Original Paper

The Importance of Cytologic Exam in The Diagnosis of the Preneoplastic and Neoplatic Lesions of the Uterine Cervix

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ABSTRACT The aim of this study represents the confirmation of the utility of cytologic investigation in the screening of the preneoplastic and neoplatic lesions of the uterine cervix,comparing the cytologic results with the histlogic diagnosis of the resected specimens.

KEY WORDS *PAP smear cytodiagnosis, Cervical cancer*

Introduction

Cervical cancer is one of the most common cancer in women, and the association between this disease and HPV is higher than that between smoking and lung cancer, being surpassed only by the association between carrier state of chronic hepatitis B and liver cancer (Franco et al, 1995).

Cervical cancer is a disease that develops gradually walking across different stages of cellular changes from normal epithelium to invasive carcinoma.

Since the introduction in 1940 of the smear Babes – Papanicolau, cervical neoplasia rate presented a drastic decline due to early detection of dysplastic lesions.

Normal superficial squamous cells have a nucleus of the size of a lymphocyte and have a high amount of cytoplasm. A gradual increase in nucleo-citplasmatic ratio correlates with progression from low grade dysplasia to high one.

Materials and methods

We idenftificated in the database the histologically confirmed cases of preneoplastic and neoplatic lesions of the cervix, during the the period 2007-2009. For these cases cytologic results were requested. Thus, 398 cervical-vaginal smears and conventional cytology in liquid medium were analyzed, stained by the Babes-smear technique using the Bethesda score.

Results

Smears were classified according to Bethesda 2001 study as follows: ASC - 164 cases, LSIL - 119 cases and HSIL cases - 99 cases and 16 cases squamous cell carcinoma (table no. 1),

preneoplastic to neoplatic lesions ratio being of 23, 87:1.

Table nr. 1   The distribution of preneoplastic and neoplastic lesions in the study group

Lesion	No cases	%
Neoplastic	16	4,02
Preneoplastic	382	95,98
1. ASC	*164*	*41,20*
2. LSIL	*119*	*29,90*
3. HSIL	*99*	*24,88*

Smears among which was identified the presence of atypical squamous cells were divided according to Bethesda 2001 classification in ASCUS - 91 cases and ASCH - 73 cases.

The defining criteria for ASCUS were increased nuclear volume (2.5 - 3 times the intermediate cell nucleus), slight nuclear hypercromasia, regular nuclear shape (Fig. 1) and for ASCH - nucleus 1.5 or 2 times than those of cell metaplasia or three times higher than the intermediate cells, hypercromasia and irregular nuclear membranes.
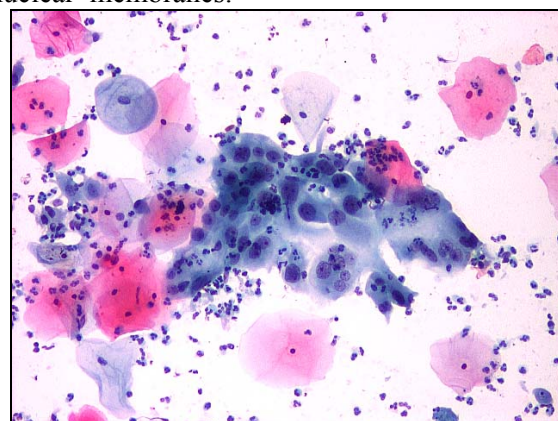

Fig. 1 - ASCUS 20X

LSIL was encountered with a higher frequency in the group of age 20-29, the values decreasing with the increase of the age.

