CARCINOMA OF THE CERVIX

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Cervical carcinoma

Cervical cancer is the second most common malignancy in women worldwide

The median age at diagnosis in North America is 47 years with nearly half the cases diagnose before the age of 35.

Women over the age of 55 have a disproportionately higher mortality from this disease as they present with more advanced disease

In the United States the relative 5-year survival rate for cervical cancer patients diagnosed with localized disease is 92% and 70% for all stages respectively

Risk factors

- lower socioeconomic status, predominantly because these individuals have not had good access to health care and cervical cancer screening programs..
- HIV seropositivity has been identified as a risk factor for cervical cancers

Other risk factors

- for cervical cancer include early age of first intercourse, history of multiple sexual partners, smoking, and a large number of pregnancies, but the single most important risk factor is a persistent infection with one of the high risk HPV types.

The clinical presentation is variable. Many patients with smallvolume microscopic disease are asymptomatic and are picked upincidentally following a loop biopsy of the cervix for preinvasive disease.

Most cervical cancers,however,arefriable,vascular masses on the cervix and patients present with abnormal bleeding, typically postcoital (PCB), prolonged, intermenstrual (IMB) or postmenopausal (PMB) bleeding Any woman with these symptoms should therefore undergo a pelvic examination, including visualization of the cervix.

In advanced disease (stagesIII–IV), patients may experience a number of distressing symptoms including pain (malignant infiltration of the spinal cord), incontinence (due to vesicovaginal fistulae), anaemia (from chronic vaginal bleeding) and renal failure (from ureteric blockage)

Cervical cancer diagnosis

- . A pelvic and speculum examination usually clinches the diagnosis as there is often a cervical mass that bleeds on contact and if advanced disease, a hardness and fixity of the tissues.
- A biopsy should be taken in the outpatient setting. Very occasionally, the diagnosis can be missed as some tumours are endophytic rather than exophytic and therefore less clinically revealing. The clinician therefore needs to retain a level of clinical suspicion in the presence of unexplained symptoms and investigate patients with persistent problems.

Pathophysiology

- The majority (70%) of cervical cancers are squamous cell carcinomas, with adenocarcinomas making up most of the remainder. In higher income countries with screening programmers, there has been a relative fall in the numbers of squamous tumours and a relative rise in the incidence of adenocarcinomas. In the UK, 30% of tumours are adenocarcinomas and are less likely to be picked up on cervical screening. Precursors of adenocarcinoma, known as cervical glandular intraepithelial neoplasia (CGIN), can also be detected at colposcopy, although lesions reside within the endocervical canal and may be difficult to visualize. Often CGIN is found incidentally in loop excision biopsies carried out for high-grade CIN; it is not uncommon for the two precursors to coexist.

Metastasis of cervical cancer

- Cervical tumours are locally infiltrative in the pelvic area, but also spread via lymphatic and, in the late stages, via blood vessels. The tumour can grow through the cervix to reach the parametria (anatomical area lateral to the cervix), bladder, vagina and rectum. Metastases can occur, therefore,in pelvic(iliac and obturator)and para-aortic nodes and, in the later stages, liver and lungs.

Staging of CA Cervix

- Assessing the stage of the disease is crucial for:
- planning treatment.
- The stage of disease also correlates with prognosis.
- Staging for cervical cancer is staged according to the FIGO system.

- Stage 0 Full thickness involvement of the epithelium without invasion into the stroma (carcinoma in situ)
- Stage I Limited to the cervix:
- IA – no visible lesion, diagnosed by microscopy
- IA1 – stromal invasion <3 mm in depth and 7 mm or less in horizontal spread
- IA2 – stromal invasion between 3 and 5 mm with horizontal spread of 7 mm or less
- IB – histologically invasive carcinoma confined to the cervix and greater than stage 1A2.
- IB1 – clinically visible lesions <4 cm in greatest dimension
- IB2 – clinically visible lesion of >4 cm in greatest dimension
- Stage II Carcinoma invades beyond the cervix but not onto the pelvic wall. Carcinoma involves the vagina but not the lower third:
- IIA – without parametrial invasion IIA1 – clinically visible lesion <4 cm in greatest dimension

