

**Adenocarcinoma in-situ
&
Microinvasive adenocarcinoma
of the uterine cervix**

ADENOCARCINOMA IN SITU

ADENOCARCINOMA IN SITU

- The Bethesda system 1991

- Descriptive diagnoses
 - Epithelial cell abnormalities
 - Glandular cell

Endometrial cell, cytologically benign, in a postmenopausal woman

Atypical glandular cells of undetermined significance (AGUS)

Atypical endometrial cells of undetermined significance

Atypical endocervical cells, favour reactive

Atypical endocervical cells, probably neoplastic

Endocervical adenocarcinoma

Endometrial adenocarcinoma

Extrauterine adenocarcinoma

Adenocarcinoma, NOS

ADENOCARCINOMA IN SITU

- The 2001 Bethesda system

- Interpretation/result
 - Epithelial cell abnormalities
 - Glandular cell

Atypical glandular cells (AGC) (specify endocervical, endometrial,
or not otherwise specified)

Atypical glandular cells, favour neoplastic (specify endocervical or
not otherwise specified)

Endocervical adenocarcinoma in situ

Adenocarcinoma

ADENOCARCINOMA IN SITU

- Abnormal cells occur in sheets, strips and rosettes with nuclear crowding and overlap; when in sheets, a honeycomb pattern is lost because of an increase in the nuclear/cytoplasmic ratio, diminished cytoplasm, and ill-defined cell borders
- A palisading nuclear arrangement with nuclei protruding from the periphery of cell clusters (feathering) is a characteristic feature.
- Nuclear enlargement, elongation, and stratification are evident in most cases.
- Variation in nuclear size and shape occurs.
- Hyperchromasia associated with chromatin that is finely to moderately granular usually is evident
- Nucleoli are small or inconspicuous.
- Mitotic figures may be seen.

ADENOCARCINOMA IN SITU

- Tumour diathesis, irregular chromatin distribution and parachromatin clearing, macronucleoli suggest invasion.

ADENOCARCINOMA IN SITU

- Epidemiology
- Prevalence of adenocarcinoma and its precursor lesions is increasing
- In most series, the ratio between AIS and high grade SIL has ranged from 1:26 to 1:237.

ADENOCARCINOMA IN SITU

- SEER registry
- Between 1973 and 1995
- 149178 “cervical cancer”
- 96% are squamous lesions, 4% glandular lesions
- 82% are in situ, 18% invasive
- 99% of the in situ lesions are squamous cell carcinoma in situ, 1% is AIS
- Of the invasive carcinoma, 16% are adenocarcinoma
- SEER 1995 age-adjusted incidence rate
 - 0.61 cases per 100,000 for AIS
 - 27.93 cases per 100,000 squamous cell carcinoma in situ

ADENOCARCINOMA IN SITU

Mean age at diagnosis : AIS 28.8 years, invasive adenocarcinoma 51.7 years

AIS that occur in association with SIL range from 24 – 75%

Most AIS is associated with HPV DNA.

ADENOCARCINOMA IN SITU

Differential diagnosis

- Reparative/reactive glandular atypia secondary to inflammation, radiation or viral infection
- Arias-Stella reaction
- Microglandular hyperplasia
- Endometriosis
- Tubal metaplasia
- Mesonephric remnants
- Invasive adenocarcinoma

MICROINVASIVE ADENOCARCINOMA

MICROINVASIVE ADENOCARCINOMA

- How to define “microinvasive” adenocarcinoma?
- How to define early invasion ?
- How to measure dimension of invasive focus?

MICROINVASIVE ADENOCARCINOMA

■ **Mod Pathol 2000 Mar;13(3):261-74**

Glandular lesion of the uterine cervix

Zaino RJ

MICROINVASIVE ADENOCARCINOMA

- How to define “microinvasive” adenocarcinoma?
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MICROINVASIVE ADENOCARCINOMA

■ Definition:

FIGO staging system for cervical cancer applies to both squamous cell carcinoma and adenocarcinoma.

FIGO IA or FIGO IA1 only?

MICROINVASIVE ADENOCARCINOMA

- Updated FIGO staging of carcinoma of uterine cervix
- Stage I Carcinoma strictly confined to the cervix

IA Preclinical invasive carcinoma (**microinvasive carcinoma**), i.e. those diagnosed only by microscopy

IA1 Stromal invasion <3 mm in depth and 7 mm or less in horizontal spread

IA2 Stromal invasion >3mm and not more than 5 mm in depth with horizontal spread <7 mm.

