Cervical Cancer

DR. NR MAHARAJ
HEAD : DEPT. OF O&G
PMMH
Definitions

Gynaecological cancer

- vaginal surface
- ectocervical ca
- Cauliflower/fungating, 5 x more common
- cervical canal
- endocervical ca
- barrel shaped
- spread
- DEATH
Impact of Ca Cx deaths

Global perspective:

- 260,000 women die annually from Ca Cx
- 80% of this happened in developing countries
- Screening programmes not stringent here
- Funding challenges
South Africa:

- Cervical cancer accounts for 23% of cancers in S.A.
- Affects 30-40 ♀ in S.A per 100 000.
- In 2002 cervical cancer caused 3700 deaths in S.A.
- Peak incidence: 30-40yr and early 50-60yr.
- 45% of surgically treatable disease occur < 40yr.
Cervical Cancer in Relation to other Malignancies
RISK FACTORS

Risk factors for Cervical Cancer:

a.) First intercourse < 16 yrs
b.) Multiple sexual partners
c.) HPV/HIV
d.) Genetic susceptibility: HLA
e.) STD’s
f.) Cigarette smoking
g.) Race
h.) High parity
i.) Low socio economic status
HPV ASSOCIATION

- HPV infection: firmly implicated as the initiating event in cervical dysplasia and carcinogenesis
- HPV infection has been detected in up to 99% of SCC.
- HPV 16 & 18 found in 62% of cervical carcinomas.
  (> 100 HPV types)
- HPV affects cellular growth & differentiation is through the interaction of viral E6 and E7 proteins with tumour suppressor genes p53 and Rb
3. HPV ASSOC. …Cont

- **Inhibition of p53** prevents cell cycle arrest & cellular apoptosis, which normally occurs when damaged DNA is present.

- **Inhibition of Rb** disrupts transcription factor E2F resulting in unregulated cellular proliferation.

- Both steps are essential for the **malignant transformation** of cervical epithelial cells.
3. HPV ASSOC. …Cont.

- 75% of HPV infection is asymptomatic
- HPV DNA persists for 6-12 months in genital tract and spontaneously regress in majority of patients. (random events)
- **High risk HPV**: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, 82.
- **Low risk HPV**: 6, 11, 40, 42, 43, 44, 54, 61, 70, 72, 81.
Changes in the cervix following HPV infection
ROLE OF HIV AND HPV INTERACTION

- HIV infection is associated with an ↑ incidence of HPV & CIN.
- Recurrent rate of CIN bet. 20-60% after Rx depending on degree of immunosuppression.
- HIV + ♀ present with invasive CaCx +/- 10yrs earlier than HIV- ♀. (JHB)
- HIV+ ♀ presented with invasive CaCx +/- 15yr earlier than HIV- ♀. (DBN)
HIV AND HPV:

- HIV+ ♀ have:
  - ↑ risk of CIN
  - ↑ genital tract neoplasia
  - ↑ genital warts
  - ↑ altered immune response to HPV & more likely to be infected with multiple HPV types.
Screening modalities

“Long lag phase between dysplasia and ca allows a window of opportunity for screening”

“screening only once in a lifetime (between 30-40yrs), reduces ca risk by 25-36%”

Developed world: pap, colposcopy, biopsy, review

Developing world: programmes ineffective due to cost, training, quality control and logistic issues
Screening modalities in low income areas

Cytology based screening (Pap):

- Slide or liquid based
- Historically shown to be effective (47-62% sens)
- Drawbacks: staff, transport, quality, follow up observer dependent, repeat screening, multiple patient visits
Screening modalities

**Visual inspection with acetic acid/cryotherapy:**

- **Naked eye view after acetic acid our iodine**
- **No lab, transport needed, little equipment**
- **All levels of health provider can be trained**
- **Immediate results, immediate treatment**
- **Operator dependent**
- **Sens : 45-79%**
Screening modalities

- HPV DNA TESTING
- Newer technology
- Sens: 66-95%
- Not operator dependent
- Good for women 30 yrs or older
- Need trained personnel
- Expensive
Newer screening tools in the horizon

- HPV test: simple, cheaper, accurate, rapid
  “care HPV“ - 2012

E6 biomarker: Arbor Vita Corporation
- still in development
Steps in the Mx of CaCx:

- HISTORY
- EXAMINATION
- SPECULUM/ PV/PR
- BIOPSY
- COUNSELLING
- STAGING
- PROGNOSIS

Investigations:
- FBC/U&E/CD4/LFT/RPR/HIV
  - Isotope GFR
  - U/S Abdomen
  - CX-ray Other: CT, MRI
Management in a nutshell:

Management:

- **Clinical Staging:**
  - Early Stage IA- II A – Surgery
  - Late Stage IIB - IVA – CCRT
  - Stage IV B – Individualise patient
  - Palliative XRT or symptomatic Rx depending on performance status.
  - CD4 < 200 – ARV’s then Standard therapy
FIGO STAGING OF CACX:
CONT....
Contd....
Cancer has grown into the tissues around the cervix.
Contd...

