



Ovary-tumor Printer Friendly Version

Last revised 21 April 2009

Last major update January 2009

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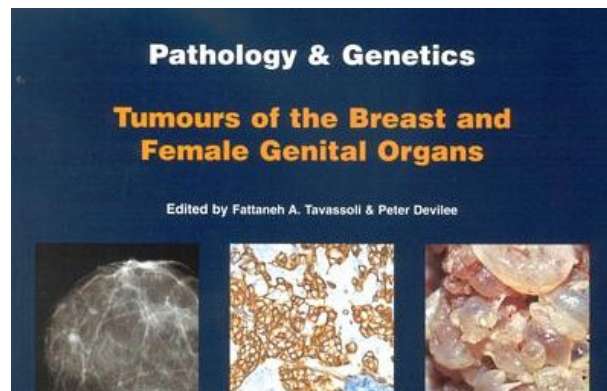


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Primary references - Ovary chapter

[AJCC Cancer Staging Manual \(6th Ed\)](#)

[American Journal of Clinical Pathology](#) [random articles are free full text-no registration], January 1975 to January 2009

[American Journal of Surgical Pathology](#), March 1977 to December 2008

[Archives of Pathology and Laboratory Medicine](#) [always free full text and no registration], January 1976 to December 2008

[Biomed Central](#) [always free full text and no registration], 27 May 1999 to 17 December 2008

[Human Pathology](#), December 1971 to January 2009

[Modern Pathology](#) [free full text and no registration after 1 year], March 1988 to December 2008

[Rosai, J: Ackerman's Surgical Pathology \(9th Ed\), Mosby, 2004](#), not 1656-1671, 1673-1689, 1702-36

[Scully: Tumors of the Ovary, Maldeveloped Gonads, Fallopian Tube, and Broad Ligament \(AFIP Atlas of Tumor Pathology, Series 3, Vol 23\); 1999.](#)

[Tavassoli: Tumours of the Breast and Female Genital Organs \(WHO, 2003\), not 114-96](#)

Websites: [PathoPic](#) - start page 5 (ovary)

Virtual slides - [USCAP](#), [vSlides](#)

Journal search terms: each disease entity listed - last searched January 2009

Please refer to these primary references for more detailed discussions and photographs

Neoplasms

Ovarian Tumors - general- Ovary chapter

#5 cause of cancer death in women; incidence has not changed recently (15,000 estimated US deaths in 2008, [American Cancer Society](#))

80% benign (usually ages 20-45 years)

90% of malignancies are carcinoma, 80% have spread beyond the ovary at diagnosis

Note: in one study, 15% of ovarian specimens required additional clinical information, which caused an altered diagnosis/revised report ([Arch Pathol Lab Med 1999;123:615](#))

Risk factors for carcinoma: nulliparity, family history, older age, childhood gonadal dysgenesis, clomiphene, hereditary nonpolyposis colon cancer, long term estrogen replacement therapy ([US National Cancer Institute](#))

Negative risk factors: history of oral contraceptives, pregnancy before age 25, prophylactic oophorectomy

BRCA1 or BRCA2 mutations: cause 10% of ovarian carcinomas; 16% with these mutations have tumors, usually serous cystadenocarcinomas; occult tumors in 4.5% of prophylactic salpingo-oophorectomies ([Cancer 2007;109:1784](#)); may be detectable only by examining entire ovary ([Am J Surg](#))

[Pathol 2001;25:1283](#), [Am J Surg Pathol 2006;30:1222](#)); BRCA1+ tumors are usually not borderline or mucinous ([Hum Pathol 2000;31:1420](#))

Higher risk of BRCA1 or BRCA2 mutation if ovarian carcinoma (any age), breast cancer (any age), early onset breast cancer

BRCA1 prevalence is 1-2% in US Ashkenazi Jews is 1-2%, 0.24% in other US whites ([Cancer Epidemiol Biomarkers Prev 2004;13:2078](#))

Note: 1-2% of patients undergoing prophylactic oophorectomy develop peritoneal adenocarcinoma, which resembles papillary serous carcinoma of ovary clinically and histologically

Origin: (a) surface coelomic epithelium, which gives rise to fallopian tubes, endometrium, endocervix; (b) germ cells which migrate to ovary from yolk sac; (c) stroma of ovary, which includes the sex cords, forerunners of endocrine apparatus

Symptoms: lower abdominal pain, abdominal enlargement, increased pressure on adjacent organs; occasionally causes bilateral diffuse uveal melanocytic proliferation, a paraneoplastic syndrome in which uveal melanocytes proliferate and cause blindness ([Am J Surg Pathol 2001;25:212](#))

CA-125: a high molecular weight glycoprotein discovered in 1981 ([J Clin Invest 1981;68:1331](#)); elevated serum levels are somewhat sensitive but not specific for ovarian carcinoma; not recommended as a screening test ([American College of Preventive Medicine](#))

Metastases from primary ovarian tumors - Ovary chapter

Contralateral ovary, peritoneal surfaces (1-5 mm tumor nodules which rarely invade deeply), para-aortic/pelvic nodes, liver, lung, pleura, omentum, diaphragm

Sister Joseph's nodule: umbilical metastasis, may be first manifestation of disease

Metastases are associated with ascites, intestinal obstruction, ureteral involvement and hydronephrosis

Metastases are often positive for WT1, ER, PR, CA125; negative for GCDPF-15, CEA (except mucinous tumors, [Am J Clin Pathol 2002;117:745](#), [Am J Clin Pathol 1997;107:12](#))

Case reports: metastasis to breast ([Am J Surg Pathol 1993;17:193](#))

Coexistence with uterine carcinoma: uncommon; may reflect metastases from uterus or ovary or two independent tumors; can differentiate with molecular techniques ([Am J Clin Pathol 1996;105:350](#), [Clin Cancer Res 2008;14:5840](#)); overall excellent prognosis ([Asian Pac J Cancer Prev 2006;7:234](#)), better than metastatic disease

Metastasis from endometrial tumor to ovary is more likely if multinodular, bilateral, small ovarian tumors, tubal lumen involvement is present, deep myometrial invasion or myometrial vascular invasion is present ([Hum Pathol 1985;16:28](#))

Tumors with endometrioid appearance in uterus and ovary are probably independent, have excellent prognosis

Metastases from cervix to ovary likely if bilateral ovary involvement, extensive extracervical disease and microscopic type is unusual for ovary, such as squamous or small cell

Other tumor histology often signifies metastases with poor prognosis

Treatment: must examine peritoneal cavity for proper staging

Benign or borderline tumors: unilateral salpingo-oophorectomy

Malignant tumors: bilateral salpingo-oophorectomy with total abdominal hysterectomy

Cytology: staging incorporates presence of malignant cells in washings or ascites fluid

Serous / endometrioid carcinomas more often have positive cytology than other carcinomas, particularly if high grade

DD: reactive mesothelial cells

Childhood ovarian tumors - Ovary chapter

Most ovarian tumors are benign; malignant tumors have favorable outcome with chemotherapy, even after recurrence ([Am Surg 2008;74:1062](#))

Usually present as unilateral mass without metastases ([Pediatr Blood Cancer 2005;44:167](#))

Of malignant tumors, germ cell tumors predominate, followed by sex-cord stromal (15%) and epithelial tumors (15%) ([Semin Pediatr Surg 2005;14:100](#))

Mature cystic teratomas are common

Excellent prognosis for germ cell tumors, even if malignant ([Pediatr Blood Cancer 2006;46:459](#))

DD: neuroblastoma, Ewings/PNET, adnexal gland carcinoma, rhabdomyosarcoma, intraabdominal desmoplastic small cell tumor

Classification of tumors of ovary - Ovary chapter

Surface epithelial (65%), germ cell (15%), sex cord-stroma (10%), metastases (5%), miscellaneous Benign, borderline (atypical proliferation, low malignant potential) or malignant; malignant may be invasive or non-invasive

Most malignant tumors are surface epithelial (90%)

WHO classification to be added

Surface epithelial tumors

Surface epithelial tumors-general - Ovary chapter

Risk of malignancy rises with increase in grossly solid areas

Derived from surface epithelium (also called coelomic or germinal epithelium) that invaginates to form glands or cysts; this epithelium is continuous with mesothelium that lines peritoneal cavity

Ovarian epithelium may undergo metaplasia/neoplasia to resemble tubal, endometrial or endocervical mucosa (mullerian differentiation)

Classify based on cell type, pattern (cystic, solid, surface), amount of fibrous stroma, invasiveness/atypia

Sample solid foci, base of papillary formations, areas adjacent to ovarian surface

Serous tumors

Serous tumors-general - Ovary chapter

25% of all ovarian tumors

60% benign, 15% borderline, 25% malignant

May also occur as primary tumors of peritoneal surface

If cystic, name as serous "cystadeno..."

If prominent fibrous component, name as adenofibroma or adenocarcinofibroma

Micro: tall, columnar, ciliated epithelial cells, resembling fallopian tube, filled with clear serous fluid; carcinomas frequently have psammoma bodies (concentric calcifications); squamous metaplasia unlikely (in contrast to endometrioid tumors)

Positive stains: CK7, CK8/18, CK19, EMA, B72.3, S100, amylase (25%), ER (50%), PR (50%), androgen receptor (50%), N-Cadherin ([Hum Pathol 1997;28:734](#)); usually CK7+ and CK20- ([Am J Clin Pathol 2002;117:944](#))

Negative stains: CEA

Serous cystadenoma / cystadenofibroma - Ovary chapter

Benign; 25% bilateral

Case reports: giant serous cystadenoma arising from an accessory ovary in a morbidly obese 11 year old girl ([J Med Case Reports 2008;2:7](#)), with mural nodules of genital rhabdomyoma ([Hum Pathol 2005;36:433](#))

Gross: smooth glistening cyst wall; papillary tumors have papillary projections on outer surface or protruding into cystic cavity

Micro: usually small, multilocular, simple papillary processes; single layer of tall, columnar, ciliated cells resembling normal tubal epithelium; stroma contains spindly fibroblasts; no atypia, no architectural complexity, no invasion

Serous cystadenofibroma - ovary chapter

More pronounced proliferation of fibrous stroma

Serous borderline tumors (serous - low malignant potential) - Ovary chapter

Younger women, often pregnant, rarely has malignant behavior

Bilateral in 1/3 if include microscopic tumors

5 year survival is 100% if confined to ovary; 90% if involves peritoneum

5 year survival is not equal to cure due to delayed recurrence or transformation to invasive carcinoma

Death due to bowel obstruction, ureteral obstruction, invasive carcinoma, sepsis and treatment complications

Define as invasive if cytologic atypia (cells round up and have increased eosinophilic cytoplasm as in squamous cell carcinoma, round nuclei, prominent nucleoli), destructive stromal invasion, stromal reaction, capsular invasion; invasive nests have loss of calretinin+ mesothelial cells and loss of stromal CD34+ fibrocytes around the nests, with presence of alpha-smooth muscle actin+ myofibroblasts present as a stromal response ([Mod Pathol 2006;19:364](#))

Define as borderline if typical histologic features (papillary, stratification, detached papillae), even if metastases exist

Serous borderline and invasive carcinomas have different genetic aberrations, indicating that invasive carcinomas do not arise from preexisting serous borderline tumors ([Hum Pathol 2002;33:632](#))

Rarely has supradiaphragmatic nodal involvement ([Am J Surg Pathol 2006;30:739](#))

Poor prognostic factors: invasive implants, micropapillary or cribriform patterns (associated with invasive implants, [Am J Surg Pathol 1999;23:397](#))

Lymph node involvement: tumors are diploid, no short term adverse prognostic significance ([Am J Surg Pathol 1994;18:904](#))

Mullerian inclusion cysts: small cysts lined by bland, cuboidal-columnar serous-type epithelium with a simple architecture; found in lymph nodes, pelvic peritoneum, omentum, bowel serosa, uterine serosa and parametrial connective tissues; often multiple sites; may be bland-appearing metastases from serous borderline tumors ([Am J Surg Pathol 2000;24:710](#))

Case reports: initial presentation as cervicovaginal psammoma bodies ([Arch Pathol Lab Med 1988;112:564](#))

Micro: (need more complete description); no stromal invasion; may have stromal microinvasion or patterns that are not destructive stromal invasion, including individual eosinophilic cells and cell clusters, cribriform pattern, simple and noncomplex branching papillae, inverted macropapillae and micropapillae; individual, discrete aggregates of invasive epithelium may be up to 12 mm, and there may be diffusely scattered invasive foci without discrete aggregates; recommended to identify stromal-epithelial alterations featuring micropapillae in pathology reports as a higher risk lesion than serous borderline possibly analogous to low grade serous carcinoma ([Am J Surg Pathol 2006;30:1209](#))

Autoimplants: usually on surface or between exophytic surface tumor papillae; consist of single cells or glands and clusters of cells with abundant eosinophilic cytoplasm and mild-moderate atypia within fibroblastic stroma, stroma dominates over epithelium in autoimplant; associated with noninvasive peritoneal implants; no apparent adverse prognostic value, so must distinguish from true stromal invasion ([Am J Surg Pathol 2006;30:457](#))

DD: ovarian clear cell carcinoma with papillary features (unilateral, nonhierarchical branching, monomorphic cells with classic features elsewhere, endometriosis, focal cytologic atypia, [Am J Surg Pathol 2008;32:269](#)), low grade serous carcinoma (has destructive stromal invasion)

References: [Mod Path 1988;1:407](#), [Am J Surg Pathol 2002;26:1129](#), [Am J Surg Pathol 2002;26:592](#)

Microinvasive serous carcinoma - Ovary chapter

Same prognosis as serous borderline tumors

Small stromal foci (up to 2 mm) of single cells / small clusters of cells, occasionally cribriform or rounded aggregates of papillae

Eosinophilic cytoplasm with minimal/absent stromal reaction ([Hum Pathol 1996;27:521](#), [Hum Pathol 1990;21:397](#))

Serous cystadenocarcinoma / carcinoma - Ovary chapter

5 year survival of 70% if confined to ovary; drops to 25% if involves peritoneum

May present as lymphadenopathy (usually inguinal or supraclavicular, has similar survival by stage as classic presentation, [Am J Surg Pathol 2004;28:1217](#))

Rarely metastasizes to breast or axillary nodes, associated with advanced stage disease; usually have papillary features but only occasionally psammoma bodies, WT1+, GCDFP-15 negative ([Am J Surg Pathol 2004;28:1646](#))

65% bilateral

Rarely produces AFP ([Arch Pathol Lab Med 1984;108:710](#))

May arise from tubal intraepithelial carcinoma ([Am J Surg Pathol 2007;31:161](#))

Treatment: high grade tumors often have extreme drug resistance

Gross: solid, hemorrhagic, necrotic

Micro: branching papillary fronds, glandular complexity, nuclear atypia and stratification, frequent mitoses, stromal invasion (irregular or destructive infiltration by small glands or sheets of cells); psammoma bodies (calcium concretions with concentric laminations, may be intracellular due to autophagocytosis)

Recommended to classify as high grade or low grade ([Am J Surg Pathol 2008;32:1667](#))

Positive stains: WT1 (78%), CA125 (78%), mesothelin (also lung, pancreas, endometrial adenocarcinomas); also CK5/6 (55%) and D2-40 (23%) ([Mod Pathol 2008;21:1147](#))

Molecular: frequent loss of heterozygosity of p53 and BRCA1 loci in high grade tumors; disseminated tumors appear to be monoclonal ([Mod Path 1996;9:166](#))

