

THE PATHOLOGY OF THE NUCLEUS IN CERVICAL LESIONS

Diana-Elena Maftai, Cristina-Elena Bărbuță

Key words: *Pap test, TBS, tumors*

INTRODUCTION

Nowadays, the tumor pathology represents an ongoing priority in public health, as it impends on lifespan worldwide, and it is regarded as the major death cause prior to the age of 70 years old. The malignant tumors impact both socially and medically within all the age groups, they grow rapidly undiagnosed in early stages [2-5].

Despite all the relevant progress in prevention, diagnosis, and cure for this pathology, the cervical cancer globally ranks fourth as frequency and as a death cause as well. This study aims the comprehension of all the paths in which HPV affects the pathogeny of the squamous intraepithelial lesions, and the overview of diagnosis (table 1, 2). The aims of The Bethesda System (TBS) were to provide effective communication from the laboratory to the clinic provider, facilitate cytologic-histologic correlation, facilitate research into the epidemiology, biology, and pathology of cervical diseases, and provide reliable data for national and international statistical analysis comparisons [11].

Table 1. The alleged diagnosis based on clinical data

Clinical data
Age
Number of births
Number of miscarriages (spontaneous/requested)
Obstetric history

MATERIAL AND METHODS

Cytological examination of the vaginal fluids represents one of the most important means of investigation for the etiological diagnosis of cervical cancers. The biological material was the vaginal fluid provided by the standard procedure.

The lab staff (the anatomo-pathologist, the biologist specialized in Cytology, the lab assistants) uses the following equipment: optic microscope, manual staining kit, slide collection, PC, printer, refrigerator, centrifuge, recipients for the used mixtures, glassware, organic solvent-resistant smear recipients and stands, recipients to collect infected fluids, toxic substances, flammable substances and drug precursors in view of neutralization; surface, instruments, and medical personnel disinfectants; fixing, dehydration, standard staining reagents; protection equipment.

The medical staff in the Clinical Cytology lab has to conform and enforce the protocol and safety regulations. Cytology and colposcopy may allow the comparison and correlations to the histological reports. Meetings are held on regular basis, addressing technical issues, training and sharing medical advice in complicated cases. The interdepartment briefings should always include anatomo-pathologists, cytotechnicians, gynecologists, debating on the colposcopy imagistics, cytological smears, and histological stained slides.

Table 2. Histopathological diagnosis of the cervix

Cytological tests for screening		Histological examination (to confirm the diagnosis)	
PAP System	TBS (The Bethesda System)	CIN	World Health Organization Classification
Class I	Normal	Normal	Normal
Class II	ASC US	Atypical	Atypical
Class III	LSIL	CIN I, and condylomatosis	Koilocytosis Mild dysplasia (low-grade intraepithelial lesion LSIL)
Class III	HSIL ASC H	CIN II	Moderate dysplasia
Class III	HSIL ASC H	CIN III	Severe dysplasia
Class IV	HSIL/In situ carcinoma	CIN III/ In situ carcinoma	In situ carcinoma
Class V	Invasive carcinoma	Invasive carcinoma	Invasive carcinoma

The Pap smear, also called Pap test, is a screening procedure for cervical cancer. It tests for the presence of precancerous or cancerous cells on the cervix. It is indicated to screen for malignant and premalignant lesions of the cervix. The recommended age at initiation of cervical cancer screening has undergone significant revision over time as the natural history of HPV infection and subsequent cervical dysplasia has been elucidated. Generally speaking, women between 25 to 65 years old should be examined every 2-3 years by means of Pap test [6, 14, 17].

The Pap test and the TBS 2001 for reporting cervical cytology are the standard most affordable methods. The cells are arranged on one layer in liquid suspension for the liquid – based cytology, preserving cell integrity, allowing the automatic examination of a larger number of cells. Regarding the HPV test by hybridization, it assesses the risk (low or high, respectively). PCR method applied on viral DNA isolates 35 types. Fluorescence in situ Hybridization (FISH) utilizes peptide nucleic acid (PNA) probes to identify specific DNA sequences.

The cervical cancer examination includes the standard Pap smear as following:

Sensitivity (percentage of patients with a positive result) of conventional Pap cytology ranges between 65-87%. Pap specificity (percentage of women who do not manifest the disease and tested negatively) ranges from 86 to 100%

HPV test's characteristics are: sensitivity 75 – 100%, specificity 85 – 96 %.

Cells from the entire transformation region should be smeared mid menstrual cycle, and be one-layer arranged for microscopic examination. The smears are tagged or the patient's name is written on the rugged side of the glass slide. The specimens to be lab examined come with the patient chart.