Cancer has grown into lower third of the vagina
Contd…
## 7. FIGO Staging of Cervical Cancer - 2009

<table>
<thead>
<tr>
<th>Stage I</th>
<th>Carcinoma is strictly confined to the cervix</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>Invasive carcinoma which can be diagnosed only by microscopy, with deepest invasion ≥ 7 mm</td>
</tr>
<tr>
<td>IA1</td>
<td>Measured stromal invasion ≤ 3 mm in depth and extension ≤ 7 mm</td>
</tr>
<tr>
<td>IA2</td>
<td>Measured stromal invasion &gt; 3 mm and &lt; 5 mm, with an extension &lt; 7 mm</td>
</tr>
<tr>
<td>IB</td>
<td>Clinically visible lesions limited to the cervix uteri, or preclinical cancers greater than stage IA</td>
</tr>
<tr>
<td>IB1</td>
<td>Clinically visible lesion ≤ 4 cm in greatest dimension</td>
</tr>
<tr>
<td>IB2</td>
<td>Clinically visible lesion &gt; 4 cm in greatest dimension</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>Stage II</th>
<th>Cervical carcinoma invades beyond the uterus, but not to the pelvic wall or to the lower third of the vagina</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIA</td>
<td>Without parametrial invasion</td>
</tr>
<tr>
<td>IIA1</td>
<td>Clinically visible lesion ≤ 4cm in greatest dimension</td>
</tr>
<tr>
<td>IIA2</td>
<td>Clinically visible lesion &gt; 4cm in greatest dimension</td>
</tr>
<tr>
<td>IIB</td>
<td>With obvious parametrial invasion</td>
</tr>
</tbody>
</table>

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<tr>
<th>Stage III</th>
<th>Tumour extends to the pelvic wall, and/or involves the lower third of the vagina, and/or causes hydronephrosis or non-functioning kidney</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIIA</td>
<td>Tumour involves the lower third of the vagina, with no extension to the pelvic wall</td>
</tr>
<tr>
<td>IIIB</td>
<td>Extension to the pelvic wall and/or hydronephrosis or non-functioning kidney</td>
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<tr>
<th>Stage IV</th>
<th>Carcinoma has extended beyond the true pelvis or has involved (biopsy proven) the mucosa of the bladder or the rectum; bullous oedema, as such, does not permit a case to be classified as Stage IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVA</td>
<td>Spread of the growth to adjacent organs</td>
</tr>
<tr>
<td>IVB</td>
<td>Spread to distant organs</td>
</tr>
</tbody>
</table>
SURGICAL OPERATIONS:

1. Stage 1A$_1$ – Cone biopsy/simple hysterectomy
2. Stage 1A$_1$ – LVSI – Type II Radical Hysterectomy/Wertheims & pelvic L.N.D
   Fertility desiring: Radical Trachelectomy
3. Stage 1A$_2$ – Type II Radical hysterectomy & pelvic LND.
   Fertility desiring: Radical Trachelectomy.
SURGICAL OPERATIONS…cont

4. **Stage 1b1** - Type III Radical Hysterectomy
   with Pelvic LND
   
   **Fertility desiring:** Radical Trachelectomy

5. **Stage 1b2** - Type III Radical Hysterectomy
   with pelvic LND
   
   - NACT then surgery
   - CCRT & XRT
Surgical Operations…

- Stage IIA: Type III Radical Hysterectomy with pelvic & para aortic LND

- MX: late stage cervical cancer:

- Stage IIB-IVA- CCRT

- Stage IVB- palliative XRT(10 Gray x 2) or symptomatic Rx.
Radical hysterectomy specimen:

Figure 1. Radical Hysterectomy specimen
Other issues

- Counseling
- Support (psychological, physical, emotional)
- Follow up: physical examination
  - pap smears
- Sexual issues
5YR SURVIVAL RATES: CACX

