Evaluation of Abnormal Cervical Cytology

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Abstract

The indicated clinical evaluation of atypical squamous cells demonstrated on Papanicolaou (Pap) smear has been determined. Although several reports and opinions suggest that these cells are of no particular significances, other studies have noted these cells in instances of advanced cervical dysplasia.

The Objective of the present study was to determine the prevalence of dysplasia in106 patients with recent Pap smear demonstrating atypical squamous cell . the study was conducted during the period 1998-2002 in the Gynecologic Clinic at Hilla Hospitals and Department of Pathology, Babylon University, Babylon, IRAQ.

Abnormal colposopy was present in 59 (55%).In 21 (36%) of the 59 patients, dysplasia was confirmed histologically. Statistical significance was present in each of the groups with tissue sampling (atypical and immature squamous metaplasia, koilocytotic atypia, and dysplasia) when ages were compared with the patients having normal colposcopy. . Pap smear is a significant indicator of cervical pathology. Although this Pap smear may not be regarded as dysplasia, neither should be ignored. Colposcopy and biopsy of any abnormality is recommended in all these patients. Two distinct patterns of initial detection of cervical dysplasia were apparent.

It is concluded that the atypical squamous cell Pap smear is a significant indicator of cervical pathology. Although this atypical Pap smear may not be regarded as dysplasia, neither should be ignored. Colposcopy and biopsy of any abnormality is recommended in all these patients.

الخلاصة

التقييم العلمي للخلأيا الحرشفية الشاذّة المُظْهَر لعنق الرحم باستخدام صبغة البابنكيلو تمت دراسته، وبالرّغم من عدّة تقارير و آراء اِقْتَرحتْ أنّ هذه الخلايا لا مَعَاني خاصّة لها، ولكن فيْ دراسات أخرى وجدت مثل هذة الخلايا في حالات سوء النشأة لعنق الرحم. استهدفت الدراسة الى تحَديْدَ شيوع سوء النشأة في المُرَضى من خلال استخدام النَاظُورالنسائي و خزعات عنق الرحم وكذلك التعرف على اهمية استخدام المسحات المتكررة لعنق الرحم .

لقد تم دراسة 106 حالة مرضية لمريضات اجريت لهن الفحص الخلوي لعنق الرحم خلال الفترة 1998–2002 اظهرن شذوذ في الخلأيا الحرشفية لعنق الرحم . اظهرت نتائج الناظور (Colposcopy) شذوذاً في 59 (55%). وكان في 21 مَريضه (36%)، سوء النشأة قد تاكد باستخدام الفحص النسجي. كَانَ هناك نتائج إحصائيه معتد بها في كلّ المجاميع الخلويه المرضيه عندما قورنت مع مثيلاتها الطبيعيه من نفس المجموعه العمريه .

استنتجت الدراسة ان فحصت البابنكيلو الخلويه تعتبر مؤشر هامّ للتغيرات المرضيه لعنق الرحم. بالرّغم من ربّما قد لا تُعْتَبَرُ هذه المسحه الخلويه الغير الطبيعيه تعبير عن سوء النشأة،ولكن لا يجب على أحد أن يُتَجَاهَلهاَ . واجراء فحص الناظور والفحص ألنسجي لأيّ من الحالات التي يظهر بها شذوذ في الفحص الخلوي لعنق الرحم اجراءات يجب التوصيه بها

Introduction

The necessary clinical management of patients with atypical squamous cells detected on cervical Papanicolaou (Pap) smears is not known. The presence of these cells has been interpreted to reflect changes caused by" infection trauma and physical or chemical stimuli (1-9). The usual management in these cases has been nonspecific, with many physicians either repeating the Pap smear or regarding the report as a variant of normal.

