Cervical Carcinoma

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Rajeev Shah and Aaron Ervine

Introduction

Cervical cancer is the second commonest cancer in females worldwide. Its incidence in Western Society is decreasing due to screening programmes and this will be improved upon by HPV (Human Papilloma Virus) vaccination Schemes. A majority of deaths related to cervical cancer are in developing countries. Risk factors for cervical intraepithelial neoplasia and cancer are HPV infection, early age at onset of sexual intercourse, multiple sexual partners, and smoking.

Cervical epithelial lesions are often detected because of an abnormal smear as part of a cervical screening programme. A persistent or high-grade abnormality is referred for colposcopic visualisation of the squamocolumnar epithelial transformation zone to delineate abnormal areas of mucosa characterised by punctation, mosaicism and loss of uptake of iodine (acetowhite epithelium). Cervical punch biopsy determines the nature of the abnormality, which if localised, is thermally ablated or resected by large loop or cone biopsy depending on its extent. The aim is to completely excise any precancerous lesion. Specimens are orientated, serially sliced and all processed with standard step sections to establish the nature (squamous cell or glandular) and grade of the lesion, the presence of any invasive component, and relationship to the ectocervical, endocervical and deep margins. Close histocytological correlation is required for accurate reporting and smear follow up of completely excised lesions is for 5–10 years with subsequent return to usual screening programme intervals. A proportion of established cervical cancers are asymptomatic, in the older age group and undiscovered due to non-attendance at cervical smear appointments. Some result from misinterpretation and undercalling, or non-representative sampling of previous smears in what is a screening programme with inevitable false negative cases. Symptomatic disease (e.g. postcoital bleeding) requires clinical examination, and if a cancer is suspected, a targeted wedge biopsy rather than a punch biopsy taken as this has a greater chance of establishing invasive disease. Tumour staging is by MRI scan (for local spread) and CT scan (for distant spread). Occasionally PET scan is done for distant metastases, and if imaging cannot exclude bladder or bowel involvement, cystoscopy and sigmoidoscopy may be required.

Cold cone knife biopsy may be considered for small cancers or if a cervical glandular lesion is suspected. However, in general, with tumours greater than FIGO stage IA, radical hysterectomy inclusive of pelvic lymphadenectomy is carried out. Laparoscopic vaginal hysterectomy is used for tumours ≤2 cm. Intraoperative frozen section

R. Shah (✉) · A. Ervine
Department of Cellular Pathology, Craigavon Area Hospital, Craigavon, UK
e-mail: rajeev.shah@southerntrust.hscni.net

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of clinically suspicious lymph nodes or sentinel lymph node mapping is sometimes indicated before proceeding to radical surgery. In occasional cases in young women with a FIGO IB tumour ≤2 cm a fertility sparing radical trachelectomy (upper vagina, cervix, parametria) with laparoscopic lymphadenectomy is performed. It can be associated with up to a 50% chance of successful subsequent pregnancy. Postoperative chemoradiation is indicated for patients with positive pelvic lymph nodes, and, radiotherapy for lymph node negative patients but with more than one third depth stromal invasion, lymphovascular invasion or tumour diameter >4 cm. Indications for pelvic exenteration are invasion of adjacent organs, recurrent disease and severe pelvic irradiation necrosis, in the absence of distant extrapelvic metastases on CT/PET scan. Advanced disease may present with ureteric obstruction and chronic renal failure, haematuria or rectal symptoms. It can be treated by primary chemoradiation with subsequent salvage hysterectomy, or exenteration if deemed appropriate by the clinical multidisciplinary team. Less than 5% of patients with recurrent disease are alive at 5 years.

Gross Description

Specimen

- Cervical smear/punch or wedge biopsy/diathermy (hot) or knife (cold) cone biopsy/LLETZ (large loop excision of transformation zone)/ hysterectomy/trachelectomy with laparoscopic lymphadenectomy/radical (Wertheim's) hysterectomy with vaginal cuff, parametria and lymphadenectomy/ pelvic (anterior/posterior/ total) exenteration (components: bladder, ureters, uterus, vagina, tubes and ovaries, rectum)
- Size (mm) and weight (g).

Tumour

Site

- Endocervix/ectocervix.
- Anterior/posterior.
- Lateral (right/left).

Size

- Length × width × depth (mm) or maximum dimension (mm).
- Early stromal invasion is breech of the basement membrane with scant stromal penetration <1 mm in depth.
- Microinvasion is a term that was inconsistently used and is no longer favoured. *Early cancer* is more appropriately designated by FIGO stage as defined by the depth and horizontal extent of invasive disease:
  - *Depth*: ≤3 mm (FIGO IA1) or if >3 mm and ≤5 mm (FIGO IA2) depth of invasion from the nearest (surface or glandular) basement membrane, usually involved by CIN/CGIN (cervical intraepithelial neoplasia/cervical glandular intraepithelial neoplasia).
  - *Horizontal extent*: ≤7 mm.
  - *Vessels*: venous or lymphatic permeation *does not alter the staging* but is taken into account for management decisions by the gynaecological oncologist.