- IIA2 – clinically visible lesion of >4 cm in greatest dimension
- IIB – with obvious parametrial invasion
- Stage III Carcinoma has extended to the pelvic wall/involves the lower third of the vagina and/or causes hydronephrosis or non-functioning kidney:
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- IIIA – tumour involves lower third of the vagina, with no extension to the pelvic wall
- IIIB – extension to the pelvic wall and/or hydronephrosis and or non-functioning kidney
- Stage IV Carcinoma has extended beyond the true pelvis or has involved the mucosa of the bladder or rectum. This stage also includes those with metastatic dissemination:
- IVA – spread of the growth to adjacent organs
- IVB – spread to distant organs

- A biopsy is crucial to confirm malignancy and assess the tumour type.
- Magnetic resonance imaging (MRI) of the abdomen and pelvis will assess the local spread of the disease in the cervix and will detect enlarged lymph nodes in the pelvic area.
- A chest X-ray is vital to exclude lung metastases.
- An examinationunder anesthesia may be helpful when, despite the above tests, the clinician is still unclear whether the tumour is operable. Doing a rectovaginal examination under anaesthetic can give crucial information on the tumour including size of disease, fixity and vaginal involvement, and a cystoscopy can help eliminate bladder involvement. Small mobile tumours favour a surgical approach, whereas larger fixed tumours favour the use of radiotherapy.
- The FIGO staging includes an intravenous urogram to ensure the integrity of the ureters; however, this is not standard practice in higher income countries, where MRI has superseded such tests.

- The staging of the disease is based on clinical findings, unlike other gynaecological tumours where there is a reliance on surgery and pathology to give the ultimate stage.

- The reasons for this are that radiotherapy is used in advanced disease and it still remains possible to stage patients in low income countries where most of the disease occurs.

Micro invasion

- Although stromal invasion can be seen in a small biopsy, the diagnosis of microinvasive cervical cancer can only be made in a conization or hysterectomy specimen
- More recently, cervical conization and large loop excision of the transformation zone (LLETZ) are considered equally efficacious when the latter is performed by experienced operators

Treatment

- Treatment for cervical cancer depends on the
- Stage of the disease,
- the requirement for future fertility
- and the patient's performance status.
- Ideally, all cancer patients should be discussed within the context of a multidisciplinary team (MDT) of doctors (surgeons, radiotherapists, radiologists and pathologists) and nurses, so that the most appropriate treatment can be offered to the patient.
- The fitness of the patient is crucial before embarking on treatment as radical surgery may not be appropriate in an unfit patient.

Preclinical lesions: stage IA

- These microscopic tumours have a low volume of cancer and are usually picked up as incidental findings after loop excision for precancerous disease. Small lesions must be removed with a clear margin of excision, and the preinvasive disease (CIN) that invariably coexists should also be completely excised as the cancer is often multifocal. If the preinvasive disease is not completely excised then a repeat loop biopsy or knife cone biopsy must be carried out. This allows fertility to be preserved and a hysterectomy is not necessary.

Clinical invasive cervical carcinoma

- stages IB–IV The tumour volumes are much greater in patients with stage 1B disease and therefore fertility-preserving treatment for this group of patients is more challenging. When small volume disease is confined to the cervix (stage IB1), radical hysterectomy and bilateral pelvic node dissection (Wertheim's hysterectomy) is standard of care.
- For young women who have not completed their families, radical trachelectomy (surgical removal of the cervix and upper part of the vagina) and bilateral pelvic node dissection is an alternative.

- It is important to remember that in early stage IB disease, pelvic radiotherapy has similar success rates to surgery and therefore this treatment is considered in women who are too overweight for radical surgery or who are anaesthetically unfit
- When the disease is beyond the cervix (stages II–IV disease), radiotherapy (with or without chemotherapy) becomes the optimal treatment.

Surgery

- Surgery The standard surgical operation for stage IB tumours is a radical hysterectomy and pelvic lymph node dissection.
- This involves removal of the cervix, upper third of the vagina, uterus and the paracervical tissue.and
- Pelvic lymph node removal includes the obturator, internal and external iliac nodes.