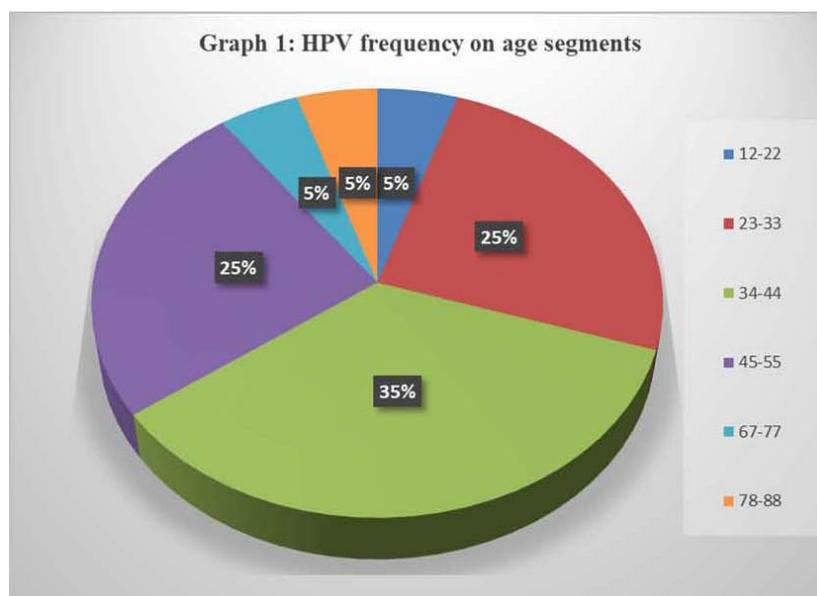
RESULTS AND DISCUSSIONS

The investigated group comprised 100 patients in the Obstetrics-Gynecology Department of the E.H. Bacău, registered within the Pathological Anatomy laboratory during January – December 2019. Of the entire group, 20% were diagnosed with cervical lesions, 46% were monitored for cervical inflammation, 7% smears containing erythrocytes and leukocytes, and 27% were examined for other alterations. The 20% cervical lesions by TBS (the Bethesda System) mean the following: 1% ASC-H, 8% ASC-US, 3% LSIL, 2% HSIL, 2% HSIL CIN3, 2% ASC-H vs HSIL CIN, 1% HSIL ASC-H CIN3, 1% ASC-US vs LSIL.

Female fertility and capacity to procreate start at the age of 14-16 years old, and end at about 45-55 years old with menopause (or climacteric). The percentage of fertile women infected with HPV compared to the climacteric women displays that the most affected are fertile women 65% (age segments of: 12-22 years old 5%, 23-33 years old 25%, 34-44 years old 35%)(graph 3). The percentage of women in premenopause or menopause is 35% (age segments of: 45-55 years old 25%, 67-77 years old 5%, 78-88 years old 5%).

Alterations in hormone levels during pregnancy might turn the cervix more sensitive, and prone to HPV. For instance, the 39 years old female patient with seven births and the 47 years old patient with two births were detected with HSIL, and the 40 years old patient (one miscarriage) and a 48 years old with (6 miscarriages) were reported with ASC-US (graph 1).

These precancerous lesions were joined by the fungus *Candida sp.* 3%, and by the bacteria *Trichomonas vaginalis* 1%, associated with ASC-US (fig.1, 2).



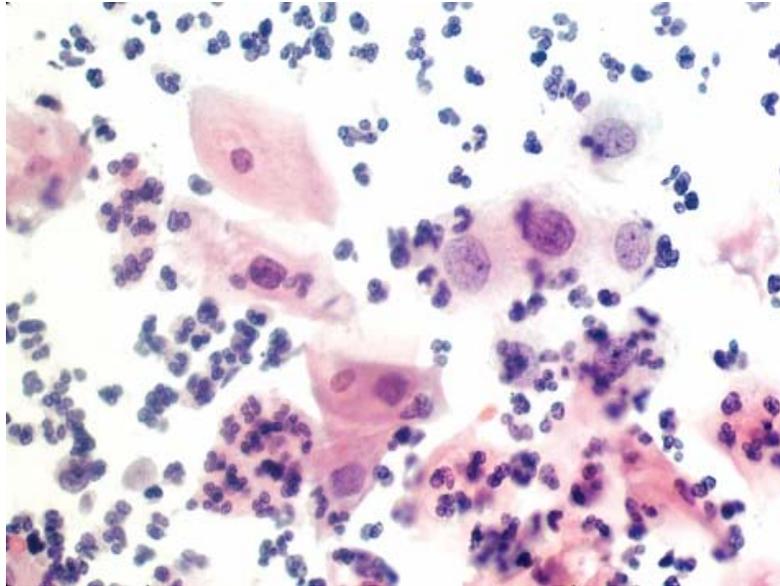


Fig. 1. Infectious cervicitis (caused by *Trichomonas*) with atypical alterations of the nucleus [18]

