The background of the slide is a high-magnification histological micrograph of fallopian tube tissue. It shows a complex network of pink-stained connective tissue stroma with numerous small, dark-stained nuclei scattered throughout. The overall appearance is dense and fibrous.

CHAPTER 3

Tumours of the Fallopian Tube and Uterine Ligaments

Tumours of the fallopian tube are much less common than the corresponding ovarian neoplasms; however, histologically the same surface epithelial-stromal tumour subtypes are recognized. Sex cord-stromal and germ cell tumours are rare. Hydatidiform moles and gestational choriocarcinoma are uncommon complications of tubal ectopic pregnancy. The wolffian adnexal tumour is also infrequent and typically occurs in the leaves of the broad ligament.

The risk factors appear similar to those of the ovary. Fallopian tube carcinomas are a component of the hereditary breast-ovarian cancer syndrome caused by *BRCA1* and *BRCA2* germline mutations.

WHO histological classification of tumours of the fallopian tube

Epithelial tumours		Soft tissue tumours	
Malignant		Leiomyosarcoma	8890/3
Serous adenocarcinoma	8441/3 ¹	Leiomyoma	8890/0
Mucinous adenocarcinoma	8480/3	Others	
Endometrioid adenocarcinoma	8380/3		
Clear cell adenocarcinoma	8310/3	Mesothelial tumours	
Transitional cell carcinoma	8120/3	Adenomatoid tumour	9054/0
Squamous cell carcinoma	8070/3		
Undifferentiated carcinoma	8020/3	Germ cell tumours	
Others		Teratoma	
Borderline tumour (of low malignant potential)		Mature	9080/0
Serous borderline tumour	8442/1	Immature	9080/3
Mucinous borderline tumour	8472/1	Others	
Endometrioid borderline tumour	8380/1	Trophoblastic disease	
Others		Choriocarcinoma	9100/3
Carcinoma in situ (specify type)		Placental site trophoblastic tumour	9104/1
Benign tumours		Hydatidiform mole	9100/0
Papilloma (specify type)		Placental site nodule	
Cystadenoma (specify type)		Others	
Adenofibroma (specify type)			
Cystadenofibroma (specify type)		Lymphoid and haematopoietic tumours	
Metaplastic papillary tumour		Malignant lymphoma	
Endometrioid polyp		Leukaemia	
Others			
Tumour-like epithelial lesions		Secondary tumours	
Tubal epithelial hyperplasia			
Salpingitis isthmica nodosa			
Endosalpingiosis			
Mixed epithelial-mesenchymal tumours			
Malignant müllerian mixed tumour (carcinosarcoma; metaplastic carcinoma)	8950/3		
Adenosarcoma	8933/3		

¹ Morphology code of the International Classification of Diseases for Oncology (ICD-O) {921} and the Systematized Nomenclature of Medicine (<http://snomed.org>). Behaviour is coded /0 for benign tumours, /3 for malignant tumours, and /1 for borderline or uncertain behaviour.

WHO histological classification of tumours of the broad ligament and other uterine ligaments

Epithelial tumours of müllerian type		Mesenchymal tumours	
Serous adenocarcinoma	8460/3	Papillary cystadenoma (with von-Hippel-Lindau disease)	8450/0
Endometrioid adenocarcinoma	8380/3	Uterus-like mass	
Mucinous adenocarcinoma	8480/3	Adenosarcoma	8933/3
Clear cell adenocarcinoma	8310/3	Others	
Borderline tumour (of low malignant potential), (specify type)			
Adenoma and cystadenoma (specify type)		Mesenchymal tumours	
Miscellaneous tumours		Malignant	
Wolffian adnexal tumour	9110/1	Benign	
Ependymoma	9391/3	Secondary tumours	

¹ Morphology code of the International Classification of Diseases for Oncology (ICD-O) {921} and the Systematized Nomenclature of Medicine (<http://snomed.org>). Behaviour is coded /0 for benign tumours, /3 for malignant tumours, and /1 for borderline or uncertain behaviour.

TNM and FIGO classification of carcinomas of the fallopian tube

TNM and FIGO classification ^{1,2}

T – Primary Tumour

TNM FIGO

Categories Stages

TX		Primary tumour cannot be assessed
T0		No evidence of primary tumour
Tis	0	Carcinoma in situ (preinvasive carcinoma)
T1	I	Tumour confined to fallopian tube(s)
T1a	IA	Tumour limited to one tube, without penetrating the serosal surface
T1b	IB	Tumour limited to both tubes, without penetrating the serosal surface
T1c	IC	Tumour limited to one or both tube(s) with extension onto or through the tubal serosa, or with malignant cells in ascites or peritoneal washings
T2	II	Tumour involves one or both fallopian tube(s) with pelvic extension
T2a	IIA	Extension and/or metastasis to uterus and/or ovaries
T2b	IIB	Extension to other pelvic structures
T2c	IIC	Pelvic extension (2a or 2b) with malignant cells in ascites or peritoneal washings
T3 and/or N1	III	Tumour involves one or both fallopian tube(s) with peritoneal implants outside the pelvis and/or positive regional lymph nodes
T3a	IIIA	Microscopic peritoneal metastasis outside the pelvis
T3b	IIIB	Macroscopic peritoneal metastasis outside the pelvis 2 cm or less in greatest dimension
T3c and/or N1	IIIC	Peritoneal metastasis more than 2 cm in greatest dimension and/or positive regional lymph nodes

M1 IV Distant metastasis (excludes peritoneal metastasis)

Note: Liver capsule metastasis is T3/stage III, liver parenchymal metastasis, M1/stage IV. Pleural effusion must have positive cytology for M1/stage IV.

N – Regional Lymph Nodes³

NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Regional lymph node metastasis

M – Distant Metastasis

MX	Distant metastasis cannot be assessed
M0	No distant metastasis
M1	Distant metastasis

Stage Grouping

Stage 0	Tis	N0	M0
Stage IA	T1a	N0	M0
Stage IB	T1b	N0	M0
Stage IC	T1c	N0	M0
Stage IIA	T2a	N0	M0
Stage IIB	T2b	N0	M0
Stage IIC	T2c	N0	M0
Stage IIIA	T3a	N0	M0
Stage IIIB	T3b	N0	M0
Stage IIIC	T3c	N0	M0
	Any T	N1	M0
Stage IV	Any T	Any N	M1

¹ (51,2976).

² A help desk for specific questions about the TNM classification is available at <http://tnm.uicc.org>.

³ The regional lymph nodes are the hypogastric (obturator), common iliac, external iliac, lateral sacral, para-aortic, and inguinal nodes.

Tumours of the fallopian tube

I. Alvarado-Cabrero
A. Cheung
R. Caduff

Malignant epithelial tumours

Definition

A malignant epithelial tumour of the tubal mucosa, usually with glandular differentiation. In order to be considered a primary carcinoma of the fallopian tube, the tumour must be located macroscopically within the tube or its fimbriated end, and the uterus and ovary must either not contain carcinoma or, if they do, it must be clearly different from the fallopian tube lesion.

ICD-O codes

Serous adenocarcinoma	8441/3
Mucinous adenocarcinoma	8480/3
Endometrioid adenocarcinoma	8380/3
Clear cell adenocarcinoma	8310/3
Transitional cell carcinoma	8120/3
Undifferentiated carcinoma	8020/3

Epidemiology

Primary fallopian tube carcinomas are rare, amounting to 0.3-1.1% of gynaecological malignancies [158]. The risk factors appear similar to those of epithelial ovarian cancer. Adenocarcinoma is the most frequent tumour of the fallopian tube [2566].

