

EVALUATION OF THE CERVICO-VAGINAL CYTOLOGY SMEARS IN POSTMENOPAUSAL WOMEN

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Abstract. Hormone-related cancers account for almost 30% of all cancer cases. Thanks to the continuous desquamation of cervical epithelium and maintenance of the estrogen responsiveness to old age, cervical-vaginal smears can be a means to study the activity of estrogen in the body because they are the only hormone able to determine the complete differentiation of cervical epithelium. This paper aims to highlight and explain, according to the latest data from the literature, cytological appearance of cervico-vaginal smears of postmenopausal women. Study was conducted at Department of Pathology of the Hospital of Obstetrics and Gynecology "Salvator Vuia" Arad during 2007-2013. In 40% of the cases analyzed, there was a non-atrophic cervical smear, superficial and intermediate type, and in 60% of cases, atrophic cervical smears, basal and parabasal type. The ability of estrogen to stimulate the development of hormone-injury is a certainty, endocrine therapy is widely used to counteract the tumorigenic effects of estrogen. The etiology of hormone-related lesions in the female reproductive tract is not known, however an important role in the development of the disease that is played by long acting estrogen unopposed by the progestogen.

INTRODUCTION

Cervico-vaginal cytology has experienced particular attention in recent years due to interest for Pap smear as a screening test in the detection of cervical neoplasia and identifying neoplastic cells of the cervix. However, any change in cervical-vaginal smear should be followed by a carefully clinical examination.

Thanks to the continuous desquamation of cervical epithelium and maintain responsiveness to the hormone estrogen to old age, cervical vaginal smear may be a means of studying the activity of estrogen in the body hormones as they are only able to determine the complete differentiation of cervical epithelium.

At the menopause, along with significant physiological decline in ovarian function and plasmatic estrogen levels decline parallels, we expect a atrophic type smear caused by complete estrogen lacking.

This paper aims to highlight and explain, according to the latest data from the literature, cytological appearance of cervico-vaginal smears of postmenopausal women.

MATERIALS AND METHODS

This study is an observational complex statistical survey carried out in the Department of Pathology of the Hospital of Obstetrics and Gynecology "Salvator Vuia" Arad, as well as private consulting rooms Obstetrics and Gynecology, during 2007-2013.

The research is an exploratory and interpretive study which analyzes and interprets data from participating. This study comprises a personal retrospective research, that analyzed using statistical methods, the cytological aspect of cervical-vaginal smear in postmenopausal women

The study is based on analysis of a total of 564 cervical-vaginal smears (I thought that the number of women studied enough to have the power to conclude the results), collected from postmenopausal women.

All samples analyzed were collected from postmenopausal women aged over 55 years, which were presented for a routine vaginal cervical smear (they were excluded from the study presenting gynecologic pathology, and those with a BMI exceeding 30).

Smears were collected with the cervical brush type Brad and fixed immediately in absolute alcohol, stained by Papanicolaou method. They were then

observed under the optical microscope (10x, 20x, 40x) analyzed particular aspects.

RESULTS

Had been taken in observations 564 patients aged over 55 years with a mean age of 63 years.

Of the total patients studied, 282 patients (50%) are included in the age group 55-60 years, 113 patients (20%) in the age group 61-65 years, 79 patients (14%) in group aged 66-70 years and 90 patients (16%) in the age group > 71 years.

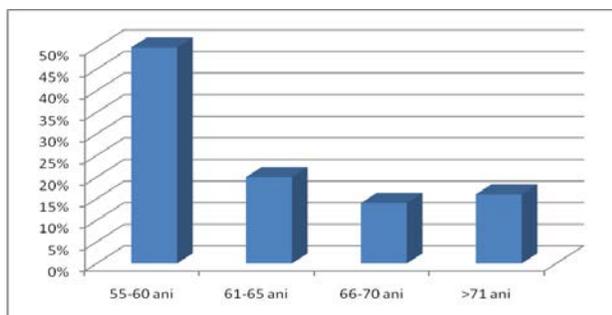


Chart 1. Distribution by age groups

The study protocol consisted of patients after enrollment in the analysis of cytological examination (Pap test).

Of smears analyzed 40% were non-atrophic smears, superficial and upper intermediate type, and 60% were atrophic smears, basal and parabasal type.

