CYTO-HISTOPATHOLOGICAL CORRELATIONS IN UTERINE CERVIX PATHOLOGY

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Abstract: Clinical significant cervical lesions are often correlated with epithelial cell abnormalities on cervical smears. The histologic lesions which are found in uterine cervix can not be always established only with conventional cytology. Thus, it is very important that any cytologic abnormality be subsequently correlated with biopsy for certification of a cervical lesion. The results of cervical smears and tissue diagnoses over a five year period were reviewed, being examined the correlations between the cervico-vaginal smears and the surgical specimens. All cervical smears with their subsequent biopsies and histerectomies, between 2003-2008 were retrospectively evaluated. The patients ages were between 18 and 70 years old. The cervical cytology records were verifyied and the cytodiagnosis were compared with the correspondent histopathological diagnosis. From the 5700 cervico-vaginal smears, diagnosticated in the mentioned period of time, 3835 were „negative for intraepithelial lesion or malignancy”. The others of 1865 presented squamous and glandular lesions, and cervical carcinoma. One case, of a 20 years old girl, had a cytodiagnostic with suspicion of sarcoma, which was confirmed on biopsy and subsequent histerectomy as a cervical embrional rhabdomyosarcoma. The exfoliative cytologic cervico-vaginal test is very important in precocious diagnosis of intraepithelial cervical lesions, especially when it its correlated with histopathologic examination. The immunohistochemical and molecular testing of high-risk HPV will contribute to a better management of cervical precancerous lesions.

INTRODUCTION

The primordial function of cervical cytology is in bringing to notice epithelial abnormalities which would otherwise escape detection because of their clinical silence (Kealy, 1986). The cervico-vaginal cytologic test is now widely used both as a screening test in asymptomatic populations and in the follow-up of patients with cervical carcinomas treated by surgery or irradiation. The accuracy of predicting cervical epithelial abnormalities from surface cell samples is now fully accepted. One aspect however in the assessment of performance in cytology is the comparison of the cytodiagnosis with the ultimate tissue appearances (Kealy, 1986). Although it is not always possible to determine the exact histologic change in the cervix on the basis of the cytology smear, when a cervical abnormality is present, this is detected by cytologic examination in the majority of cases (Rosai, 2004). The great success of the cervico-vaginal cytologic test led to the conception among clinicians and large population that it can detect every case of carcinoma. It is important to realise that it is only a screening test and, thus, it will be associated with false-negative results.

MATERIALS AND METHODS

The results of cervical smears and tissue diagnoses over a five year period were reviewed, being examined the correlations between the cervico-vaginal smears and the surgical specimens. All cervical smears with their subsequent biopsies and histerectomies, between 2003-2008 were retrospectively evaluated. The patients ages were between 18 and 70 years old. The cervical cytology records were verifyied and the cytodiagnosis were compared with the correspondent histopathological diagnosis. All the cytologic specimens were conventional smears, and these were selected for the present study only among those which were „satisfactory for the result”. The smears were stained with classic Papanicolau technique and diagnosticated using Bethesda 2001 Terminology (Solomon, 2004). The biopsies and histerectomies were done to the pacients with cyrtologic diagnosis of ASCUS (atypical squamous cells of unknown significance) , AGC (atypical glandular cells), HSIL (high grade intraepithelial squamous lesion), and carcinoma (Smith, 2002). The surgical specimens were routinely fixed, paraffin-embedded and stained with Hematoxylin and Eosin. Epithelial abnormalities in tissues were graded as cervical intraepithelial neoplasia I-III (CIN I-III) and squamous intraepithelial lesions (LSIL, HSIL). The cytodiagnoses were correlated with the adequated histopathologic diagnoses.

RESULTS AND DISCUSSIONS

From the 5700 cervico-vaginal smears, diagnosticated in the mentioned period of time, 3835 (67,28%) were „NILM (negative for intraepithelial lesion or malignancy)”: 1200 (21,05%) were „within normal limits” and 2635 (46,22%) were „benign cellular changes”. The others of 1865

(32,72%) presented squamous and glandular lesions, and cervical carcinoma, as follows: 1230 (21,57%) were diagnosticated as LSIL (low grade intraepithelial squamous lesion), 408 (7,15%) as HSIL, 120 (2,10%) as ASCUS, 96 (1,68%) as AGC, and 12 (0,21%) as cervical squamous carcinoma. One case, of a 20 years old girl, had a cytodiagnostic with suspicion of sarcoma, which was confirmed on biopsy and subsequent histerectomy as a cervical embrional rhabdomyosarcoma (figures 1 and 2).