Macroscopy

On macroscopic examination, the tube shows abnormal dilatation or nodular thickening resembling a hydrosalpinx or haematosalpinx and contains a dominant localized tumour mass. When found in the proximal part of the tube, the

tumour may protrude through the fimbriated end. On the sectioned surface the adenocarcinoma usually consists of soft, grey-brown, villous or polypoid tissue.

Tumour spread and staging

The tumour spread is very similar to that of ovarian carcinoma and involves adjacent organs, the peritoneum and regional lymph nodes. Involvement of the adjacent ovary may make it difficult to determine whether the tumour is primary in the tube or ovary. When the origin remains unclear, the tumour is classified as tubo-ovarian carcinoma [1256].

Surgical staging is performed according to the FIGO classification system [51,2976].

Histopathology

All carcinoma subtypes documented in the ovaries have been identified in the fallopian tube. Serous carcinoma is the most common cellular subtype. In one series of 151 cases, 80% of the tumours were serous [158]. In other large series, about half of these carcinomas were serous, one-fourth endometrioid, one-fifth transitional cell or undifferentiated and the remainder of other cell types [75].

Serous adenocarcinoma

Most serous carcinomas of the tube are invasive tumours with a high histological grade. In one series 50% of the cases were grade 3 [75]. Occasional serous



Fig. 3.01 Carcinoma of the fallopian tube. The sectioned surface shows a dilated fallopian tube filled with papillary tumour exhibiting foci of haemorrhage.

carcinomas have an extensive inflammatory cell infiltration that may simulate a salpingitis of non-tuberculous type [472].

Mucinous adenocarcinoma

These tumours are extremely rare and often are associated with other mucinous neoplasms of the female genital tract [2617]. Reported cases have been predominantly in situ mucinous carcinomas [2450]. A case of synchronous, trifocal mucinous papillary adenocarcinoma involving the uterine cervix and both fallopian tubes has been reported [1316]. We are only aware of a single case of an invasive mucinous adenocarcinoma. The histological appearance of these tumours resembles that of ovarian mucinous carcinomas, and goblet cells may be prominent.

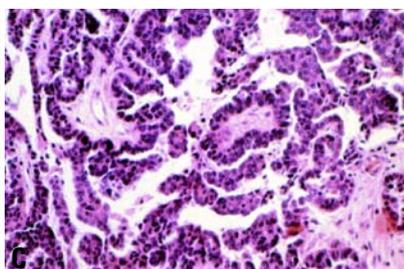
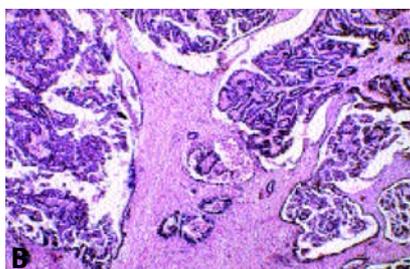
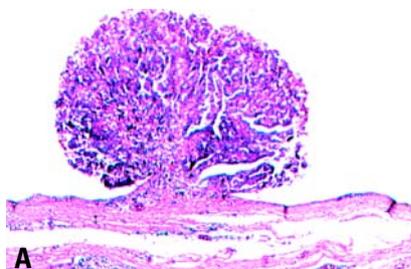


Fig. 3.02 Serous papillary adenocarcinoma of the fallopian tube. **A** Pedunculated papillary tumour arises from the wall of the tube. There is no invasion of the muscular wall. **B** Note the well differentiated papillary fronds. **C** This papillary tumour shows prominent budding from the primary papillae. The nuclei show stratification and atypia.

Endometrioid adenocarcinoma

Endometrioid carcinomas of the tube are characteristically non-invasive or only superficially invasive and have a generally favourable prognosis [1985]. The typical variant is the most common form of endometrioid carcinoma encountered in the tube. By definition these tumours closely resemble their uterine counterparts. Endometrioid carcinomas with a prominent spindle-shaped epithelial cell component [2942] or with the glands lined exclusively by oxyphilic cells [2258] also occur in the tube. An unusual form of endometrioid carcinoma resembling the patterns seen in the wolffian adnexal tumour has been found relatively often in the fallopian tube [641,1985]. These tumours are characterized by a prominent pattern of small, closely packed cells punctured by numerous glandular spaces, a large number of which contain a dense colloid-like secretion. The finding of areas with the typical appearance of endometrioid carcinoma enables one to make the correct diagnosis.

Clear cell adenocarcinoma

These neoplasms constitute 2-10% of all fallopian tube carcinomas [75,1181a,3031]. The majority of the reported cases have shown a tubulocystic pattern varying from flattened cuboidal epithelium to an irregular pattern with prominent hobnail and clear cells. A papillary pattern featuring the hobnail type of epithelium lining fibrovascular stalks has also been described [3031].

Transitional cell carcinoma

These carcinomas are rare in the female genital tract but occur relatively more often than in the ovary [2676]. The fre-

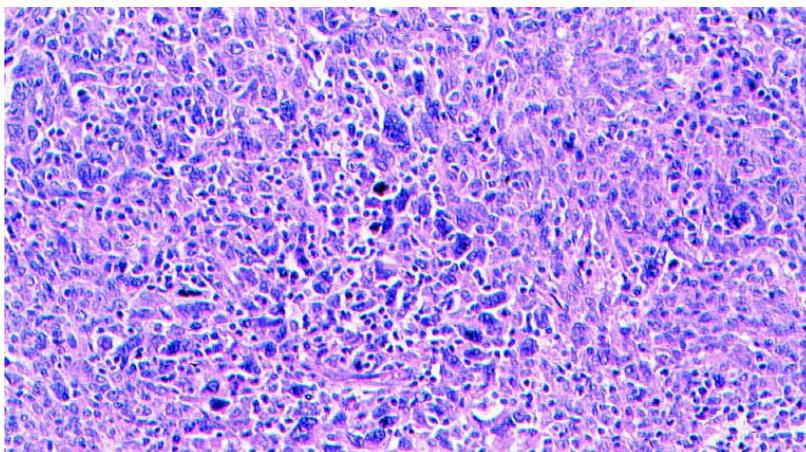


Fig. 3.03 Undifferentiated carcinoma of the fallopian tube. Note the sheets of cells with scattered tumour giant cells.

quency of transitional cell carcinoma of the fallopian tube in previous reports has varied from 11-43% [75,2974]. Transitional cell metaplasia of the epithelium has been suggested as a possible source of tubal carcinoma of the same cell type [750].

Undifferentiated carcinoma

These carcinomas fail to show evidence of either glandular or squamous differentiation. The tumour displays a diffuse growth pattern composed of sheets of small cells resembling those of small cell carcinoma of the lung. These densely cellular tumours may have a relatively conspicuous myxoid matrix. Some tumours have large epithelial cells arranged in nests surrounded by a dense lymphocytic infiltrate resembling a lymphoepithelioma-like carcinoma. Extensive tumour areas consisting predominantly of multinucleated giant cells may also be present [75].

Hormone-producing carcinoma

Ectopic beta-human chorionic gonadotropin (-hCG) production has been reported in two women with serous or undifferentiated carcinoma of the tube [75,399]. Each of the tumours contained syncytiotrophoblast-like cells, many of which stained positively for -hCG. Unusual reported cases include a renin-producing tumour [3234] and an alpha-fetoprotein producing carcinoma that had a hepatoid appearance [111].

Miscellaneous epithelial tumours

Rare examples of unusual neoplasms arising in the tube include cases of squamous cell [290,470,1747], adenosquamous, glassy cell [75,1191] and lymphoepithelioma-like carcinoma [75].