Appearance

- Polypoid/papillary/nodular/solid/ulcerated/ burrowing. Ulcerated cancers generally infiltrate more deeply than polypoid ones.

Edge

- Circumscribed/irregular.

Extent

- Infiltration of cervical wall, parametria/paracervix, corpus uteri, vagina.

Histological Type

Squamous Cell Carcinoma

- *80% of cases.*
- Classical:
  - Keratinising
  - Non-keratinising: large cell/small cell. Non-keratinising large cell is recognisably squamous in character with cell stratification and intercellular bridges but no keratin pearls are present.

- Variants:
- *Verrucous:* exophytic and locally invasive, it may recur after excision and radiotherapy. It shows bland cytology with bulbous processes and a pushing deep margin.
- *Warty:* surface koilocytosis and an invasive deep margin.
- *Spindle cell:* upper aerodigestive tract analogue with tumour cell fibroplasia (sarcomatoid carcinoma).
- *Papillary:* two types of papillary neoplasm with either CIN like changes/in situ squamous cell epithelium, or, squamotransitional cell type epithelium. The latter occurs in post menopausal women and is associated with late recurrence and metastases (25%). Invasion at the base may be superficial or associated with more usual squamous cell carcinoma.
- *Basaloid:* an aggressive neoplasm comprising nests of basaloid cells with peripheral palisading and central keratinisation or necrosis.
- *Lymphoepithelioma like:* circumscribed margin, lymphocytic infiltrate, large uniform cells with a prominent nucleolus. It may have a better prognosis and is radiosensitive. ±EBV (Epstein Barr Virus) positive.

Adenocarcinoma

- *10–15% of cases*.
- *Endocervical:* 70% of cervical adenocarcinomas and variably glandular/mucinous related to the degree of differentiation which is usually well to moderate.
- *Endometrioid:* 25% of cervical adenocarcinomas, and exclude a uterine adenocarcinoma extending to cervix. Typically at the junctional zone arising from endometriosis/tuboendometrial metaplasia, and may coexist with usual endocervical type adenocarcinoma. A minimal deviation variant exists.
- *Minimal deviation (adenoma malignum):* late presentation and poor prognosis with bland epithelium showing mitoses and irregular gland extension deep (>50%) into the cervical stroma. CEA and p53 over expression may be of diagnostic help. Associated with Peutz-Jeghers syndrome.
- *Villoglandular:* good prognosis in young females. Papillary with CGIN type covering epithelium, connective tissue cores and indolent invasion at the base. More aggressive moderately differentiated variants occur and it can be associated with more usual cervical cancer subtypes. Also consider implantation from an endometrial primary.
- *Clear cell:* clear, hobnail cells, glycogen PAS positive, solid, tubules, papillae. Some are associated with in utero exposure to diethylstilboestrol.
- *Serous papillary:* poor prognosis and potentially multifocal in endometrium and ovary. High-grade cytological appearances ± psammoma bodies—exclude low-grade villoglandular adenocarcinoma.
- *Mesonephric:* from mesonephric duct remnants deep in the posterior or lateral cervical wall. Small glands with eosinophilic secretions.
- *Non-Müllerian mucinous:* intestinal including colloid and signet ring cell carcinomas. There is also a gastric type. Poor prognosis compared to usual endocervical-type adenocarcinoma (30% vs. 70% 5 year survival), and exclude a gastrointestinal secondary adenocarcinoma.

Poorly Differentiated Carcinoma

- *Scirrhous, undifferentiated.*
- In undifferentiated carcinomas also consider differential diagnoses such as sarcoma (epithelioid leiomyosarcoma), malignant melanoma and malignant lymphoma.

Mixed Tumours

- *Mixed type* (e.g. squamous cell/adenocarcinoma) and *differentiation* (e.g. endocervical/endometrioid adenocarcinoma).
- *Adenosquamous, solid with mucus production*: varies from well differentiated glandular and squamous cell components, to solid poorly differentiated squamous cell carcinoma with stainable PAS positive mucin production (up to 30% of cases) and which is *more aggressive* than usual squamous cell carcinoma.

Miscellaneous Carcinoma

- *Glassy cell:* a poorly differentiated adenosquamous carcinoma in young women.
- *Adenoid basal:* indolent and often an incidental finding at hysterectomy or cone biopsy. Organoid lobules and nests of cells with punched out lumina ± eosinophilic secretions. Strong association (90%) with overlying high-grade CIN or microinvasive squamous cell carcinoma.
- *Mucoepidermoid* and *adenoid cystic*: low-grade and indolent behaviour although recurrence/metastasis if incompletely removed.

Small Cell Carcinoma

- *Primary* or *secondary*. A poorly differentiated/high-grade neuroendocrine carcinoma. Chromogranin(focal)/synaptophysin/CD56 positive with poor prognosis. High Ki-67 index, TTF-1/CD99/p16/p63±. Treated by chemotherapy and not surgery.

