IJPRP

Original Research Article

A Study of Histopathological Correlation with Diagnostic Finding of Cytological Smear Evaluated Within the Criteria of TBS

Shweta Goyal

Consultant Pathologist, Department of Pathology, Jindal Super Speciality Hospital, Bharatpur, Rajasthan 321001, India.

Abstract

Corresponding Author:

Shweta Goyal, Consultant Pathologist, Department of Pathology, Jindal Super Speciality Hospital, Bharatpur, Rajasthan 321001, India.
E-mail:
rajendragoyal30061981@gmail.com

The cervical Pap smear is one of the most successful screening tests utilized in medicine. Since its introduction in the 1950s, the cervical cancer rate in the United States has fallen dramatically. While cervical cancer is still the most common malignancy in women in developing countries, in the United States and other developed countries, it is much less common. In all patients cervico-vaginal smear will be made by means of Ayers – spatula and cotton swab stick. The smears will immediately fixed in 95% alcohol for 30 minutes and then will stained by Papanicolaou method. In this study Colposcopy and cervical biopsy was taken by Gynaecologist. Cytohistological correlation was done by Pathologist in these cases. Among 3 cases of ASC-H 1 showed CIN I could be confirmed as invasive carcinoma 1 (33.33%). However, 1 (33.33%) showed benign changes on histology. There were 8 cases of LSIL by cytology, while diagnosis would be histologically confirmed in 4 (50 %) cases. it show CINII in 1 (12.5%) cases and confirmed as invasive carcinoma in 3 (37.5%) of cases. The remaining 4 (50%) cases were histologically benign.

Keywords: TBS; Histopathology; Cervix.

Introduction

There are often no symptoms with early stages of cervical cancer. Therefore, beginning at age 18 (or when first sexually active), women should receive annual Pap smears to detect pre-cancerous or cancerous cervical cells. The following symptoms may be associated with cervical cancer and should be reported to a physician for further investigation. However, these symptoms can indicate a number of conditions other than cervical cancer.

Symptoms that may be associated with cervical cancer include:Unusual vaginal discharge (include spot/light bleeding between menstrual periods), Pain during sexual intercourse, Bleeding after sexual intercourse [1].

Since the 1950s when the was introduced, a plethora of terms has been used to describe these cytologic exams, some of them dubious or redundant. To quell the ensuing diagnostic chaos and improve patient care, the Bethesda System of cervical-vaginal nomenclature was developed to standardize and define these terms and diagnostic descriptions. Dr. Henry reports on the results of this now widely used system.

The cervical Pap smear is one of the most successful screening tests utilized in medicine. Since its introduction in the 1950s, the rate in the United States has fallen dramatically. While cervical cancer is still the most common malignancy in women in developing countries, in the United States and other developed countries, it is much less common. For example, in the United States only about 15,000 new cases of cervical cancer are diagnosed each year, most often in poor and elderly women who lack access to screening programs. Indeed, a recent consensus conference sponsored by the National Institutes of Health concluded that virtually all of the deaths caused by cervical squamous cell carcinoma could be prevented by a program of routine cervical Pap smears and education of the female population. For the Pap smear to be effective in cancer screening, however, three things must occur.

First, an adequate specimen must be obtained from the patient and submitted to the laboratory. Second, the specimen must be properly prepared, screened, and interpreted. Third, it is imperative that when communicating the diagnosis, laboratorians use terminology that is understood clearly by the clinician. In the laboratory, diagnostic terminology is used both as a framework for communication with clinicians and as the basis for education and research. At times, these dual purposes conflict. While analysis of subtle morphologic differences and creation of multiple subgroupings of lesions may be important in a research or educational setting, only those diagnostic categories with clinical relevance are important when communicating laboratory results to the clinician [2].

The diagnostic terminology applied to cervical smears has evolved since its inception in the early 1950s. The original Papanicolaou system consisted of a numeric system of five classes (1 to V) designed to convey the degree of atypical changes present [3].

As time passed, however, laboratories created their own idiosyncratic versions of the Pap classes, some including complex subgroupings such as Class III A1, III A2, III B, etc. In addition, as the morphologic correlates of benign, infectious and/or reactive processes were described, the designation "Class II" proved inadequate to accommodate the diversity of these lesions.

As gynecologic cytology gained credibility and expanded as a diagnostic field, additional diagnostic schemes and sets of terminology were developed to provide more meaningful diagnostic information. Dysplasia was a term promulgated by Dr. James Reagan to designate lesions that were less than cancerous. Soon pathologists began to use mild, moderate, and severe dysplasia and carcinoma in situ Cervical intraepithelial neoplasia. [4]

In 1968, Richart introduced the term cervical intraepithelial neoplasia with subcategories for grades 1, 2, and 3, to identify the degree of abnormality or disease in cervical biopsies and promote the concept of a continuum of precursors leading to invasive cancer (see illustration, "Multiple nomenclatures"). The CIN classification became widely adopted in histopathology, and many laboratories began to use the terms in gynecologic cytology as well. Mild dysplasia roughly corresponds to CIN 1, and moderate dysplasia roughly corresponds to CIN 2. However, CIN 3 encompasses both severe dysplasia as well as carcinoma in situ, thus eliminating this difficult and sometimes arbitrary cytologic distinction between these two similar terms. Richart actually considered the various grades of CIN irrelevant when determining clinical management. Rather, he emphasized that once invasion is ruled out, the size and distribution of preneoplastic lesions are far more important factors in determining clinical management of patients than a pathologic grade for CIN [5].