Advantages of surgery

- The ovaries in premenopausal women can be spared.
- There is higher morbidity with this procedure over the standard total abdominal hysterectomy.
- Bladder dysfunction (atony), sexual dysfunction (due to vaginal shortening) and lymphoedema (due to removal of the pelvic lymph nodes) are not uncommon.
- Anatonic bladder is frequent in the immediate postoperative period due to neuronal damage from the surgery, and intermittent self-catheterization may be required until the bladder tone returns. Lymphoedema is variable and is described by patients as a wooden, heavy feeling to the legs with swelling and reduced mobility. Management includes leg elevation,good skin care (e.g. avoid shaving), massage and occasionally compression stockings. Despite these potential problems, surgery is the preferred treatment as the cure rate is high, ovarian tissuecan be preserved and the patient avoids the complicationsof radiotherapy

Radiotherapy

- Radiotherapy The aim of radiotherapy is to deliver a lethal dose of radiation to thetumour and minimize damage to the surrounding tissues.
- Treatment is overseen by a radiotherapist and team. Treatment is delivered in two ways: external beam radiotherapy (as teletherapy)and internal radiotherapy (brachytherapy).In external beam radiotherapy, the sourceof the radiation is from a machine called a linear accelerator, and radiation isdelivered to the pelvis a distance from the patient .
- The dose of radiotherapy is carefully calculated according tothe patient weight and the tumour, and is usually administeredas 45 Gy in total. This is given in several treatments or 'fractions' as an outpatient over 4 weeks. Although this treatment is given daily, then time of each fraction is no more than 10 minutes.

- Brachytherapy is a radiotherapy technique where the radiation is delivered internally to the patient. The source of the radiation is usually selenium and patients generally have to undergo an examination under anaesthetic to insert the rods into the uterus. These rods are then attached to the radiotherapy source; the patient receives this internal treatment in isolation to protect the staff. Brachytherapy delivers a high dose of radiation to the tumour source and its harmful effects on the bladder and bowel are minimized as its effects are targeted only 5 mm from the rod. Patients frequently suffer lethargy with treatment and may experience both bowel and bladder urgency, which is due to the initial inflammatory effects of the radiation. Skin erythema-like sunburn is not uncommon after external beam radiotherapy. Symptomatic treatment is usually required, such as antiinflammatory creams for skin. Around 5% of patients experience a serious side-effect that might interrupt treatment, for example bowel perforation.

- There are manylong-term complicationsof radiotherapy that affect only a minority of patients but do have a significant impact on patients' quality of life. The initial inflammatory process is replaced by fibrosis in the long term. Vaginal stenosis can cause sexual pain, bladder damage can lead to cystitis-like symptoms, haematuria and bowel damage lead to malabsorption and mucous diarrhoea. None of thesecomplicationscan be managed easily. Patients who are premenopausalwill undergo a radiotherapy-induced menopause as the ovaries are very sensitive to small doses of irradiation.

Chemotherapy

- Chemotherapy (cisplatin) is ideally given in conjunction with the radiotherapy, as this combination increases cure rates more than when radiotherapy is used in isolation. It probably works by enhancing the effects of radiotherapy and might also address micrometastases that are outside the radiotherapy field

