REACTIVE CELLULAR CHANGES AND INFECTIONS OF FEMALE GENITAL TRACT

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Aim:
- The aim of the presentation is clarifying the cause of infectious disease of female genital tract and the reactive cellular changes to interpretate/ recognize by cytology.

PRESENTATION PLAN
- What Bethesda includes under this title?
- Causes of infectious disease
- Reactive cellular changes
- Repair process
- Cellular changes due to the RT
- Atrophy
- Others...

REACTIVE CELLULAR CHANGES AND INFECTIONS OF FEMALE GENITAL TRACT

- “Negative for intraepithelial lesion and malignancy” was represented quite heterogenous cytomorphologic features in Bethesda
- Wide spectrum of benign lesions

Bethesda System 2001

Negative for intraepithelial lesions and malignancy
- Organisms
  - Trichomonas vaginalis
  - Fungal infectious
  - Bacterial vaginosis
  - Actinomyces
  - Cellular changes depend on HPV infection
- Other neoplastic features (not obligatory to mention in report)
  - Reactive cellular changes
  - Inflammation
  - Radiation
  - IUD
  - Glandular cells following hysterectomy
  - Atrophy
CELLULAR CHANGES AND INFECTIONS OF FEMALE GENITAL TRACT

○ Common point of the heterogenous benign lesions of this category is not to be included the cytomorphologic features of "(ASC-US)" and further...

When we diagnose:

○ Case;
  - Age?
  - Last mens date
  - Hormonal effects,
  - The presence of infectious disease,
  - Atypia history in old smears
  - And if she take any therapy

○ All these that mentioned above have serious effects on cell morphology and clinical information should be included to the whole evaluation process.

REACTIVE CELLULAR CHANGES AND INFECTIONS OF FEMALE GENITAL TRACT

○ Cervical cytology is a screening test
○ The aim of the test is to diagnose squamous cell carcinoma and its precursors by cytology.
○ To know "what is normal" is the base note of the interpretation of the sample regardless conventional or liquid base methods.
○ Squamous and endocervical cells are seen in same morphology in LBP as well as conventional method.

REACTIVE CELLULAR CHANGES has...

○ Well described criteria
○ Lack of reproducibility
○ Should be noted the presence of microbial agents in reports
○ Other changes might be mentioned depends of the different requirements of the different clinical departments.

TRICHOMONAS VAGINALIS

○ Usually small (especially in liquid base), 15-30µm, oval-round
○ Eccantrically placed faint-vesicular nucleus
○ Cytoplasmic debris can be distinguished from organism itself by analyzing the inner structure
○ difficult to see flagella but can be seen in detailed analysis
TRICHOMONAS VAGINALIS

- Flagella and pear shaped forms as seen in living organism can be recognizable
- Eosinophilic cytoplasmic granules
- Leptotrich can be observed in the background
- Kite-shape cells can be seen in LPB

- Presence of inflammatory cells, perinuclear halo in squamous cells and bi-chromatic staining
- Organism also can be seen without accompanying of inflammatory cells
**CANDIDA SPECIES**

- Grouping of cells is typical
- Squamous cells can phagocyte neutrophils also is another clue of this infection.
- Herringbone pattern or shish-kebab pattern with polydust also are useful diagnostically.

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**CANDIDA SPECIES**

- Vacuolated copy paper or moth hole appearance of cytoplasm or reactive nucleus can commonly be observed.

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**CANDIDA SPECIES**

- It is important to differentiate mucus flaments from pseudohyphae
CANDIDA SPECIES

- Mucus flaments/strands extend out of the cell groups however it is easy to notice the width of flaments are different and irregular in high magnification.
- No hyphae and spors can be seen.

Budding yeast forms may occur in Candida infection.
BACTERIEL VAGINOSIS
(Cocobasil predominance in the background)

- The replacement of normal lactobacilli with by shorter bacilli (coccobacilli), curved bacilli and mixed bacteria that gives a filmy appearance in the background is a hallmark of this infection (in conventional smears)
- Every each squamous cells are covered by the organisms, known as “clue cells”
- No lactobacilli

BACTERIAL VAGINOSIS

- On the contrary of conventional smears, LBP s represents clean background associated with clue cells

ACTINOMYCES

- Numerous Gram (+), filamentous organisms with acute angle branching patterns can be observed in clumps forms.
- Numerous filamentous structures radiating from the center (wolly clumps)

ACTINOMICCES

- Acute inflammatory response associated with polymorphonuclear leucocytes are usually seen
- In close proximity to IUD in most of the patients
ACTINOMICIES

HERPES SYMPLEX VIRUS

- Ground glass nuclei, margination of chromatine and distinct membrane are diagnostic clues.
- Multinucleation and nuclear molding are easily identifiable.
HERPES SYMPLEX VIRUS
- Eosinophilic nuclear inclusions are prominent which is even more distinctive in LBPs, also without any drying and/or mechanic artifacts.