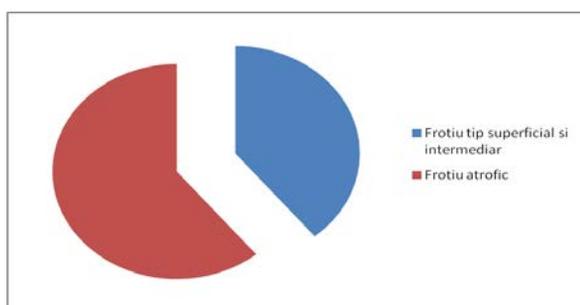


Chart 2. Distribution of types of smear

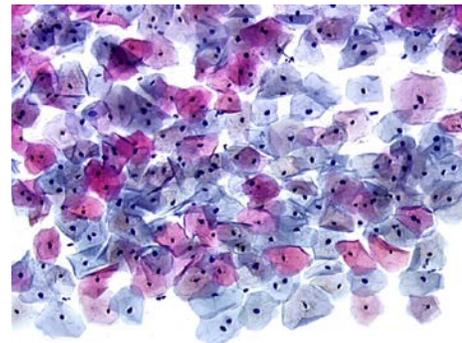


Fig.1 Non-atrophic smear of superficial and intermediate type (HE 10x) in a patient aged 67 years

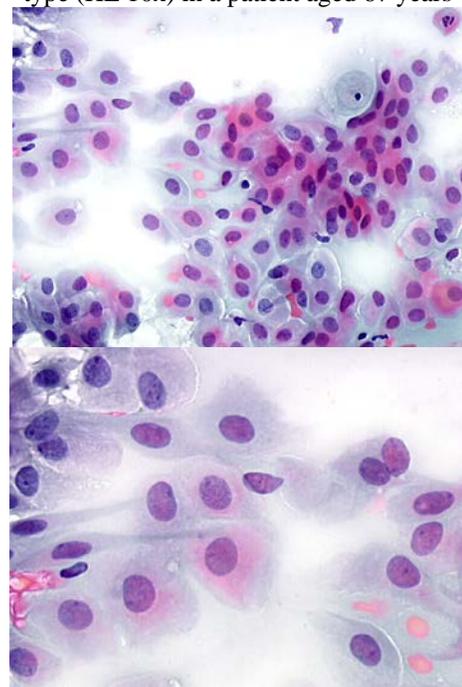


Fig.2. Atrophic smears, basal and parabasal type (HE 20x, 40x) in a patient aged 59 years

Distribution of changes in cervical smear by age:

- Age group 55-60 years:
 - Non-atrophic smears, superficial and intermediate type 144 cases (25,5%),
 - Atrophic smears, basal and parabasal type 138 cases (24,5%);
- Age group 61-65 years:
 - Non-atrophic smears, superficial and intermediate type 34 cases (6%),
 - Atrophic smears, basal and parabasal type 79 cases (14%);
- Age group 65-70 years:

- Non-atrophic smears, superficial and intermediate type 26 cases (4,5%),
- Atrophic smears, basal and parabasal type 53 cases (9,5%);
- Age group over 70 years:
 - Non-atrophic smears, superficial and intermediate type 22 cases (4%),
 - Atrophic smears, basal and parabasal type 68 cases (12%)
- Table 1. Distribution of changes in cervical smear by age

Age group	Non-atrophic smear	Atrophic smear
55-60	144	138
61-65	34	79
66-70	26	53
>70	22	68

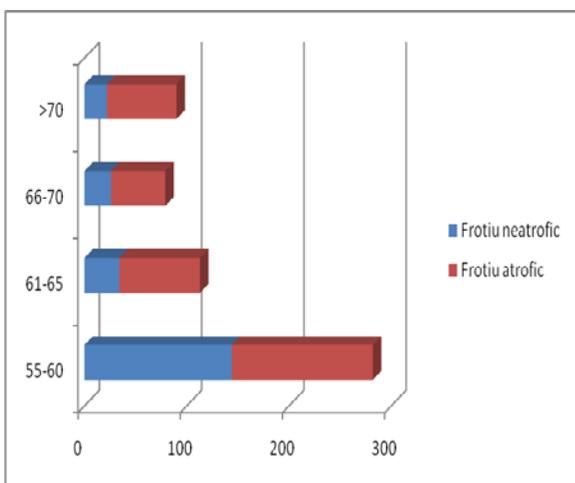


Chart 3. Distribution of changes in cervical smear by age

33% of the smears analyzed were type-I, respectively 67% type-II associated to the presence of non-specific inflammation.

In smears of type I, 32% are non-atrophic smears, superficial and upper intermediate type, and 68% are atrophic smears, basal and parabasal type.

In the smears of type II, 43% are non-atrophic smears, superficial and upper intermediate type, and 57% are atrophic, basal and parabasal type.

