded neoplastic cells with vacuolated cytoplasm and an eccentric nucleus with a "shrunkened" appearance and may occasionally exhibit a "signet ring" appearance (however, they cells contain lipid rather than mucin). These cells are mixed with variable numbers of fibroblasts and areas of collagenous deposition ("sclerosis") are frequently found. Mitotic figures are infrequent. In the rare case of a functioning sclerosing stromal tumor one may encounter luteinized cells similar to those seen in luteinized thecomas. Occasionally, nonfunctioning sclerosising stromal tumors may contain prominent typically luteinized cells.

The differential diagnosis includes ovarian fibromas and thecomas. Sclerosing stromal tumors exbibit a more heterogeneous appearance than either of these tumors which lack a pseudolobular appearance, prominent vascularity, and intimate admixture of vacuoalted tumor cells and fibroblasts. Krukenberg tumors may be confused with sclerosing stromal tumors but the signet ring cells contain mucin rather than the lipid found in sclerosing stromal tumors. The prominent vascular pattern may suggest a hemangiopericytoma, but these tumors do not exhibit any of the other characteristic features of sclerosing stromal tumors.

10. SERTOLI CELL TUMOR

These relatively uncommon ovarian tumors account for about 4% of all ovarian stromal tumors, generally following a benign clinical course. They occur in all age ranges with a mean of 30 years. They usually present as a pelvic mass but may produce various hormone- related symptoms in the rare case of a functioning tumor. Hormonal production may include estrogens, androgens, and rarely progesterones and renin (leading to hypertension).

These tumors are usually unilateral and present as a solid, lobular cut surface which is usually yellow or brown.The average diameter is about 9.0 cm. Microscopically, the most characteristic finding is the production of tubules which are always present and, depending upon the degree of differentiation, may be abundant. The tubules may be hollow or solid and are thought to represent the recapitulaion of seminiferous tubules. They are occasionally present in lobules that are separated by fibrous stroma which may show areas of hyalinization. The individual tubules are lined by cuboidal cells which may be either eosinophilic or pale and vacuolated. These cells are typically reactive for cytokeratin and occasionally for vimentin. About 50% of the tumors are reactive for inhibin. Nuclear atypia and mitotic activity are usually minimal but may be present to a greater degree in poorly differentiated lesions.

The differential diagnosis includes well-differentiated Sertoli–Leydig cell tumors. Pure Sertoli cell tumors lack the Leydig cells found in the Sertoli–Leydig cell tumors. Occasionally, a Sertoli cell tumor is confused with a granulosa cell tumor which may exhibit a pronounced trabecular pattern simulating the appearance of the tubules found in a Sertoli cell tumor. However, the other distinctive features of a granulosa cell tumor are not present. Granulosa cell tumors usually produce a variety of patterns which aids in making that diagnosis.

11. REFERENCES

1. Kurman RJ, Norris HJ, Wilkinson E, *Tumors of the Cervix, Vagina, and Vulva* (Armed Forces Institute of Pathology, Washington, DC, 1992).
2. Silverberg SG, Kurman RJ, *Tumors of the Uterine Corpus and Gestational Trophoblastic Disease* (Armed Forces Institute of Pathology, Washington, DC, 1992).
3. Gompel C, Silverberg S, *Pathology in Gynecology and Obstetrics* (J.B. Lippincott, Philadephia, PA, 1994).
4. Kurman R, *Blaustein's Pathology of the Female Genital Tract,* (Springer-Verlag, New York, NY, 1994).
5. Scully RE, Young RH, P.B. C, *Tumors of the Ovary, Maldeveloped Gonads, Fallopian Tube, and Broad Ligament* (Armed Forces Institute of Pathology, Washington, DC, 1998).
6. Clement PB, Young RH, *Atlas of Gynecologic Surgical Pathology* (W.B. Saunders, Philadephia PA, 2000).
7. Robboy SJ, Anderson MC, Russell P, *Pathology of the Female Reproductive Tract* (Churchill Livingstone, London, UK, 2001).

http://www.springer.com/978-0-387-25357-2

Updates in Diagnostic Pathology
Chhieng, D.C.; Siegal, G.P. (Eds.)
2005, XVI, 198 p., Hardcover
ISBN: 978-0-387-25357-2