Atypical squamous cells demonstrate certain cytologic features that are abnormal but yet fall short of the characteristics of dysplasia, i.e., cervical intraepithelial neoplasia (CIN). Published guidelines by many authors have provided excellent advice for the evaluation of Pap smears with the features of dysplasia (10-14), but there is little or no information correlating the significance of the Pap smear findings of atypical squamous cells with a simultaneous evaluation by Colposcopy and histological study of biopsied cervical tissue. This prospective study was undertaken to determine the prevalence of dysplasia in these patients through the Pap smear. An appropriate clinical management of these Pap smears was also evaluated.

Materials and Methods

All Pap smears were obtained, using the fast smear method of Frost (15), from patients examined in the Obstetric-Gynecologic Clinic at Hilla Hospitals during the period 1998-2002.

The smears were processed and screened. All abnormal cases were reviewed. At the time of microscopic evaluation of cervical biopsies, all Pap smears were available for correlation. For the purpose of this report, mild, moderate,and severe dysplasia/carcinom – in – situ (CIS) will be used interchangeably with CIN I CIN II, and

CIN III, respectively. Although somewhat subjective, atypical squamous cells are defined as cervical and/or vaginal epithelial cells demonstrating slight nuclear enlargement (average nuclear areas of 50 to 100 um2) with regular nuclear membranes and evenly dispersed, finely granular chromatin. Mildly dysplastic cells (CIN I), on the other hand have larger nuclear areas (120-200um2), are more hyperchromatic, with more variability in the coarseness and distribution of the chromatin (Fig.1&, Fig.2). Nucleoli are absent or inconspicuous in both, atypical squamous cells and CIN I cells. The total cell areas are the same for both, resulting in a higher nuclear-to-cytoplasmic ratio in the CIN I cells another distinguishing characteristic. Squamous cells demonstrating changes interpreted as secondary to repair or inflammation are not included in this classification of atypical squamous cells. Patients with atypical squamous cell Pap smears were referred to a special clinic where evaluation repeats Pap smears, identification of any inflammatory or infectious processes and colpscopy. More than one Pap smear was usually obtained. Repeat Pap smears were performed at least 30 days apart. Colposcopy was always performed and biopsies were obtained to from all abnormal areas. Patients with history of dysplasia were not referred to this clinic, In addition, if active vaginitis or other inflammatory processes were present, avoiding misleading colposcopic findings. Colposcopy and resultant – indicated biopsies were the final diagnostic procedures in the evaluation of these patients.

Results

A total of 105 patients ranging in age from 15 to 65 years with a median age of 29 years were evaluated. All patients were studied colposcopically. Normal colposcopic findings were present in 48 patients, ranging in age from 16 to 66 years with a median of 31 years. Abnormal findings were present and subsequent biopsies were performed in 59 patients (55%). In 35 of the 59 women the cervical biopsies revealed nondysplastic tissue, either koilocytotic atypia (12 patients) or immature or atypical squamous metaplasia (26 patients). The remaining 21 patients had histologically proven dysplasia. Statistical significance was present in each of the groups with tissue sampling (atypical and immature squamous metaplasia, koilocytotic atypia, and dysplasia) when ages were compared with the patients having normal Colposcopy. The distribution of ages and p values are presented in Table 1. Two distinct patterns of initial detection of cervical dysplasia were apparent. In one group (12 patients) repeat Pap smears first detected cells interpreted as dysplastic and will be referred to as cytology – detected dysplasia (Table 2). In a second group (9 patients) cervical dysplasia was not detected by repeat Pap smears but by colposcopy and biopsy and will be referred to as biopsy – detected dysplasia. The repeat Pap smears in the biopsy-detected dysplasia group are shown in (Table 3). 5 of these 9 patients had atypical squamous cells on at least some of their subsequent Pap smears, whereas the remaining 3 patients had only normal smears. Review of the degree of cervical dysplasia associated with the atypical squamous cell Pap smear for both groups of patients is summarized in (Table 4). Remarkably, 15(70%) of the 21 total patients had CIN II or CIN III histological lesions.