Genetic susceptibility

The discovery of the *BRCA1* cancer predisposition gene in 1994 and the *BRCA2*

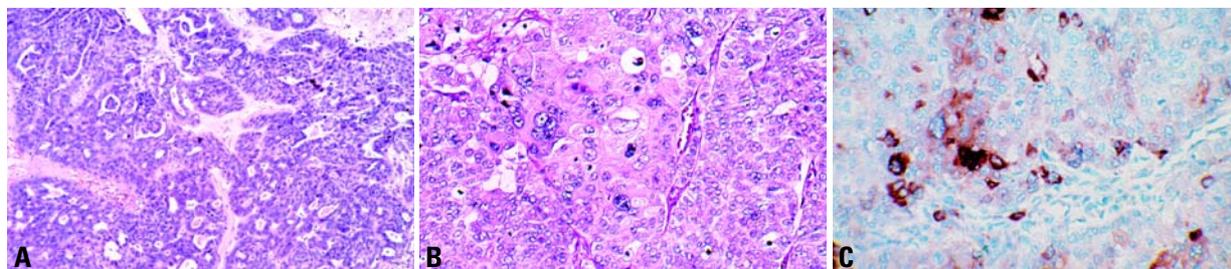


Fig. 3.04 Carcinoma of the fallopian tube. **A** The poorly differentiated tumour shows papillary fronds and gland-like spaces. **B** Note the syncytiotrophoblast-like multinucleated tumour giant cells in the centre. **C** The syncytiotrophoblast-like giant cells stain positively for beta-human chorionic gonadotropin (-hCG).

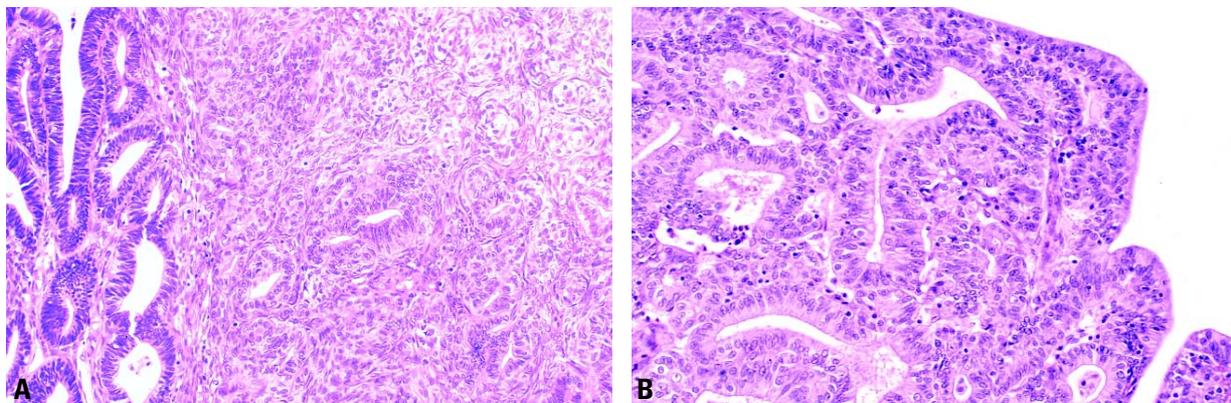


Fig. 3.05 Endometrioid carcinoma of the fallopian tube. **A** Closely packed tubules of endometrioid carcinoma are present adjacent to a focus of endometriosis composed of larger glands present on the left. **B** The tumour forms closely packed glands lined by pseudostratified epithelium.

cancer predisposition gene in 1995 has allowed the identification of a group of women who are at a greatly increased risk of developing breast and ovarian cancer {8,499}. Two previous series in which 5% and 11% respectively of patients with tubal cancer also had breast carcinoma suggest an association between breast cancer and tubal carcinoma {75,2225}. Recently, several high-risk "breast-ovarian cancer families" with *BRCA1* mutations and fallopian tube cancer have been reported. Additionally, a family history of fallopian tube cancer was found to be predictive of the presence of a *BRCA1* mutation in a panel of 26 Canadian "breast-ovarian cancer families" {2939}. A slightly increased risk of

ovarian cancer and of early-onset breast cancer was found in the first-degree relatives of the fallopian tube cancer cases {144}. Thus, fallopian tube carcinoma should be considered to be a clinical component of the hereditary breast-ovarian cancer syndrome and may be associated with *BRCA1* and *BRCA2* mutations. See Chapter 8.

Prognosis and predictive factors

The surgical stage is an independent prognostic factor {75,158} and is critical for determining whether adjuvant therapy is appropriate. Stage I carcinomas that occur in the tubal fimbriae appear to have a worse prognosis than stage I tubal carcinomas that are nonfimbrial {74}.

Borderline epithelial tumours

Borderline epithelial tumours of the fallopian tube are rare and include cases of serous, mucinous and endometrioid types {74}. Borderline serous tumours involve the tube, including its fimbriated portion, and have histological features similar to those of the ovary {74,1421,3257}. Mucinous tumours are sometimes associated with mucinous metaplasia of the fallopian tube or the Peutz-Jeghers syndrome {1806,2617}. Patients that have multiple organ involvement or pseudomyxoma peritonei may have a metastatic lesion to the tube, and in all cases the appendix needs to be ruled out as a source.

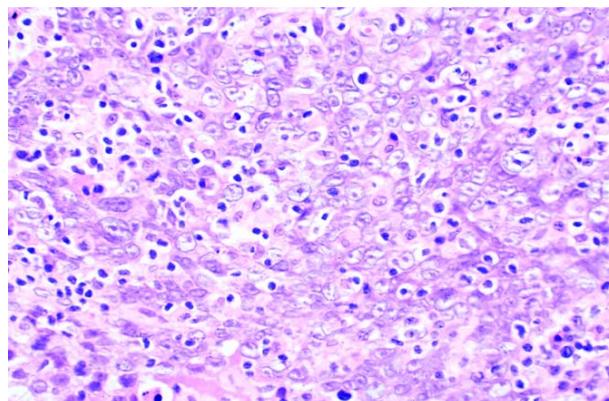


Fig. 3.06 Lymphoepithelial-like carcinoma. The tumour is composed of pale epithelial cells with large vesicular nuclei and prominent nucleoli. Note the lymphocytic infiltration.

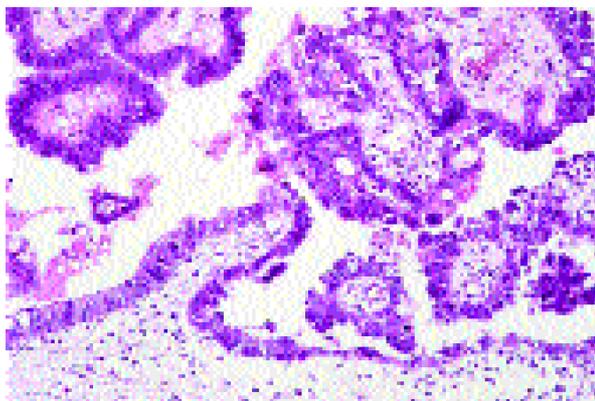


Fig. 3.07 Serous borderline tumour. The tumour consists of papillae with connective tissue cores lined by epithelium showing cellular stratification and tufting, resembling its ovarian counterpart.

Two examples of adenofibroma of borderline malignancy have been reported {74,3257}. One of the tumours appeared in a pregnant woman and on ultrasound was interpreted as an ectopic pregnancy; the other was detected incidentally during an elective tubal ligation. Both neoplasms were located at the fimbriated end of the fallopian tube. One tumour was of serous type and the other endometrioid.

Although relatively few cases of tubal borderline tumours have had long term follow up, the prognosis appears favourable, and it has been suggested that they can be managed conservatively {3257}.

Carcinoma in situ

Rare cases of tubal intraepithelial carcinoma have been reported, and one of these occurred after tamoxifen therapy of breast carcinoma {2747}. With the exception of one case in which a small papillary tumour was found {1875}, the tumours are not detectable on macroscopic examination.

