Non-neoplastic gynecological cytology

Rietje Salet-van de Pol
Department of Pathology
Radboud University Nijmegen Medical Centre
Nijmegen
The Netherlands

Trieste  June 6th 2011
Normal smears
cells of the transformation zone

Bethesda: at least 10 well preserved endocervical or squamous metaplastic cells must be present, singly or in clusters
Normal smears
Endocervical cells

uniform nuclei

Strip with basally located nuclei
Normal smears
Endocervical cells
honeycomb pattern
Normal smears
Endocervical cells

Oval shaped nuclei, finely evenly distributed chromatin
Normal smears
Endometrial cells

First 10-12 days of menstrual cycle, are grouped in 3-dimensional clusters, bone shaped or round to oval nuclei
Normal smears
Tubal metaplasia

*Columnar cells can have hyperchromatic nuclei and increased n/c ratio. Look for terminals bars and cilia*
Normal smears
histiocytes
Normal smears
Cytolysis

Cellular degeneration due to bacterial overgrowth (lactobacilli) in late menstrual cycle, pregnancy or due to hormonal contraceptives
Normal smears

Atrophic smears

- Composed of parabasal type cells
- Cells arranged in aggregates with indistinct cell border
- Round to oval nuclei
- Relatively high n/c ratio
- Granular chromatin
- Nucleoli not present
Normal smears
Atrophic smears

LBC: Background of cellular debris with dispersed atrophic cells
Normal smears
Atrophic smear with inflammation
blue blobs (degenerate cells or inspissated mucus)
Normal smear

Glycogen associated with excessive hormonal influences (pregnancy)
Hyperkeratosis (anucleated squames)

- Abnormal differentiation
- Under influence of chronic stimulations such as prolaps of the uterus
- Inflammatory processes
- As a reaction of hyperestrinism of long duration
Parakeratosis

- Relatively small superficial squameus cells
- Shapes from round to oval, polygonal or spindle shaped
- Cytoplasm staining eosinophilic
- Small often pyknotic nuclei
- Beware of hyper- and parakeratosis overlying abnormal cell changes
- Advice 2 smears one to remove keratosis
Cell changes in inflammatory conditions

- Enlargement and binucleation
- Degenerative changes
  - irregular nuclear membranes (chromatin becomes blurry beaded along nuclear margins)
  - hyperchromasia
  - karyorrhexis and pyknosis
  - vacuolization and included granulocytes
  - degenerative color changes: pseudoeosinophilia
  - perinuclear halo
Cell changes in inflammatory conditions

Hyperchromasia

Degenerative color change: pseudoeosinophilia
Cell changes in inflammatory conditions
Enlargement, chromatin along nuclear margin
Blurry chromatin
Cell changes in inflammatory conditions
Perinuclear halo
Cell changes in inflammatory conditions
Binucleation, perinuclear halo and hyperchromasia
Cell changes in inflammatory conditions
Vacuolization and included granulocytes
Cell changes in inflammatory conditions
Degenerated endocervical cells
Cell changes in inflammatory conditions
Karyorrhexis and karyopyknosis
Cell changes in inflammatory conditions

When there is a persistent irritation (infectious or non-infectious) the epithelial cells undergo morphologic changes:

• Tissue repair
• Metaplastic changes (Replacement of simple columnar epithelium by a stratified squamous epithelium)
  • Immature squamous metaplasia
  • Mature squamous metaplasia

• Endocervical columnar epithelium
  • Columnar cell hyperplasia (chronic irritation: IUD)
  • Polyp formation
  • Tubal metaplasia (normal only 5-10% ciliated ec)
Cell changes in inflammatory conditions
Squamous metaplastic cells

**Mature**

- Isolated or in sheets
- Densely cyanophylic cytoplasm
- Relatively large round to oval nuclei
- Increased n-c ratio
- Finely granular evenly distributed chromatin
- Often micronucleoli

**Immature**

- Isolated or less frequently in sheets
- Distinct cytoplasmic borders
- Cells are round to oval or polyhedral
- Cytoplasm has densely staining outer zone
- Two tone cytoplasm
- Nuclei relatively small, uniform with finely granular evenly distributed chromatin
- Chromocentra and nucleoli may occur
Cell changes in inflammatory conditions
Squameus metaplastic cells
Cell changes in inflammatory conditions
Squameus metaplastic cells
Cell changes in inflammatory conditions
Squamous metaplastic cells