Other Neuroendocrine Tumours

- *Atypical carcinoid* like tumour of intermediate-grade malignancy as well as classical well differentiated/low-grade *carcinoid tumour* (rare), and high-grade *large cell neuroendocrine carcinoma*.

Metastatic Carcinoma

- *Direct spread*: endometrium (commonest), colorectum, bladder.
- *Distant spread*: breast (especially infiltrating lobular), stomach, ovary.

Differentiation

Varies according to lesion type: e.g. keratinising squamous cell carcinoma is well to moderately differentiated, non-keratinising large cell moderate, and non-keratinising small cell poorly differentiated. About 60% are moderately differentiated. Tumour grade does not reliably predict prognosis and is only broadly indicative. However, grade 1 (small amount (≤10%) of solid growth with mild nuclear atypia) has a better prognosis than grade 3 (solid pattern (>50%) with severe nuclear atypia) adenocarcinoma. Undifferentiated carcinomas show no squamous cell or glandular differentiation (grade 4). Small and large cell neuroendocrine carcinomas are high-grade or poorly differentiated.

Extent of Local Tumour Spread

- Border: pushing/infiltrative.
- Lymphocytic reaction: prominent/sparse.

Infiltration

- Cervical wall, parametria, endometrium, myometrium, vagina.
- Depth through the cervical stroma and parametrium and distance to the nearest parametrial resection margin (mm).
- Infiltration of the superficial and deep thirds of the cervix have average disease free intervals of 94% and 73% respectively.

FIGO/TNM

FIGO staging is recommended with additional TNM8 comments on lymph node status. The classifications are applicable to cervical carcinomas

I	Carcinoma confined to the uterus (extension to the corpus is disregarded)
IA	Lesions detected only microscopically; maximum size 5 mm deep and 7 mm across; venous or lymphatic permeation does not alter the staging
IA1	Stromal invasion ≤3 mm deep and ≤7 mm horizontal axis
IA2	Stromal invasion >3 mm to ≤5 mm deep and ≤7 mm horizontal axis
IB	Clinically apparent lesion confined to the cervix or microscopic lesion larger than stage IA2 (occult carcinoma)

IB1	clinical lesions ≤4 cm in greatest dimension
IB2	Clinical lesions >4 cm in greatest dimension
II	Invasive carcinoma extending beyond the uterus but not to pelvic wall or lower third of vagina.
IIA	Without parametrial invasion
IIA1	Clinical lesion ≤4 cm in greatest dimension
IIA2	Clinical lesion >4 cm in greatest dimension
IIB	With parametrial invasion
III	
IIIA	Tumour involves lower third of vagina
IIIB	Tumour extends to pelvic wall wall, or causes hydronephrosis or non-functioning kidney
IV	Tumour involving mucosa[a] of urinary bladder mucosa and/or rectum or extends beyond the true pelvis. Adjacent organ involvement (IVA) or distant metastases (IVB).

[a]Bladder/rectal mucosal involvement requires confirmation by biopsy and involvement of bladder/rectal wall only is FIGO stage III

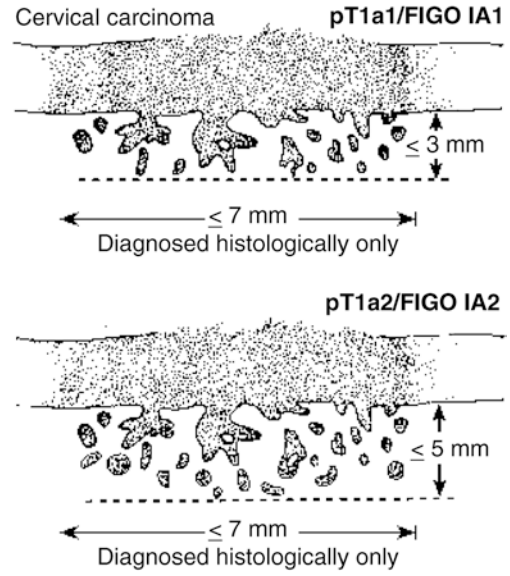

Fig. 25.1 Cervical carcinoma. Reproduced, with permission, from *TNM Atlas: Illustrated guide to the TNM/pTNM classification of malignant tumours, 5th ed.*, © 2005, Springer-Verlag

FIGO III refers to grossly or histologically evident continuous invasion beyond the myometrium into the parametrium and to "frozen pelvis"—a clinical term meaning extension to pelvic wall(s). Parametrial involvement is an indicator of poor prognosis and likely lymph node metastases. Positive peritoneal fluid is not considered in the FIGO classification.

Tumour spread: is typically to vagina, uterine corpus, parametria, lower urinary tract (ureters) and uterosacral ligaments. Involvement of regional lymph nodes relates to the stage of disease with lungs, brain and bone the commonest (5–10%) sites of distant metastases (Figs. 25.1, 25.2, 25.3, 25.4, 25.5, 25.6, and 25.7).