Table 2. Distribution of smear type I, II according to age

Pap type	%	Smear type	no	Age group			
				55-60	61-65	66-70	>71
I	33	Non-	60	42	10	2	6

	%	atrophic smear					
		Atrophic smear					
II	67 %	Non-atrophic smear	164	102	24	22	14
		Atrophic smear	214	98	44	42	30

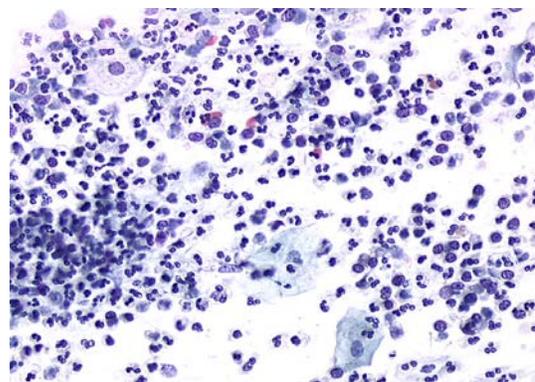


Fig.3. Type II smear - superficial and intermediate smear with marked nonspecific inflammation, numerous polymorphonuclear and histiocytes (HE 20x) in a patient aged 69 years.

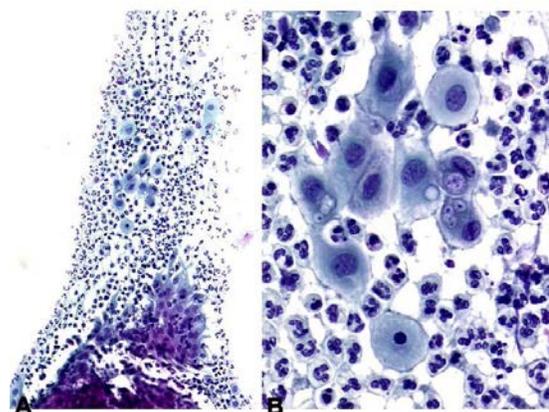


Fig.4. Smear type II - type atrophic smear with with marked nonspecific inflammation (HE 10x, 40x) in a patient aged 60 years

Other changes in the analyzed smears consisted of hyperkeratosis changes (9% of cases) and parakeratosis changes (17% of cases), evenly distributed across age groups.

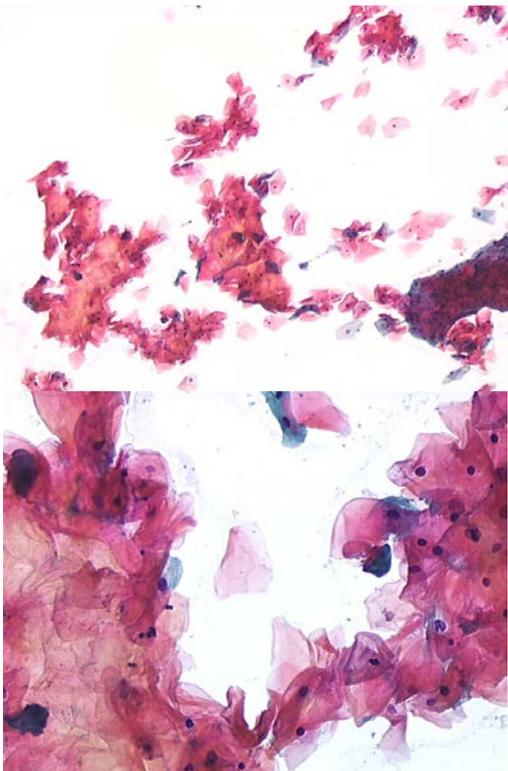


Fig.5. Cervical smear with hyperkeratosis changes (HE 5x, 20x) in a patient aged 63 years

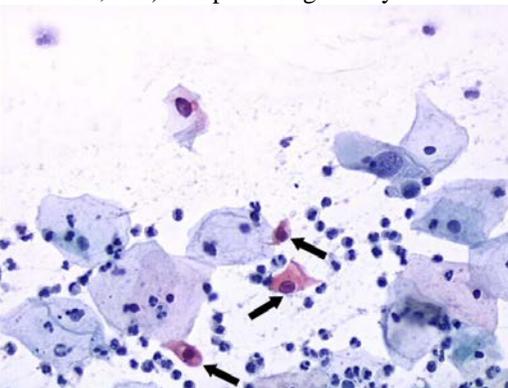


Fig.6. Non-atrophic cervical smear, superficial and intermediate type, with parakeratosis changes (HE 20x) in a patient aged 55 years

DISCUSSIONS

Pap test was introduced into practice by George Papanicolaou gynecologist about 80 years ago and still is one of the best methods of diagnosis and prevention of cervical neoplasia. This test consists of microscopic analysis of cells exfoliate from the surface of the cervix, cells sensitive to estrogens.

