Impact of Surgical Pathologic Features to Clinical Management of Cervical Cancer

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- Carcinoma of cervix:
  - Squamous cell carcinoma
  - Adenocarcinoma
  - Other epithelial tumor (adenosquamous CA, ACC, neuroendocrine tumor)

- Staging system – FIGO (2009) based on clinical evaluation not surgical examination
**Evaluation:**

- Define lesion as invasive carcinoma
- Measure depth of stromal invasion
- Measure greatest lateral extent of the lesion
- Lymphovascular invasion
- Surgical resection margins
Evaluation:

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Microinvasive Squamous Cell Carcinoma

- In the UK – some FIGO stage IA1 and IA2 while in others IA1
- In the USA - stage IA1
- The Society of Gynaecologic Oncology - lesions up to a depth of 3 mm with no limit on the size of horizontal spread, neoplasms with lymphovascular invasion are excluded.
- In order to avoid confusion, the British Association of Gynaecological Pathologists working group has recommended for histological reporting of cervical neoplasia a preference for avoiding the term 'microinvasive carcinoma' and for using the specific FIGO stage as a descriptor
Microinvasive Squamous Cell Carcinoma

Criteria

- Stromal invasion ≤3mm in depth and ≤7mm width. (regardless of vascular invasion)
- Diagnosis based on histologic examination of cone biopsy or hysterectomy specimen that includes the entire cervical lesion
- Early stromal invasion – invasion less than 0.1 cm. in depth and management same as high grade CIN

Microinvasive Squamous Cell Carcinoma

Pathologic Features:

- Presence of one or more tongues of malignant cells penetrating the basement membrane of the squamous epithelium
- Cells are better differentiated with abundant eosinophilic cytoplasm and prominent nucleoli as compared to the associated SIL (aberrant differentiation)
- Papillary architecture
- Marked inflammatory infiltration
- Scalloping/Blurring of the margins of the epithelium at the dermal-epidermal interface
Differential diagnosis

- Entrapped or buried dysplastic squamous epithelium in the superficial cervical stroma at the site of a previous biopsy (pseudoinvasion)
- Tangentially sectioned epithelium, benign or neoplastic
- Inflammatory or reparative changes in CIN, including pseudoepitheliomatous changes
- Obscuring of the epithelial-stromal interface by inflammation or other artifacts
- Crypt (gland) involvement that is inflamed or tangentially sectioned
- Cautery or crush artifact

Early Invasive Adenocarcinoma

- Difficult to define
  - AIS-like gland architecture may accompany invasion
  - AIS itself may be quite complex
  - Irregular distribution of endocervical crypts in the stroma makes it difficult to differentiate between early stromal invasion and AIS
- Generally not advisable to diagnose early invasion from small biopsies
- Three patterns of invasion that typify adenocarcinoma, infiltrative, expansile, and exophytic patterns
- Close proximity to thick-walled blood vessels
Evaluation:

- Define lesion as invasive carcinoma
- Measure depth of stromal invasion
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- Surgical margins
- Lymphovascular invasion
Depth of Invasion

- Depth of invasion must be measured in all cases.
- This measurement is taken from the base of the epithelium (surface or glandular) from which the carcinoma arises, as specified in the FIGO classification.
- If there is no obvious epithelial origin, the depth must be measured from the tumour base (the deepest focus of tumour invasion) to the base of the nearest surface epithelium.

ความลึกวัดจาก basement membrane ของ surface epithelium หรือ endocervical gland ที่อยู่ใกล้เคียง ถึงจุดที่ลึกที่สุด.
Depth of Invasion

• When the distinction of intraepithelial and invasive components cannot be made, a measure of thickness is most appropriate

Depth of Invasion

• In glandular neoplasms with an admixture of AIS and foci of stromal invasion, it may be difficult to identify the precise origin of the invasive component - measurements may be taken from the tumor surface to the deepest point of invasion - tumor thickness
Evaluation:

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Tumor Volume and Horizontal Extent

- Introduced the concept of tumor volume as applied to MICA and have reported no pelvic node metastases in patients with 420 mm$^3$ of cancer or less, time-consuming!
- Other investigators and FIGO have used lateral extent of spread as a surrogate for measuring tumor volume
Tumor Volume and Horizontal Extent

- Horizontal spread (width/lateral extent) of unifocal tumours must be measured using the section in which the width of the tumour is greatest
- The measurement is from one lateral edge of the tumour to the other

1.1. \( A \) lateral extension = A
1.2. ให้ใช้วัด A หรือ B ที่สัดส่วนที่สูง (ระยะเวลาตามลำดับ มากกว่า 1 มิลลิเมตร)