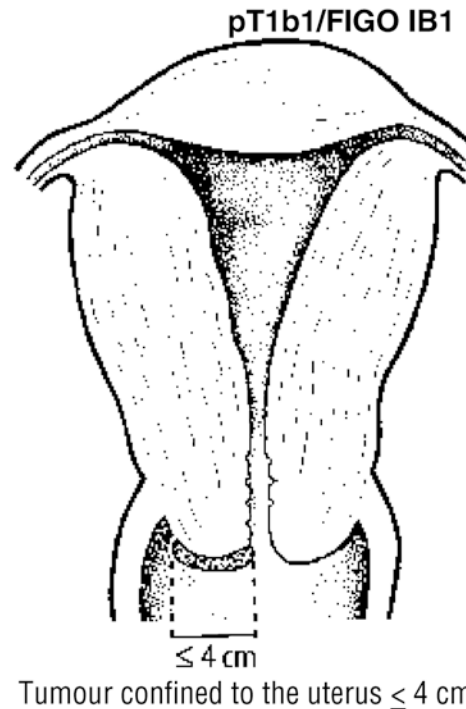

Fig. 25.2 Cervical carcinoma. Reproduced, with permission, from *TNM Atlas: Illustrated guide to the TNM/pTNM classification of malignant tumours, 5th ed.*, © 2005, Springer-Verlag

Lymphovascular Invasion

- Present/absent.
- Intra−/extratumoural.
- Lymphovascular invasion should be noted on biopsy material as it may influence the choice of more extensive surgical resection. Its presence and extent are a *strong indicator of poor*

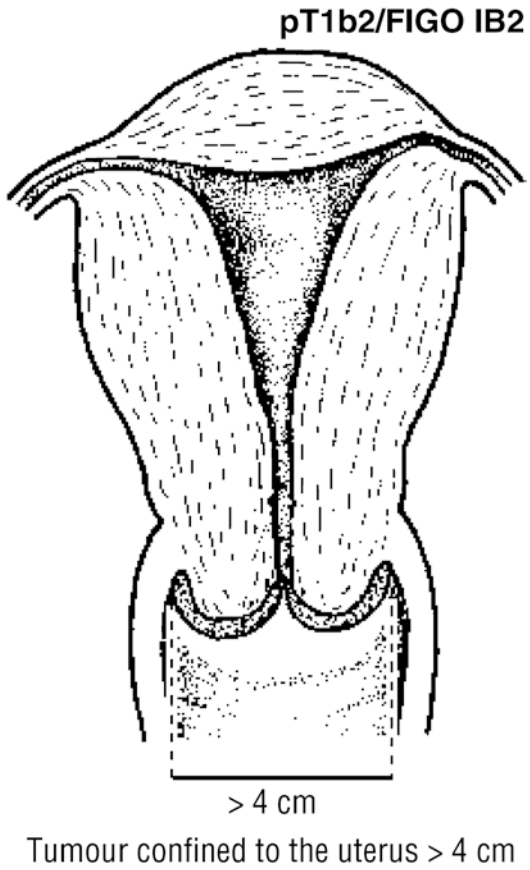

Fig. 25.3 Cervical carcinoma. Reproduced, with permission, from *TNM Atlas: Illustrated guide to the TNM/pTNM classification of malignant tumours, 5th ed.*, © 2005, Springer-Verlag

prognosis and the likelihood of lymph node metastasis and recurrence of tumour.

Lymph Nodes

- Site/number/size/number involved/extracapsular spread.
- Parametrial involvement increases regional lymph node metastases to about 35% of cases.
- Regional nodes (Fig. 25.8): paracervical[1], parametrial[2], hypogastric[3] (internal iliac, obturator), common[5] and external iliac[4], presacral[6], lateral sacral[7]. Para-aortic lymph nodes are not regional. A regional lymphadenectomy will ordinarily include a minimum of six lymph nodes. Intraoperative frozen section examination of suspicious lymph nodes may be done as a prequel to radical surgery, and if positive, a more conservative approach adopted.

pN0	no regional lymph node metastasis.
pN1	metastasis in regional lymph node(s).

Excision Margins

Distances (mm) to the nearest deep cervical (anterior and posterior), lateral parametrial and inferior vaginal resection margins.

In a trachelectomy specimen distances (mm) to the nearest deep cervical, lateral parametrial, proximal endocervical and distal ectocervical resection margins.

Other Pathology

HPV	Human papilloma virus infection causing an anogenital field change of viral lesions (flat koilocytosis/condyloma accuminatum), intraepithelial neoplasia and carcinoma.
CIN	Cervical intraepithelial neoplasia.
SIL	Squamous intraepithelial lesion (Bethesda system).
AIS/CGIN	Adenocarcinoma in situ (AIS) / high-grade cervical glandular intraepithelial neoplasia (CGIN).
SMILE	Stratified mucin producing intraepithelial lesion
VAIN	Vaginal intraepithelial neoplasia
VIN	Vulval intraepithelial neoplasia.
AIN	Anal intraepithelial neoplasia.
Bowenoid papulosis	A now less often used clinical term describing brown perineal patches in young women. HPV induced with histology of VIN 3 and a negligible risk of progression to carcinoma.