- Stage I-IIA - 85-90%
- Stage IIB - 65%
- Stage III - 40%
- Stage IV ≤ 20%
Conclusion

- **Prevention, Prevention, Prevention !!!**

- **Acknowledgements:**
  - Dr Sunpath
  - Dr TR Moodley
9. THE MX OF CERVICAL CANCER IN PREGNANCY

- Incidence 1-10/10000
- 3% of cervical cancers diagnosed in pregnancies.
- Stage 1: 69-83%
- Stage 2: 23%
- Stage 3: 3-8%
- Stage 4: 0-3%
9. THE MX OF CERVICAL CANCER IN PREGNANCY

...CONT

- Diagnostic and Therapeutic mx of Cervical Cancer in pregnancy is difficult because mother & fetus involved.

- The physiological changes associated with pregnancy makes diagnosis of Cervical Cancer difficult.
9. THE MX OF CERVICAL CANCER IN PREGNANCY ...

Cont.

Diagnosis:

- Clinical evaluation of cancer in pregnancy
- Cytological assessment
- Colposcopy ± Directed biopsy

- Symptomatic patients present with abnormal vaginal bleeding mostly post coital or PV discharge.
- Average duration of symptoms before diagnosis of Cervical Cancer in pregnancy is 4.5 months.
9. THE MX OF CERVICAL CANCER IN PREGNANCY

...Cont.

- Colposcopy used to exclude micro-invasive & invasive carcinoma.

- Colposcopy directed biopsy only absolute indication is invasive Cervical Cancer.
  - Bleeding 1-3%
  - Premature labour

- LLETZ avoided in pregnancy, used to exclude micro-invasive dx where diagnosis alters time or mode of delivery.
9. THE MX OF CERVICAL CANCER IN PREGNANCY ...

Cont.

- Cone biopsy is performed in 2\textsuperscript{nd} trimester if micro-invasive Cervical Cancer present.

(14-20 wks)

Micro-invasive Cervical Ca < 24 wks gest. – Cone biopsy choice

Micro-invasive Cervical Ca > 24 wks gest. – Cone biopsy postponed until fetal maturity.
9. THE MX OF CERVICAL CANCER IN PREGNANCY ...

Cont.

- The mx of invasive Cervical Cancer in pregnancy depends on gestational age at diagnosis, stage of disease, lesion size, patient’s desire for the pregnancy and desire for future fertility.

- Mx is stage for stage!

- Stage 1A1 - cervical cancer with + margins for invasive dx ----> cone biopsy.

- Stage 1A2, 1B, II A----> radical hysterectomy with fetus

- ≥ Stage IIB Radiotherapy: external beam, when aborts then intracavitatory brachytherapy.
10. MX OF RECURRENT CERVICAL CANCER

- Late stage of dx experience recurrence.
- Prognosis in recurrent dx is very poor & Rx options limited.
- Symptomatic patients require extensive investigations to detect the extent of dx.
- Present with bleeding, pelvic pain, vaginal discharge, leg swelling, wt loss
10. Mx of Recurrent Cervical Cancer:

- Recurrence can be divided into: central or distant.
- If 1° Surgery then CCRT
- If 1° CCRT - then palliative XRT/chemo
  - exenteration if centrally located
  2. Posterior exenteration-removal of rectum, vagina, cervix and uterus
  3. Total exenteration-removal of bladder, rectum, vagina, cervix, uterus
10. Mx of recurrent cervical cancer: contd....

- 5yr survival - 23%.
- Most recurrence occur within 18/12
- Strict criteria used to select patients.
- Chemo: has limited role due to low response rate & severe toxicity.
- Radiotherapy: after surgical Rx, offers a very good prospect of survival- 33%
- Palliative radiotherapy is intended to relieve symptoms of pain or bleeding in advance disease.
11. CONCLUSION

- Cervical cancer in the developing world is still rising.
- HPV testing and vaccines are 2 important steps in the eradication of cervical cancer.
- Education of health care workers, public, school and politicians is important.
- Investment in prevention will repay itself over next few decades but will also eradicate the suffering caused by cancer of the cervix!
THE END:

THANK YOU!
Invasive Cervical Cancer
Cervical Dysplasia
Cervical Changes:

- Normal cervix
- Cervical dysplasia
- Normal cervical cells
- Cancerous or pre-cancerous cervical cells
Cervical Dysplasia
Cervical Dysplasia: CIN 3
Cervical Dysplasia: CIN 3
Advanced Cervical Cancer