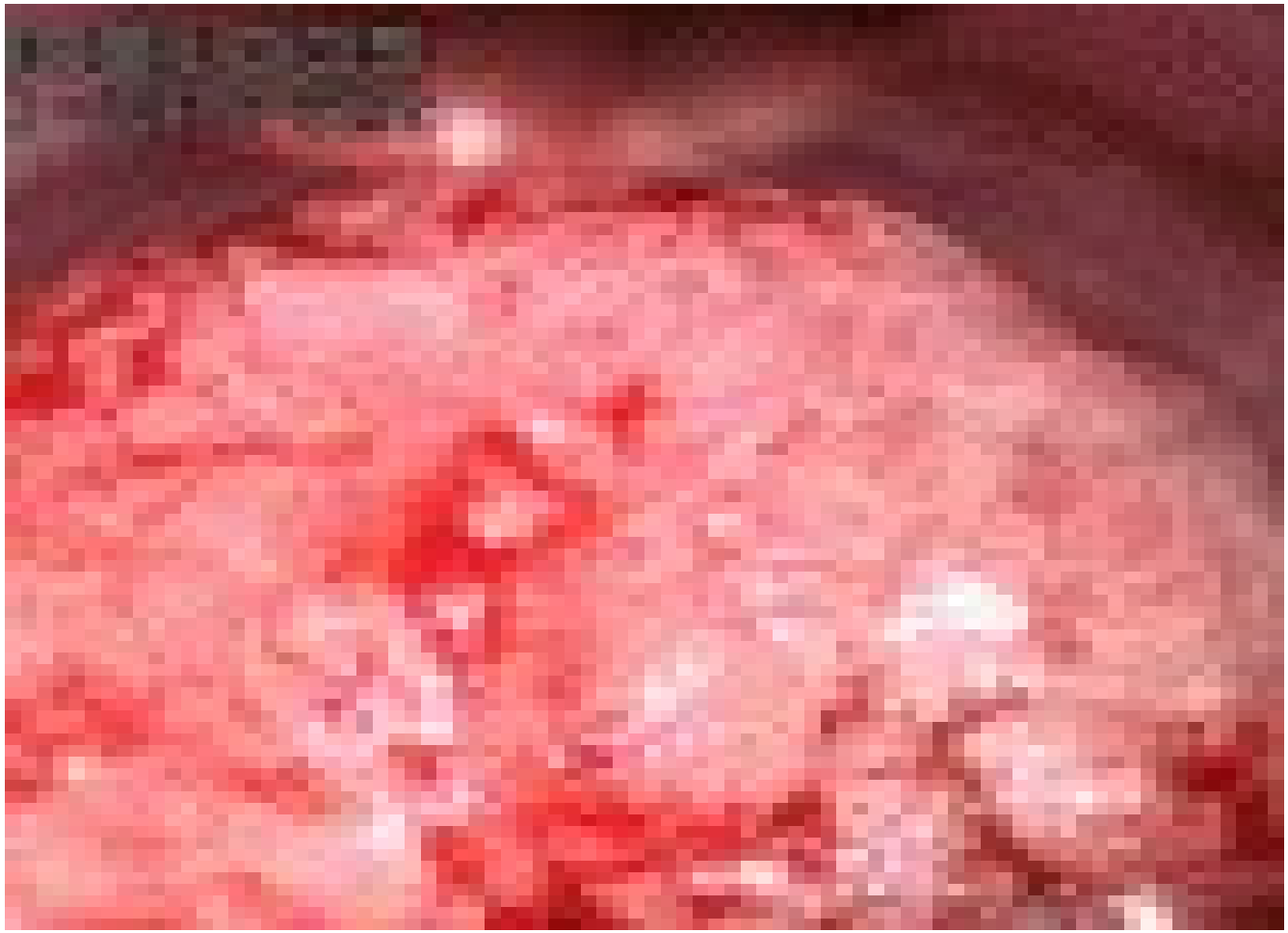
Palliative treatment

- Palliative treatment When it is not possible to offer curative treatment, palliation of symptoms becomes important and early involvement of the palliative care team is essential for symptom control. The disease can be hidden from family and friends even in the late stages of the disease; patients may be experiencing a number of symptoms from local infiltration of the pelvis by the cancer. Malignant pain, recto and/or vesicovaginal fistulae and bleeding may occur. Distant spread is often a very late stage of the disease. Radiotherapy may be considered with a palliative intent; for example, a one-off treatment may be used for symptomatic bone metastases.