In the smears diagnosed with LSIL (fig. 2) there were large cells with mature cytoplasm, nuclei three times bigger than those of the intermediate cells and with a ratio nucleus:cytoplasm slightly elevated, hypercromasia, bi (fig.3) and multinucleated, absent or inconspicuous nucleoli, situated in the deep 1/3 of the epithelium, the stratification of cells being kept.
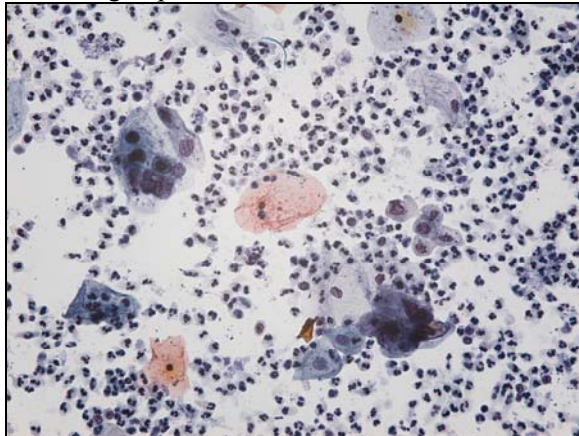

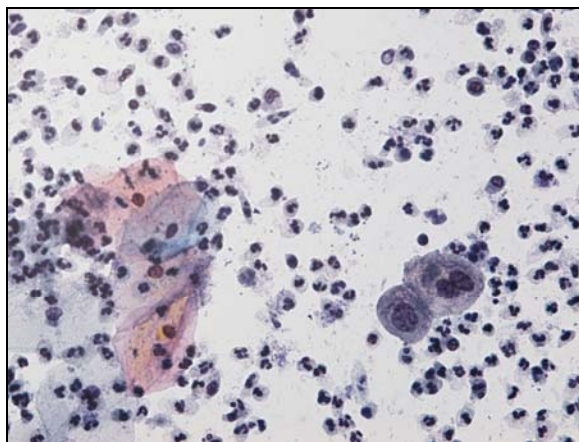*Fig.2 - LSIL – large cells, hypercromasia 40x*

Fig.3- LSIL – the presence of binucleated cells in the smear, 40x.

Koilocytes, evidence of HPV infection typical cells were identified by these aspects: tahicromatic nucleus of cells shaped like a ball, well preserved chromatin, irregular shape, with no apparent nuclear membrane, without inclusion nucleolus or body, surrounded by a clear halo and bordered on the periphery of a very dense cytoplasm. Koilocytes were arranged isolated or in groups. (Fig.4)

HSIL was observed in the presence of atypical cells - with dark nuclei, with variations in size and shape, the ratio N: C increased, micro or macrogranular chromatin, with uniform distribution, nucleus with irregular outline and nuclear membrane with numerous indentations, with variable cytoplasm -arranged isolated or aggregated in layers (Fig.5, 6).
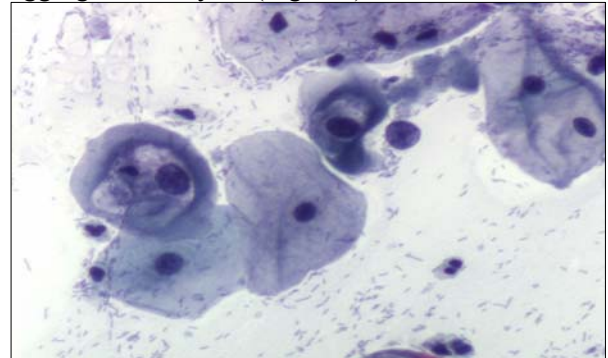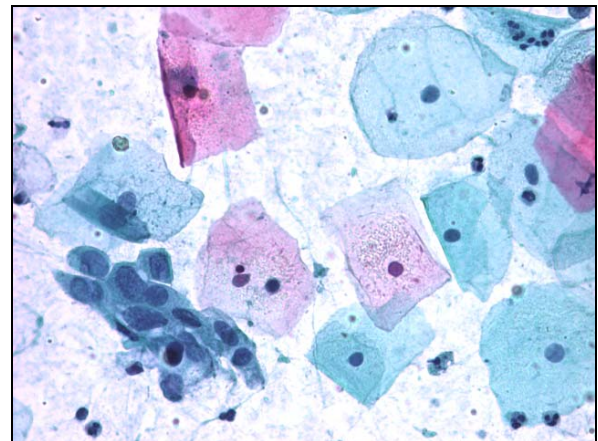