They are characterized by replacement of the tubal epithelium by malignant glandular epithelial cells with pleomorphic nuclei {178,2835}. Florid epithelial proliferation, sometimes even with a cribriform or sieve-like pattern, may occur in association with salpingitis and should not be mistaken for carcinoma in situ {472}.

Benign epithelial tumours

Polypoid adenofibromas, papillomas, benign serous cystadenoma and endometrioid tumours are rarely found in the fallopian tube, including the fimbria {74,1615}. They may be complicated by torsion, especially during pregnancy.

Papilloma and cystadenoma

Serous papilloma and cystadenoma are uncommon lesions of the fallopian tube. Papillomas may be intramural or involve the fimbriated end {74}. Papillomas typically are loosely attached to the tubal mucosa and consist of delicate branching fibrovascular stalks lined by epithelial cells that are indifferent in appearance or resemble those of the fallopian tube lining. The lesion may cause tubal obstruction

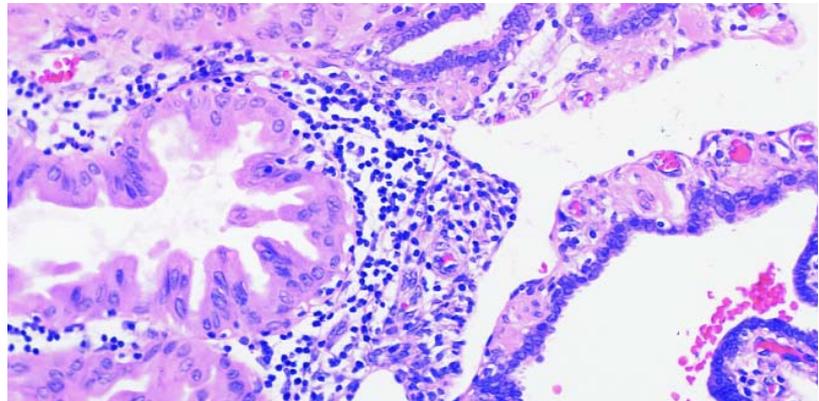


Fig. 3.08 Metaplastic papillary tumour. The tumour is composed of variably sized papillae showing a proliferation of atypical epithelial cells with cellular budding and abundant eosinophilic cytoplasm.

{1012,1407}. Cystadenomas are similar but lack papillary features {74}. Mucinous cystadenomas also have been reported {2617}.

Adenofibroma and cystadenofibroma

Fallopian tube adenofibromas and cystadenofibromas are rare. About fifteen examples of these tumours have been documented {74,3257}. The age range is from the third to the eighth decade with a mean age of 49 years. Most women are asymptomatic, and the majority of the tumours are incidental findings at the time of an operation for another gynaecological disorder {3257}. The neoplasm presents as a round, solitary mass (average 0.5-3 cm) that is either intraluminal or attached to the fimbriated end or the serosal surface and may have a smooth or papillary surface. In one case the tumour was bilateral {451}.

Histologically, two components are present, a connective tissue stroma without nuclear pleomorphism or mitoses and papillary structures on the surface or tubal structures lined by epithelial cells. The epithelial cell type has been serous in most of the cases but occasionally may be endometrioid {647}.

Metaplastic papillary tumour

Metaplastic papillary tumour is an uncommon lesion that typically occurs as an incidental histological finding in segments of fallopian tube removed during the postpartum period for sterilization {187,1425,2504}. Only rare lesions occur

in women who were not recently pregnant. The intraluminal tumour usually involves part of the mucosal circumference and is composed of variable sized papillae covered by atypical epithelial cells that superficially resemble a serous borderline tumour. The epithelial lining shows cellular budding and the presence of abundant eosinophilic cytoplasm in most of the tumour cells. Some of the cells may contain intracellular mucin, and extracellular mucin may be abundant. Mitotic figures are rarely observed.

Endometrioid polyp

Endometrial (adenomatous) polyps occur in the interstitial portion of the fallopian tube {1170,1180}. They are commonly found in radiographic studies of infertile patients. They may obstruct the lumen and result in infertility or tubal pregnancy. They are often attached to the tubal epithelium by a broad base and, thus, macroscopically resemble intrauterine endometrial polyps. They may be occasionally associated with ectopic endometrial epithelium elsewhere in the tube {342}.

Tumour-like epithelial lesions

Definition

Proliferations of the tubal mucosa that simulate neoplasms.

Tubal epithelial hyperplasia

Pseudocarcinomatous hyperplasia in chronic salpingitis may mimic adenocar-

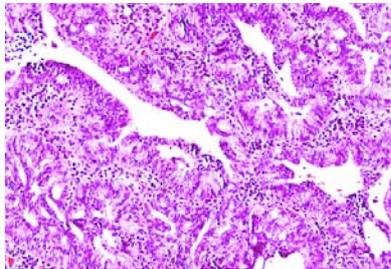


Fig. 3.09 Prominent mucosal hyperplasia. A glandular proliferation producing a cribriform pattern simulates a neoplastic process within the plicae of the fallopian tube.

cinoma histologically because of the pseudoglandular and cribriform permeation of the tubal wall by hyperplastic epithelium and the florid mesothelial hyperplasia [472]. The typically young age of the patients, the presence of marked chronic inflammation, the absence of a macroscopically detected tumour or solid epithelial proliferation, the mildness of the nuclear atypia and the paucity of mitotic figures facilitate the differential diagnosis.

Recently, atypical hyperplasia of the fallopian tube has been observed in patients on tamoxifen therapy for breast cancer [2244].

Salpingitis isthmica nodosa

Salpingitis isthmica nodosa is a manifestation of tubal diverticulosis and is associated with female infertility and ectopic pregnancy [1064]. These nodules in the isthmus are composed of hypertrophic myosalpinx and glandular spaces lined by tubal epithelium.

Endosalpingiosis

Endosalpingiosis is the benign transformation of the mesothelium into tubal epithelium with ciliated and secretory cells. Psammoma bodies and atypical changes may be found [2919]. Endosalpingiosis is distinguished from endometriosis by the absence of endometrial stroma since tubal type epithelium can also occur occasionally in endometriosis. Endosalpingiosis occurs in the peritoneum and may involve the serosal surfaces of the uterus and its adnexa.

Endosalpingiosis may either present as pelvic pain or may be discovered as an

incidental finding [659,1591]. Rarely, endosalpingiosis can present clinically as a cystic mass and can be confused with a neoplasm on macroscopic examination [518a].

Mixed epithelial and mesenchymal tumours

Definition

Neoplasms composed of an admixture of neoplastic epithelial and mesenchymal elements. Each of these components may be either benign or malignant.

ICD-O codes

Malignant müllerian mixed tumour 8950/3
Adenosarcoma 8933/3

Malignant müllerian mixed tumour

As a group, these malignancies are uncommon. The fallopian tube is the least common site for malignant müllerian mixed tumours in the female genital system, accounting for less than 4% of the reported cases [1124]. Patients are almost always postmenopausal (mean age, 57 years) and usually present with abdominal pain, atypical genital bleeding or abdominal distension [1124,1284]. The histological appearance of these tumours resembles that of ovarian malignant müllerian mixed tumour. The prognosis is poor [1124,1284,3079].

Adenosarcoma

This tumour is exceedingly uncommon. Only one well documented case that arose in the fimbriated end of the tube and recurred on the pelvic wall has been reported [1036]. Another example of a tubal tumour of this type was characterized by marked adenoacanthotic atypia of its epithelial component [2605].

Gestational trophoblastic disease

Definition

A heterogeneous group of gestational and neoplastic conditions arising from trophoblast, including molar gestations and trophoblastic tumours.