Evidence indicates that *"high-risk" HPV infection* results in *high-grade CIN (SIL)* with a higher rate of progression to carcinoma (high risk HPV types 16 and 18 are responsible for approximately 70% of cervical cancers). *"Low-risk" HPV* and *low-grade CIN* may potentially regress. HPV infection is also an aetiological factor in cervical glandular dysplasia (CGIN), which often

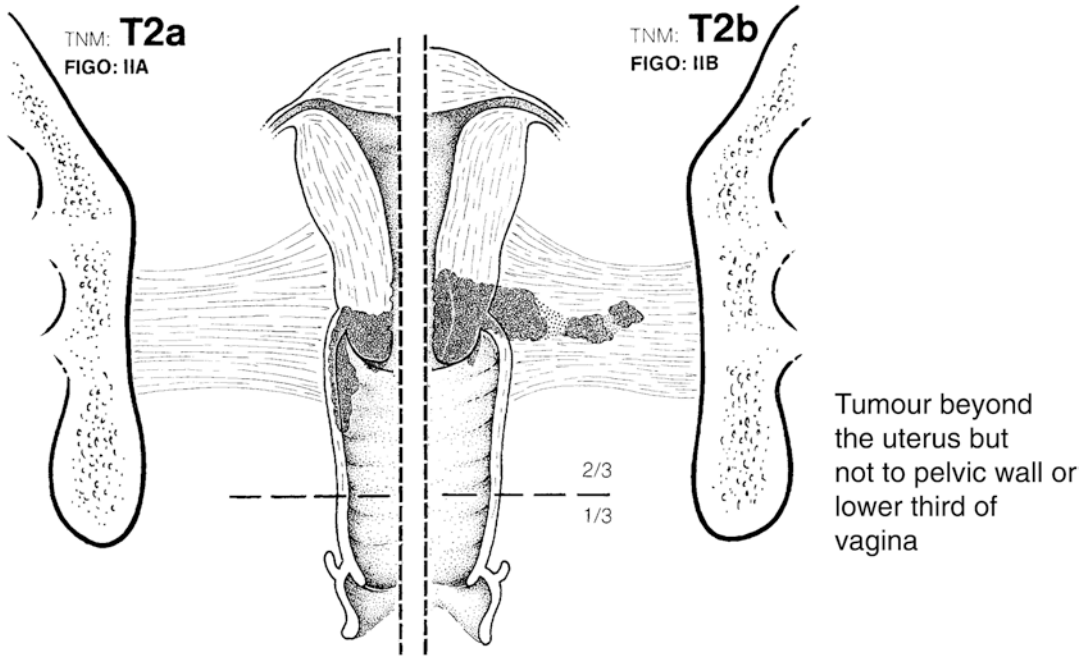

Fig. 25.4 Cervical carcinoma. Reproduced, with permission, from *TNM Atlas: Illustrated guide to the TNM/pTNM classification of malignant tumours, 5th ed*., © 2005, Springer-Verlag