Fig.4- Koilocyte, 400x

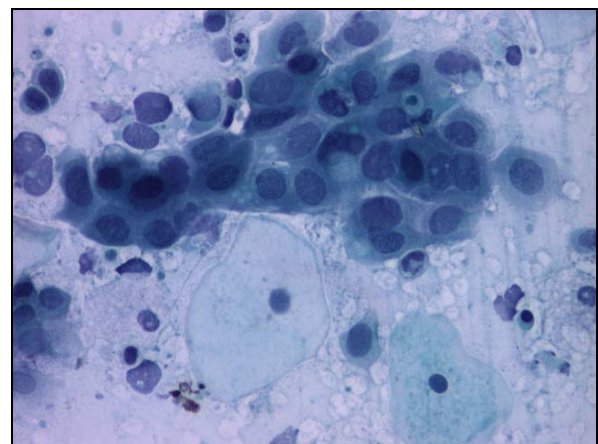*Fig.5 - HSIL- atypical cells , 200x*

Fig.6 – HSIL – atypical cells, 400x

Squamous cell carcinoma presented hypercelllar smears, the tumor cells arranged in aggregates or isolated. Cytoplasm was moderate or abundant, with irregular dark, nuclei. In all cases tumor diathesis was present: necrotic debris and red blood cells (fig.7, 8).
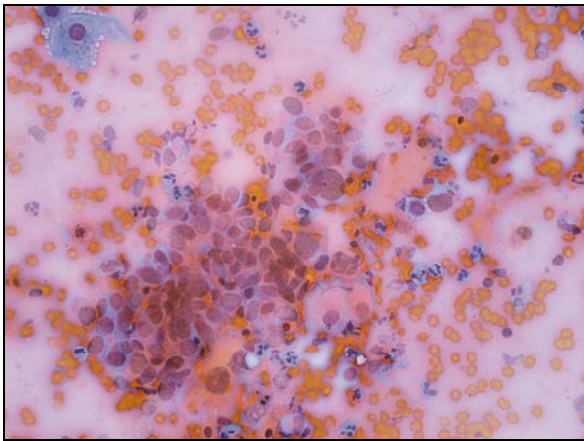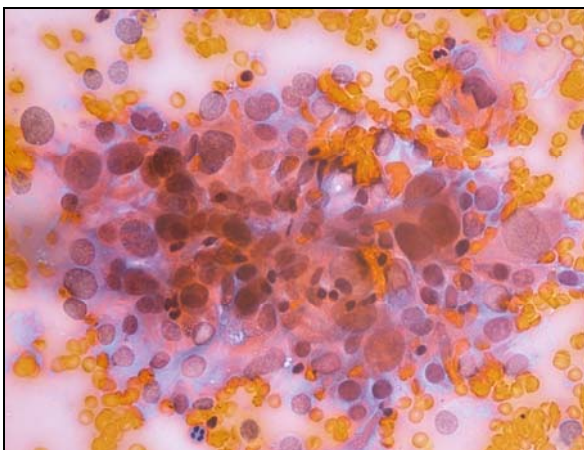
Fig. 7 - Squamous cell carcinoma, 200x

Fig.8 - Squamous cell carcinoma, 400x

In our study has been carried out a comparative analysis of cytological and histological diagnosis, thus establishing the accuracy of cytological diagnosis (Table 2).