ICD-O codes

Choriocarcinoma 9100/3
Placental site trophoblastic tumour 9104/1
Hydatidiform mole 9100/0

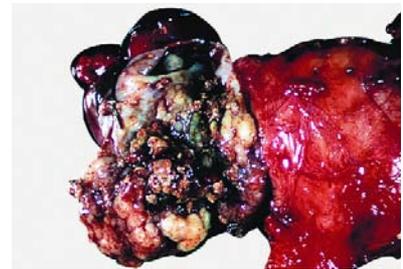


Fig. 3.10 Malignant müllerian mixed tumour of fallopian tube. The fallopian tube is distended and distorted by a multinodular tumour mass that has extended through the serosa.

Choriocarcinoma

Tubal choriocarcinomas account for approximately 4% of all choriocarcinomas [660]. Most of the cases are discovered by chance during an ectopic pregnancy, but about 40% present with an enlarging adnexal mass [2078]. Histological examination shows typical features of gestational choriocarcinoma. In the older literature before the advent of modern chemotherapy, choriocarcinomas associated with ectopic pregnancy were frequently very aggressive, and 75% showed metastases at the time of diagnosis. The response to modern chemotherapy generally has been encouraging [1717,1953].

Placental site trophoblastic tumour

This neoplasm is composed predominantly of intermediate trophoblast. It is generally benign but occasionally may be highly malignant [1540]. To date, only one case of tubal placental site trophoblastic tumour has been reported [2810].

Hydatidiform mole

Approximately thirty tubal hydatidiform moles have been reported [1999]; however, only four valid examples of this lesion were accepted in 1981 [2078]. Those authors concluded that the remaining "moles" were actually ectopic pregnancies with villous hydrops. This tumour usually occurs as an isolated growth, but it may be associated with an intrauterine pregnancy [1048]. The histological appearance may be that of a complete, partial or invasive mole with clear

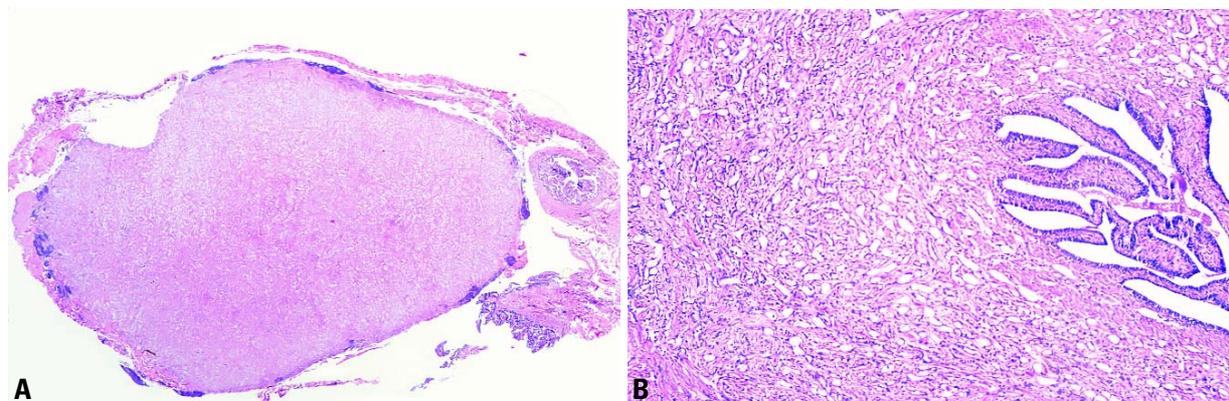


Fig. 3.11 Adenomatoid tumour. **A** The wall of the fallopian tube contains a solid mass. Note the uninvolved cross section of the tube on the right. **B** Variably shaped small cystic spaces and tubule-like structures proliferate in the wall of the tube. The mucosa is on the right.

evidence of trophoblastic proliferation in addition to hydropic swelling of the villi.

Placental site nodule

Placental site nodule is an asymptomatic non-neoplastic proliferation of intermediate trophoblast from a previous gestation that failed to involute. This lesion has recently been reported to occur at the site of an ectopic gestation; two were located in the fallopian tube and one in the broad ligament in direct contact with the tube {391,1514}.

Other tumours

Adenomatoid tumour

ICD-O code 9054/0

The adenomatoid tumour is the most frequent type of benign tubal tumour and usually is found as an incidental finding in a middle-aged or elderly woman {1290}. It typically appears as a grey, white or yellow nodular swelling measuring 1-2 cm in diameter located beneath the tubal serosa. The tumour may be large enough to displace the tubal lumen eccentrically {2787}. Rare examples are bilateral {3230}. It originates from the mesothelium and is composed of gland-like structures lined by flat to cuboidal cells {2787}.

Germ cell tumours

To date only about 50 teratomas of the tube have been reported {1242,3051, 3189}. Many of them were found incidentally, measuring 1-2 cm in diameter, and none has been diagnosed preoperatively. The patients have the risk factors for ectopic pregnancy such as prior salpingitis and tubal occlusion {1953}. A malignant mixed germ cell tumour has been reported {1652}.

Soft tissue tumours

Primary sarcomas of the fallopian tube are exceedingly rare; approximately 37 cases have been reported in the literature in more than 100 years {1322}. The clinical signs and symptoms are usually non-specific and include lower abdominal pain and pelvic pressure. The age at diagnosis varies from 21-70 years with a median of 47 years.

Leiomyosarcoma is the most common type and may arise from the tube or broad ligament {1322}. Other reported fallopian tube or broad ligament malignancies include chondrosarcoma {2245}, embryonal rhabdomyosarcoma {361}, myxoid liposarcoma {2708} and Ewing tumour {1692}. The prognosis is poor, although several long-term survivors have been reported {1322}.

Malignant lymphoma and leukaemia

Tubal involvement by lymphoma is rare and is associated almost invariably with simultaneous involvement of the ipsilateral ovary {2119}. In one large series more than 25% of patients with ovarian lymphoma had tubal involvement, most often by Burkitt or Burkitt-like (small non-cleaved cell) lymphoma or diffuse large-cell lymphoma {2119}. One example of an apparent primary malignant lymphoma of the fallopian tube has been observed {2605}. The tube may also be infiltrated in cases of leukaemia {428}.

Secondary tumours

Metastatic tumours involving the tube usually are the result of secondary spread from carcinomas of the ovary or endometrium {3145}. In most cases, the spread is by direct extension. In one study 89% of secondary carcinomas in the tube were of ovarian origin, and the remainder originated in the endometrium. Blood-borne metastases from breast carcinomas or other extrapelvic tumours may also occur {862,3145}. The authors are aware of a case of adenocarcinoma of the gallbladder metastatic to the fallopian tube {862}.

Tumours of the uterine ligaments

S.F. Lax
R. Vang
F.A. Tavassoli

Definition

Benign and malignant tumours that arise in the broad ligament and other uterine ligaments.

ICD-O codes

Serous adenocarcinoma	8460/3
Endometrioid adenocarcinoma	8380/3
Mucinous adenocarcinoma	8480/3
Clear cell adenocarcinoma	8310/3
Wolffian adnexal tumour	9110/1
Ependymoma	9391/3
Papillary cystadenoma (with von Hippel-Lindau disease)	8450/0
Adenosarcoma	8933/3

Epithelial tumours of müllerian type

Definition

Epithelial tumours of müllerian type are the most frequent neoplasms of the broad and other ligaments {2919}. In general, tumours of every müllerian cell type and of every degree of malignancy can occur in this location but are infrequent compared to their occurrence in the ovary. The criteria for malignancy and for the borderline category are the same as described for müllerian type epithelial tumours occurring in the ovary and the peritoneum.