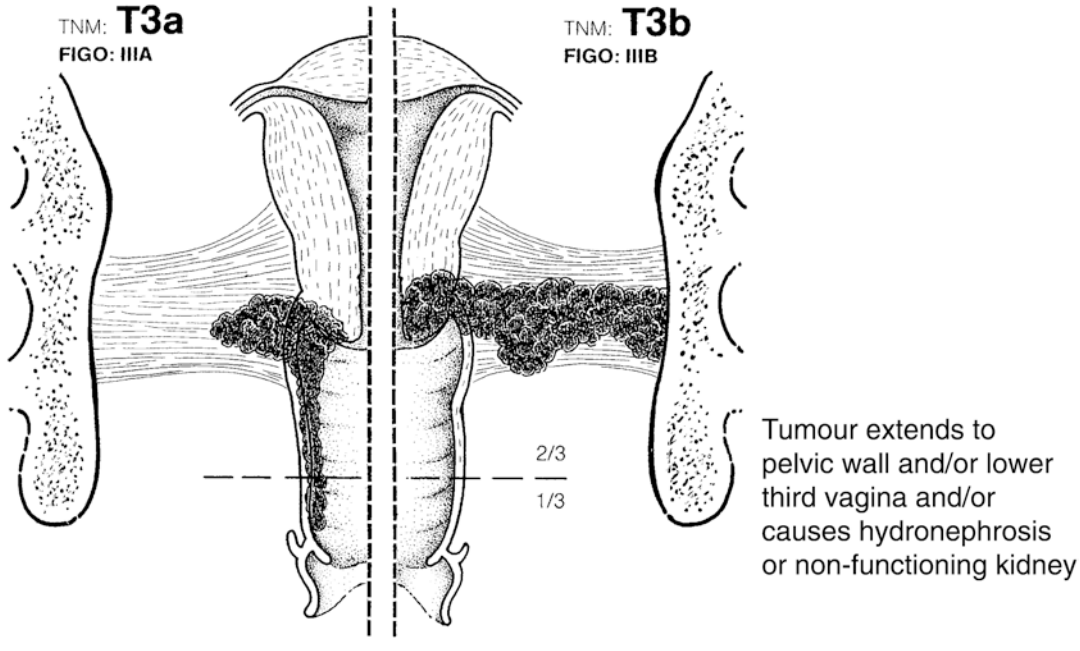

Fig. 25.5 Cervical carcinoma. Reproduced, with permission, from *TNM Atlas: Illustrated guide to the TNM/pTNM classification of malignant tumours, 5th ed*., © 2005, Springer-Verlag

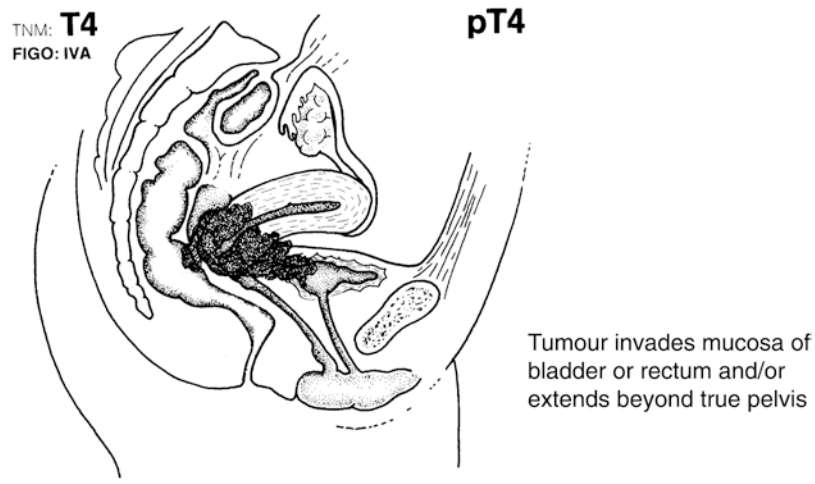

Fig. 25.6 Cervical carcinoma. Reproduced, with permission, from *TNM Atlas: Illustrated guide to the TNM/pTNM classification of malignant tumours, 5th ed.*, © 2005, Springer-Verlag

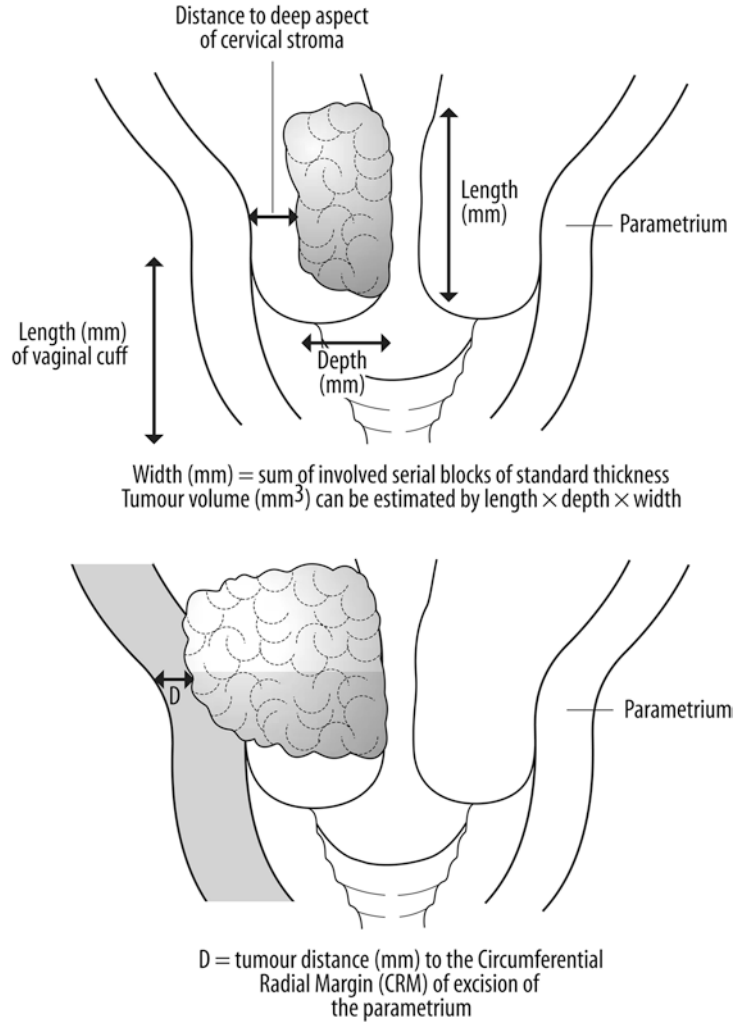

Fig. 25.7 Cervical carcinoma. Reproduced, with permission, from *Histopathology Reporting: Guidelines for Surgical Reporting*, *2nd ed.,* © 2006, Springer