SECONDARY REACTIVE CHANGES TO INFLAMMATION
- Slight nuclear enlargement (2 folds of the nuclei of intermedier cell)

REACTIVE CHANGES
- It has critical importance to distinguish non-specific halos from the ones associated with HPV infections.
- Cytoplasmic vacuolation and bi-chromatic staining pattern may also be seen.

REACTIVE CHANGES
- Clumping neutrophils are demonstrable in the background.
- Cellular details are increased due to extended fixation.
- These cells are seen with slightly enlargement of the nuclei associated with mild hyperchromasia and nucleoli.

REACTIVE CHANGES
- Nuclear changes might bring to mind ASC-US diagnosis however, important to require all nuclear changes of ASC-US to refrain any.
- Slight irregularity of nuclear membrane can be noticed.
- However uniformity can be noticed due to the cytoplasmic degeneration.
SECONDARY REACTIVE CHANGES TO REPAIR

Epithelial cell layers phagocyted the neutrophils is remarkable
- Cell groups are more spheric and deep focus are necessary due to LBP.
- No mechanic artefacts

FISH SCHOOL

Nuclei with thin chromatin, irregular membranes and presence of nucleolei are noticeable with the uniform cell sheets.

“Eyeliner” effect
Differences between repair and SIL

- Cells are arranged as sheets in repair and this gives a peculiar tissue-culture appearance to the cytoplasmas of the cells.
- Despite of the enlargement of nucleus, chromatin pattern is seen evenly distributed and homogenous with the regular cell borders.
- Nucleoli can be prominent but not in all cell population.

RADIATION CHANGES

- Cell size is increased without any changing in N/C ratio (cytomegali).

Differences between repair and SIL

- To detect SIL cells in epithelial sheets requires further concentration and focusing.
- Size of the nuclei is different and polarity represents prominent.
- Nucleoli can be multiple and prominent.

RADIATION CHANGES

- Bizarre cell morphology can be observed.
- Large nucleus with pale chromatin and folding are common in degenerative changes.
- Binucleation and multinucleation also are common.
RADIATION CHANGES

- Nuclei with marked size variation can be observed.
- Enlarged nuclei and normal size nuclei can be seen in the same cell groups.

RADIATION CHANGES

- Slight nuclear hyperchromasia.
- If there is any association of repairment, nuclei can be observed in multiple form as well as the single form.

Cytoplasmic vacuolation and cytoplasmic polychromatic staining pattern can be encountered.

ATROPHY WITH AND WITHOUT INFLAMMATION

- Flat sheets of parabasal-like cells with honeycomb arrangement.
- Relatively high nucleo/cytoplasmic ratio with the particular size of the nuclei (Genel bir nükleus büyüklüğü vardır (3-5 folds of intermediate cell nuclei)).
- Nuclear enlargement is relatively decreased compared to the conventional smears.

ATROPHY

- Intermediate cells tend to be normochromatic, however, parabasal cells represent slight hyperchromasia with the nuclear elongation.
- Chromatin is evenly distributed.
- Naked nuclei can be observed due to autolysis, which is much rare in LBPs.
ATROPHY

- Abundant inflammatory exuda and basophilic granular background can mimic tumor diathesis.

- Variable in size and shape histiocytes with multiple round, epithelioid nuclei and foamy-dense cytoplasm.

OTHER NON-NEOPLASTIC CONDITIONS THAT DO NOT REPLACED IN 2001 BETHESDA SYSTEM
Tubal metaplasia

- Endocervical columnar cells that arranged in small to pseudostratified crowded groups.
- Nuclei is oval, round and enlarged, pleomorphism and hypochromasia can be encountered.
- Evenly distributed chromatin without nucleoli.
- Nucleus-to-cytoplasmic ratio increased.
- Vacuolation and goblet cell changes might be observed in cytoplasm of the cells.
- Presence of cilia/terminal bars is typical for these cells, however isolated cells with cilia is not enough to described as metaplasia.

Parakeratosis

- Various numbers of small, superficial squamous cells with dense-orangeophilic cytoplasm.
- Nuclei is small and picnotic.
- If there is any accompanying morphologic features of atypia, then must be called as atypical cellular changes (ASC).
- Isolated cell layers or whorls arrangement is common.
- Cells can be seen oval, round, polygonal or spindle in shape.

Hyperkeratosis

- Anucleated mature, polygonal squamous cells.
- Keratohyaline granules are commonly observed as well as ghost cells.

Lymphocytic (Follicular) cervicitis

- Clusters of polymorphic lymphoid cells, macrophages are encountered in mucus deposits.
- Lymphoid cells can mostly be seen as single cells as well as clusters in LBPs.
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