Table no. 2 – Correlation between cytologic and histologic diagnosis

Histologic diagnosis	Cytologic diagnosis					
	ASCUS	ASCH	LSIL	HSIL	Squamous carcinoma	Total
CIN1	54	22	101	2	0	179
CIN2	23	24	11	23	0	81
CIN3	13	26	7	47	0	93
Squamous carcinoma	1	1	0	27	16	45
Total	91	73	119	99	16	398

The cytological diagnosis of cervicovaginal smear led to the following results:% 22.86 ASCUS, ASC-H 18.34%, 29.90% LSIL, 24.88% HSIL and 4.02% squamous cell carcinoma. Corresponding histopathology of these smears were represented as follows: 44.97% CIN1, CIN 2 20.35%, 22.36% CIN3 and 12.32% squamous cell carcinoma. It was not identified any false positive result for squamous cell carcinomas.

Discordances between cytological and histological examination of LSIL and HSIL lesions type were divided into two categories: overdiagnostis (CIN1 diagnosed as HSIL on cytology) - two cases and underdiagnosis (diagnosed LSIL on cytology and CIN 2, CIN3 or squamous cell carcinoma on histology) - 18 cases.

Discussions

The incidence of cervical cancer is situated initially in 20 to 29 age group and grows rapidly, reaching a peak around age 45-49 years (Parkin et al, 2001). In one study, the proportion of advanced stages of cervical squamous cell cancer was 30% in women <50 years and 52% in those ≥ 50 years (Armstrong et al, 2002). Population mobility, persistence of risk in migratory populations, higher risk in ethnic minorities, young age of onset of sexual life, higher proportion of advanced stage at diagnosis, are reasons for which cervical cancer remains a major health problem even in countries where the incidence decreased.

The youngest patient of our study was 25 years and the oldest 84 years old. Comparing data from our study with the literature, we found similar values. Thus the study of Robyr et al (2002) identified patients aged 21 and 78 years and an average of 43.7 years and that of Autier et al. (1996) patients aged between 20 and 90 years and an average of 46 years.

In the 21-30 yearsold age group of patients we found 7.46% cases. Of these 68.57% were LSIL lesion type and the majority (70.83%) for the national screening program, suggesting that young womenprofit the most of thecervical cancer screening program.

The importance of cytologic diagnosis in preneoplastic and neoplastic lesions of the cervix has its origins in the years 1927-1928 (Babes, 1928), when two studies were published on the appearance of tumor cells present in cervical and vaginal smears, the names of two researchers giving the name test currently used for screening and monitoring of these lesions posttherapeutic: Babes-Papanicolau test.

In our study the relationship between preneoplastic and neoplastic lesions identified by cytologic 23,87:1 was comparable to that of Klinkhaemer et al (1988) where the ratio was 29:1. However, we identified a wide variety of literature data regarding this report: Mostafa et al (2000) identified a lower rate of preneoplastic lesions (3,2:1) and Lozowski et al (1982) a much higher rate (62.5:1). A good diagnostic acuity is obtained by combining cytology, colposcopy and histology. Although the ideal would be to have a high concordance in terms of diagnosis between these

methods, literature sometimes presents variations. The cytohistological discrepancy may reach alarming rates, even 47% (Adad et al, 1999).

College of American Pathologists (CAP) uses the ratio ASCUS / SIL as a quality indicator of management and recommends maintaining it <2-3 (Jones et al, 2000). Although in our study this ratio cannot be regarded as a true index of quality because the group was composed exclusively of histologically confirmed cases, the ratio was 0.22 (91/398).

Liquid based smears medium were described as having lower risk compared with the conventional error by reducing unsatisfactory smears (Kirschner et al, 2006), but this comparison was not performed in our study.

Accuracy of cytological diagnosis in regard to identification of squamous carcinoma was 100%, this being seen in studies of Lozowski et al (1982) and Klinkhaemer et al (1988). Mostafa et al's study (2000) identified a low rate of diagnostic accuracy (68%). This can be attributed to the underdiagnosis or errors of interpretation.

Although cervicovaginal cytodiagnosis was and is still the subject of many studies evaluating its effectiveness, it is still a simple method, with low cost and satisfactory results, reducing mortality and morbidity associated with cervical cancer.

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