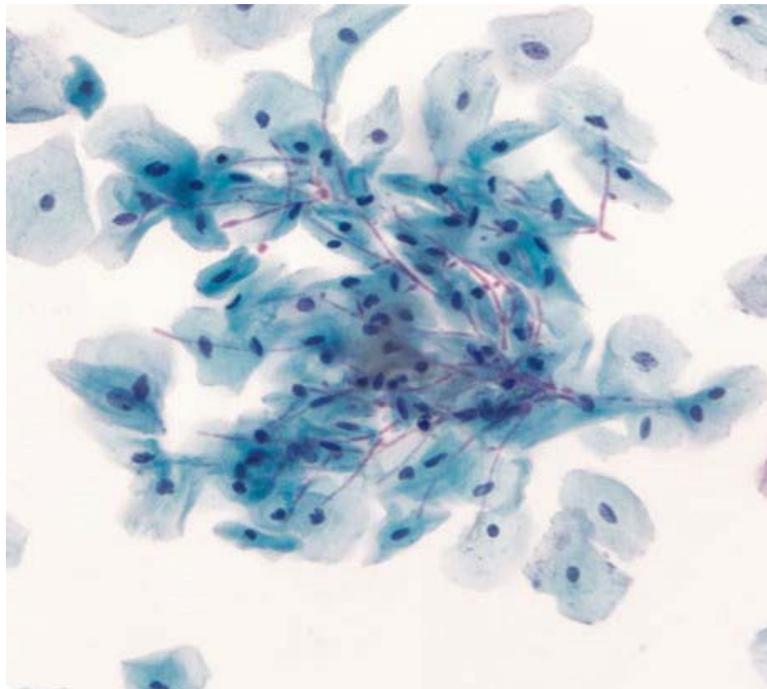


Fig. 2. Fungi (morphological traits of *Candida*) - vegetative growth form of pseudohyphae [18]

CONCLUSIONS

A percentage of 20% of the 100 examined smears are precancerous cervical lesions, of which the majority were detected ASC-US (8%)

Most affected by HPV infection are fertile women (65 %), whilst the percentage of menopausal women is 35%.

The specific pathogens were *Candida sp* (3 %) and *Trichomonas vaginalis* (1 %).

The precancerous lesions were examined and monitored, in order to establish their type. The histopathological classification was cytologically determined. Therefore, the histopathological diagnosis CIN 1 stands for the cytological alteration LSIL, and CIN 2 and 3, represent the cytology of HSIL.

HPV testing will be only useful in high risk genotypes (oncogenes). Low risk strains (non-

oncogenes) are not significant in the diagnosis of cytological abnormalities.

The misdiagnosis may either be caused by a lack of knowledge and experience, but usually reflects incomplete or shallow examination.

The Pap test should be done yearly for early diagnosis of a possible cancer. The first two stages of cervical cancer mean over 90% life chance for the female patient; the 3rd and 4th stages mean expensive care for the cure for a short life expectancy.

The cure in precancerous lesions should start immediately after a certain diagnosis. The treatment is effective for CIN II, CIN III/CIS and AIS type of lesions; CIN I type of lesions are periodically monitored.

Surgery is the main cure as it follows: the preserving surgery (LLETZ and conization) or the invasive one – hysterectomy, recommended in AIS lesions or recurrent/persistent disease.

Cervical cancer first starts as a precancerous lesion, never on a healthy cervix.

Cervical cancer is curable as long as one is aware of it. Romania has a high occurrence and death rate caused by cervical cancer.

Nevertheless, the death rate by cervical cancer decreased by more than 30% during the last 30 years in Europe, as a consequence of screening, prevention, monitoring. Acting synergically, the vaccine and the screening are an effective strategy to fight cervical cancer.

Romanian women should be aware of the triggering factors for cervical cancer, as the prevention may decrease the risk by 80%.

Diagnosis and treatment of precancerous lesions assess patients' life quality individually, socially, and professionally.

ABSTRACT

Romania has a high occurrence and death rate caused by cervical cancer. Most affected by HPV infection are fertile women (65 %) whilst the percentage of menopausal women is 35%.

This study aims the comprehension of all the paths in which HPV affects the pathogeny of the squamous intraepithelial lesions, and the overview of diagnosis.

The specific pathogens were *Candida sp* (3 %) and *Trichomonas vaginalis* (1 %). The cure in precancerous lesions should start immediately after a certain diagnosis. Cervical cancer is curable as long as one is aware of it.

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AUTHORS' ADDRESS

MAFTEI DIANA – ELENA - ‘Vasile Alecsandri’ University of Bacău, Faculty of Sciences, no 157 Mărășești Street, Bacău, Romania, e-mail: diana.maftei@ub.ro;

BĂRBUȚĂ CRISTINA – Elena ‘Vasile Alecsandri’ University of Bacău, Faculty of Sciences, no 157 Mărășești Street, Bacău, Romania, e-mail: bogatucristina144@yahoo.com.