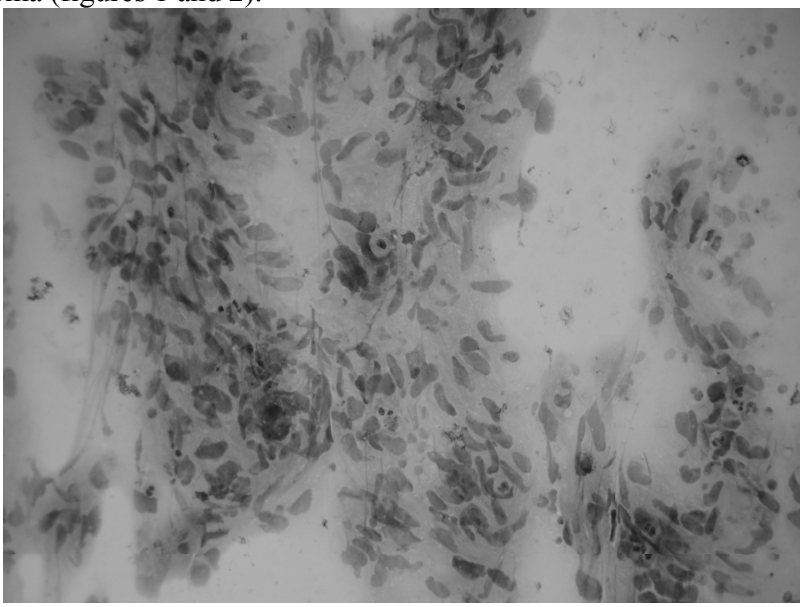

Fig. 1 - Sarcomatous stromal cells, conventional smear, Papanicolau staining x 20

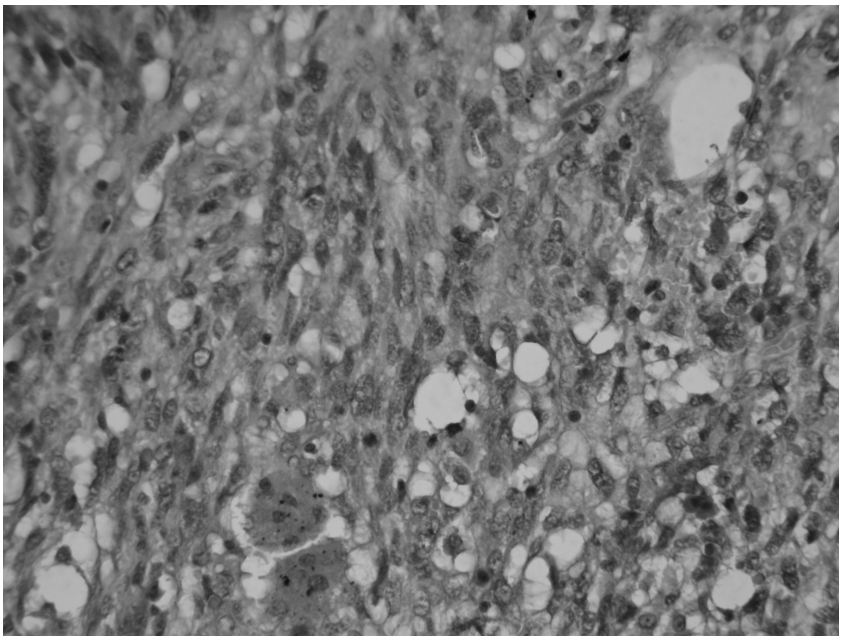

Fig. 2 – Rhabdomyosarcoma, tumoral giant cells, with pleomorphic nuclei, HE x 20

From NILM smears, 53 cases (1,38%) developed cytological cervical lesions, confirmed on subsequent biopsies, at 6 months and one year follow-up. From the 636 abnormal smears with

HSIL, ASCUS, AGC, and cervical cancer there were performed only 380 (59,74%) biopsies. A total of 340 (89,47%) cases presented a total concordance between cytodiagnostic and histopathology, and 40 (10,52%) cases presented minor diagnosis differrences. From those 216 cases with ASCUS and AGC, there were performed only 86 (39,81%) biopsies, which confirmed 54 LSIL (CIN I) (figure 3), 22 HSIL (CIN II-III/carcinoma *in situ*) (figure 4), seven endocervical polyps, two glandular-cystic hyperplasia and one in situ endocervical adenocarcinoma (AC). All of the cytologic cervical carcinomas (12 cases) were histologically confirmed. Only 34 patients had total histerectomy with bilateral adnexecomy.