Table 1. Demographic characteristics of patients having atypical squamous cell Papanicolaou smears and abnormal Colposcopy with directed cervical biopsies.

Tissue report	Age range (years)	Median	P[a]	No. of patients
Immature and atypical				
Squamous metaplasia	16-50	31	<0.02	26
Koilocytotic atypia	15-51	25	<0.001	12
Dysplasia	17-48	27	<0.001	21

[a]p value is determined by comparison to patients with normal Colposcopy.

Table 2 Cytology – detected cervical dysplasia

Initial detection of dysplastic cells on repeat Papanicolaou smear	No. of patients
1st Pap smear	6
2nd Pap smear	3
3srd Pap smear	2
≥4th Pap smear	1
Total	12

Table 3. Results of Papanicolaou smear report in biopsy – detected dysplasia group (9 patients)

	Number of repeat Pap smears				
Pap smear report	One	Two	Three	Four	Total Patients
Normal reports only	1	2	1	0	4
Persistent atypical squamous					
Cell reports	2	0	0	0	2
Both	-	1	1	1	3

[a]Both atypical squamous cell reports and normal reports revived received on various Pap smears performed at separate times.

Table 4 Histologically confirmed dysplasia of the cervix in 21 patients

Method of detection	Mild dysplasia (CIN I)	Moderate dysplasia (CIN II)	Severe dysplasia (CIN III)
Cytology-detected group	2	6	4
Biopsy-detected	4	4	1

CIN, cervical intraepithelial neoplasia.

Discussion

The goal of cervical screening by Pap smear is the detection and subsequent treatment of dysplasia, thereby decreasing the chance of the development of invasive carcinoma. Although effective protocols exist for the evaluation of dysplastic cells detected on Pap smear, the management of the

patient with an atypical Squamous cell Pap smear is not well understood. These cells are not normal, yet most pathologists would not classify them as dysplastic16. How aggressive one should be when these cells are detected can only be detailed after an evaluation of the relationship of this cell type to cervical pathology. Some authors (9,17) encourage a practice of no investigation of these Pap smears, and others have found significant pathology associated with atypical squamous cell Pap smear reports (12,18-23). Some have relied on repeat cytology to diagnose the status of patients (19.21,22). Studies that rely only on cytologic follow-up of patients may potentially miss many abnormalities due to the well- documented false-negative rate of cervical cytology of 12-40% (23-29). Other factors such as patient compliance could also affect the efficacy of only repeating the cytology. Benedet et al. detected dysplasia in 68% of the patients (30). Although our survey does not document as high a dysplasia occurrence in these patients, one must conclude that a significant potential is present. Nyirjesy recommended histologic sampling only after a repeat Pap smear demonstrated atypical squamous cells, despite a 3.5 and 25% respective incidence of invasive cancer and CIS (19). Sandmire et al. reported the same conclusion despite similar serious histologic findings (21).

As can be seen in Table 2 and 3 the first repeat Pap smear failed to detect dysplastic cells in a substantial number, of patients. Although the first repeat Pap

smear did detect dysplasia in 6 patients, the remaining 15 dysplasia patients went undetected. Additionally, in those patients with documented dysplasia many had two or more Pap smears that failed to identify dysplastic cells. From the biopsy-detected dysplasia group, 3 dysplasia-proven patients demonstrated two or more normal repeat Pap smears, and 3 had an admixture of atypical squamous cell and normal Pap smear report (Table 4). In total, 12 patients with biopsy confirmed dysplasia did not have dysplastic cells identified on two or more repeat Pap smears (Table 2 and 3). Thus, data from the present study underscore the potential for significant cervical pathology in presents with atypical squamous cells detected on Pap smear. To have adopted a policy of just repeating the Pap smear and evaluating only dysplastic reports in these 105 patients could have potentially resulted in the evaluation of only those 6 patients whose first repeat Pap smear demonstrated dysplasia.