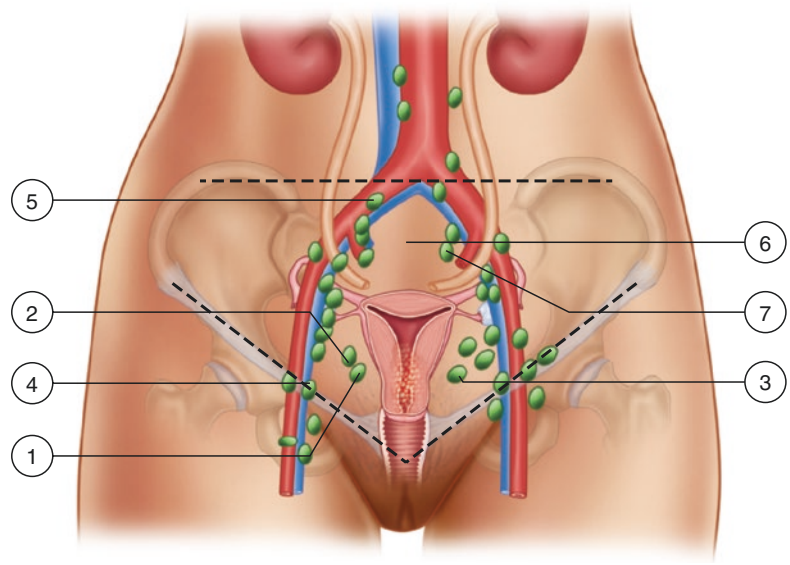

Fig. 25.8 Cervical carcinoma: regional lymph nodes. Reproduced, with permission, from *TNM Atlas: Illustrated guide to the TNM/pTNM classification of malignant tumours, 5th ed.*, © 2005, Springer-Verlag

coexists with squamous epithelial dysplasia (CIN, SIL), and occasionally SMILE of intermediate squamocolumnar character.

High-grade CGIN also potentially progresses to invasive disease with a strong association between high-grade CGIN and invasive lesions. CGIN should also be distinguished from *benign mimics*: e.g. tuboendometrial metaplasia (TEM), endometriosis, endocervical microglandular hyperplasia, mesonephric remnants and endocervical gland tunnel clusters. CGIN shows an abrupt junction with normal epithelium, nuclear atypia, mitoses and apoptosis. Ciliation is less frequent than in metaplasia. Immunohistochemistry may also be of help in that CGIN has a high Ki-67 proliferation index (>10%), stains strongly with p53, shows strong diffuse "block" positivity with p16, and is focal or negative for bcl-2. Benign mimics such as TEM have a converse immunophenotype with this panel. Endocervical (commonest), intestinal and endometrioid variants are described. Ki-67 positive cells in the upper two thirds of the epithelium also reliably identifies CIN lesions in biopsy material. Retention of distinct immunophenotype may also help to distinguish neoplastic squamous or glandular epithelia from thermal cautery artifact at diathermy loop or conisation specimen tissue margins.

Low-risk	HPV types 6, 11	Koilocytosis, CIN 1
High-risk	HPV types 16, 18, 31, 33, 35, 39, 51	CIN 2/3
		Squamous carcinoma
		Typing by in situ hybridisation
CIN (SIL)	Low-grade	CIN 1, SIL 1
	High-grade	CIN 2, CIN 3, SIL 2

"High-risk" HPV DNA subtyping has a role in primary screening, quality assurance checking, and the closer follow up of women whose cervical smears shows BNA (borderline nuclear abnormalities)/ASC-US (atypical squamous cells of uncertain significance) changes.

Immunophenotype: cervical squamous cell carcinoma is AE1/AE3, CK5/6, p63 positive, and adenocarcinoma p16 and CEA positive.

FIGO IA Carcinoma

The higher the grade and larger the CIN lesion the more likely it is to show early invasion with a *35% risk of CIN 3 progressing to carcinoma over a ten year period.* FIGO IA carcinoma is not designated on small, limited biopsy samples but rather on a large biopsy specimen, e.g. cone

biopsy which allows removal and assessment of the whole lesion. Five year survival rates are about 95%. Risk factors for progression to clinically invasive carcinoma are increasing depth of invasion, increasing lateral extent (horizontal axis) of the lesion, lymphovascular invasion and incomplete removal by LLETZ/cone biopsy. Adverse factors in occult carcinoma (i.e. bigger than FIGO IA but not clinically detectable) are a depth of invasion >5 mm and lymphovascular invasion. Very occasional cases, where CIN has focal areas suspicious of penetrating the stroma but lacking definite evidence of invasion, may warrant a designation of "equivocal stromal invasion". Commonly occurring tangential cutting and extension of CIN into endocervical crypts must be excluded and is supported by an intact circumscribed basement membrane. An uncommon differential is squamous cell carcinoma with a CIN 3 like growth pattern, for which widespread, deep expansion with luminal necrosis are useful diagnostic clues. A rare mimic of cervical cancer is buried or entrapped atypical epithelium in the superficial cervical stroma following a previous biopsy.