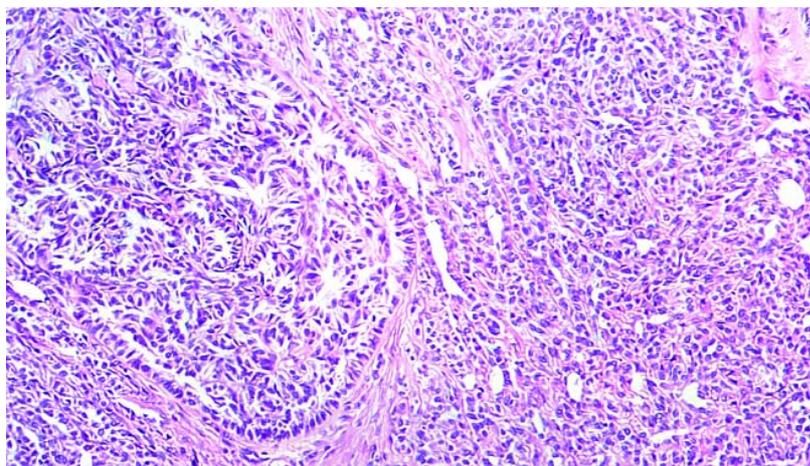


Fig. 3.13 Wolffian adnexal tumour. The tumour is composed of crowded tubules.

Carcinomas

Less than 20 cases have been reported, of which most were of serous, endometrioid and clear cell types {127a,604a,715a,1481a,1850a,2402a,2775a,2912a}. An association with endometriosis was observed in some endometrioid and clear cell carcinomas. The age of the patients ranged from 28-70 years. The tumours were cystic, solid or mixed, and their diameter ranged from 4.5-13 cm. All carcinomas were unilateral, but some had spread beyond the broad ligament. Due to the small number of cases and limited follow-up in many of the cases, the prognosis of these tumours cannot be established.

Borderline tumours

More than 30 cases, mostly serous cystic tumours (age range 19-67 years; mean age 33 years) have been reported {73,127,434,606,740,1341,1702,2626}. One mucinous tumour has been reported {1342}. The tumours measured 1-13 cm in greatest diameter, were unilateral, clearly separated from the ovary and confined to the broad ligament.

Benign tumours

Serous cystadenoma is the most common type {962}. As in the ovary, the distinction

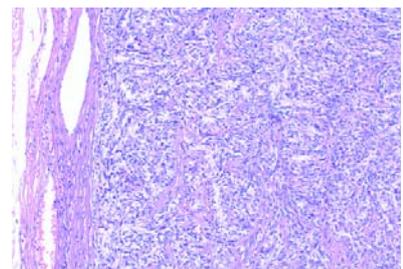


Fig. 3.12 Wolffian adnexal tumour. The tumour is circumscribed and composed of closely packed tubules.

from non-neoplastic serous cysts is ill defined. A suggested distinction is that serous cystadenomas have a thick wall composed of cellular stroma resembling ovarian stroma and lack folds and plicae in contrast to the histology of serous cysts {1236,1335}. Several Brenner tumours ranging from 1-16 cm in diameter have occurred {1120}, and they may be associated with serous or mucinous cystadenomas {169,1628,2302,3040}.

Wolffian adnexal tumour

Definition

A tumour of presumptive wolffian origin characterized by a variety of epithelial patterns.

Synonyms

Retiform wolffian adenoma, retiform wolffian adenocarcinoma.

Sites of involvement

Wolffian tumours occur mainly within the leaves of the broad ligament but may appear as pedunculated lesions arising from it. Less than 50 examples have been described that are predominantly located within the area where mesonephric remnants are distributed. They occur mainly in the broad ligament but also in the mesosalpinx, the serosa of the fallopian tube, the ovary and the retroperitoneum {637,670,682,1400,2653,2877,2926,3212}.

Clinical features

Patients range in age from 15-81 years, and most present with a unilateral adnexal mass. Ultrasound studies may show an ill defined mass [637].

Macroscopy

These predominantly solid tumours range from 0.5-18 cm in diameter. The sectioned surface may contain variably sized cysts and is yellow-tan to grey-white [2877]. The tumour is firm to rubbery and occasionally may have areas of haemorrhage and necrosis.

Tumour spread and staging

Tumour implants may be present at the time of diagnosis and indicate an aggressive tumour [637,2653].

Histopathology

The tumour shows a variable admixture of diffuse, solid and sieve-like cystic areas, with the solid pattern dominating in the majority of cases. The diffuse, solid areas show a compact proliferation of ovoid to spindle-shaped cells reflecting closed tubules bound by a basement membrane and separated by variable amounts of fibrous stroma or none at all. The round to ovoid nuclei may show indentations. The hollow tubules have a retiform or sertoliform appearance. When the closed tubules dominate, the lesion resembles a mesenchymal tumour; a PAS or reticulin stain helps unmask the tubular pattern. The cells lining the tubules are cuboidal to low columnar with a minimal amount of eosinophilic

cytoplasm and round to spindle-shaped, uniform nuclei. Sieve-like areas display clusters of variably sized cysts lined by attenuated cells. Most cases do not show atypia or mitotic figures.

Immunoprofile

The tumour cells are positive for most cytokeratins and vimentin and are often positive for calretinin (91%), inhibin (68%) and CD10 [2110]. They are usually negative for epithelial membrane antigen, estrogen receptor (ER) and progesterone receptor (PR) and are negative for cytokeratin 20, 34betaE12 and glutathione S-transferase [682,2926].

Cytometry

The ploidy of a metastatic tumour was assessed and found to be diploid [2653].

Electron microscopy

At the ultrastructural level, the tubules are surrounded by basal lamina and lined by cells with complex interdigitations, desmosomes and/or tight junctions and a few microvilli along the luminal border; no cilia are identifiable [670]. The cytoplasmic organelles are not distinctive and include lysosomes, a small amount of smooth endoplasmic reticulum and a few lipid droplets.

Differential diagnosis

The main tumours in the differential diagnosis are Sertoli cell tumour, Sertoli-Leydig cell tumour, and well differentiated endometrioid carcinoma. The presence of a sieve-like pattern and the

absence of Leydig cells help distinguish wolffian tumours from all these lesions. The absence of immunoreactivity with either ER or PR also would distinguish wolffian tumours from well differentiated endometrioid carcinomas; the latter are invariably positive for ER and PR; however, positive immunostaining does not exclude the possibility of a wolffian tumour [682].

Prognosis and predictive factors

The tumour stage as well as cytological atypia and frequent mitotic figures are important predictors of aggressive behaviour. Careful follow-up of all women with wolffian adnexal tumours is prudent [637,2653].

Most wolffian adnexal tumours are benign and adequately treated by unilateral salpingo-oophorectomy. About 10% either recur or metastasize. Recurrences and metastases to the lungs and liver have been reported within 1 year or as late as 8 years after diagnosis [637,2653]. The metastatic tumour often has more atypia compared to the primary. Some aggressive tumours have had no significant atypia or mitotic activity in either the primary or the metastatic lesion [2653].

Ependymoma

Definition

Tumours closely resembling neoplasms of the central nervous system that show ependymal differentiation.