KEY LEARNING POINTS

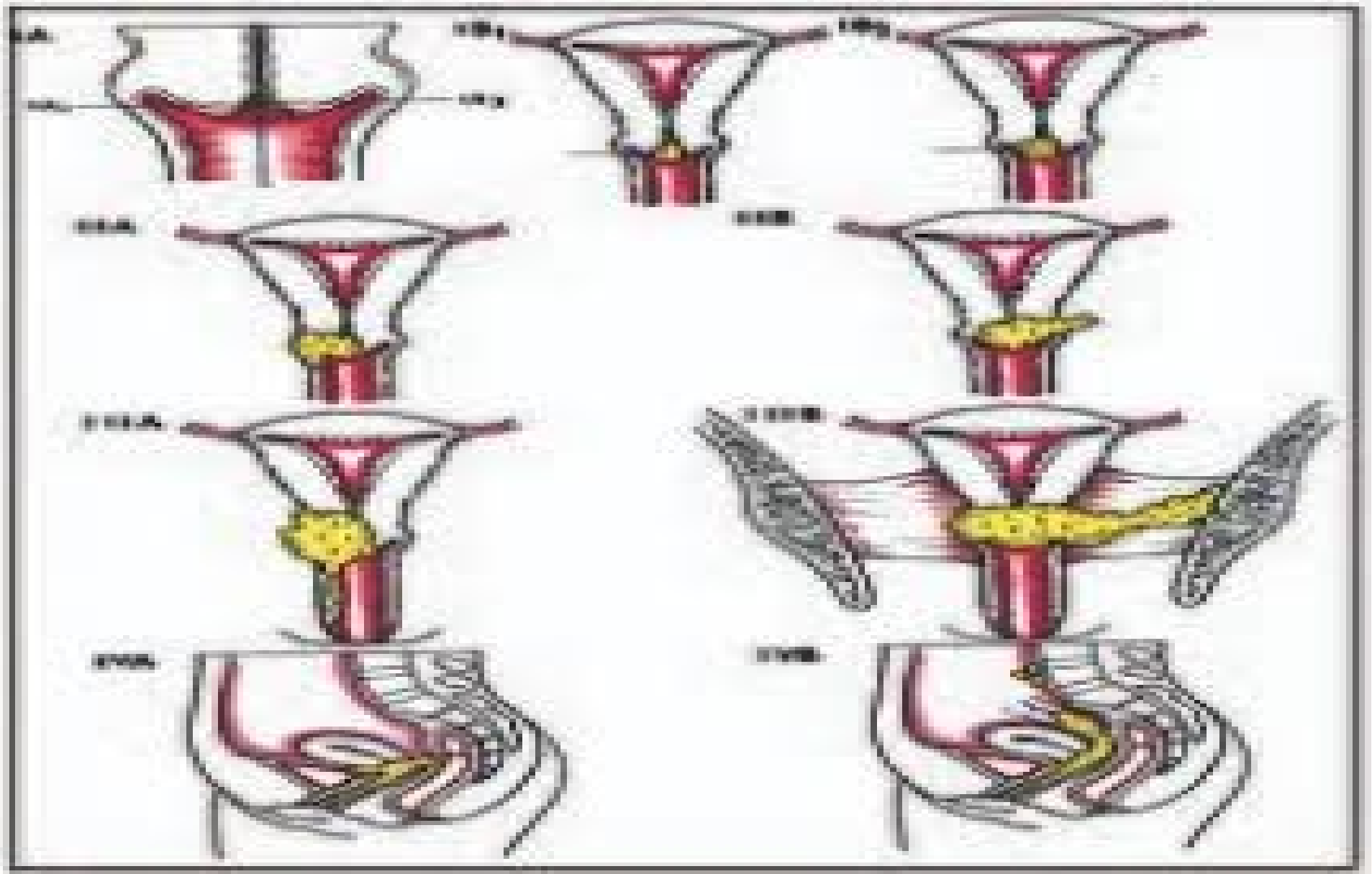
- • Cervical cancer affects young women who may not have completed their families.
- • Many cervical tumours are picked up when they are microscopic or very small volume, making fertility-sparing treatment a possibility.
- • Cone biopsy or radical trachelectomy with bilateral pelvic lymphadenectomy allows preservation of the ovaries and uterus, permitting pregnancy in the future.
- • The long-term cure rate of radical trachelectomy is less well established than radical(Wertheim's) hysterectomy.

Stage 1a



Linear accelerator for teletherapy

FIGO classification

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