DD: peritoneal mesothelioma (usually h-caldesmon+, calretinin+, ER-, Ber-EP4-, [Am J Surg Pathol 2007;31:1139](#); calretinin+, D2-40+, podoplanin+, BerEP4-, MOC31-, [Mod Pathol 2006;19:34](#)); also metastatic invasive micropapillary carcinoma of breast (GCDFP-15+ (38%), WT1-, [Hum Pathol 2008;39:666](#))

Serous micropapillary carcinoma - Ovary chapter

Also called low grade serous carcinoma

Behaves like low-grade adenocarcinoma; appear to be derived from serous borderline tumor or adenofibroma

Recurr as classic serous carcinoma

10 year survival is 70% vs. ~100% for borderline tumors

Invasive if destructive infiltrative growth; most are non-invasive

Survival: dependent on stage and invasiveness of implants; stage I invasive or noninvasive has 100% disease free survival; stage II/III noninvasive or invasive with noninvasive implants has 80% disease free survival, stage II/III noninvasive with invasive implants has 55% 10 year survival; stage II/III invasive with invasive implants has 45% 10 year survival

Micro: filigree pattern of small, uniform, elongated, stroma-poor or stroma-free papillae, at least five times as long as wide, arising directly in a nonhierarchical fashion from large fibrotic, edematous, or myxoid papillary stalks or from cyst walls; or a cribriform pattern of epithelial cells lining the stalks or cyst walls; or both; either or both patterns should be present on a confluent area at least 5 mm in greatest dimension on at least one slide; occasionally also have large macropapillae

Noninvasive: numerous delicate micropapillae (length > 5x width) with no/rare fibrovascular cores; radiates in "medusa" nonhierarchical branching pattern from thick fibrous stalks; may be cribriform due to fusion; micropapillae are covered by cuboidal/columnar cells with minimal cytoplasm, variable psammoma bodies, no cilia, no/rare mitotic figures; more recurrences but similar survival as serous borderline tumors ([Am J Surg Pathol 2002;26:1129](#))

Invasive: by definition, have destructive infiltrative growth; invasive areas may be < 3 cm (microinvasion) or larger; stromal invasion is characterized by micropapillae and solid epithelial nests surrounded by a cleft or space and fibroblastic stroma; may also have noninvasive component; variable psammoma bodies; rarely mitotic figures or atypical mitotic figures; macropapillary component may signify invasive disease ([Am J Surg Pathol 2008;32:1800](#)); single cells or small clusters

of cells appearing to be in spaces within nonreactive stroma are considered to NOT represent stromal invasion

Molecular: chromosomal imbalances intermediate between serous borderline tumors and serous carcinomas ([Hum Pathol 2002;33:47](#))

References: [Am J Surg Pathol 2003;27:725](#), [Am J Surg Pathol 2002;26:592](#), [Am J Surg Pathol 2001;25:419](#)

Serous psammomacarcinoma - Ovary chapter

Rare variant of serous carcinoma with massive psammoma body formation and low grade cytologic features

Behaves similar to serous borderline tumors

Serous surface tumor - Ovary chapter

Grows exophytically on ovarian surface, with little involvement of underlying organ (surface papilloma, surface borderline papillary tumor, serous surface papillary adenocarcinoma)

Malignant tumors tend to be bilateral, aggressive, have widespread dissemination to peritoneum at presentation

May develop in women with family history of ovarian cancer even after prophylactic oophorectomy

Micro: features of typical serous carcinoma; contiguous with hyperplastic mesothelium of ovarian surface or other locations; confined to ovarian surface or with focal minimal invasion

Positive stains: neutral or acidic mucins ([Hum Pathol 1990;21:99](#)), keratin, EMA, B72.3 (85%), LeuM1 (45%), vimentin (35%), CEA (25%)

Molecular: 65% have loss of heterozygosity of p53 and BRCA1 loci ([Hum Pathol 1999;30:203](#))

EM: epithelial differentiation

DD: ovarian implants (in patients with primary ovarian tumors)

References: [Hum Pathol 1989;20:426](#)

Ovarian implants - Ovary chapter

In patients with primary ovarian tumors, implants are deposits of ovarian tumor on peritoneal surfaces, lateral pelvic gutters, right side of diaphragm or omentum, usually close to primary

Entire peritoneum may contain tumor nodules < 1 cm, resembling miliary tuberculosis

Implants are seen in 1/3 of patients with serous borderline tumors, mortality is 25%; some may arise from peritoneal mesothelium; destructive invasion and cytologic atypia are associated with disease progression

May regress spontaneously leaving psammoma bodies behind

Criteria: *ovarian carcinoma* if multiple peritoneal nodules with features of ovarian serous borderline tumor or carcinoma and some minimal ovarian involvement; *extraovarian serous carcinoma* or *papillary tumor of peritoneum* if no ovarian involvement

Criteria for implants associated with primary benign or borderline tumor - *invasive*: either invasion of underlying normal tissue, micropapillary architecture or solid epithelial nests surrounded by clefts; ***noninvasive*:** none of these features

Invasion by these criteria is associated with adverse outcome ([Am J Surg Pathol 2001;25:419](#)); features that do not correlate with invasion are nuclear atypia, mitoses, calcification, necrosis, and individual cell infiltration of the stroma

Micro: tufting, stratification, atypia, psammoma bodies; invasive cases usually had micropapillary pattern and solid epithelial nests surrounded by clefts

Positive stains: LeuM1, B72.3, CEA

DD: desmoplastic response in noninvasive tumors

Mucinous tumors

Mucinous tumors-general - Ovary chapter

15% of ovarian neoplasms, rare before puberty or after menopause

80% are benign, 10% are borderline and 10% are carcinoma

Compared to serous neoplasms, have more cysts, larger size (up to 25kg), more often unilateral
Filled with sticky, gelatinous fluid rich in glycoproteins
Fibromas rare

Based on genetic analysis, some ovarian and appendiceal lesions are independent, others are related
Features favoring appendiceal (non-ovarian) origin: ovarian surface involvement only; signet ring cell differentiation with appendiceal tumor identified (current or prior) of similar morphology, bilateral tumor consistent with appendiceal or colonic primary, unilateral tumor consistent with appendiceal or colonic primary with a history of appendiceal or colonic adenocarcinoma; also normal/slightly enlarged ovaries, bilateral ovarian involvement, simple or focally proliferative mucinous epithelium with abundant extracellular mucin in cases with predominantly surface involvement of the ovaries; multifocal or extensive abdominal cavity mucin in cases with stromal involvement, ruptured appendiceal adenoma and unruptured ovarian tumor of similar histology; presence of an associated mucinous intestinal tumor ([Hum Pathol 1995;26:509](#))

May be associated with mature cystic teratoma ([Am J Surg Pathol 2007;31:854](#))

Positive stains: CEA (particularly malignant tumor of intestinal type), keratin, EMA, amylase (present in 75% of malignant tumors, 20% of benign tumors); usually CK7+/CK20+ (similar to upper GI and endocervical tumors, [Am J Surg Pathol 2006;30:1130](#)); or CK7+/CK20- ([Am J Clin Pathol 2002;117:944](#), [Hum Pathol 1997;28:1039](#))

Negative stains: N-Cadherin ([Hum Pathol 1997;28:734](#))

Mural nodules in mucinous cystic neoplasms - Ovary chapter

Associated with benign, borderline or malignant mucinous cystic tumors ([Am J Surg Pathol 2002;26:1467](#))

Sarcoma-like mural nodules - Ovary chapter

Usually young women (mean 39-47 years old)

Considered benign or reactive

Excellent prognosis; presence does not affect the outcome of the tumor

Gross: typically multiple, small (0.6 to 6 cm), discrete, sharply demarcated, red-brown

Micro: well circumscribed with hemorrhage and necrosis but no vascular invasion; either (1) pleomorphic and epulis-like, composed of heterogeneous cell population including numerous multinucleated giant cells of the epulis type, atypical spindle cells with prominent mitotic activity and inflammatory cells, (2) pleomorphic and spindle cell, consisting predominantly of atypical spindle cells with large, hyperchromatic nuclei, prominent nucleoli, frequent atypical mitotic figures, mixed with histiocytes and inflammatory cells or (3) giant cell-histiocytic, composed of regular, round, well differentiated mononucleated giant cells

Positive stains: vimentin, CD68

Negative stains: keratin (may be a few scattered keratin+ cells)

Sarcomatous nodules - Ovary chapter

Older population

Poor prognosis

Gross: large, poorly circumscribed

Micro: monotonous spindle cell population, vascular invasion

Negative stains: cytokeratin, EMA

Positive stains: variable desmin and actin

Anaplastic carcinoma foci - Ovary chapter

May not affect prognosis in stage I tumors if unruptured ([Am J Surg Pathol 2008;32:383](#))

Case reports: with multicystic mass and anaplastic carcinoma in mural nodule ([Arch Pathol Lab Med 2002;126:871](#))

Gross: large, poorly circumscribed

Micro: rhabdoid, sarcomatoid or pleomorphic features; no prominent inflammatory reaction, no multinucleated giant cells

Positive stains: keratin, EMA

Mucinous cystadenoma - Ovary chapter

5% bilateral

Associated with carcinoid tumors in same ovary and endocervical adenocarcinoma; rarely with Zollinger-Ellison syndrome

Case reports: with cholesterol granuloma in draining lymph nodes ([Arch Pathol Lab Med 1985;109:1124](#))

Micro: tall, columnar, nonciliated cells, basal nuclei, abundant intracellular mucin; usually endocervical type; also intestinal type (picket fence architecture with Paneth cells) or mixed; stroma may be hypercellular or luteinized

Positive stains: CEA, keratin, EMA, amylase (20%); usually CK7+/CK20- ([Am J Clin Pathol 2002;117:944](#))

Mucinous adenofibroma - Ovary chapter

Rare; mean 51 years old (24-76 years)

Benign

Gross: unilateral, 1-25 cm

Micro: glands lined by single layer of mucin-containing columnar cells; may have crowded glands with atypia

DD: metastatic adenocarcinoma

References: [Am J Surg Pathol 1991;15:227](#)

Primary retroperitoneal mucinous cystadenoma - Ovary chapter

Uncommon, found only in women

Resembles ovarian mucinous cystadenoma but is not attached to ovary

Appears to arise from mesothelial cell inclusions and subsequent mucinous metaplasia to form a cystadenoma

Case reports: 30 cm retroperitoneal cystic mass in 25 year old woman ([Arch Pathol Lab Med 2001;125:691](#))

Gross: thin walled (1 mm) multilocular cyst containing clear serous fluid; smooth inner lining

Micro: lining composed of tall columnar cells with clear cytoplasm and basal nuclei and low cuboidal cell resembling mesothelial cells, in densely cellular collagenous stroma composed of closely packed spindle cells

Positive stains: PAS/diastase and Alcian blue (pH 2.5) in tall columnar cells; ER in stroma and low cuboidal cells; calretinin in low cuboidal cells; both cell types positive for CAM 5.2, CK7, CK20

Negative stains: PAS/diastase and Alcian blue (pH 2.5) in low cuboidal cells; ER and calretinin negative in tall columnar cells; all cells negative for B72.3, PR, CEA

Mucinous borderline tumors - Ovary chapter

Also called atypical proliferative mucinous tumor of ovary or mucinous ovarian tumor of low malignant potential

10% bilateral

Pure borderline tumors and borderline tumors with intraepithelial carcinoma are almost always Stage 1 and clinically benign, but must sample tumor extensively to rule out invasion

High stage borderline tumors with abdominal cavity mucin may represent ovarian metastases rather than primary borderline tumors - must examine appendix to correctly interpret ([Am J Surg Pathol 2000;24:1447](#))

Micro: resemble villous or tubular adenomas of intestines; endocrine cells common; are noninvasive with intraglandular or intracystic epithelial proliferations; either endocervical (mullerian) or intestinal types

Classification: borderline may have slight atypia (grade 1 nuclei); borderline with intraepithelial carcinoma have grade 2/3 nuclei, 4+ layers or cribriform or stroma-free papillary growth pattern

Molecular: 40% have K-ras mutations (vs. 11% of mucinous carcinomas, [Am J Surg Pathol 1999;23:323](#))

References: [Am J Surg Pathol 2002;26:139](#)

Endocervical type - Ovary chapter

Tumors usually mixed, but clinically resemble serous tumors due to papillary architecture, serous-type differentiation, frequent bilaterality, smaller size, indolent clinical behavior (only rare deaths, [Am J Surg Pathol 2002;26:1529](#))

Mean 39 years (younger patients), range 25-64 years

Associated with endometriosis in 41% of cases, endosalpingiosis in 32%

Malignancy is based on cytology, not number of cell layers

Almost always stage I, excellent prognosis with no evidence of disease at followup, even with intraepithelial carcinoma or microinvasion ([Am J Surg Pathol 2004;28:1311](#))

Micro: proliferation of branching papillary structures resembling borderline serous tumors; papillae composed of fibrovascular cores of variable size covered by variable epithelium; mucinous cells have basal nuclei; some papillary tips lack fibrovascular cores; small detached clusters of cells may be observed over the papillary tufts; hobnail cells also present; occasionally intraepithelial carcinoma or stromal microinvasion, but no stromal invasion; associated with noninvasive desmoplastic implants

References: [Am J Surg Pathol 2002;26:139](#), [Am J Surg Pathol 2000;24:1447](#)

Intestinal type - Ovary chapter

Comprises most borderline mucinous cases

Occurs in older patients, not associated with endometriosis

Excellent prognosis

Must count cell layers (1-3 layers is borderline tumor, 4 or more layers is malignant)

Microinvasive mucinous adenocarcinoma - Ovary chapter

Same prognosis as mucinous borderline tumor

Small stromal foci (up to 2 mm) of single cells / small clusters of cells, occasionally cribriform

Eosinophilic cytoplasm with minimal/absent stromal reaction ([Hum Pathol 1996;27:521](#))

Pale nuclear staining, fibrous reaction or edema in stroma, particularly in intestinal subtype

References: [Am J Surg Pathol 2002;26:139](#)

Mucinous cystadenocarcinoma / carcinoma - Ovary chapter

77% are ovarian metastases (see below), 23% are ovarian primaries ([Am J Surg Pathol 2003;27:985](#))

Features favoring primary ovarian carcinoma vs. metastasis are: unilateral, "expansile" pattern of invasion, complex papillary pattern, size > 10 cm, smooth external surface, microscopic cystic glands, necrotic luminal debris, mural nodules and accompanying teratoma, adenofibroma, endometriosis or Brenner tumor ([Am J Surg Pathol 2003;27:281](#))

Definition: stromal invasion distinguishes these tumors from borderline tumors

Survival: 95% for stage 1 vs. 32% for stages 2+

10 year survival: borderline stage 1 - 95% (better than previously thought; prior series may have included metastases from intestine and pancreas); noninvasive malignant - 90%, invasive malignant - 66%

Distant metastases are rare

Expansile tumors are usually stage 1 and behave "benign"; infiltrative tumors may demonstrate malignant behavior and cause death even if stage 1 ([Am J Surg Pathol 2002;26:139](#))

Poor prognostic factors for stage 1 tumors: infiltrative invasion (destructive stromal invasion, [Mod Pathol 2005;18:903](#)), high nuclear grade, tumor rupture

Anaplastic components in intact tumors do not affect prognosis ([Am J Surg Pathol 2002;26:139](#))

Gross: primary tumors are usually unilateral, > 10 cm, smooth capsule, cystic and solid areas of tumor evenly distributed throughout ovary without discrete nodularity

Micro: stromal invasion; also more solid growth, atypia, stratification, papillae, loss of glandular architecture, necrosis (resembles colon carcinoma), greater complexity of glands than borderline tumors

Stromal invasion may be infiltrative (disorderly penetration of stroma by neoplastic glands, single cells or cell clusters, may have desmoplastic response) or expansile (complex arrangement of glands, cysts or papillae lined by malignant epithelium with minimal or no intervening stroma)