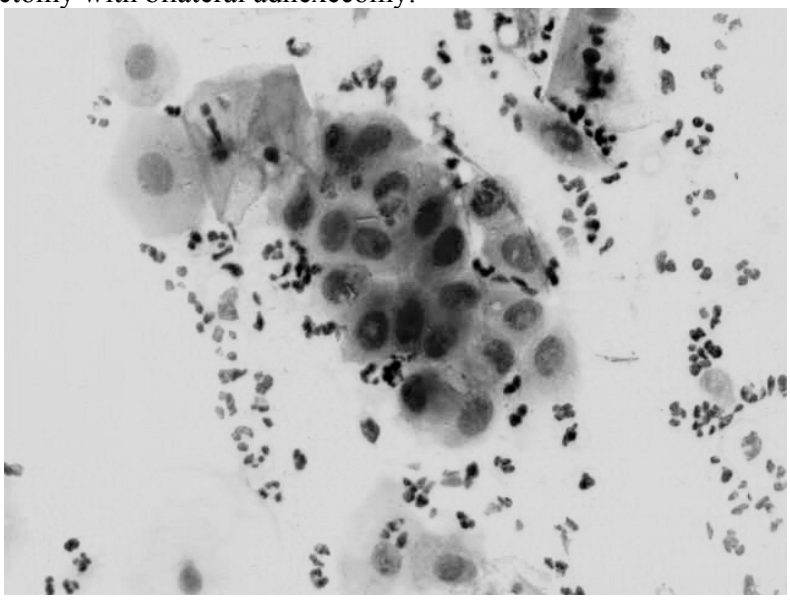

Fig. 3 – LSIL, conventional smear, Papanicolau staining x 40

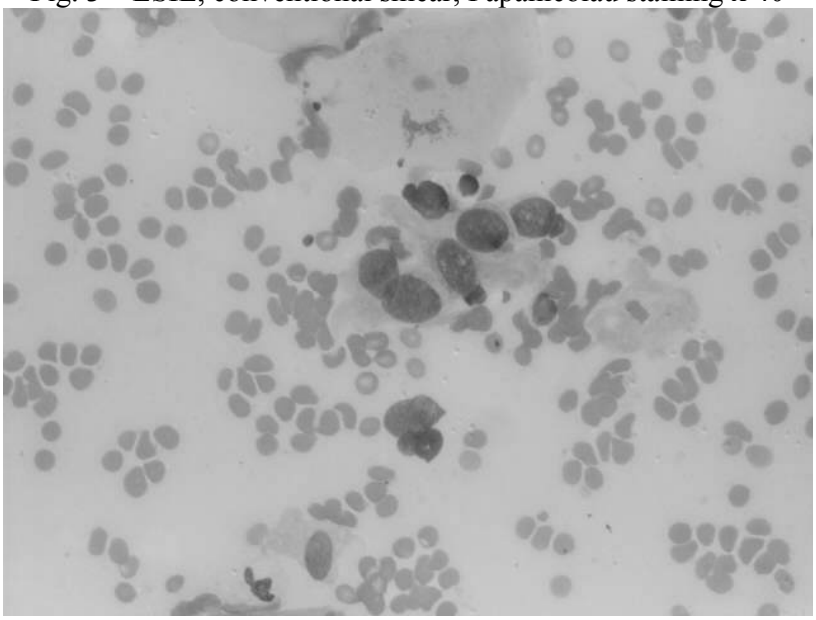

Fig. 4 – HSIL, conventional smear, Papanicolau staining x 100

The discrepancies which appeared between cytodiagnostic and histopathologic exam were due both to certain fals positive results (postmenopausal pseudokoilocytosis, absence of complete clinical data which could explain the appearance of certain cytologic modifications, like: intrauterine devices, pregnancy, hormonal substitution treatments) and certain prelevation errors of biopsies, which required the repetition of the surgical procedure (Balan, 2007; Tuganova, 2009). The non-concordance between cytodiagnostic and histopathologic exam can be due to a inadequate fixation and staining of the smears. Drying fixation smears are inadequate. Although the squamous cells can be rehydrated, these can not reproduce fine structural details (Kurman, 2002). The glandular cells are more affected by the inadequate fixation. The discrepance between cytology and biopsy can appear by performing certain superficial histologic sections, which not succeed to enter deep in the lesion. Thus, making deeper sections or turning round the paraffin block for a complete visualization of the epithelium could solve this problem (Kurman, 2002). Most cases which presented on smears cytopatic effect of human papilloma virus (HPV) infection (koilocytes) were confirmed as HPV positive on biopsy (figure 5). The non-concordances were due to pseudokoilocytosis process which appear in atrophic smears. Both the immunocytochemical and immunohistochemical investigation of HPV and molecular testing for high risk-HPV can reduce the diagnostication of advanced forms of precancerous lesions or even invasive carcinoma (Jones, 1996). The correlation between cytology and histology is useful also in verifying the laboratory internal quality and in control of histologic and cytologic processed errors. These problems can be also solved through the microscopic interpretation of smears and surgical specimens by different pathologists (Castle, 2007).