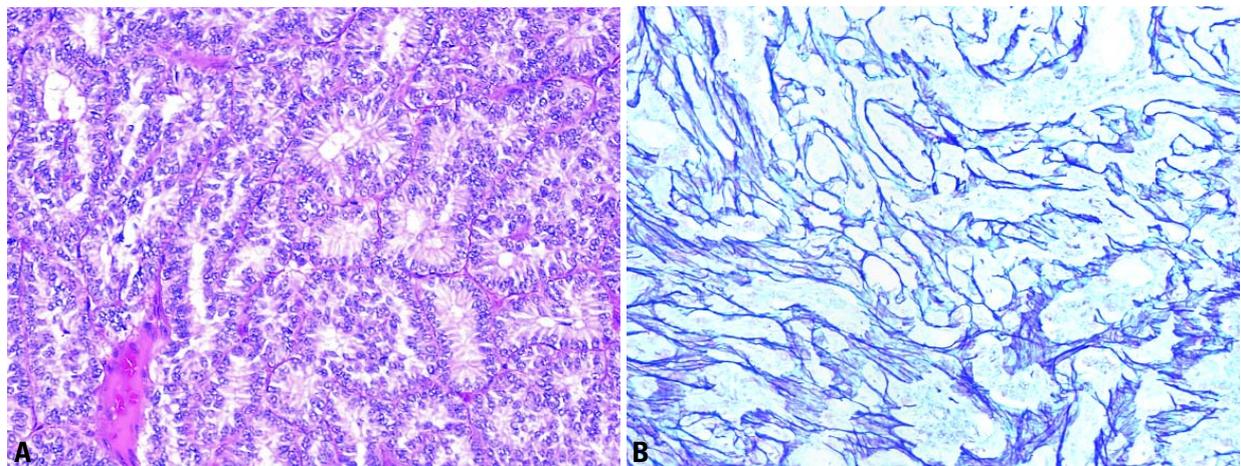


Fig. 3.14 Wolffian adnexal tumour. **A** The pattern of closely packed tubules simulates a Sertoli cell tumour. **B** Reticulin stain accentuates the tubular pattern.

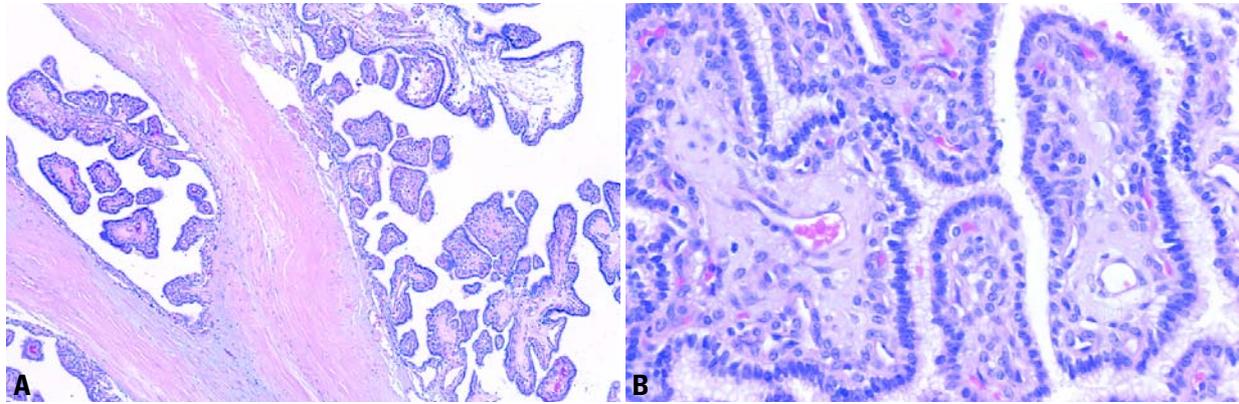


Fig. 3.15 Papillary cystadenoma associated with VHL. **A** A cystic lesion with multiple papillary excrescences is characteristic. **B** The papillae are lined by a single layer of cuboidal to low columnar cells with bland nuclei; there is no atypia or notable mitotic activity.

Localization

Only four endometriomas have been described in the uterine ligaments, three in the broad ligament and one in the uterosacral ligament [208,727,1068].

Clinical features

Patients were 13-48 years of age with a mean of 38 years and presented with a mass associated with lower quadrant tenderness.

Macroscopy

The tumours are solid or multicystic, soft in consistency and vary from 1 cm to massive in size. The sectioned surface shows haemorrhage and necrosis in the larger tumours.

Histopathology

The lesions are characterized by papillae lined by flat to columnar ciliated cells with central to apical, round to elongated nuclei that protrude into cystic spaces. In more cellular solid areas, the cells form true perivascular endometrial rosettes and pseudorosettes. Mitotic figures may be few or numerous. A few psammoma bodies and small nodules of mature cartilage may be present.

At the ultrastructural level the cells have cilia, blepharoplasts and intermediate filaments [208,727].

Differential diagnosis

The papillary architecture and psammoma bodies closely resemble serous papillary carcinoma. The endometrial cells are immunoreactive for glial fibrillary acidic protein, however, helping to distin-

guish the two lesions. The cells are also positive for cytokeratin and vimentin.

Prognosis and predictive factors

These are malignant tumours capable of spread beyond the ligaments [208,727,1068]. Two of the reported cases had spread beyond the broad or uterosacral ligament at presentation, whilst a third had two recurrences over a 24 year period.

Papillary cystadenoma associated with von Hippel-Lindau disease

Definition

A benign tumour of mesonephric origin that occurs in women with von Hippel-Lindau (VHL) disease.

Clinical features

Reported in women 20-46 years of age, one case was not only bilateral but also the first manifestation of the disease; the remaining three were unilateral [939,949,988,1505].

Imaging

Ultrasonography shows a sonolucent mass containing an echogenic region [1505]. By computed tomography the lesion appears as an adnexal mass with both water attenuation and soft tissue attenuation areas and curvilinear calcification [939].

Macroscopy

The tumours are up to 4 cm in diameter and cystic with polypoid papillary protrusions.

Histopathology

Histologically, the lesion is characterized by a complex, arborizing, papillary architecture. Generally, a single layer of non-ciliated cuboidal cells with vacuolated to lightly eosinophilic cytoplasm and bland round nuclei line the papillae [939,949,988,1505]. The papillary stalks vary from cellular to oedematous and hyalinized. Atypia and necrosis are absent, and mitotic figures are rare to absent. The cells contain glycogen but not mucinous material. A prominent basement membrane is evident beneath the epithelial cells. The cyst wall is fibrous and may have small bundles of smooth muscle or focal calcification.

Genetic susceptibility

VHL disease is an autosomal dominant disorder with inherited susceptibility to a variety of benign and malignant neoplasms including haemangioblastomas of the retina and central nervous system, renal cell carcinoma, pancreatic microcystic adenomas and a variety of other cysts, adenomas and congenital abnormalities. Papillary cystadenomas of mesonephric origin are rare VHL-associated lesions that occur more often in the epididymis but also rarely in the retroperitoneum and broad ligament in women; only four examples of the latter have been documented.

Genetics

The tumour suppressor gene responsible for VHL disease has been mapped to chromosome 3p25 and subsequently identified. Genetic studies on a variety of

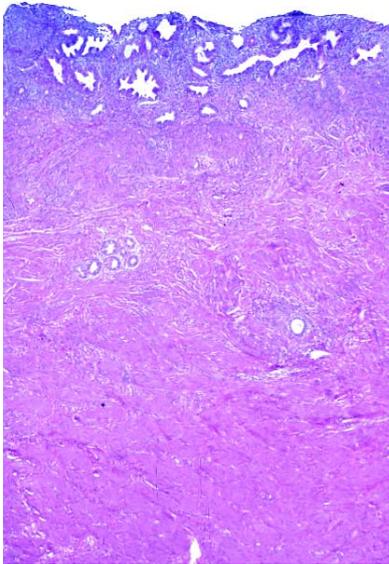


Fig. 3.16 Uterus-like mass. The cystic mass resembles the uterus and is composed of a layer of endometrium consisting of glands and stroma overlying smooth muscle.

tumours from patients with VHL disease have demonstrated loss of heterozygosity at chromosome 3p within the VHL gene region. Two papillary cystadenomas (one from broad ligament, the other retroperitoneal) were studied by polymerase chain reaction and single-strand conformation polymorphism with four polymorphic markers spanning the VHL gene locus (D3S1038, D3S1110, D3S2452, 104/105) {2640}. Both tumours showed loss of heterozygosity at one or more of the markers providing evidence that somatic loss of the VHL gene is responsible for the genesis of these papillary cystadenomas {2640}.