Glands are almost always intestinal type and not endocervical type
Carcinoma often merges with borderline or benign mucinous tumors
Rarely has signet ring cells, but differs from Krukenberg tumor ([Am J Surg Pathol 2008;32:1373](#))
Grading: grade 1-no solid areas, grade 2-up to 50% solid foci; grade 3-more than 50% solid foci;
severe nuclear atypia can raise grade 1 or 2 carcinomas by one grade

Positive stains: CEA, CK7, CK20, CA125 (weak)

Molecular: K-ras mutations are common

DD: metastatic tumor (bilateral tumors of any size, unilateral tumor <10-12 cm, exceptions are often metastatic colorectal and endocervical carcinomas, [Am J Surg Pathol 2008;32:128](#))

References: [Am J Surg Pathol 2000;24:1447](#), [Am J Surg Pathol 2002;26:1529](#)

Metastatic mucinous carcinoma to ovary - Ovary chapter

Primary sites: 45% GI, 20% pancreas, 18% gynecologic, 8% breast, 10% unknown

Features favoring metastasis and not primary ovarian tumor are history of extra-ovarian primary mucinous adenocarcinoma, bilaterality, surface implants (gross or microscopic), infiltrative pattern of stromal invasion; also nodular invasive pattern, ovarian hilar involvement (due to tumor emboli), single cell invasion, signet ring cells, vascular invasion, surface mucin ([Am J Surg Pathol 2003;27:281](#)); CDX2+ tumor cells suggests GI primary ([Mod Path 2003;16:913](#))

Surface implant: nodular protrusion above adjacent cortical surface, composed of neoplastic glands and single cells

Gross: usually bilateral tumors or unilateral tumors < 10 cm, involves surface / superficial cortex, typically with nodular pattern; also surface implants

Micro: nodular pattern of invasion characterized by circumscribed aggregates of glands surrounded by zones of normal ovarian stroma, particularly in superficial ovary; may be mixed with haphazard infiltrative mucinous glands irregularly distributed throughout the ovarian stroma; borderline-like areas usually display much greater cytologic atypia than borderline / benign mucinous tumors; metastatic pancreatic carcinoma may contain bland mucinous epithelium simulating mucinous cystadenoma

References: [Am J Surg Pathol 2003;27:985](#)

Pseudomyxoma peritonei - Ovary chapter

Clinically represents mucinous ascites accompanied by peritoneal lesions with bland to low-grade adenomatous mucinous epithelium intimately associated with pools of extracellular mucin and fibrosis, diagnosed pathologically as disseminated peritoneal adenomucinosis

Peritoneal mucinous tumor/ascites almost always has mucinous epithelium present, if adequately sampled

Virtually all cases have appendiceal, not ovarian origin

Rare cases lacking mucinous epithelium usually do not recur

Three types of pseudomyxoma peritonei: (1) superficial; mucin contains hyperemic organizing vessels and fibroblasts; (2) dissecting with fibrosis; (3) metastatic mucinous carcinoma

Mucin is associated with cystic epithelial implants on peritoneal surfaces, adhesions to bowel, abdominal wall and bladder; intestinal obstruction and peritonitis

Due to production of MUC2, a gel-forming mucin that forms strong bonds with stroma

Treatment: excise as much tumor as possible, plus chemotherapy

References: [Am J Surg Pathol 2000;24:1447](#)

Peritoneal mucinous carcinomatosis - Ovary chapter

Rarely ovarian in origin

Micro: histologic features of carcinoma, usually signet-ring morphology

Endometrioid tumors

Endometrioid tumors-general - Ovary chapter

20% of surface ovarian tumors, usually carcinomas

15-40% are accompanied by endometrial carcinoma, but are considered independent primaries; often have a good prognosis;

may represent (a) single clonal tumor with concordant genetic alterations (based on identical loss of homozygosity, identical PTEN mutation or sporadic microsatellite instability patterns) or (b) single clonal tumor with genetic progression or (c) double/triple clonal tumors ([Hum Pathol 2002;33:421](#))

Presence of endometriosis in ovary usually means ovarian tumor is primary

Mixed tumors with endometrioid and serous / mucinous patterns also exist

Benign tumors are often cystadenofibromas

Gross: 40% bilateral, usually associated with extension beyond genital tract

Micro: tubular glands resembling endometrium; usually foci of squamous differentiation; often arises in background of fibroma / adenofibroma

Endometrioid cystadenoma - Ovary chapter

Micro: cystic tumor with endometrioid features; no cytologic atypia, no architectural complexity; benign lesions may be adenofibroma, adenoma or cystadenoma

Endometrioid adenofibroma - Ovary chapter

No recurrence or deaths in patients with atypia

Micro: endometrioid and fibroma-like features; may have mild to severe cytologic and architectural atypia

References: [Am J Surg Pathol 1985;9:205](#)

Endometrioid borderline tumor - Ovary chapter

Rare (<200 cases reported)

Mean age 55 years, range 28-86 years

97% present with stage I disease

Typically no recurrent disease or metastasis on follow-up, even if intraepithelial carcinoma or microinvasion ([Am J Surg Pathol 2003;27:1253](#))

Micro: composed of aggregates, glands or cysts of endometrioid-type epithelium that is atypical or cytologically malignant but lacks destructive stromal invasion, glandular confluence or stromal disappearance; often has adenofibromatous pattern (47%) or squamous differentiation (47%); may have foci of intraepithelial carcinoma (7%, high grade/grade 3 nuclei are large, pleomorphic with coarse chromatin or hypochromasia, large irregular nucleoli; also many mitotic figures; associated with villoglandular architecture or microinvasion); microinvasion if areas of invasion are 10 mm² or less (7%)

References: [Am J Surg Pathol 2000;24:1465](#)

Endometrioid carcinoma - Ovary chapter

10-25% of primary ovarian carcinomas

15% coexist with endometriosis; tumors may arise from endometriotic cysts

15-30% of patients have endometrial hyperplasia or carcinoma; these tumors are often well differentiated with squamous metaplasia

Associated with keratin granulomas of peritoneum ([Am J Surg Pathol 1990;14:925](#))

Mean age 51 years, range 26-87 years

Prognosis: better than serous/mucinous tumors because usually stage 1 and well differentiated; not as good as borderline tumors; may have malignant behavior if limited destructive stromal invasion

([Mod Pathol 2005;18:903](#))

Sample thoroughly, as serous or undifferentiated carcinoma component lowers 5 year survival from 63% (pure) to 8% ([Am J Surg Pathol 1994;18:687](#))

Tumors with yolk sac component are unusually aggressive ([Am J Surg Pathol 1996;20:1056](#))

Cytologic atypia and microinvasion do not appear to affect prognosis ([Am J Surg Pathol 2000;24:1465](#))

Gross: cystic, solid, hemorrhagic; papillary formations are absent or inconspicuous; 5% bilateral; mean 11 cm, range 3-22 cm

Micro: either non-cystic villoglandular pattern, glandular confluence or stromal disappearance; resembles endometrioid adenocarcinoma of uterus, usually well differentiated; 50% have squamous metaplasia (morules or keratin pearls, formerly called adenoacanthomas), 40% of well differentiated tumors have adenofibromatous component; 10% are associated with luteinized stroma cells; may

contain luminal but not cytoplasmic mucin, may have clear cells (but lacks the architecture of clear cell carcinoma, [Am J Surg Pathol 2007;31:1203](#)); vascular invasion rare
Stromal invasion is defined as confluent glandular growth, stromal disappearance or obvious stromal invasion

Positive stains: keratin, CEA (some), HPL (some), N-Cadherin ([Hum Pathol 1997;28:734](#))

EM: paranuclear microfilaments, "mesh basket" nucleoli

Molecular: PTEN mutations in 21%

DD: Sertoli-Leydig tumors (usually younger patients with endocrine symptoms, no squamous metaplasia, no typical endometrioid features elsewhere, no mucin, no adenofibroma component, keratin negative), metastatic colonic carcinoma, metastatic endometrial carcinoma (bilateral, multinodular, surface implants, prominent angiolymphatic invasion within ovarian stroma)

References: [Am J Surg Pathol 1982;6:513](#), [Am J Surg Pathol 2003;27:1253](#)

Granulosa cell tumor like variant of endometrioid carcinoma of ovary - Ovary chapter

Micro: resembles granulosa cell tumor but has nonmorular nests with nuclear clearing and biotin activity; may have classic endometrioid features

Positive stains: PR

DD: granulosa cell tumor

Sertoliform variant of endometrioid carcinoma of ovary - Ovary chapter

Uncommon; resembles Sertoli and Sertoli-Leydig cell tumors

Usually age 60-70 years, older than Sertoli tumors (mean 25 years)

Good prognosis if limited to ovary ([Arch Pathol Lab Med 2007;131:979](#))

Micro: compact anastomosing cords and small tubules within fibrous stroma without desmoplasia; usually low grade nuclear features, mucin at apical border of tumor cells; associated with classic endometrioid carcinoma in all cases, often with squamous metaplasia; usually focal adenofibroma component

Positive stains: keratin (CK7), EMA, ER, PR

Negative stains: inhibin (except for luteinized stromal cells, [Mod Path 1999; 12:933](#)), calretinin

Spindle cell variant of endometrioid carcinoma of ovary - Ovary chapter

Classify as endometrioid based on typical endometrioid glands, foci of squamous differentiation or adenofibromatous component

Similar behavior as typical endometrioid carcinoma

Micro: predominance of spindle-shaped epithelial cells

Positive stains (spindle cells): EMA, keratin

DD: sex cord stromal tumor, female adnexal tumor of wolffian origin, mixed mullerian tumor

References: [Am J Surg Pathol 1995;19:1343](#)

Brenner tumors

Brenner tumors-general- Ovary chapter

One of two types of transitional cell tumors - also transitional cell carcinoma

1-2% of ovarian neoplasms

Usually age 40+; median age 50 years

Slow growth, rarely ascites

Adenofibromas in which epithelial component consists of sharply demarcated nests of urothelial-like cells

Associated with hyperestrogenism (endometrial hyperplasia and uterine bleeding), mucinous cystadenoma, struma ovarii, urothelial carcinoma of bladder

Has true urothelial differentiation based on immunostains ([Am J Surg Pathol 2003;27:1434](#))

Epidermoid cysts may originate from epithelial cell nests of Brenner tumor ([Am J Clin Pathol 1980;73:272](#))

Case reports: cervical carcinoma metastatic to Brenner tumor ([Mod Path 1995;8:307](#))

Gross: unilateral, firm, white/yellow; resembles fibroma/thecoma except for cystic areas with yellow-brown fluid

Micro: solid and cystic nests of urothelium-like cells surrounded by abundant dense, fibrous stroma; epithelial cells have sharp outlines; clear to pale cytoplasm, small but distinct nucleoli and nuclear grooves, similar to granulosa cell tumors

Positive stains: keratin, EMA, CEA, glycogen, chromogranin (focal), NSE; also EGFR ([Am J Surg Pathol 2008 Nov 19 \[Epub ahead of print\]](#))

Negative stains: p16, p53

References: [Hum Pathol 1989;20:787](#)

Benign Brenner tumor- Ovary chapter

Derived from ovarian surface epithelium and metaplasia; similar to Walthard nests

6% bilateral

Micro: sharply demarcated solid epithelial nests in dense fibrous stroma; cells are uniform, polygonal with pale cytoplasm and often grooved nuclei; frequent microcysts within epithelial nests

Metaplastic - with prominent cystic formation, accompanied by florid mucinous changes similar to cystitis glandularis

Proliferating - with papillary pattern and low grade nuclear atypia (resembles low grade urothelial carcinoma of bladder)

Positive stains: CK7, thrombomodulin, uroplakin III (focal)

Negative stains: CK20

References: [Am J Surg Pathol 2003;27:1434](#)

Borderline Brenner tumor- Ovary chapter

Mean age 60 years, older than for benign Brenner tumor

Larger tumor with mass related symptoms

May be associated with bladder urothelial carcinoma

Rare local recurrence, otherwise benign behavior

Gross: unilateral, multilocular cysts, 10-25 cm with papillary or polypoid projection into lumen

Micro: solid and papillary epithelial proliferation with high grade nuclear atypia; papillary areas lined by multilayer epithelium (looks like high grade urothelial carcinoma), cells have prominent nucleoli, nuclear grooves, no stromal invasion

Positive stains: CK7

Negative stains: CK20

References: [Am J Surg Pathol 2003;27:1434](#)

Malignant Brenner tumor- Ovary chapter

Atypical cytology and stromal invasion

May be bilateral

Better prognosis than urothelial (transitional cell) carcinoma

Micro: resembles urothelial, squamous or undifferentiated carcinoma, but associated with benign or borderline Brenner component; stromal invasion is present

Other surface epithelial tumors

Clear cell adenocarcinoma - Ovary chapter

Also called mesonephroid adenocarcinoma

Associated with endometriosis or endometrioid carcinoma of the ovary

Usually ages 40-59 years

Stage for stage, similar prognosis to other ovarian carcinomas

Gross: spongy, cystic

Micro: tubular-cystic, papillary or solid; papillary cores have prominent hyalinization; large tumor cells, some with nuclei that protrude into lumina (hobnail), clear cytoplasm (glycogen, mucin, fat); resembles mucinous tumor on frozen section

Positive stains: keratin, Leu-M1 (90%), hyaline globules are PAS+ diastase resistant but AFP negative; VHL gene product (90%, [Am J Clin Pathol 2008;129:592](#)), hepatocyte nuclear factor 1 beta ([Mod Pathol 2006;19:83](#))

Negative stains: AFP, WT1, ER, usually GPC3

DD: high grade serous carcinoma (usually WT1+, hepatocyte nuclear factor 1 beta negative, often ER+, [Am J Surg Pathol 2009;33:14](#)), yolk sac tumor (AFP+, GPC3+, [Am J Surg Pathol 2008;32:600](#)), dysgerminoma (Oct3/4+)

References: [Am J Clin Pathol 1989;91:511](#)

Oxyphilic variant of clear cell adenocarcinoma - Ovary chapter

Abundant eosinophilic cytoplasm, but also typical clear cell areas ([Am J Surg Pathol 1987;11:661](#))

Urothelial carcinoma (transitional cell carcinoma) - Ovary chapter

1-2% of surface epithelial tumors of ovary

Mean age 56 years, range 33-94 years

Resembles urothelial carcinoma of bladder but no coexisting Brenner component

Poorer prognosis than malignant Brenner tumor

Median survival for stage 3/4 disease is 28 months, similar to serous carcinoma ([Hum Pathol 1996;27:1267](#))

Gross: mean 10 cm, range 3-30 cm, 60% solid and cystic, 41% bilateral

Micro: undulating, diffuse, insular or trabecular patterns; papillary structures lined by urothelium-like cells and nests of epithelial cells with high grade features, pale granular cytoplasm, large nucleoli or longitudinal grooves, separated by fibrous stroma; usually necrosis; may have other ovarian epithelial components (usually serous)

Positive stains: CK7, WT1, p53, p16, ER ([Arch Pathol Lab Med 2005;129:194](#))

Negative stains: uroplakin III, CK20, EGFR ([Am J Surg Pathol 2008 Nov 19 \[Epub ahead of print\]](#))

References: [Am J Surg Pathol 2003;27:1434](#), [Am J Surg Pathol 2004;28:453](#)

Mixed epithelial-papillary cystadenoma of borderline malignancy of mullerian type - Ovary chapter

Associated with endometriosis, favorable prognosis

Mean age 35 years

Micro: mucinous, serous, endometrioid and squamous epithelium; may have squamous overgrowth, prominent neutrophilic infiltration of epithelium ([Am J Surg Pathol 2003;27:242](#))