IB Clinically visible lesion confined to the cervix or microscopic lesion greater than IA2.

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- Depth of invasion is measured from base of the epithelium, either surface or glandular, from which it originates.
- Lymphovascular invasion does not alter the stage, but this should be stated if present.
- Ulcerated lesions – not as microinvasive carcinoma.

MICROINVASIVE ADENOCARCINOMA

- How to define “microinvasive” adenocarcinoma?
- How to define early invasion ?
- How to measure dimension of invasive focus?

MICROINVASIVE ADENOCARCINOMA

PROBLEM of assessing invasion

- The irregular distribution and architecture of the normal endocervical crypts in the cervical stroma make it difficult to differentiate between early stromal invasion and pure adenocarcinoma in situ.
- Less well defined criteria of diagnosis of early invasion

MICROINVASIVE ADENOCARCINOMA

- Pathological features:

- Ostor

- The first histologic sign of invasion was thought to be the presence of finger-like extension of epithelium with abundant pink cytoplasm into the stroma from a gland demonstrating the histologic features of AIS.
- More advanced areas of invasion showed glands that lack the lobular architecture of crypts involved by AIS. These glands are often separated by stroma and may be within the zone of normal endocervical mucosa. There may or may not be a stromal response with edema, inflammation and desmoplasia.

MICROINVASIVE ADENOCARCINOMA

- Lee and Flynn
- Histologic patterns they considered indicative of invasion:
 1. small detached tumour cell islands adjacent to AIS that elicit a stromal response
 2. closely packed collections of glands that have lost their smooth outlines
 3. smooth contoured, dilated glands with complex intraglandular cribriform or papillary growth patterns

MICROINVASIVE ADENOCARCINOMA

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MICROINVASIVE ADENOCARCINOMA

- **Obstet Gynecol 2001 May; 97 (5 Pt 1):701-6**
- Population-based study of microinvasive adenocarcinoma of the uterine cervix.
- *Webb JC*
- 1988-1997. 301 cases
- Only 1 out of 140 women who had lymphadenectomy had a single positive LN. 4 tumour related death (one with IA1, and three with IA2)
- Prognosis is excellent for microinvasive adenocarcinoma of the uterine cervix. Simple hysterectomy alone proved adequate.

MICROINVASIVE ADENOCARCINOMA

- **Int J Gynecol Pathol 2000 Jan;19(1):29-38**
 - Early invasive adenocarcinoma of the uterine cervix
 - *Ostor AG*
 - Cases + lit. review, 436 cases
 - 2% of 219 cases had pelvic LN mets
 - 15 recurrences and 6 tumour related deaths
 - Early invasive adenocarcinoma behaves in the same way as its squamous counterpart
- Conization or simple hysterectomy is the treatment of choice.

MICROINVASIVE ADENOCARCINOMA

- **Cancer 2000 Sep 1;89(5):1048-55**
- Early invasive adenocarcinoma of the cervix
- *Lee KR*
- 40 cases
- Mean age 40.9yr.
- 78% in squamocolumnar junction.
- 85% had AIS. AIS is the precursor to most adenocarcinoma of the cervix, with an average interval between clinically detected AIS and early invasion of approximately 5 year.
- Multifocal invasion is uncommon (4 /40), as is vascular invasion (2/40).

MICROINVASIVE ADENOCARCINOMA

- **Aust N Z J Obstet Gynaecol 1999 Nov;39**
- Microinvasive adenocarcinoma of the cervix
- *Nicklin JL*
- 1986-1998
- 1995 FIGO
- 29 case
- asymptomatic, disease discovered at the time of routine Pap smear
- 43% incidence of coexisting CIN. Multifocal disease found in 17% of patients, lymphovascular positivity in 7%
- 18 case treat with radical surgery – no mets found
- 13 case with conservative surgery
- No recurrence 3-116 month

MICROINVASIVE ADENOCARCINOMA

- **Ostet Gynaecol 1997 Jan;89(1):88-93**
- Microinvasive adenocarcinoma of the cervix: a clinicopathologic study of 77 women
- *Ostor A*
- No lymph node mets. Vault recurrence in one case.

MICROINVASIVE ADENOCARCINOMA

■ Prognostic factor

Depth of invasion

Tumour volume

Type and grade

Lymphovascular invasion

Resection margin



