Prognosis and predictive features

All lesions reported so far have been benign.

Uterus-like mass

Definition

A tumour-like lesion composed of endometrial tissue and smooth muscle, histologically resembling the uterus.

Clinical features

Patients present with a pelvic mass. Most arise within the ovary, but extraovarian

cases have been described. Cases reported in the uterosacral and broad ligaments have occurred in women under 50 years of age {48}.

Macroscopy

The lesions form a cystic mass.

Histopathology

The inner lining consists of benign endometrial glands and endometrial stroma with an arrangement resembling endometrium. The outer layer of the cyst wall consists of thickened smooth muscle bundles appearing similar to myometrium.

Immunoprofile

Lesions may express ER and PR in the endometrial and myometrial components.

Differential diagnosis

"Endomyometriosis" is likely the same entity as uterine-like mass. "Endometriosis with smooth muscle metaplasia" is histologically related to uterus-like mass, if not the same. Adenomyoma is distinguished from uterus-like mass by lacking the uterus-like organization. A uterus-like mass lacks the classic features of endometrioid carcinoma and extrauterine adenosarcoma.

Genetics

A deletion on the short arm of chromosome 2 has been identified.

Prognosis and predictive factors

Benign behaviour would be expected.

Adenosarcoma

A single case of a high grade adenosarcoma arising from the round ligament was reported {1396}.

Mesenchymal tumours

Mesenchymal tumours originating from the broad and other ligaments are rare. Almost any kind of malignant or benign mesenchymal tumour may occur.

Malignant tumours

Sarcomas are extremely rare, the most frequent being leiomyosarcoma, {465, 689, 1192, 1608, 1630, 2210} for which the same diagnostic criteria should be applied as for its uterine counterpart.

Approximately 10 cases have been reported, and the prognosis is poor. Other sarcomas reported include endometrioid stromal sarcoma arising in endometriosis {2220}, embryonal rhabdomyosarcoma (occurring in children and having a poor prognosis) {991}, alveolar rhabdomyosarcoma (in an adult) {558}, mixed mesenchymal sarcoma {2822}, myxoid liposarcoma {2708} and alveolar soft part sarcoma {2017}.

Benign tumours

The most common tumours are leiomyomas and lipomas {340,962}. It is often difficult to determine the site of origin of leiomyomas within the broad ligament. It has been suggested that leiomyomas be designated as ligamentous only if clearly separated from the myometrium. A leiomyoma of the broad ligament was imitated by Dracunculosis {70}. Lipomas are usually small and located within the mesosalpinx {847} and may be mixed with leiomyomas. Cases of other mesenchymal tumours of the broad and round ligament have been reported including two benign mesenchymomas {2069}, neurofibromas, schwannomas {246,1047,2910} and a fibroma with heterotopic bone formation {2899}. Massive ascites and bilateral pleural effusion has been described in association with broad ligament leiomyoma and with paraovarian fibroma (pseudo-Meigs syndrome) {357,364, 992}.

Miscellaneous tumours

A variety of miscellaneous tumours have been described. Many of them are of ovarian type, such as germ cell and sex cord-stromal tumours. Although the question of origin from accessory ovarian tissue may be raised, in most cases no pre-existing ovarian tissue is identified. Mature teratomas, in particular dermoid cysts, occurred bilaterally within accessory ovaries of the broad ligament {941}. A dermoid cyst containing pituitary tissue occurred in the uterosacral ligament {1179}. A yolk sac tumour was found in the broad ligament {1270}. Other reported cases included granulosa cell tumours, but some of these were in fact wolffian adnexal tumours {962,1427,2347,2997}. Several broad ligament tumours of the thecoma-fibroma group, some of which had estro-

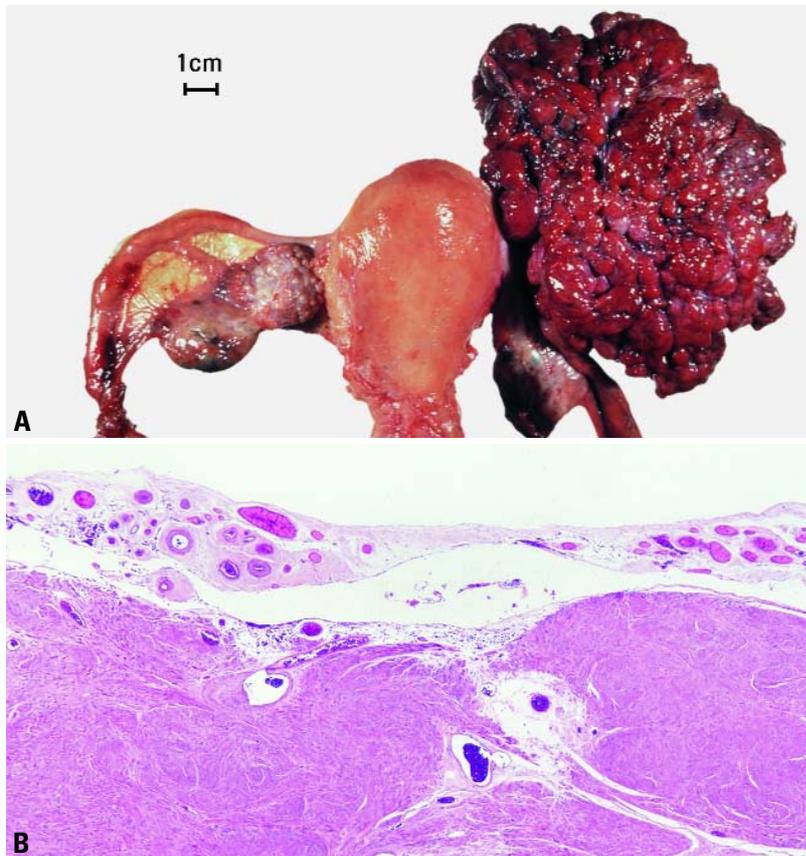


Fig. 3.17 Cotyledonoid dissecting leiomyoma. **A** Viewed posteriorly, an exophytic, congested, multinodular mass resembling placental tissue arises from the right cornual region of the uterus and extends laterally. **B** In the extrauterine component, a cotyledonoid process composed of smooth muscle is covered by connective tissue containing congested vessels.

genic effects, have been reported. Several cases of steroid cell tumour with possible origin from accessory ovaries or adrenocortical remnants have been described {38,2462,2538,2996}. Three phaeochromocytomas, two that caused hypertension and elevated vanillylmandelic acid levels and one non-functional tumour {54,58,122}, and a carcinoid {1325} have been described.

Secondary tumours

Any type of malignant tumour originating from the uterus, its adnexae, other sites within the abdomen or from any other organ of the body may spread to the uterine ligaments by direct extension, lymphatics or blood vessels. In particular, intravenous leiomyomatosis {523, 1122,1940,2051}, diffuse uterine leiomyomatosis {2394} and endometrial stromal sarcoma from the uterus may present as a mass within the broad ligament. Although it is far more common to spread to the broad ligament from the uterus, intravenous leiomyoma may exceptionally arise in the broad ligament {1154}. Cotyledonoid dissecting leiomyoma, the Sternberg tumour, is an unusual benign uterine smooth muscle neoplasm that spreads to the broad ligament {2470}. It is characterized by dissecting growth within the uterus, degenerative changes and a rich vascular component but does not have intravascular extension.