DD: borderline Brenner tumor

Germ cell tumors

Germ cell tumors - general- Ovary chapter

20% of ovarian tumors; resemble germ cell tumors in testis

Usually children and young adults

Usually benign cystic teratomas

8% are mixed

Survival: 95% disease free survival due to chemotherapy with bleomycin, etoposide and cisplatin

Case reports: systemic mast cell disease 3 months after chemotherapy for mixed malignant germ cell tumor ([Hum Pathol 1998;29:1546](#))

Carcinoid tumors - Ovary chapter

May be a form of monodermal teratoma; 15% have cystic teratoma or mucinous neoplasm in contralateral ovary

Good prognosis if ovarian primary

1/3 are associated with carcinoid syndrome; may cause constipation due to secretion of peptide YY

Case reports: primary ovarian carcinoid with metastases and simultaneous borderline mucinous tumor and colonic adenocarcinoma ([Arch Pathol Lab Med 1996;120:393](#))

Treatment: excision, although mucinous types are more aggressive

Gross: mean 10 cm, yellow, solid cut surface; usually unilateral

Micro: resembles carcinoid tumors elsewhere; patterns are insular (resembles appendix or small bowel tumors), trabecular (resembles stomach or rectal tumors); strumal (below), mucinous; may have abundant fibrous stroma; rarely has prominent pleomorphism, mucinous features (below) or signet ring pattern

Positive stains: chromogranin, synaptophysin, neuron specific enolase (NSE)

Negative stains: inhibin

EM: neurosecretory granules

DD: fibroma-thecoma, Brenner tumor; GI metastasis (bilateral, associated with peritoneal implants, no other teratomatous elements)

References: [Arch Pathol Lab Med 1987;111:440](#)

Mucinous (goblet cell) carcinoid - Ovary chapter

Rare; usually stage 1

Presence of frank carcinoma may be poor prognostic factor

Gross: solid nodules/areas of thickening in wall of mature cystic teratoma or solid tumors associated with other cystic tumors

Micro: often well-differentiated with small glands, many floating in mucin pools; glands lined by goblet cells and columnar cells, some neuroendocrine

References: [Am J Surg Pathol 2001;25:557](#)

Atypical mucinous carcinoid - Ovary chapter

Micro: crowded glands, some confluent with cribriform pattern and scattered microcystic glands; glands are lined by cuboidal and columnar cells, some neuroendocrine and goblet cells

Carcinoma arising in mucinous carcinoid - Ovary chapter

Micro: islands, larger nodules, closely packed glands or single cells of mainly signet ring cell type; most cells lack mucin and are severely atypical, with marked mitotic activity and necrosis

DD: metastatic mucinous carcinoid from appendix or elsewhere (ovarian origin suggested if ovarian teratoma or surface epithelial tumor present, no angiolymphatic invasion, involves only one ovary), strumal carcinoid, insular carcinoid

References: [Am J Surg Pathol 2001;25:557](#)

Strumal carcinoid - Ovary chapter

Has features of carcinoid tumor and struma ovarii

Associated with MEN IIA/III

Case reports: associated with MEN IIA ([Arch Pathol Lab Med 1992;116:200](#))

Micro: often other teratomatous elements

Positive stains: neuron specific enolase, chromogranin, synaptophysin, thyroglobulin, PAP (similar to rectal carcinoids)

Negative stains: calcitonin

EM: numerous electron-dense neurosecretory granules, [Am J Clin Pathol 1978;69:356](#)

Choriocarcinoma - Ovary chapter

Most ovarian choriocarcinomas are metastases from uterine tumors

Pure ovarian choriocarcinomas are rare, develop from ovarian pregnancy or as a germ cell tumor (pure or mixed)

Rarely arise from surface ovarian carcinomas with choriocarcinomatous differentiation

After puberty, origin from an ovarian ectopic pregnancy cannot be excluded

Have high levels of serum hCG; monitoring serum levels is helpful in predicting recurrence

In contrast to placental tumors, nongestational tumors are usually fatal and unresponsive to chemotherapy; metastases to lungs, liver, bone and viscera are common at diagnosis

Micro: mixture of syncytial and cytotrophoblastic elements in a hemorrhagic and necrotic background

Positive stains: hCG, CD10

Dysgerminoma - Ovary chapter

Less than 1% of ovarian malignancies

Counterpart of testicular seminoma

Usually young patients (81% under age 30)

5% associated with gonadal dysgenesis/Swyer syndrome ([World J Surg Oncol 2007 Jun 23;5:71](#)), androgen insensitivity or pseudohermaphroditism; rarely associated with hypercalcemia

Metastasize to opposite ovary, retroperitoneal nodes, peritoneal cavity

Rarely transforms to yolk sac tumor ([Mod Path 1995;8:881](#))

Survival: 95%

Mixture with choriocarcinoma, yolk sac or embryonal carcinoma worsens prognosis

Treatment: surgery and chemotherapy (NOT radiotherapy, although it is effective for seminoma)

Gross: 15% bilateral; solid, nodular, small to huge, gray-pink (resembles cerebral cortex); hemorrhage and necrosis common but less prominent than other malignant tumors

Micro: nests of tumor cells separated by fibrous stroma with T lymphocytes; large vesicular cells with well defined cell borders, cleared cytoplasm containing glycogen, central nuclei; 1+ prominent nucleoli; occasional granulomas; may have hCG+ syncytiotrophoblastic cells close to blood vessels or hemorrhagic foci with increased serum hCG; may have abortive yolk sac elements with increased serum AFP; may be present in wall of mature teratoma; may have pseudotubular or cord-like architecture

Early carcinomatous differentiation: 30+ mitoses per 10 high power fields, may worsen prognosis

Positive stains: OCT4 (strong nuclear staining in 90%+ cells, [Am J Surg Pathol 2004;28:1341](#)), c-kit (87%, [Mod Pathol 2005;18:1411](#)), CAM5.2 (20%), AE1-AE3 (8%, [Hum Pathol 2006;37:1015](#))

Negative stains: CK7, CK20, EMA, HMW keratin, CD30, vimentin

Molecular: 12p abnormalities in 81% ([Mod Pathol 2006;19:611](#))

Embryonal carcinoma - Ovary chapter

Similar to testicular embryonal carcinoma

Median age 15 years, patients often present with precocious puberty, also vaginal bleeding, amenorrhea, hirsutism

Serum hCG always high (positive pregnancy test), AFP sometimes high

Gross: median 17 cm, smooth and glistening, variegated cut surface with extensive hemorrhage and necrosis

Micro: sheets and nests of large primitive cells, occasional papillae and abortive glands; syncytiotrophoblast-like tumor cells seen (hCG+)

Mixed Germ Cell tumor of Ovary - Ovary chapter

Molecular: often isochromosome 12p in teratomatous and non-teratomatous components ([Mod Pathol 2006;19:766](#))

Polyembryoma - Ovary chapter

Embryonal carcinoma composed primarily of embryoid bodies

Embryoid body has amniotic cavity-like structure and is continuous with intestinal duct, and rarely has squamous cell nests, while "yolk sac" is continuous with hepatic tissue

Embryoid body is not considered to be a real or teratomatous embryo, but a product of divergent differentiation into intestine and liver from the plastic epithelium, which seems to be derived from embryonic gut ([Hum Pathol 1988;19:1144](#))

Struma ovarii - Ovary chapter

Rare monodermal teratoma composed predominantly of mature thyroid tissue

May show pathologic changes of thyroid gland including hyperfunctioning; malignancies are usually papillary thyroid carcinoma

Associated with mucinous cystadenoma, Brenner tumor, carcinoid tumor, dermoid cyst

Case reports: struma salpingis ([Am J Surg Pathol 1993;17:1187](#)), follicular variant of papillary carcinoma with intraluminal crystalloids ([Arch Pathol Lab Med 1991;115:145](#))

Gross: resembles red-brown thyroid tissue but usually multilocular cystic; usually unilateral
Micro: thyroid follicles with colloid; other teratomatous elements may be present; rarely has solid or pseudotubular patterns, microfollicles, abundant eosinophilic cytoplasm, abundant clear cytoplasm or minimal thyroid follicles

Positive stains: thyroglobulin

Molecular: BRAF mutations frequent in malignant but not benign tumors ([Am J Surg Pathol 2007;31:1337](#))

DD: metastatic thyroid carcinoma to ovary

References: [Am J Surg Pathol 1995;19:21](#), [Am J Surg Pathol 1994;18:785](#), [Arch Pathol Lab Med 1978;102:180](#)

Teratoma-mature - Ovary chapter

Mature if only contains adult tissues

Usually teenage women (solid) or children (cystic)

Excellent prognosis, even if peritoneal implants are present

Rarely associated with hemolytic anemia

May rupture into peritoneal cavity causing foreign body reaction that simulates metastatic carcinoma or miliary tuberculosis

Tumors arise from a single germ cell after first meiotic division

Cystic tumors may contain squamous cell carcinoma, carcinoid tumor or adenocarcinoma

Dermoid cyst: usually means teratoma resembles skin; some use dermoid cyst and mature teratoma interchangeably

Gliomatosis peritonei: peritoneal implants exclusively composed of mature glial tissue; benign if all tissue is mature and other teratomatous elements are absent

Case reports: corticotroph pituitary adenoma ([Am J Surg Pathol 1987;11:218](#)), glomus tumor ([Arch Pathol Lab Med 2000;124:1373](#)), homunculus (fetiform) coexisting with intrauterine pregnancy ([Arch Pathol Lab Med 1986;110:1192](#)), mature teratoma with anti-Ri antibodies and memory impairment ([Int Semin Surg Oncol 2004 Nov 10;1\(1\):11](#)), mucinous tumor ([Am J Surg Pathol 2003;27:650](#)), nodal gliomatosis ([Arch Pathol Lab Med 1986;110:975](#)), peptic ulcer with spindle cell nodule, ([Arch Pathol Lab Med 1990;114:529](#)), pituitary tissue ([Arch Pathol Lab Med 1978;102:122](#)), prostate tissue ([Am J Surg Pathol 1992;16:780](#), [Arch Pathol Lab Med 1985;109:675](#)), skin adnexal tumor ([Arch Pathol Lab Med 1993;117:846](#))

Gross: solid or cystic; cystic content may contain greasy material composed of keratin, hair, teeth; rarely is "fetiform" (partial human body-like structure) or contains partial mandible; teeth may be found in Rokitansky's protuberance-a well defined nipple-like structure covered with hair

Micro: ectodermal structures in 100%, mesodermal in 93%, endodermal in 71%; skin and glial tissue common; prostate tissue in 10%; still considered mature if microscopic foci of immature tissue

DD: immature teratoma grade 1 (sample extensively to distinguish); epidermoid cyst (no skin adnexae or other tissues)

References: [Am J Surg Pathol 2003;27:650](#)

Malignant change in cystic teratoma - Ovary chapter

Tumor is apparently derived from germ cell elements of teratoma, but behavior is based on phenotype

Squamous cell carcinoma: most common malignant change in cystic teratoma; 5 year survival is 52%, dependant on histologic grade and vascular invasion; appears to arise from columnar epithelium ([Am J Surg Pathol 1989;13:397](#))

Case reports: apocrine adenocarcinoma, ([Arch Pathol Lab Med 1993;117:647](#)), carcinosarcoma arising from dermoid cyst ([BMC Cancer 2006 Mar 1;6:47](#)), Paget's disease in squamous epithelium ([Am J Surg Pathol 1991;15:1002](#)), small cell epidermoid carcinoma ([Arch Pathol Lab Med 1995;119:551](#)), squamous cell carcinoma in situ ([Arch Pathol Lab Med 1991;115:172](#))

Teratoma-immature - Ovary chapter

Malignant tumor, whose tissue resembles embryonal or fetal tissue

Usually prepubertal or young women (mean 18 years)

Most recurrences within 2 years; presence of yolk sac component is best predictor of recurrence in pediatric tumors ([Am J Surg Pathol 1998;22:1115](#))

Common errors are classifying differentiating tissue as immature and not recognizing hepatoid and well-differentiated glandular patterns of yolk sac tumor

Case reports: 17 year old woman with predominant malignant retinal anlage component, tumor parthenogenetically derived, GFAP+, neuroglia by EM ([Am J Surg Pathol 1985;9:221](#))

Treatment: surgery, multiagent chemotherapy; better prognosis if only mature teratoma found after chemotherapy, although abnormal karyotype is maintained in mature teratoma

Gross: bulky, solid or cystic with necrosis, hemorrhage

Micro: usually neurogenic elements (GFAP+); mesodermal elements common; some tumors derived primarily of esophageal, liver and intestinal structures (endodermal)

Grading: histologic grade is based on proportion of tissue containing immature neuroepithelium
Norris grading system (correlates best with extraovarian spread, survival)

1 - abundant mature tissue, loose mesenchymal tissue with occasional mitoses, immature cartilage, tooth anlage

2 - less mature tissue than grade 1, rare foci of neuroepithelium with mitoses, < 4 low power fields in any one slide

3 - little/no mature tissue; numerous neuroepithelial elements merging with cellular stroma occupying 4+ low power fields

Immature teratoma variants

Endodermal teratoma - Ovary chapter

High serum AFP, low serum hCG, no neuroectodermal component

Micro: early endoderm - liver, esophagus, intestine

Positive stains: AFP, alpha-1-antitrypsin

References: [Hum Pathol 1993;24:364](#)

Ependymoma - Ovary chapter

May derive from teratoma

Neuroectodermal component composed entirely of primitive ependymal structures

Appears to derive from distinct precursors or to differentiate along distinct pathways from CNS ependymoma based on different immunostaining patterns ([Am J Surg Pathol 2008;32:710](#))

Case reports: PR+ bilateral tumors in pregnant woman ([Hum Pathol 1992;23:962](#)), 68 year old woman ([Am J Surg Pathol 1993;17:623](#)), tumor of broad ligament ([Am J Surg Pathol 1984;8:203](#))

Micro: resembles CNS ependymoma; cells have fibrillary cytoplasmic processes, often arranged around blood vessels forming perivascular pseudorosettes

Positive stains: CK18 (100%), ER (100%), CK7 (80%), PR (80%), 34betaE12 (60%), CAM5.2 (60%); GFAP, vimentin, neuron-specific enolase, S100, EMA

EM: cilia on surface of cysts and within intracellular lumina, abundant intermediate filaments in cytoplasmic processes, intercellular junctions

References: [Hum Pathol 1984;15:632](#)

Growing teratoma syndrome - Ovary chapter

Treatment: long term follow up since recurrent masses can appear many years after primary tumor, although most nodules appear within 2 years of initial primary

Case reports: carcinoid teratoma arising in mature teratoma of liver ([Am J Surg Pathol 2007;31:1913](#))

Yolk sac tumor - Ovary chapter

Also called endodermal sinus tumor

May be derived from embryonal carcinoma

Usually children or young adults (median age 19 years) with abdominal pain and rapidly growing mass, increasing alpha fetoprotein (AFP) and alpha-1-antitrypsin serum levels; negative hCG

Fatal without chemotherapy since most have subclinical metastases at presentation

Case reports: with associated virilization ([Am J Surg Pathol 1981;5:385](#))

Gross: mean 15 cm, smooth and glistening external surface, cystic cut surface with hemorrhage and necrosis; often has benign teratoma component; rarely is found in pelvis unattached to ovary

Micro: numerous patterns; Schiller-Duval body is pathognomonic - central blood vessel enveloped by germ cells within a space similarly lined by germ cells, resembles glomerulus; hyaline droplets present in all tumors (positive for AFP, PAS and alpha-1-antitrypsin)