Conventional same patient LBC
Cell changes in inflammatory conditions

Repair

• In sheets with distinctive cell borders
• Nuclear enlargement (1-2.5 x intermediate nucleus)
• Anisokaryosis
• Regular chromatin, finely granular
• Chromocenters
• Prominent nucleoli and multiple
• Regular shaped nucleoli
• Abundant cytoplasm with granulocytes
• Normal mitosis
• Cellular cohesion, rarely solitary cells
Cell changes in inflammatory conditions

Repair
Cell changes in inflammatory conditions
Repair
Cell changes in inflammatory conditions
Repair
Chronic inflammation
Follicular cervicitis

- Lymphoid follicles in subepithelial areas
- Mature and reactive lymphoid cells
- Tingible-body macrophages

- More difficult in LBC because of dispersed lymphocytes
- Distinguished from: lymphoma, endometrial cells
Chronic inflammation
Follicular cervicitis
Inflammation
Granulomateus reaction

• Large aggregates of epithelioid cells
• Occasionally with Langhans-type multinucleated giant cells
• May occur in presence of foreign bodies (IUD) or specific infections, such as tuberculosis
Inflammation
Granulomateus reaction
Specific infections
Organisms

- Bacterial infection
- Actinomyces
- Fungal infections
- Trichomonas infection
- Viral infections:
  - Herpes simplex virus (HSV)
  - Cytomegalovirus (CMV)
  - Human papilloma virus (HPV)
Bacterial infection

- Cells covered by bacteria
- Also bacteria in the background
Actinomyces

- Occurs in the presence of intrauterine or intravaginal devices
- Vaginal pessaries
- Foreign bodies incl. forgotten tampons
Actinomyces

- Spidery, amorphous clumps, darker in the center
- Numerous filamentous structures radiating from the center
Chronic irritations of IUD gives cellular changes

- Reactive and reparative in squamous cells
- Hyperplastic changes in endocervical cells with bubble gum cytoplasm
- Endometrial cells with multinucleation, degeneration, also in second half menstrual cycle
- Psammoma body formation
Endometrium IUD
Fungal infection
Candida

- Numerous eosinophilic filamentous organisms revealing pseudo-and true hyphal and yeast forms
- Often fernlike arrangements of squamous cells with hyphen
Trichomonas infection

- Protozoan organism
- Small round to oval structure (size varies from leukocyte to parabasal cell)
- Distinct faint nucleus, mostly eccentric
- Sometimes eosinophilic granules (LBC)
- Occurrence of aggregates of leukocytes covering squamous epithelial cells
- Represents a number of organisms feeding on sq.ep.cells
Trichomonas infection
Viral infections
Herpes Simplex Virus (HSV)

- May effect squam. and endoc. cells
- Cytomegaly, karyomegaly, n/c ratio not altered
- Combination of reactive and degenerative changes
- Chromatin becomes finely divided, some against nuclear membrane (ground glass appearance)
- Nucleoli may be present

Later stage of infection
- Multinucleation and molding
- Large, single intranuclear inclusions, usually round or oval with halo
Viral infections
Herpes Simplex Virus (HSV)
Viral infections
Herpes Simplex Virus (HSV)
Viral infections

Cytomegalovirus (CMV)

- CMV bearing cells in endocervical glands and not many cells may be observed in epithelium of endocervical canal
- Cells may be multinucleated and enlarged
- Round very large intranuclear inclusion with a clear zone of halo around it
- Chromatin around nuclear membrane
- Intracytoplasmic inclusions also possible
Viral infections

Human papilloma virus (HPV)

• Belongs to the family Papovaviridae
• More than 100 HPV types identified
• Approx. 40 different types affect anogenital tract
• Depending on their risk to develop cancer:
  • Low risk types (most commonly 6-11)
  • High risk or oncogenic types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68, 73, 82) found in CIN II/CIN III and carcinomas
Viral infections
Human papilloma virus

- Diagnostically the koilocyt is an excellent indicator of HPV infection
- Loss of polygonal form with blunt or rounded corners
- Large clear-cut perinuclear halo
- Thickened cellular margin
- Bi-and multinucleation
- Also dyskeratosis, parakeratosis and hyperkeratosis
- Cells have tendency to clump
Viral infections
Human papilloma virus

• Nuclei: no specific changes, may degenerate, hyperchromatic, pyknotic, chromatin margination, bi- and multinucleation, may be enlarged, but chromatin is finely divided
• Membrane can be wrinkled (raisin like)
• Nucleoli absent or inconspicuous
Viral infections
Human papilloma virus
Viral infections
Human papilloma virus
Dyskeratosis
The End