In post menopausal women, estrogen secretion ovarian function is completely canceled, this reflected cytological in atrophic cervical smears basal and parabasal type (60% of cases analyzed).

In 40% of cases analyzed, there was a non-atrophic cervical smear, superficial and intermediate type. This can be explained by the persistence of the action of estrogen on the cervical epithelium, the estrogen hormone is the only able to induce changes in the level.

Age distribution of cervical smear changes shows a ratio of 1: 1 non-atrophic smear: atrophic smear in the age group 55-60 years, which is halved compared to the age group 61-70 years, and becoming 1: 3 in the age group > 71 years. These data show a gradual decrease of estrogenic activity on cervical epithelium with age. The existence of estrogenic activity in women aged over 70 years is a problem due to the ability of estrogen to produce changes in the female reproductive tract.

After installation of postmenopausal ovarian failure, varying amounts of estrogen are secreted by the adrenals as a precursor - androstenedione. Morphological, postmenopausal estrogen persistence, even at low levels, induces a slow process of atrophy in the cervix, keeping it a trophicity fairly good, this being observed in cervical cytological smears by the presence of superficial type and intermediate type cells.

Estrogens modulators of cell growth and differentiation in the female reproductive tract can cause in excess in postmenopausal women the appearance of pathologies of the most serious consisting of hormone-related injuries, which can range from simple glandular hyperplasia to carcinoma development at this level. Estradiol is a weak mutagenic and carcinogenic factor capable of inducing genetic damage (3).

In 17% of the examined cases, have been observed and change of parakeratosis, and in 9% of cases, changes of hyperkeratosis. Responsible for these changes are estrogens, which stimulates the proliferation of exocervical squamous epithelium, resulting in a superficial layer of well-developed cells covered by a fairly thick layer of parakeratosis cells which are keratinized prematurely.

In hyperestrogenism, either endo or exogenous nature, can become excessive keratinization leading to the appearance of a layer of hyperkeratosis in which cells may be anucleated.

Proliferative effects of estrogen in addition, promotes the repair of columnar epithelium or epithelial defects, which are oversized through the regeneration of original exocervical epithelium.

Cervical smear expresses estrogenic activity on the cervical epithelium. Postmenopausal persistence of high estrogenic activity and thus a non-atrophic cervical smear is important given that increased activity of the postmenopausal estrogen may have mutagenic effects on the female reproductive tract.

Numerous studies (2, 4, 9, 10) shows that the imbalance of estrogen-progesterone with the growth of the concentration of estrogen promotes glandular hyperplasia development of the female reproductive tract, while exposure to increasing amounts of progesterone has a protective effect.

Basically, estrogen increases the activity of mitogenic stimulation at both endometrial glandular and in the mammary gland, which significantly increases the likelihood of accumulation of random mutations and finally leading to malignant transformation. Estrogens act more as tumor promoters rather than as carcinogens on female reproductive tract, considering that their action is mitogenic, not mutagenic (3, 4).

A prompt and thorough investigation is recommended for patients who have non-atrophic cervical smears through the menopause.

CONCLUSIONS

Data obtained from this observational study shows in 60% of analyzed cases, atrophic type smears - expected and physiological aspect in postmenopause. In 40% of cases, cytology shows non-atrophic smears, superficial and intermediate type, unexpectedly in postmenopause. Also, 17% of the cases was observed parakeratosis changes and in 9% of cases hyperkeratosis changes.

Estrogens being the only hormones that act in the cervix, we concluded that the persistence of these hormones, even in low concentrations in postmenopausal women can cause this aspect on cervical smear.

The ability of estrogen to stimulate the development of hormone-related injury is a certainty; endocrine therapy is widely used to counteract the tumorigenic effects of estrogen. The etiology of hormone-related lesions in the female reproductive tract is not known, but a major role in the development of the disease it plays estrogen long acting non-counterbalanced by progesterone.

For these reasons, we consider important and prompt investigation of all the patients who have non-atrophic cervical smears, superficial and intermediate type in the postmenopausal period. Study of the interrelation estrogen - hormone-related injuries in postmenopausal women raises new controversy.

We believe that a study, on the correlation of cervico-vaginal cytology aspect and the histopathological appearance of pieces of biopsy and serum estrogen levels, is necessary under the conditions that glandular hyperplasia of the female reproductive tract is the most important precursor in the development of neoplastic lesions at this level.

Postmenopausal women should be educated on the importance for regular cervical-vaginal smears and performing the necessary investigations in the genital area.

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