Patterns: reticular or microcystic patterns formed by a loose network of flat/cuboidal cells; polyvesicular vitelline pattern: in 25%; vesicular structures with eccentric constrictions surrounded by a dense spindle cell stroma; may have better prognosis in pure form

Other patterns - hepatoid (large polyhedral cells with hyaline bodies but no bile, resembles metastatic hepatocellular carcinoma), intestinal differentiation, glandular (may be cribriform or resemble endometrioid carcinoma), solid, parietal yolk sac (thick layers of basement membrane) and undifferentiated

Positive stains: keratin, AFP (yolk sac elements, hepatic or intestinal epithelium in teratomas), CD10

Molecular: usually aneuploid or tetraploid

References: [Am J Surg Pathol 1987;11:767 \(endometrioid pattern\)](#)

Sex cord-stromal tumors

Sex cord-stromal tumors-general - Ovary chapter

5% of ovarian neoplasms, 7% of malignant ovarian neoplasms

Derived from ovarian stroma, itself derived from sex cords of embryonic gonad (predecessor of Sertoli, Leydig, granulosa and theca cells)

Theca cells produce estrogens; Leydig cells produce androgens

Morphology and clinically evident hormonal activity may go together, but classify based on morphology

Positive stains: alpha-inhibin, mullerian inhibiting substance, alpha-inhibin (>95%), calretinin (more sensitive, less specific than inhibin ([Am J Surg Pathol 2002;26:1477](#)), CD99 ([Arch Pathol Lab Med 2000;124:563](#)), MART1/MelanA, WT-1

Negative stains: EMA, PLAP, CEA

Notes: anti-Mullerian hormone staining is present in only a small percentage of granulosa or Sertoli tumor cells, but is specific for these tumors ([Hum Pathol 2000;31:1202](#)), particularly compared to endometrioid tumors ([Hum Pathol 1998;29:840](#))

Strong alpha-inhibin staining is relatively specific for ovarian sex-cord stromal proliferations, although luteinized cells from other tumors are also immunoreactive ([Hum Pathol 1997;28:1387](#), [Am J Surg Pathol 1997;21:583](#))

Fibroma - Ovary chapter

Common; benign; arise after puberty

40% of tumors > 6 cm are associated with ascites

Also associated with right sided hydrothorax, Meigs syndrome, basal cell nevus syndrome

Meigs syndrome: ovarian fibromas, right sided hydrothorax, ascites; after tumor excision, hydrothorax and ascites disappear

Basal cell nevus syndrome (Gorlin syndrome): autosomal dominant disease of multiple basal cell carcinomas, odontogenic keratocysts, palmoplantar pits, congenital skeletal abnormalities and ectopic calcifications, caused by mutational inactivation of the PTCH gene; also have calcified, bilateral, often multinodular ovarian fibromas

Fibrothecoma: combined fibroma and thecoma; also a generalized term for these two closely related tumors

Case reports: fibrothecoma with ascites and elevated CA125 ([Arch Pathol Lab Med 2005;129:701](#)), 69 year old woman with fibrothecoma containing minor sex cord elements and fibrosarcoma ([Arch Pathol Lab Med 2003;127:81](#))

Treatment: excision, does not recur

Gross: mean 6 cm, usually unilateral, solid, lobulated, firm, white, may have myxoid change; not associated with adhesions

Micro: closely packed spindle cells in "feather-stitched" or storiform pattern; may have hyaline bands and edema; no atypia

Positive stains: CD56 (not specific), WT1, ER-beta, PR, variable smooth muscle actin, occasional S100 and CD34 ([Am J Surg Pathol 2008;32:884](#))

Molecular: trisomy 12

DD: cellular fibroma (up to 3 mitoses/10 high power fields), fibrosarcoma (4+ mitoses/10 HPF), massive edema, fibromatosis, thecoma, Brenner tumor, Krukenberg tumor

References: [Am J Surg Pathol 2002;26:1477](#)

Cellular fibroma of ovary - Ovary chapter

Recommended to call mitotically active cellular fibroma ([Am J Surg Pathol 2006;30:929](#))

Treatment: excision and long term follow up; occasionally recurs locally, particularly with rupture or adherence

Gross: mean 9 cm, usually solid, may have cystic component, occasionally ovarian surface adhesions or extraovarian involvement

Micro: cellular intersecting fundles of spindle cells with bland nuclei, 4+ MF/10 HPF

DD: fibrosarcoma (severe nuclear atypia, 4+ MF/10 HPF, aggressive clinical course)

Fibroma with minor sex cord elements - Ovary chapter

Case reports: 45 year old woman ([Diagn Pathol 2007 Dec 4;2:46](#))

Gonadoblastoma - Ovary chapter

Also called dysgenetic gonadoma

Mixture of germ cell tumor and sex-cord stromal tumor

Usually occurs in individuals with abnormal sexual development and indeterminate gonads; usually gonadal dysgenesis with Y chromosome (i.e. XY gonadal dysgenesis, XO-XY mosaicism, not XX gonadal dysgenesis); 25% risk of neoplasia in these gonads

Also present in phenotypically normal women, even during pregnancy, although ovary is never normal Y chromosome material appears to participate in gonadoblastoma tumorigenesis ([Am J Clin Pathol 1997;108:197](#))

Associated with ataxia-telangiectasia

80% are phenotypic women, 20% are phenotypic men with undescended testicles and female internal secondary organs

50% have coexisting dysgerminoma

Excellent prognosis if completely excised; almost never malignant

Gross: 36% bilateral, tumors usually small, may be microscopic

Micro: primitive germ cells and sex cord stromal cells surrounded by ovarian-type stroma; nests of dysgerminoma-like germ cells and sex cord derivatives resemble immature Sertoli and granulosa cells; arranged in nests surrounded by ovarian stroma containing Leydig or lutein-type cells; hyalinization and calcification are common; may be dysgerminoma if overgrowth of this component

([Am J Clin Pathol 1997;108:197](#))

Positive staining: anti-Mullerian hormone focally ([Hum Pathol 2000;31:1202](#))

DD: incidental finding in ovaries of normal infants/children (associated with follicular cysts, microscopic foci resembling gonadoblastoma or sex cord tumor with annular tubules)

Granulosa cell tumor-adult - Ovary chapter

Differentiation towards follicular granulosa cells

Usually women age 15+ years; 75% associated with hyperestrogenism, causes precocious puberty in children, metrorrhagia (bleeding between periods), endometrial hyperplasia / carcinoma (usually well differentiated and superficial), breast fibrocystic changes in adults

Endometrial hyperplasia regresses after tumor excision

10 year survival >90%; tends to recur locally, up to 20 years later

5-25% risk of malignancy, cannot predict from histology

Prognostic factors: stage, size, tumor rupture, nuclear atypia

Case reports: [Case of the Week #96](#), tumor to tumor metastasis from breast cancer ([Hum Pathol 2002;33:445](#)), collision tumor with colonic adenocarcinoma ([World J Surg Oncol 2007 Oct 20;5:118](#)),

recurrence after 30 years ([Int Semin Surg Oncol 2004 May 11;1\(1\):4](#)), associated with unusual germline p53 mutation ([Mod Pathol 2004;17:868](#))

Gross: >95% unilateral and confined to ovary; encapsulated with smooth lobulated surface, gray or yellow, solid or cystic with straw colored or mucoid fluid; may resemble cystadenoma; androgenic tumors tend to be large

Micro: small, bland, cuboidal to polygonal cells in various patterns, including Call-Exner bodies (small follicle-like structures filled with acidophilic material), macrofollicular, trabecular, solid, insular patterns; cells may be luteinized (plump with ample cytoplasm), particularly during pregnancy; may have theca cell component

Cells have coffee bean nuclei with folds/grooves; may see floret giant cells, indicative of degeneration
Rarely focal hepatic cell differentiation (large cells with abundant eosinophilic, slightly granular cytoplasm; central round nuclei with single prominent nucleoli; often bile pigment in canaliculi between large cells ([Am J Surg Pathol 1999;23:1089](#), [Am J Surg Pathol 1993;17:85](#)), pseudopapillary pattern ([Am J Surg Pathol 2008;32:581](#))

Positive stains: inhibin alpha, vimentin, calretinin ([Am J Surg Pathol 2002;26:1477](#)), CD99 ([Mod Pathol 1998; 11:769](#)), smooth muscle actin, desmoplakin, S100 (50%), keratin (dot like in 30-50%, primarily low molecular weight, [Am J Surg Pathol 1992;16:962](#)), anti-Mullerian hormone focally ([Hum Pathol 2000;31:1202](#)), desmin (35%), silver stains demonstrate reticulin surrounding cluster of cells

Negative stains: EMA

Cytology: little cytoplasm, intense indentation of nuclear membrane; resembles mesothelial cells ([Am J Clin Pathol 1986;85:402](#))

Molecular: monosomy 22 (~40%), trisomy 12 (~30%), +14 (~30%), monosomy X (~10%), monosomy 17 (5%), although most tumors (80%) are diploid or near-diploid ([Mod Pathol 2002;15:951](#))

EM: abundant intermediate filaments, desmosomes

DD: poorly differentiated ovarian surface epithelial carcinoma (diffuse cytoplasmic keratin staining, [Virchows Arch A Pathol Anat Histopathol 1989;414:439](#)), carcinoid tumor, endometrial stromal sarcoma, endometrioid carcinoma, small cell carcinoma of hypercalcemic type, pregnancy related granulosa cell proliferation (microscopic, multiple, associated with atretic follicles, [Hum Pathol 1988;19:657](#))

Granulosa cell tumor-juvenile - Ovary chapter

5% of ovarian tumors in children

Mean age 13 years, range 0-67 years, 80% occur before age 20, 97% before age 30

Most prepubertal patients present with sexual precocity due to excessive estrogen production; rarely produce androgens ([J Endocrinol Invest 2006;29:653](#)); older patients have nonspecific abdominal swelling and pain

Rarely associated with enchondromatosis (Ollier's disease), Mafucci syndrome, abnormal karyotype / ambiguous genitalia ([Am J Surg Pathol 1985;9:737](#))

Case reports: [Case of the Week #59](#), cystic tumor in 43 year old woman ([Arch Pathol Lab Med 2002;126:1123](#)), bilateral tumor in newborn with dysmorphic features ([Am J Surg Pathol 1981;5:789](#))

Treatment: excision is usually adequate for limited disease, although late recurrence may occur ([Am J Obstet Gynecol 2004;191:366](#))

Gross: usually unilateral, up to 12 cm; multiloculated, cystic and solid tumor with yellow-white solid areas; may have hemorrhage and necrosis

Micro: diffuse or macrofollicular patterns with microcysts containing eosinophilic secretions, tumor cells either have scant cytoplasm or are luteinized; round/oval hyperchromatic nuclei with small nucleoli, irregular nuclear contours; no/rare nuclear grooves; high mitotic rate (mean 7/10 HPF); may have hobnail-type cells, pseudopapillary pattern ([Am J Surg Pathol 2008;32:581](#))

Positive stains: inhibin, calretinin

Negative stains: HER2

Molecular: consistent trisomy 12 (as with adult granulosa cell tumors); more aneuploidy in juvenile than adult granulosa cell tumors

DD: adult granulosa cell tumors (more regularly shaped follicles with basement membrane material, prominent nuclear grooves, no hyperchromasia), thecoma (older patients, no follicles, no atypia, no mitotic figures), clear cell carcinoma (older patients, diffuse hobnail cells, no follicles, no juvenile granulosa type cells)

References: [Am J Surg Pathol 1984;8:575](#), [Arch Pathol Lab Med 1989;113:40](#)

Gynandroblastoma - Ovary chapter

Sex cord stromal tumor with equal numbers of granulosa-theca cells and Sertoli-Leydig cells
Very rare; variable hormones

Case reports: 24 year old woman with polycystic ovarian syndrome ([Arch Pathol Lab Med 2006;130:225](#))

Leydig cell tumor (hilus cell tumor) - Ovary chapter

Rare, derived from hilar cells

Almost always benign

Call a nonhilar Leydig cell tumor if it occurs in ovarian cortical stroma

Symptoms: virilization, elevated 17-ketosteroid excretion, unresponsive to cortisol suppression

Treatment: excision

Gross: unilateral

Micro: large lipid laden cells with distinct borders; Reinke crystals common

Lipid (steroid, lipoid) cell tumor - Ovary chapter

Any age, usually associated with virilizing syndrome (defeminization and amenorrhea)

Cells either lutein (theca/stroma), hilar (Leydig, with Reinke crystals) or adrenal cortical type

If Cushing syndrome present, tumor often called "adrenal cortical type"

Exact origin of tumor is unknown

May be biologically active or inactive

Malignant: 25%, usually large (7 cm or more), necrosis, hemorrhage, nuclear atypia, mitoses, may have peritoneal implants

Gross: usually unilateral, yellow/brown nodules separated by fibrous trabeculae

Micro: large rounded or polyhedral cells with abundant eosinophilic or vacuolated cytoplasm

Positive stains: fat stains on fresh/frozen tissue, vimentin (75%), keratin (50%), actin (30%)

EM: increased smooth endoplasmic reticulum, mitochondria have tubulovesicular cristae

DD: tumors with secondary proliferation of steroid hormone-producing cells (stromal luteoma, luteinized granulosa cell tumor [usually juvenile], fibroma-thecoma, stromal Leydig cell tumor, proliferations at periphery of other tumors)

Myxoma - Ovary chapter

Some consider it a variant of fibroma-thecoma ([Arch Pathol Lab Med 1993;117:802](#))

Gross: solid and cystic, with blood filled cysts

Micro: scattered fibroblastic cells in well-vascularized myxoid background

Sclerosing stromal tumor - Ovary chapter

Rare, benign, resembles fibroma-thecoma but in younger patients

Prominent vasculature is associated with vascular endothelial growth factor expression ([Am J Surg Pathol 1998;22:83](#))

Micro: lobular growth pattern of cellular and hypocellular areas composed of dual cell population (collagen producing spindle cells and lipid-containing round/oval cells); interlobular fibrosis, marked vascularity

Positive stains: desmin, smooth muscle actin

Molecular: trisomy 12 by FISH

EM: luteinized theca like cells, spindle-shaped fibroblastic cells, primitive mesenchymal cells

DD: Krukenberg tumor

References: [Arch Pathol Lab Med 1989;113:372](#)

Sertoli cell tumor - Ovary chapter

Rare; excellent prognosis

Mean 30 years old, range 2-76 years

Tends to secrete estrogen/progesterone, but diagnose based on morphology, not hormones
Similar to a well differentiated Sertoli-Leydig tumor without a Leydig component; may have abundant cytoplasmic lipid

Associated with Peutz-Jeghers syndrome

Usually stage I and clinically benign ([Am J Surg Pathol 2005;29:143](#))

Case reports: 67 year old whose tumor has various histologic patterns ([Arch Pathol Lab Med 2006;130:e70](#))

Gross: lobulated, solid, yellow-brown, unilateral, mean 9 cm, up to 30 cm

Micro: closely packed solid or hollow tubules lined by well differentiated cuboidal to columnar epithelial cells; few or no Leydig cells, often fibromatous or sclerotic; may have amyloid-like material; other patterns include cord-like and diffuse; variable stroma; occasional cells with bizarre nuclei; minimal mitoses, minimal atypia

malignant: moderate to severe cytologic atypia and 5+ MF/10 HPF

Positive stains: inhibin, vimentin, CD99, CD10, AE1-3 or CAM5.2 (usually), calretinin (50%), variable smooth muscle actin and S100

Negative stains: EMA, chromogranin

EM: tight junctions, desmosomes, abundant rough endoplasmic reticulum and lipid

DD: endometrioid carcinoma (EMA+, inhibin-), carcinoid (chromogranin+, EMA+, inhibin-)