The first stage of *early invasive squamous cell carcinoma* is recognised by budding of invasive cells with morphology similar to that of the overlying CIN lesion through the basement membrane. With lesion progression the tongues of tumour become *more differentiated or "hypermature" (so called paradoxical maturation/differentiation)* with cytoplasmic eosinophilia and nuclear clearing. A *stromal fibro-inflammatory reaction* is also seen. The distinction between adenocarcinoma in situ and early invasive adenocarcinoma is more difficult to define and measure with features such as *depth* beyond the normal endocervical gland field, *cribriform complexity and budding* of glandular architecture, *stromal fibroinflammatory reaction* and *proximity of abnormal glands to thick walled stromal vessels* of use.

Measurement of tumour extent in cervical carcinoma is readily obtained in the longitudinal and deep axes, whereas the transverse dimension depends on summation of the number of involved adjacent blocks of known thickness. About 10% of cervical carcinomas show multifocal stromal invasion characterised by clear separation of tumour by uninvolved tissue or an origin from different lips of the cervix. In this case the pathological stage is based on the width and depth of the largest tumour and not the combined dimensions of the various cancers.

Treatment

Treatment of cervical carcinoma is based on the tumour stage, patient age and consideration of fertility. Early invasive carcinoma may be treated with *loop or cold knife cone biopsy* ensuring a minimum 3 mm clearance of margins (note that there can be a small risk of skip or higher endocervical canal lesions), or *simple hysterectomy*. A fertility sparing procedure such as *radical trachelectomy* (removal of the upper vagina, cervix and surrounding parametria with laparoscopic lymphadenectomy) may be considered in young women with up to a FIGO IB1 tumour <2 cm in maximum dimension. *Radical hysterectomy* is indicated for larger tumours or where there is lymphovascular invasion. *Radiotherapy* produces tumour cell necrosis, degeneration, pleomorphism, maturation, inflammation and fibrosis. *Combination radio−/chemotherapy* (±brachytherapy) is used to augment radical surgery for tumours ≥ FIGO IB, or on its own for palliative control in high stage disease. Small cell neuroendocrine carcinoma is treated by chemotherapy rather than surgery.

Prognosis

Prognosis relates to tumour type and volume, invasion of endometrium, parametrium and vessels, and most importantly *stage of disease*. Overall 5 year survival rate is 55%, with stage I carcinoma 85–90% and 35%/10% for stages III/IV. Tumours with a glandular component, lymphovascular invasion and young age at diagnosis (<30 years) are more aggressive and more often positive for pelvic lymph node metastases. The incidence of cervical adenocarcinoma is increas-

ing and presents on average 5 years younger than squamous cell carcinoma. Anecdotally it has a worse prognosis than squamous cell carcinoma and radical surgery is undertaken. This adverse outlook may relate to presentation with more bulky disease and greater resistance to radiotherapy. However the risk of lymph node metastasis is broadly similar for equivalent early stage cervical adenocarcinoma and squamous cell carcinoma. Therefore, early FIGO 1A1 cervical adenocarcinoma can also be treated by local excision, or small 1B1 tumours by trachelectomy if preservation of fertility is a concern. Mixed differentiation tumours, and the coexistence of CIN and CGIN particularly on the surface and in crypts respectively, are sometimes seen. High-grade CGIN or adenocarcinoma in situ is usually treated by hysterectomy although conservative conisation may be used if the patient is young (<36 years) and wishes to remain fertile.

Other Malignancy

Malignant Melanoma

- Usually metastatic.
- Primary lesion is rare: 40% 5 year survival.

Embryonal Rhabdomyosarcoma

- Infancy/childhood.
- Syn. Sarcoma botryoides.
- Cellular subepithelial cambium zone/myxoid zone/deep cellular zone.
- Small cells/rhabdomyoblasts/desmin, myogenin and myo D1 positive.
- ±Heterologous elements.

Leiomyosarcoma

- 40–60 years.
- Cellular atypia, necrosis, and >5 mitoses/10 high-power fields.
- >10 mitoses/10 high power fields required if no atypia.

Adenosarcoma

- Polypoid.
- 25% have heterologous elements (striated muscle, cartilage, fat).
- A low-grade malignancy.

Stromal sarcoma and malignant mixed mesodermal tumour are more likely to represent spread to the cervix from an endometrial lesion rather than a primary cervical tumour.

Malignant Lymphoma

- More often secondary spread from systemic/nodal disease.
- Primary: 70% are intermediate to high-grade of large B cell type.
- 5 year survival is about 75%.

Leukaemia

- Granulocytic sarcoma as a presentation of chronic myeloid leukaemia.
- CD34/CD43/CD68/CD117/chloroacetate esterase /myeloperoxidase and neutrophil elastase positive.
- Relapse of AML, blast transformation of CML.

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