Those patients having tissue-proven dysplasia, Koilocytotic atypia, and immature or atypical squamous metaplasia were younger in age than those patients with normal Colposcopy. The comparison in ages reached statistical significance in all instances (Table 1). These data indicate that colposcopy can be expected more often to be normal in the older patient, but due to the frequent instances of similar ages in normal and abnormal coloposcopy patients.

In conclusion, the atypical squamous cell Pap smear is a significant indicator of cervical pathology. Although this Pap smear may not be regarded as dysplasia, neither should be ignored. Colposcopy and biopsy of any abnormality is recommended in all these patients. We feel this management is reasonable and practical considering the relationship of this cell type to dysplasia and the documented ineffectiveness of evaluating abnormal Pap smears by repeat Pap smear.

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Fig.1. A Pap smear. The dysplastic cells arrowed, overall with darker, more irregular nuclei.

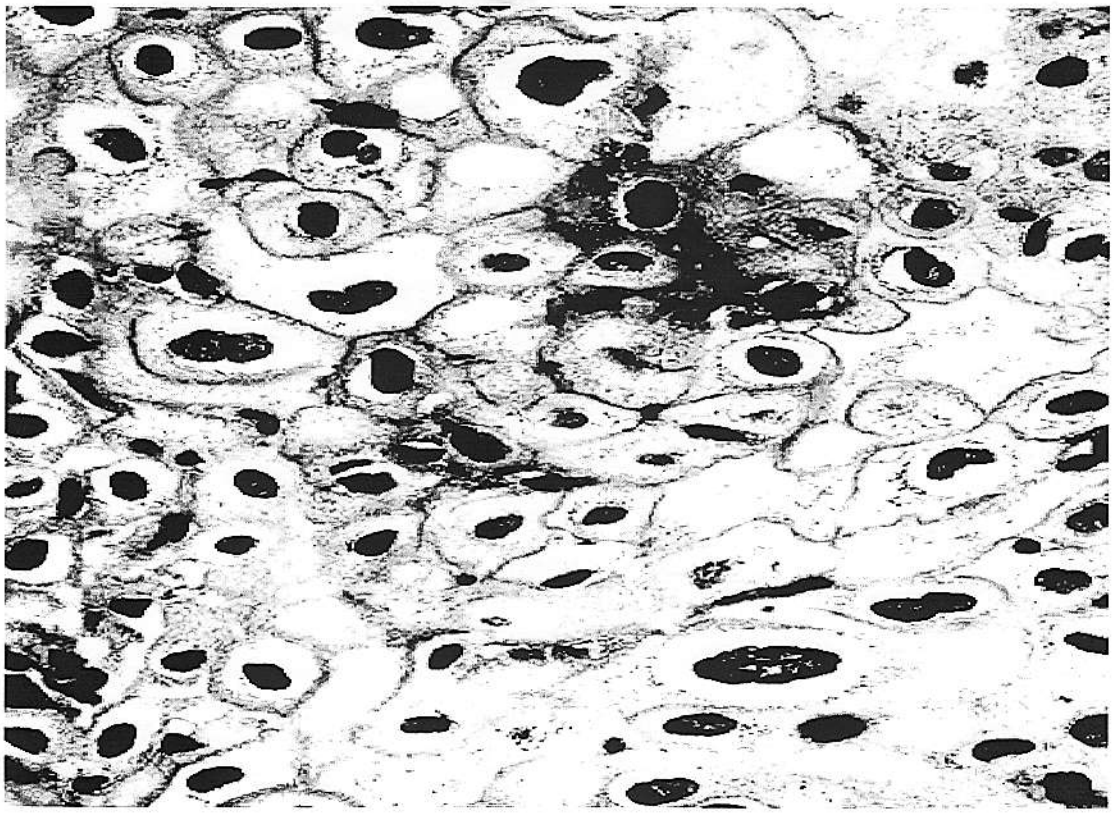

Fig. 2. Histological section of cervical dysplasia (H&E×40).