Lipid rich variant of Sertoli cell tumor - Ovary chapter

Large Sertoli cells with abundant cytoplasmic lipid

May be associated with isosexual pseudoprecocity, Peutz-Jeghers syndrome

“Adenomas” are common in testes of those with testicular feminization (most common tumor after seminomas), but are actually hamartomas, usually bilateral

Sertoli-Leydig tumor - Ovary chapter

Also called Sertoli-stromal cell tumor; formerly called androblastoma, arrhenoblastoma

Rare, < 0.1% of ovarian neoplasms

Morphologically resembles cells of testis at various stages of development, but ultrastructurally resembles ovarian granulosa cell tumors and contains female sex chromatin

Usually young women (mean age 25 years, 75% < age 30), but 10% > age 50; some with edema are diagnosed during pregnancy

Virilization in 30-50% with oligo/amenorrhea, loss of secondary sex characteristics, breast atrophy, masculinization [clitoral hypertrophy, hirsutism, deepening of voice]; also increased RBC count, increased serum testosterone and androstenedione, variable increases in serum alpha-fetoprotein, usually normal serum 17-ketosteroids

Feminine characteristics return after surgery, but manifestations of masculinization disappear more slowly

50% have no endocrine abnormalities

2% bilateral, 97% stage I, 2% spread beyond ovary

5% recur/metastasize

Well differentiated: older age, usually not associated with masculinization; usually clinically benign

Intermediate differentiated: associated with virilization; 11% clinically malignant

Poorly differentiated: 59% clinically malignant; case report of AFP production ([Arch Pathol Lab Med 1986;110:65](#))

Tumors with heterologous elements: 19% clinically malignant

Retiform pattern: often young girls; tumors are stage I

Some cells show differentiation into both Sertoli cells and cells of rete testis, but lack presence of sex-determining region Y ([Hum Pathol 2001;32:796](#), [Hum Pathol 1997;28:1206](#))

Treatment: conservative surgery if tumor confined to ovary

Case reports: 4 year old girl with retiform pattern ([Arch Pathol Lab Med 2002;126:377](#)), 13 year old girl with elevated serum AFP, heterologous elements (hepatocytes) and retiform pattern ([Am J Surg Pathol 1984;8:709](#)), 17 year old girl with elevated AFP and clusters of hepatocytes ([Arch Pathol Lab Med 1995;119:1075](#)), 22 year old woman with retiform pattern and mucinous component ([Arch Pathol Lab Med 2004;128:e93](#))

Gross: similar to granulosa cell tumors - golden-yellow but fewer blood filled cysts, almost never have unilocular cyst

Micro: hemorrhage/necrosis suggests poorly differentiated tumors or heterologous elements; edematous papillae suggests retiform subtype

Degenerative changes (bizarre and multiple nuclei) have no prognostic significance

Multiple subtypes may exist in same tumor (so % add up to > 100%)

Well differentiated (Meyer type I): 11%, may be nodular; tubular (hollow > solid), easily identifiable Leydig cells and Sertoli cells in a tubular pattern; may resemble endometrioid carcinoma or atrophic seminiferous tubules; crystals of Reinke in 20%

Intermediate differentiated (Meyer type II): 54%, outlines of immature tubules with immature Sertoli cells and large Leydig cells; may have mucus filled epithelial cells, cartilage, skeletal muscle

Poorly differentiated (Meyer type III): 13%, resemble indifferent gonad; may have sarcomatous appearance, Leydig cells in 2/3; may have mucus filled epithelial cells, cartilage, skeletal muscle

Pure Sertoli cell tumors (tubular androblastoma): similar to well differentiated Sertoli-Leydig cells but no Leydig cells and no primitive stromal elements; cytoplasm may have abundant lipid; tubular or follicle-like patterns; variable amyloid

With heterologous elements (teratoid androblastoma): 22%, associated with mucinous epithelium of GI type, liver, skeletal muscle, cartilage

Retiform ("netlike"): 15%, irregular branching, elongated and narrow tubules and cysts, which often have papillary structures; also ribbons of immature Sertoli cells; degenerative cells (large, bizarre cells without mitotic activity); usually associated with intermediate or poorly differentiated tumors; often have homologous or heterologous tissues including hepatocyte differentiation (positive for AE1-AE3, CAM5.2, AFP, ferritin, [Hum Pathol 1999;30:611](#)); resemble yolk sac tumors (Schiller-Duval bodies, AFP+), serous borderline tumors (older patients, no ribbons of immature cells)

Positive stains: testosterone, estradiol, cytokeratin, AFP (in hepatoid areas), CD99 ([Mod Path 1998;11:769](#)), inhibin alpha, low molecular weight cytokeratin, anti-Mullerian hormone focally ([Hum Pathol 2000;31:1202](#)), progesterone receptor, androgen receptor, vimentin ([Hum Pathol 1997;28:1206](#))

Negative stains: EMA, PLAP, CEA, CA19-9, CA125, S100 (use to distinguish from carcinosarcoma)

Molecular: Trisomy 8 in case report ([Hum Pathol 2001;32:559](#))

EM: elongated nuclei with deep indentations and annulate lamellae (resemble Sertoli cells), apical microvilli and frequent desmosomes (resemble rete testis)

DD: endometrioid carcinoma with sex cord-like elements, carcinoid tumor

References: [Am J Surg Pathol 1985;9:543](#), [Am J Surg Pathol 1984;8:405](#), [Am J Surg Pathol 1983;7:755 \(retiform pattern\)](#)

Sex cord tumor with annular tubules - Ovary chapter

Distinctive ovarian tumor associated with hyperestrinism (50%)

1/3 with tumor have Peutz-Jegher's syndrome

Peutz-Jegher's syndrome: autosomal dominant with variable penetrance; patients have ovarian sex cord stromal tumors or tumorlets with annular tubules (almost all patients, usually bilateral, often with calcifications, tumorlets are benign); mucocutaneous melanin pigmentation (lips, oral mucosa, digits, palms, soles, genitalia); GI hamartomatous polyposis (florid epithelium supported by broad bands of smooth muscle in stalk, causes intussusception and GI bleeding); occasional adenocarcinomas of GI tract, pancreas, breast, lung; occasional cervical adenoma malignum, ovarian mucinous carcinomas; Peutz was Dutch physician 1886-1957; Jeghers was American physician born 1904

Patients without Peutz-Jegher's syndrome have large, unilateral tumors, with transitions to granulosa cell tumors, 40% secrete estrogen, 20% are malignant

Arise in ovarian cortex from follicular granulosa cells

Micro: mixture of simple and complex annular tubules with eosinophilic hyaline bodies, often calcified; resembles granulosa cell tumor with Sertoli growth pattern; simple annular tubules are ring shaped, with peripheral oriented nuclei around a central hyalinized body composed of basement membrane material; most of ring is anuclear cytoplasmic zone

Complex annular tubules are made of intercommunicating rings revolving around multiple hyaline bodies, often calcified

EM: granulosa cell and Sertoli cell features (granulosa cell-deeply indented nuclei, interdigitating plasma membranes joined by abundant desmosomes; Sertoli cell-variable Charcot-Bottcher filaments as cytoplasmic inclusions), [Am J Clin Pathol 1981;75:11](#)

DD: Sertoli cell tumors, granulosa cell tumors, gonadoblastoma (different clinical background, has germ cell component)

Steroid cell tumor, NOS - Ovary chapter

< 0.1% of all ovarian tumors

Mean age 42 years, range 2 to 80 years

Usually associated with androgenic changes (56-77%); estrogen secretion in 6-23%, Cushing syndrome in 6-10%

Usually benign in prepubertal children

Clinically malignant in 25-43%, associated with 2+ mitosis per high-power field (92% malignant); necrosis (86% malignant); 7 cm or larger (78% malignant); hemorrhage (77% malignant); and grade 2 or 3 nuclear atypia (64% malignant); some clinically malignant cases are histologically benign

Case reports: 8 year old girl with virilization ([Arch Pathol Lab Med 1991;115:150](#)), 22 year old woman with virilization ([J Med Case Reports 2007 Dec 18;1:182](#)), 24 year old woman with hirsutism and multiple sclerosis ([Arch Pathol Lab Med 2003;127:890](#)), 29 year old woman with virilization and tumor in accessory ovary in broad ligament ([Arch Pathol Lab Med 1996;120:405](#)), 35 year old woman with virilization ([Arch Pathol Lab Med 2006;130:113](#))

Gross: up to 45 cm, solid, well-circumscribed, yellow-orange to red-brown to brown-black cut surface (depending on amount of lipid and lipochrome pigment); 6% bilateral; occasional hemorrhage and cystic degeneration

Micro: usually diffusely arranged cells, also nests, clusters, cords, columns; scant stroma may be fibromatous, edematous or myxoid; tumor cells are round/polygonal with spongy to granular, eosinophilic cytoplasm with clear intracytoplasmic vacuoles; distinct cell borders; central nuclei, prominent nucleoli; no Reinke crystals, no significant nuclear atypia or mitotic activity

Positive stains: inhibin, fat stains (75%), vimentin (75%), CAM 5.2 (46%), AE1/AE3 (37%), EMA (8%), S100 (7%)

Negative stains: chromogranin A, CD15 (Leu-M1), myoglobin, neurofilament, AFP, CEA, HMB-45

DD: stromal luteoma, clear cell carcinoma, metastatic renal cell carcinoma, luteoma of pregnancy

References: [Am J Surg Pathol 1987;11:835](#)

Thecoma - Ovary chapter

Usually > 40 years old, 65% after menopause

May be hormonally active, associated with estrogenic and occasionally (if steroid cells present) androgenic symptoms

Usually benign

Luteinized thecomas: thecoma plus features of steroid hormone secreting cells including edema, focal mitotic activity; may be associated with sclerosing peritonitis and ascites ([Am J Surg Pathol 1994;18:1](#), [Arch Pathol Lab Med 1996;120:303](#))

Leydig cell containing thecoma: if Reinke's crystalloids are present in cytoplasm

Gross: unilateral (90%), well defined, firm, solid, covered by intact ovarian serosa; variable size; usually yellow; often a mixture with fibroma (white)

Micro: spindle cells with moderate pale cytoplasm containing lipid droplets and central nuclei; intervening stroma has collagen deposition and focal hyaline plaque formation; some tumors are heavily calcified; may have prominent stromal hyperplasia (hyperthecosis)

Positive stains: Oil red O or Sudan black (fat stains) on fresh/frozen tissue; silver stains demonstrate reticulin fibers surrounding individual cells (note: reticulin surrounds clusters of cells in granulosa cell tumors)

Molecular: trisomy 12

Tumor of adrenogenital syndrome - Ovary chapter

Case reports: 36 year old woman with congenital adrenal hyperplasia with sudden aggravation of virilizing symptoms ([Am J Surg Pathol 2001;25:1443](#))

Gross: soft brown masses in ovarian or paraovarian tissue

Micro: identical to the testicular tumor of the adrenogenital syndrome

Unclassified sex cord stromal tumors - Ovary chapter

Differential diagnosis is usually between granulosa cell tumor and Sertoli-Leydig tumor

Predominance of primitive spindle-cell stroma or cords, trabeculae or tubules with features of both tumors in different areas

5 year survival is 92% (behavior resembles Sertoli-Leydig tumors of intermediate differentiation)

References: [Am J Surg Pathol 1996;20:699](#), [Arch Pathol Lab Med 1998;122:52](#)

Other ovarian tumors

Female adnexal tumor of wolffian origin - Ovary chapter

Originally described as arising from broad ligament, also ovary, fallopian tube and retroperitoneum

Not a sex-cord stromal tumor since wolffian/mesonephric origin, but resembles them

No stromal cells of steroid hormone secreting type, no hormonal manifestations

Wide age range (15-81 years)

Usually benign, rarely malignant with metastases to omentum, liver, lung

Case reports: 60 year old with benign appearing primary but hepatic metastases ([Arch Pathol Lab Med 2000;124:431](#))

Gross: solid or solid/cystic, smooth surface, yellow-tan, usually unilateral, 1-20 cm, focal hemorrhage and necrosis

Micro: epithelial cells form cystic structures, hollow or solid tubules, diffuse sheets; sieve-like on low power; tubules outlined by well-defined basement membrane; cells are low cuboidal with minimal eosinophilic cytoplasm, oval hyperchromatic nuclei, finely granular chromatin, no atypia, no/rare mitotic activity; hemorrhage and necrosis may be present

PAS+ basement membranes are prominent around epithelial aggregates

Positive stains: CD10, CAM5.2, vimentin, variable EMA

Negative stains: mucin, B72.3, CEA, S100, inhibin alpha (may be weak / focal positive)

EM: thick layer of basal lamina surrounding tubules; prominent desmosomes, distinct junctional complexes; irregular nuclei, prominent nucleoli; cilia present

DD: Sertoli-Leydig cell tumor (has Leydig cells, clinical hormonal effects, not in broad ligament, inhibin alpha+), endometrioid adenocarcinoma of ovary (marked atypia and mitotic activity) or fallopian tube (intraluminal mass)

References: [Am J Surg Pathol 2003;27:178](#)

Microcystic stromal tumor - Ovary chapter

First described in 2008 ([Am J Surg Pathol 2008 Oct 28. \[Epub ahead of print\]](#))

Mean age 45 years, range 26-63 years

Usually unilateral

Appear to have benign behavior and stromal derivation

Gross: mean 9 cm (range 2-27 cm), usually solid-cystic; solid component is firm, tan or white-tan

Micro: conspicuous microcystic change with small round/oval cystic spaces that may coalesce to larger irregular channels; often intracytoplasmic vacuoles; also solid cellular areas with fibrous bands and hyaline plaques, similar to thecoma; cells have moderate, finely granular, lightly eosinophilic cytoplasm, bland round/oval or spindle nuclei with fine chromatin and indistinct nucleoli; may have foci of bizarre nuclei; up to 2 MF/10 HPF; no morphologic features diagnostic of other sex cord stromal tumors, no epithelial elements, no germ cell elements

Positive stains: CD10, vimentin; variable keratin (25%)

Negative stains: inhibin, calretinin, EMA

Small cell carcinoma of ovary, hypercalcemic type - Ovary chapter

Mean age 23, range 9-43 years), associated with hypercalcemia in 2/3 which disappears after excision

More common than pulmonary type

Poor prognosis due to extra-ovarian spread (50% in stage IA die of disease); better prognosis if 30 years or older, normal preoperative serum calcium, < 10 cm size, no large cells ([Am J Surg Pathol 1994;18:1102](#))

Often associated with surface epithelial tumor

Not associated with hyperestrogenic effects

May be of germ cell origin ([Hum Pathol 1987;18:175](#))

Case reports: 26 year old woman ([Arch Pathol Lab Med 2006;130:e56](#)), 32 year old woman with bilateral pleural effusions and ovarian mass ([Arch Pathol Lab Med 2003;127:e271](#)), ectopic parathyroid hormone production ([Arch Pathol Lab Med 2005;129:531](#))

Gross: mean 15 cm (range 6-26 cm), solid, fleshy mass with hemorrhage and necrosis

Micro: diffuse sheets of small, closely packed round cells with scant cytoplasm, small hyperchromatic nuclei with irregular chromatin clumps, small but identifiable nucleoli; cytoplasmic hyaline globules, follicle-like structures with eosinophilic fluid, frequent mitotic figures; tumor necrosis with perivascular sparing; 50% have large cells with abundant eosinophilic cytoplasm and large nuclei with prominent nucleoli; 10% have mucinous epithelial cells with intracytoplasmic mucin; no crush artifact or Azzopardi effect