- Normal
- HPV / CIN
- MICA

1.3. ค่า lateral extension = C

- Normal
- HPV / CIN
- MICA
Third dimension

- Invasive carcinoma that is presenting sections from three or more consecutive 2.5–3 mm thick blocks of a loop or cone biopsy exceeds 7 mm in horizontal extent, more than FIGO stage IA2
- Ensure that present in the same part of the specimen in the contiguous sections

Multifocal tumors

- Usually occurs in squamous, rather than glandular neoplasms
- Field changes from high-risk HPV infection
- More than one focus of neoplastic transformation may develop and invade as several buds (multifoci ?)
Multifocal tumors

- However, this localized form of multifocal invasion does not indicate multifocal neoplasia
- They are not independent foci of neoplasia but reflect invasion from a single zone of transformed epithelium and will over time, coalesce to form the single invasive tumor that represents unifocal disease
- The staging is based on the width (and depth) of the tumour across all of the infiltrative buds in a single focus of neoplasia.

Multifocal tumors

- Multifocal tumors should be diagnosed if foci of invasion are:
  1. Separated by blocks of uninvolved cervical tissue (levels must be cut to confirm this)
  2. Located on separate cervical lips
  3. Situated far apart from each other in the same section
- Measures width (and depth) of the largest of the largest tumors, not on their combined width.
Evaluation:

- Define lesion as invasive carcinoma
- Measure depth of stromal invasion
- Measure greatest lateral extent of the lesion
- Surgical margins
- Lymphovascular invasion
Surgical Margins

• The status of the margin is also a predictor for recurrent disease
• Ablative (Electrical Excision, LEEP or LLETZ, Cone Biopsy, or Cryocautery), margins should be designated only where a cautery artifact can be identified
• If the lesion extends to an edge but the edge does not contain thermal artifact, margin involvement is not confirmed

Evaluation:

• Define lesion as invasive carcinoma
• Measure depth of stromal invasion
• Measure greatest lateral extent of the lesion
• Surgical margins
• Lymphovascular invasion
Lymphovascular Space Invasion (LVSI)

- LVSI also appears to be a predictor of the presence of invasive carcinoma in subsequent hysterectomy specimens and lymph node metastasis
- Although FIGO does not take LVSI into account in staging, the prevailing opinion in the United States is that LVSI should be assessed in women with early invasive squamous cell carcinoma

Lymphovascular Space Invasion (LVSI)

Criteria
(1) Rounded nests of tumor cells
(2) Enclosed within a sharply defined space
(3) Molding of the tumor nests to the vascular space
(4) An absence of a surrounding stromal response
Grading, squamous cell carcinoma

- Poor clinical correlation
- Nevertheless, the following system may be used
- WHO recommends the use a two-tiered system separating squamous cell carcinomas into keratinizing and non-keratinizing

1. Large cell nonkeratinizing carcinoma (most common).
2. Keratinizing carcinoma. (requires the presence of keratin pearl formation)
3. Small cell nonkeratinizing carcinoma (not basaloid carcinoma or small cell neuroendocrine carcinoma)
Grading, squamous cell carcinoma

1. Well-differentiated (grade 1: mature squamous cells with abundant keratin pearl formation and intercellular bridges)
2. Moderately differentiated (grade 2: less cytoplasm, less distinct cell borders, nuclear pleomorphism, and mitoses)
   Approximately 60% of squamous cell carcinomas belong to this group.
3. Poorly differentiated (grade 3: primitive-appearing small cells with scant cytoplasm and hyperchromatic nuclei with increased mitoses)

Grading, adenocarcinoma

Architecture - percentage of solid growth, excluding squamous

• Grade 1 —well-differentiated (10% or less solid growth)
• Grade 2 —moderately differentiated (11 to 50% solid growth)
• Grade 3 —poorly differentiated (over 50% solid growth
  + Nuclear atypia
Cervical Biopsy

1. Histologic type
2. Tumor grade
3. Degree of invasion (if present)
4. Lymphovascular space invasion (if present)

Cervical conization / LEEP / LLETZ / Hysterectomy for preinvasive lesion

1. Histologic type
2. Tumor grade
3. Degree of invasion (if present)
4. Lymphovascular space invasion (if present)
5. Status of surgical margin (ectocervical / endocervical / deep)
# Hysterectomy for invasive lesion

1. **Histologic Type:**
2. **Tumor Grade:**
3. **Extent of invasion:** Confinement to cervix / extend beyond cervical wall
4. **Location:** Exocervical / squamo-columnar / endocervical / confine to polyp.
5. **Lymphatic invasion:** Present / not seen
6. **Involvement of the other structures:** Not seen / present (specify)
7. **Associated premalignant changes:** Not seen / present (specify)
8. **Margins:**
   - Vaginal margin: Negative for malignancy / positive (specify location and histologic type)
   - Parametrium: Negative for malignancy / positive (specify location and histologic type)
9. **Lymph node metastasis:** Not seen / present (specify group)
10. **Other findings:** Non-neoplastic cervical lesions

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## References

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