During the investigated period, there was a significant continuous increase in cytological AGC diagnoses. This was probably due to a more intensive education and training of the cytologists and a more defensive cytological practice due to a lack of reliable cytological criteria, aspects which were also described in literature (Scheiden, 2004; Soofer, 2000; Burja, 1999).

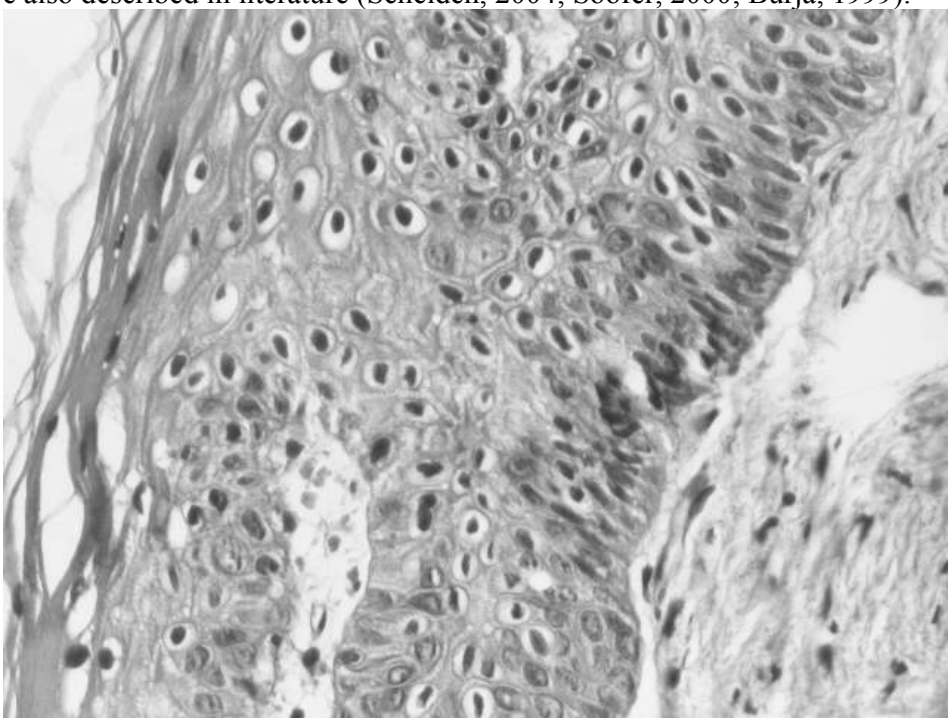

Fig. 5 – LSIL, cytopatic effect HPV, HE x 20

It is widely accepted that the cytological distinction between reactive, inflammatory, and dysplastic or neoplastic alterated squamous and/or glandular proliferations is complex and may be controversial for the cytopathologists and surgical pathologists (Solomon, 2004; Scheiden, 2004; Johnson J, 1996).

CONCLUSIONS

The cytotest (Pap test) remains a screening test and it will be inevitably associated with a rate of false negative results. The cervico-vaginal smears are very important in precocious diagnosis of cervical lesions, especially when it is correlated with histopathologic examination. Non-concordance between cytodiagnostic and histopathologic exam is sometimes due to non-observance of some cytologic and histologic processing techniques. The immunohistochemical and molecular testing of high-risk HPV will contribute to a better management of cervical precancerous lesions. Although exfoliative cytology has been proven to be an efficient technique for the detection of precancerous and cancerous squamous lesions of the cervix, it is not a speciffic test for endocervical, glandular endometrial lesions, and other types of neoplasia.

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