Cytology: highly cellular with poorly cohesive uniform small cells with scant cytoplasm, round/oval hyperchromatic nuclei, inconspicuous nucleoli, occasional mitotic figures

Positive stains: CAM 5.2, vimentin (50%), variable chromogranin, laminin, PTH-related protein, EMA (30%)

Negative stains: B72.3, S100 ([Am J Clin Pathol 1989;92:140](#)), inhibin

Molecular: diploid

EM: poorly differentiated; abundant dilated rough endoplasmic reticulum; no neurosecretory granules ([Am J Clin Pathol 1988;90:523](#))

DD: lymphoma (Burkitt's), dysgerminoma, ovarian small cell carcinoma of pulmonary type, granulosa cell tumor (different morphology, not associated with hypercalcemia)

Small cell carcinoma of ovary, pulmonary type - Ovary chapter

Mean age 59 years (range 28-85 years)

Resembles conventional pulmonary small cell carcinoma

Poor prognosis

Case reports: small cell and large cell tumor in 40 year old mother and 21 year old daughter ([Arch Pathol Lab Med 1995;119:523](#))

Gross: 50% bilateral, most have extraovarian spread at diagnosis, mean 13 cm (4-26 cm), solid with variable cysts

Micro: sheets and nests of small/medium size round/spindle cells with hyperchromatic nuclei, fine regular chromatin (not clumped), inconspicuous nucleoli, minimal cytoplasm; also crush artifact, Azzopardi effect; occasionally associated with endometrioid carcinoma; may have squamous, mucinous, Brenner differentiation

Positive stains: keratin, EMA, neuron specific enolase; occasional chromogranin

Negative stains: vimentin

Molecular: aneuploid

EM: neurosecretory granules

References: [Am J Surg Pathol 1992;16:926](#)

Other tumors (not specific to ovary)

Adenoid cystic and basaloid carcinoma - Ovary chapter

Rare; resembles salivary gland or cutaneous carcinomas, pure or mixed with conventional patterns

Adenoid cystic carcinomas are more aggressive than basaloid carcinomas; present at older age

Case reports: with myoepithelial differentiation ([Arch Pathol Lab Med 2000;124:1529](#) and [Mod Pathol 1996;9:413](#))

Micro: small uniform and basaloid cells in tubular pattern with cribriform and focal solid areas; minimal pleomorphism or mitotic activity, no necrosis

Positive stains: CAM 5.2, AE1-AE3, CEA, muscle-specific actin, S100

EM: convoluted nuclei and filamentous structures associated with dense bodies; PAS+ basement membrane material appears as reduplicated basal lamina

References: [Mod Path 1995;8:731](#)

Angiomyolipoma - Ovary chapter

Angiosarcoma - Ovary chapter

Rare in ovary

Median age 31 years (range 25-42 years)

Gross: unilateral, hemorrhagic, median 13 cm

Micro: variable; vascular nature often not immediately apparent, but at least focal vasoformative channels or discrete cytoplasmic vacuoles; fascicular growth pattern composed of spindle cells with ovoid nuclei and ample eosinophilic cytoplasm mimicking leiomyosarcoma; also reticular growth pattern resembling yolk sac tumor; may also resemble clear cell carcinoma of ovary

Positive stains: vascular markers for vasoformative channels

References: [Am J Surg Pathol 1998;22:620](#)

Benign papillary mesothelioma - Ovary chapter

Typically an incidental finding

Has hyaluronidase-sensitive acid-mucin staining

Endometrial stromal sarcoma - Ovary chapter

Micro: high or low grade; plump oval cells arranged around spiral artery-like vessels

Fibromatosis - Ovary chapter

May be related to massive edema, probably not related to fibromatosis of soft tissue

Menstrual abnormalities common

Gross: firm, white cut surface

Micro: spindle cells separated by dense collagen, luteinized cells present

Fibrosarcoma - Ovary chapter

Aggressive

Trisomy 8 may be helpful in distinguishing from cellular fibroma ([Am J Surg Pathol 1997;21:52](#))

Case reports: 8 year old girl with nevoid basal cell carcinoma syndrome ([Am J Surg Pathol 1984;8:231](#))

Gross: large, solid, with adhesions

Micro: 4 or more mitotic figures per 10 high powered fields

Granulocytic sarcoma - Ovary chapter

May be initial clinical presentation of disease

Associated with AML in bone marrow

Often fatal

Case reports: with dysplastic nevus syndrome ([Arch Pathol Lab Med 1991;115:830](#))

Gross: often green, bilateral

Micro: diffuse growth pattern with focal cords and pseudoacinar spaces; sclerosis often present; myeloid differentiation usually not prominent

Positive stains: chloroacetate esterase, lysozyme, myeloperoxidase, CD68, CD43

DD: lymphoma

Hemangioma - Ovary chapter

Case reports: large cavernous hemangioma in 68 year old woman ([Arch Pathol Lab Med 1986;110:77](#))

Infantile hemangioendothelioma of ovary - Ovary chapter

Also called cellular hemangioma of infancy

Case reports: newborn ([Am J Surg Pathol 1997;21:1231](#))

Micro: well-formed blood vessels and proliferating endothelial cells arranged in solid cordlike structures; tumor entraps normal ovarian follicles

Positive stains: Factor VIII, CD34, alpha smooth-muscle actin

EM: endothelial cells focally associated with pericytes

Leiomyoma - Ovary chapter

Rare, mean 50 years (range 42-76 years) in one study of 6 patients ([Arch Pathol Lab Med 1992;116:1068](#))

Associated with synchronous leiomyomas of uterus

Do not recur locally or metastasize, even if mitotically active

Case reports: bilateral massive leiomyomas in 21 year old ([Mod Path 1992;5:586](#))

Gross: median 3 cm (range 0.3 to 20 cm), often in hilar region

Micro: may be cellular, have prominent mitotic activity or occasionally have bizarre nuclei or myxoid stroma

Leiomyosarcoma - Ovary chapter

Rare

62% die of disease within mean 24 months ([Am J Surg Pathol 2004;28:1436](#))

Case reports: 58 year old with primary tumor ([Arch Pathol Lab Med 1991;115:941](#))

Micro: usually 2 of 3 - moderate/severe cytologic atypia, 10+ MF/10 HPF, tumor cell necrosis

Positive stains: desmin, vimentin, muscle specific actin

Myxoid leiomyosarcoma - Ovary chapter

Poor prognosis

Large gelatinous mass with cystic change, necrosis, hemorrhage

Micro: elongated cells surrounded by abundant basophilic material, low mitotic count

Positive stains: smooth muscle actin

References: [Hum Pathol 1991;22:1268](#)

Lymphoepithelioma-like carcinoma - Ovary chapter

Rare in female genital tract

Case reports: 51 year old woman with ovarian tumor and nodal metastases ([Arch Pathol Lab Med 2007;131:1715](#))

Micro: undifferentiated carcinoma with pleomorphic epithelioid cells and marked lymphocytic infiltrate, resembling nasopharyngeal tumor

Lymphoma - Ovary chapter

Usually B cell

55% bilateral

Children - usually Burkitt's lymphoma

Adults - usually diffuse large cell or follicular lymphoma

May be difficult to determine if primary or secondary

5 year survival is 80% after surgery or chemotherapy in primary disease vs. 33% in secondary disease

Case reports: diffuse large cell lymphoma in 23 year old ([Arch Pathol Lab Med 2003;127:e169](#))

Micro: Burkitt's lymphoma cells tend to grow in cords or nests, forming pseudoacini, accompanied by sclerosis, resembling carcinoma; diffuse large cell lymphoma cells may appear as short fascicles and form interlacing bundles of spindle cells, resembling a stromal tumor

Negative stains: ER, PR

References: [Mod Path 2001;14:1093](#), [Am J Surg Pathol 1993;17:154](#), [Arch Pathol Lab Med 1994;118:647](#)

Malignant mixed mullerian tumor - Ovary chapter

Also called malignant mixed mesodermal tumor, MMMT

Postmenopausal, low parity

Very poor prognosis; stage is best predictor; most patients present at advanced stage

Micro: homologous (nonspecific malignant stroma) or heterologous (malignant elements of a different tissue type, particularly cartilage); often contains hyaline droplets containing alpha-1-antitrypsin in cytoplasm ([Hum Pathol 1982;13:930](#)); rare trophoblastic tissue ([Hum Pathol 1988;19:1235](#))

Positive stains: keratin; **tumor cell droplets** - PAS, diastase resistant; alpha-1-antitrypsin

DD: immature teratoma (children)

References: [Am J Surg Pathol 1980;4:37](#), [Arch Pathol Lab Med 1991;115:918](#)

Mesothelioma - Ovary chapter

Rarely presents as ovarian masses

Median age 52 years old, range 16-63 years

Patients usually present with widespread peritoneal tumor, but occasionally is limited to 1-2 ovaries

Gross: 3-15 cm, often bilateral, solid with occasional small cysts

Micro: serosa and parenchyma involved by epithelial or biphasic tumor with papillary, tubular-glandular or solid patterns; tumor cells have moderate atypia and low mitotic rate; stroma is hyalinized, occasionally with striking hyalinized cores, psammoma bodies

References: [Am J Surg Pathol 1996;20:1067](#)

Metastases to ovary - Ovary chapter

Common site for metastases; 7% of ovarian tumors are metastases

Usually are bilateral, small, multinodular surface tumors with extensive extraovarian spread

Often have unusual patterns of dissemination, unusual histologic features, angiolymphatic invasion, desmoplasia

Most common metastases are appendix (adenocarcinoid or mucinous adenocarcinoma), breast, carcinoid, colon, pancreas, stomach

May have associated ovarian stromal luteinization with masculinization

Rarely chordoma ([Arch Pathol Lab Med 1990;114:208](#))

Abdominopelvic sarcoma of perivascular epithelioid cells metastatic to ovary - Ovary chapter

Rare tumor at any site (4 cases) described in 2001 in women 19 to 41 years presenting with mass of serosa of the ileum, uterus or pelvic cavity

Resembles angiomyolipoma and clear cell "sugar" tumor of lung

Considered a sarcoma of uncommitted perivascular epithelioid cells without smooth muscle or adipose ([Mod Path 2001;14:563](#))

Micro: sheets of large polygonal cells with glycogen-rich clear or eosinophilic cytoplasm, moderately pleomorphic nuclei, delicate vasculature, resembling clear cell carcinoma; angiolymphatic invasion common, metastases to lymph nodes and ovary; also coagulative necrosis, occasional mitotic figures, intracytoplasmic brown pigment; no spindled cells, smooth muscle or fat

Positive stains: HMB45, MART-1

Negative stains: S-100, vimentin, muscle-specific actin, desmin and chromogranin A

Breast carcinoma metastatic to ovary - Ovary chapter

25-38% of ovarian metastases, often microscopic

Positive stains: GCDFP-15 ([Hum Pathol 1991;22:368](#))

Negative stains: Pax8 (usually positive in ovarian carcinomas except mucinous types, [Am J Surg Pathol 2008;32:1566](#)), WT1 (positive in 2% versus 63% of ovarian tumors, usually negative in ovarian clear cell, mucinous and endometrioid subtypes), CA125 (weak/negative in breast carcinomas, 90% of ovarian carcinomas are CA125+, [Am J Surg Pathol 2005;29:1482](#))

Cervical carcinoma metastatic to ovary - Ovary chapter

Endocervical primaries are usually HPV related and p16+ ([Am J Surg Pathol 2007;31:653](#))

Colon carcinoma metastatic to ovary - Ovary chapter

Associated with advanced primary lesions, but ovarian mass may be first indication of disease
Often large, unilateral or young patient ([Am J Surg Pathol 2006;30:177](#))

Gross: 43% bilateral, cystic, mucin producing, hemorrhagic and necrotic

Micro: well differentiated, cribriform growth, intraluminal "dirty" necrosis, segmental destruction of glands, no squamous metaplasia

Stains: (a) usually CK7 negative/focal, CK20+, CEA+, HAM56-, MUC5AC-, CA125- vs ovarian primary with opposite staining; (b) diffuse expression of CDX2, beta-catenin and P504S is virtually diagnostic ([Mod Pathol 2005;18:19](#))

DD: endometrioid or mucinous adenocarcinoma of ovary

References: [Hum Pathol 1995;26:852](#), [Mod Path 1996;9:426](#), [Mod Path 1994;7:396](#), [Hum Pathol 2000;31:672](#), [Hum Pathol 1998;29:491](#), [Am J Surg Pathol 1987;11:114](#)

Desmoplastic small round cell tumor metastatic to ovary - Ovary chapter

May metastasize to ovary; common in teenage girls

Extensive extraovarian tumor at presentation

Gross: often bilateral

Micro: prominent nodular ovarian growth; nests of small cells with scant cytoplasm, hyperchromatic nuclei, prominent desmoplastic stroma

Positive stains: cytokeratin, EMA, desmin, vimentin, Leu-7/CD57, S100

EM: frequent intercellular junctions, basal lamina, cytoplasmic filaments, sparse, small dense granules of either neuroendocrine or lysosomal type

References: [Hum Pathol 1992;23:454](#)

Gastric carcinoma (intestinal type) metastatic to ovary - Ovary chapter

Rare; signet-ring metastases (Krukenberg tumor, see below) are much more common

Mean 55 years old

Usually identified after gastric primary is known

Very aggressive with death within 1 year ([Am J Surg Pathol 2006;30:1382](#))

Gross: solid and cystic

Micro: pseudoendometrioid with tubulo-glandular, cribriform and papillary patterns; may have mucinous appearance; prominent necrosis

Gastrointestinal stromal tumor metastatic to ovary - Ovary chapter

Rare

Mean age 59 years, range 44-81 years

Primary usually in small bowel or its mesentery (4/5 cases)

Often death due to disease, possibly due to misdiagnosis ([Am J Surg Pathol 2005;29:920](#))

Gross: often bilateral, solid, tan, lobulated

Micro: spindle cells and epithelioid cells, low grade features

Positive stains: CD117; variable h-caldesmon, smooth muscle actin and CD34

Negative stains: desmin

DD: leiomyosarcoma (tumor in uterus, high grade, desmin+, c-kit negative)

Intrahepatic cholangiocarcinoma metastatic to ovary - Ovary chapter

Mimics primary mucinous neoplasms

Often simultaneous detection of hepatic and ovarian masses or ovarian masses detected first ([Am J Surg Pathol 2007;31:1788](#))

62% bilateral

Micro: surface implants in 80%, infiltrative stromal invasion in 86%, multinodular growth in 48%; variably sized glands with cystic dilation, also small clusters and individual cells; tumor cells vary from tall columnar mucinous cells to flat/cuboidal cells with nonspecific features

Positive stains: CK7, variable CK20

Krukenberg tumor - Ovary chapter

Metastatic signet ring cell adenocarcinoma of ovary; usually from GI tract (signet ring type), often stomach (2/3, due to retrograde lymphatic spread, [Arch Pathol Lab Med 2006;130:1725](#)), appendix, colon or breast; primary is often clinically occult and very small

1-2% of ovarian tumors, but higher in Japan (which has higher prevalence of gastric carcinoma)

Initially described by German gynecologist and pathologist [Friedrich Ernst Krukenberg](#) (1871-1946)

Mean 45 years, range 13-84 years, 43% under age 40 years ([Am J Surg Pathol 2006;30:277](#))

In young patients, may be mistaken for granulosa cell tumor or lipid rich tumor

Most patients die within 2 years

Symptoms: abdominal pain or swelling, ascites (with positive cytology), occasionally vaginal bleeding or virilization

Case reports: bilateral ovarian tumor due to appendiceal adenocarcinoid ([Arch Pathol Lab Med 1985;109:930](#))

Gross: multinodular enlargement of ovaries, bilateral (63-80%), mean 10 cm, intact bosselated external surfaces without adhesions; solid, firm to edematous / gelatinous cut surface, cysts in 1/3

Micro: multiple nodules separated by normal stroma in small tumors and focally in large tumors; more cellular at periphery and edematous / gelatinous centrally; mucin-producing signet-ring cells comprise at least 10% of neoplasm, but have variable appearance and patterns; must see intracytoplasmic mucin; commonly vascular space invasion; may have marked stromal proliferation with storiform growth and variable luteinization (pregnant and nonpregnant patients); frequently focal tubules ([Am J Surg Pathol 1981;5:225](#)), glands and cysts

Lung carcinoma metastatic to ovary - Ovary chapter

Rare, may occur without lung symptoms

Mean age 47 years, range 26-76 years

Prior diagnosis of lung cancer in only 53%, usually small cell or adenocarcinoma ([Am J Surg Pathol 2005;29:997](#))

Case reports: 42 year old woman with pulmonary papillary adenocarcinoma ([Arch Pathol Lab Med 2002;126:1101](#))

Gross: mean 10 cm, often bilateral

Micro: multinodular growth, widespread necrosis, extensive lymphovascular invasion; involvement of ovarian surface is rare

Positive stains: CEA, TTF-1

Negative stains: CA125

Melanoma metastatic to ovary - Ovary chapter

Rare; mean age 38 years (range 21-60 years)

50% had metastatic tumor outside the ovary, 60% had known cutaneous melanoma, 15% had other pigmented lesions excised

Most die within a few years of ovarian excision ([Am J Surg Pathol 2004;28:771](#))

Gross: often bilateral, mean 10 cm, 30% brown/black, often cystic

Micro: sheets or nodules of large cells with abundant eosinophilic cytoplasm, prominent nucleoli, occasional cytoplasmic pseudoinclusions in nuclei or cytoplasmic melanin pigment; necrosis common; follicle-like spaces common; occasionally tumors have small cells with scanty cytoplasm, spindle cells or nevoid appearance

Positive stains: S100, HMB45, MART-1, vimentin; usually tyrosinase and MITF, occasionally inhibin

Negative stains: keratin, calretinin

EM: melanosomes

DD: juvenile granulosa cell tumor, small cell carcinoma

References: [Am J Surg Pathol 1991;15:849](#), [Am J Surg Pathol 1987;11:959](#)

Neuroendocrine carcinoma metastatic to ovary - Ovary chapter

Pancreatic acinar cell carcinoma metastatic to ovary - Ovary chapter

May be detected in ovary before pancreatic primary is identified ([Am J Surg Pathol 2008;32:1540](#))

Micro: highly cellular with minimal fibrous stroma; often acinar growth pattern of cells with eosinophilic granular cytoplasm, uniform nuclei with prominent nucleoli; resembles carcoid tumor but chymotrypsin+, trypsin+, synaptophysin-, chromogranin-; also focal alpha-inhibin+

Pancreatic ductal carcinoma metastatic to ovary - Ovary chapter

May simulate primary ovarian cancer

Gross: large, multiloculated cystic neoplasm, usually bilateral with surface desmoplastic implants and extraovarian spread

Micro: may focally resemble benign, borderline or malignant mucinous tumor

References: [Am J Surg Pathol 1989;13:748](#)

Renal cell carcinoma metastatic to ovary - Ovary chapter

Rare, <15 cases reported

Case reports: 48 year old woman with no history given of renal mass ([Arch Pathol Lab Med 2003;127:e123](#))

Gross: hemorrhagic and multiloculated cystic mass with focal golden-yellow solid areas

Micro: solid areas with clear, polygonal tumor cells arranged in sheets or nests surrounded by delicate, thin-walled vascular septa; bland nuclei without mitoses; dilated tubules with intratubular eosinophilic fluid or blood; no desmoplasia

Positive stains: EMA, RCC, CD10

Negative stains: AE1/AE3 (may be weak), CAM5.2 (may be weak), 34betaE12, ER, CA125, inhibin, calretinin, CD34, AFP

DD: primary clear cell carcinoma of ovary (usually unilateral, clear cells with hobnail cells lining cysts and tubules, PAS+ material in papillary cords, usually CK7+, RCC-, CD10-, renal cell carcinoma is opposite, [Int J Gynecol Pathol 2003;22:272](#)), steroid cell tumor (usually androgenic or estrogenic symptoms, not bilateral, lipid rich tumor with clear intracytoplasmic vacuoles, inhibin+, EMA-), dysgerminoma (usually 20-40 years old, unilateral, clear cells have prominent nucleoli, lacks vasculature of renal cell carcinoma, fibrous stroma has mature lymphocytes, PLAP+, EMA-)

Mullerian adenosarcoma - Ovary chapter

Low grade variant of mixed mullerian tumor; more commonly seen in endometrium and cervix

Mean age 54 years, range 30-84 years

67% have tumor rupture at or before excision

Poorer prognosis than uterine adenosarcoma, perhaps due to lack of anatomic barrier to spread

Tends to recur as pure sarcoma or adenosarcoma

Poor prognostic factors: extraovarian spread (high stage), tumor rupture, high grade, high-grade sarcomatous overgrowth, < age 53 years

Survival: 5 year-64%, 10 year-46%

Gross: 97% unilateral, mean 14 cm (range 5-50 cm); usually solid with occasional small cysts

Micro: (1) conspicuous non-invasive mullerian-type glands within a predominant malignant stroma, either homologous or heterologous; (2) periglandular cuffs of cellular stroma (80%), intraglandular protrusions of cellular stroma (60%) or both, (3) at least mild stromal atypia (33%); (4) variable stromal mitotic count; usually marked stromal cellularity (resembling endometrial stromal sarcoma or cellular ovarian fibroma), other features - glands widely spaced throughout stroma (90%), occasional sarcomatous overgrowth (30%), sex cord-like elements (15%), heterologous elements (12%); may have hypocellular stromal areas

DD: benign tumor (adenofibroma, endometriosis - lack periglandular cellular cuffs of cellular stroma, no stromal atypia), immature teratomas (younger patients, usually embryonal neuroectodermal elements, no periglandular cellular cuffs of cellular stroma), endometrial stromal sarcoma (sample thoroughly to rule out glandular component), malignant mixed mullerian tumor (glandular and stromal epithelium is obviously malignant vs. at most atypical glands in stromal sarcoma)

References: [Am J Surg Pathol 2002;26:1243](#)

Myofibroblastoma - Ovary chapter

Case reports: 22 year old woman with 9 cm tumor entirely replacing ovary ([Mod Path 1999;12:907](#))

Micro: encapsulated, composed of cytologically bland spindled cells arranged in patterns of solitary fibrous tumor and hemangiopericytoma

Positive staining: smooth muscle actin, muscle-specific actin; focal/weak for CD34

Negative staining: S100, desmin, AE1/AE3

EM: myofibroblastic differentiation

DD: solitary fibrous tumor, hemangiopericytoma

Nephroblastoma (Wilm's tumor) - Ovary chapter

Case reports: 19 cm multilocular mass in 21 year old woman ([Hum Pathol 2000;31:761](#))

DD: retiform Sertoli-Leydig cell, adenosarcoma

Neuroendocrine carcinoma (non-small cell type) - Ovary chapter

Rare and aggressive

Associated with coexisting mucinous carcinoma, endometrioid carcinoma or mature cystic teratoma

Mean 47 years, range 22-63 years

Case reports: 22 year old woman with coexisting borderline mucinous tumor ([Arch Pathol Lab Med 1994;118:1032](#))

Treatment: TAHBSO, chemotherapy; patients with stage III/IV disease often die of disease

Gross: usually unilateral, cystic or solid/cystic, mean 16 cm (5-26 cm)

Micro: solid pattern, nests or trabeculae of large to intermediate round/oval cells with brisk mitotic activity

Positive stains: keratin cocktail, CK7, CAM 5.2, usually CK20, synaptophysin; usually chromogranin A, CD58, c-kit

References: [Am J Surg Pathol 2007;31:774](#)

Osteoclast-like giant cell tumor - Ovary chapter

Case reports: 8 cm tumor in 76 year old woman ([Am J Surg Pathol 2003;27:854](#))

Micro: diffuse, bland-appearing osteoclast-like giant cells mixed with pleomorphic mononuclear cells; hemorrhage, large areas of necrosis, frequent mitotic figures among mononuclear cells; infiltrative border, vascular invasion; no cystic tumor; no epithelial component

Positive stains: *osteoclast-like giant cells* - CD68, vimentin, alpha-1-antichymotrypsin, CD45; *mononuclear cells* - vimentin, PCNA

Negative stains: *mononuclear cells* - keratin, EMA, CK7, CD45, CD68, S100

Osteosarcoma - Ovary chapter

Case reports: primary osteosarcoma in 47 year old Japanese woman ([Am J Surg Pathol 1988;12:567](#))

Gross: large multilocular cysts with blood and solid tissue

Micro: anaplasia, blood filled spaces lined with tumor cells

Paraganglioma - Ovary chapter

Rare as primary or metastasis

May be associated with hypertension

Gross: 8 to 22 cm, solid, tan, brown or yellow; often extraovarian involvement

Micro: nested Zellballen pattern with clusters of cells surrounded by vascular stroma; tumor cells have abundant, eosinophilic cytoplasm with occasional clear cells or bizarre giant tumor cells

Positive stains: neuroendocrine markers, variable S100+ sustentacular cells, variable inhibin and calretinin

Negative stains: keratin

EM: dense core neuroendocrine granules

References: [Am J Surg Pathol 2006;30:600](#)

PNET / Ewing's sarcoma - Ovary chapter

Case reports: 29 year old woman ([Am J Surg Pathol 1998;22:1417](#))

Micro: solid nests and sheets of monotonous, primitive, small round cells with occasional rosettes

Positive stains: CD99

Molecular: t(11;22)(q24;q12), EWS-FLI-1 chimeric RNA

DD: small cell carcinoma of the ovary

Rhabdomyosarcoma - Ovary chapter

Presents as disseminated tumor in neonates or young children, with difficulty determining primary tumor site (other pediatric tumors with similar presentations include infantile myofibromatosis, neuroblastoma, lymphoma, malignant rhabdoid tumor)

Subtypes in children and 5 year survival: embryonal (49% of cases, 66%), alveolar (31% of cases, 88%), botryoid (6% of cases, 95%), spindle cell (3% of cases, 88%)

Case reports: alveolar subtype in 2 year old girl with ovarian mass and pleural effusions ([Arch Pathol Lab Med 2003;127:e56](#))

Cytology: highly cellular, with background reactive mesothelial cells and lymphocytes; tumor cells are bizarre, discohesive giant cells with pleomorphic hyperchromatic nuclei, variable eosinophilic cytoplasm with occasional vacuoles, frequent mitotic figures

Positive stains: desmin, myogenin

Molecular: t(2;13)(p36;q14) found in 60% of alveolar subtypes (Pax3 and FKHR genes), associated with older age, truncal tumors, advanced stage, poorer prognosis; t(1;13)(p36;q14) involves Pax7 and FKHR genes, associated with better prognosis

Squamous cell carcinomas - Ovary chapter

May represent extreme expression of squamous metaplasia in endometrioid carcinomas, transformation of ovarian teratomas, HPV related transformation

Often associated with dermoid cyst (50%) and endometriosis (20%)

Case reports: associated with HPV DNA 16/18 in ovary, high grade VIN and high grade SIL ([Am J Surg Pathol 1996;20:767](#)), 12 years after hysterectomy for endometriosis ([Arch Pathol Lab Med 1987;111:864](#))

Gross: 6-35 cm, often forming mural nodules with intracavitary protrusion, focal necrosis, hemorrhage

References: [Am J Surg Pathol 1996;20:823](#)

Undifferentiated carcinoma - Ovary chapter

Mean 54 years (range 39-72 years)

Usually stage III/IV

Micro: large groups or sheets with desmoplastic stroma; foci of papillary serous, urothelial, adenocarcinoma often present; necrosis common; vascular invasion in 20%

References: [Arch Pathol Lab Med 1991;115:377](#)

Staging - Ovary chapter

Staged by surgery and pathologic examination, including biopsies of frequently involved sites to rule out high stage disease

Primary tumor (T) - Ovary chapter

TNM category (FIGO stage)

pTX: primary tumor cannot be assessed (example-malignant cytology of pleural or peritoneal fluid)

pT0: no evidence of primary tumor

pT1 (I): tumor limited to one or both ovaries

pT1a (IA): tumor limited to one ovary, capsule intact, no tumor on ovarian surface, no malignant cells in ascites fluid or peritoneal washings

pT1b (IB): tumor limited to both ovaries, capsule intact, no tumor on ovarian surface, no malignant cells in ascites fluid or peritoneal washings

pT1c (IC): tumor involves one or both ovaries with any of the following: ruptured capsule, tumor on ovarian surface, malignant cells in ascites fluid or peritoneal washings

pT2 (II): tumor involves one or both ovaries with pelvic extension or implants

pT2a (IIA): extension to or implants on uterus or fallopian tube; no malignant cells in ascites fluid or peritoneal washings

pT2b (IIB): extension to or implants on other pelvic tissues; no malignant cells in ascites fluid or peritoneal washings

pT2c (IIC): pelvic extension or implants (T2a or T2b) with malignant cells in ascites fluid or peritoneal washings

pT3 (III): tumor involves one or both ovaries with microscopically confirmed peritoneal metastasis outside the pelvis

pT3a (IIIA): microscopic peritoneal metastasis beyond pelvis (no macroscopic tumor)

pT3b (IIIB): macroscopic peritoneal metastasis beyond pelvis 2 cm or less in greatest dimension

pT3c (IIIC): peritoneal metastasis beyond pelvis more than 2 cm in greatest dimension or regional lymph node metastasis

Notes:

Liver capsule metastasis is T3 (Stage III); liver parenchymal metastasis is M1 (Stage IV)

Pleural effusion must have positive cytology to be considered M1 (Stage IV)

Non-malignant ascites is not classified; ascites does not affect staging unless malignant cells are present

Regional lymph nodes (N) - Ovary chapter

pNX: regional lymph nodes cannot be assessed

pN0: no regional lymph node metastasis

pN1 (IIIC): regional lymph node metastasis

Distant metastasis (M) - Ovary chapter

pMX: Distant metastasis cannot be assessed

pM0: No distant metastasis

pM1 (IV): Distant metastasis (extraperitoneal metastasis, including liver parenchyma [not surface involvement], lung, skeleton, supraclavicular nodes, axillary nodes)

Stage grouping - Ovary chapter

Stage I: T1 N0 M0

Stage IA: T1a N0 M0

Stage IB: T1b N0 M0

Stage IC: T1c N0 M0

Stage II: T2 N0 M0

Stage IIA: T2a N0 M0

Stage IIB: T2b N0 M0

Stage IIC: T2c N0 M0

Stage III: T3 N0 M0

Stage IIIA: T3a N0 M0

Stage IIIB: T3b N0 M0

Stage IIIC: T3c N0 M0 or any T N1 M0

Stage IV: Any T any N M1

Features to report - Ovary chapter

[Editorial note](#)

Specimen type
Tumor site
Specimen integrity (intact, ruptured, fragmented, other)
Tumor size
Histologic type
Histologic grade (benign, borderline, malignant - poor, moderate or well differentiated)
Invasion sites within ovary
Surface involvement
Involvement of fallopian tube, opposite ovary, other tissues
Implants: noninvasive epithelial, noninvasive desmoplastic, invasive
Margins
Angiolymphatic space involvement:
Lymph nodes positive / number of nodes examined
Extranodal extension
Presence of endometriosis or other findings

End of Ovary tumor chapter

See also [Ovary-non tumor](#) chapter

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