Koilocytic changes are defined as perinuclear clearing of the cytoplasm with a well circumscribed margin and peripheral cytoplasmic condensation. Koilocytic changes in squamous cells were originally recognized by numerous cytologists including Papanicolaou, and were considered to be part of the spectrum of "atypical" or precancerous lesions but were not indicative of a distinct clinical entity. There are also associated changes in the cell nucleus, such as enlargement, smudging of the cell's chromatin, as well as binucleation and membrane wrinkling. Koilocytic atypia was a term for these changes first proposed by Koss and Durfee. Meisels and Fortin were the first to recognize koilocytic changes as a manifestation of genital human papilloma virus (HPV) infection. This association between HPV and koilocytic atypia led to the creation of a separate diagnostic category of HPV cytopathic changes or condyloma, which was considered to be less serious than true dysplasia. When koilocytic changes were seen in association with dysplasia, it was thought that the underlying HPV change should be morphologically distinguished

and reported separately. This led to even more complexity in diagnostic terminology as various terms for HPV effect were used in conjunction with dysplasia, CIN, or the Papanicolaou classification [6].

As various techniques for identifying papilloma virus have become more sensitive, viral DNA has been found in the vast majority of cervical neoplasias studied. Human papilloma virus is now considered to be a key link in the pathogenesis of the entire continuum of squamous precursors and cervical cancer. Scores of subtypes of the virus have been identified and categorized as low-risk or high-risk types. So-called "HPV only" or "condyloma" lesions, as a group, contain both the low-risk and high-risk forms of the virus. This same heterogeneity of viral types is also found in mild dysplasia and CIN 1 lesions (see illustration, "Multiple nomenclatures". Therefore, isolation of koilocyticatypia or "HPV effect" as a separate entity from dysplasia/CIN is probably no longer biologically valid [7].

Despite the well-known deficiencies of the original Papanicolaou classification scheme, in the late 1980s most laboratories continued to include a numerical class designation in the laboratory report. While many of these same laboratories used descriptive diagnostic terminology, such as varying degrees of dysplasia or CIN in conjunction with the Papanicolaou classification, often the class number took precedence and dictated clinical management of the patient.

Methodology

In all patients cervico-vaginal smear will be made by means of Ayers–spatula and cotton swab stick. The smears will immediately fixed in 95% alcohol for 30 minutes and then will stained by Papanicolaou method. In this study Colposcopy and cervical biopsy was taken by Gynaecologist. Cytohistological correlation was done by Pathologist in these cases.

Requirements

1. Cusco 's self retaining speculum
2. 2- Ayre's spatula/cytobrush/cotton swab stick
3. Fixative 95 %ethanol in coplin jar
4. Glass slides

Method of Collection and Preparing Smear

Patients was advised to avoid coitus ,vaginal douche or any other local medication 48 hrs prior to sample collection. Examination should be done in lithotomy position. Place the cusco 's self retaining speculum, without any lubricant and prior to per vaginum examination, to visualize vagina and cervix for any abnormality then put endocervical brush placed inside endocervix and rolled firmly Then Ayer's spatula will be placed against cervix with its longer limb within the endocervical canal And firmly rotated 360 degree to scrape the entire transformation zone, sample obtained will immediately smeared on glass slides and wet fixed.

General rules in obtained smear

1. Bottle of fixative should kept open and readily accessible before the smear was obtained. Cells dry rapidly the moment they are spread out on slide ,the slide must be immediately dropped into the fixative while the smear is still wet.
2. The fixative fluid most commonly will be used is mixure of equal parts of ether and 95% ethyl alcohol but other alcohols such as formyl alcohol, 95% ethyl alcohol alone or a combination of three parts of tertiary butyl alcohol and I part of 95% ethyl alcohol are also good.
3. While introducing the speculum lubricants should not used.
4. Smear should obtain from te patients who had no internal examination or douching during past 24 hours.
5. Care should be taken to spread the material evenly on the slides ,so that a uniformly thin smear was obtained.
6. The smear will be prepared in such a way to avoid contamination of cells from the skin of the patient or examiner.
7. Slides shoulde be kept in fixative at least for 20-30 minutes . After that they should remove and stain immediately.

Results

Out of 25 cases diagnosed cytologically as NILM, the histology (benign) matched cytological diagnosis in 20 (80%) cases. In others 3 (12%) were CIN I, 1 (4%) were CIN II, 1 (4%) were CIN III by histology.

Shweta Goyal / A Study of Histopathological Correlation with Diagnostic Finding of
Cytological Smear Evaluated Within the Criteria of TBS
875

There were 6 cases of ASCUS out of which 4 (66.7%) confirmed to be benign by histology. Among the remaining CIN I and CIN II was seen histologically in 1 (16.7%) case each.

Among 3 cases of ASC-H 1 showed CIN I could be confirmed as invasive carcinoma 1 (33.33%). However 1 (33.33%) showed benign changes on histology. There were 8 cases of LSIL by cytology, while diagnosis would be histologically confirmed in 4 (50%) cases. it show CINII in 1 (12.5%) cases and confirmed as invasive carcinoma in 3 (37.5%) of cases. The remaining 4 (50%) cases were histologically benign.

In all 8 cases of HSIL, 4 (50%) cases were invasive, 1 (12.5%) were CIN III and 1 (12.5%) cases were CIN

Table 1: Correlation between cervical cytology and Histopathological findings

PAP	Chronic cervicitis	CIN Grade I	CIN Grade II	CIN Grade III	SCC	Total
NILM	20	3	1	1	0	25
	80.0%	12.0%	4.0%	4.0%	.0%	100.0%
ASC-US	4	1	1	0	0	6
	66.7%	16.7%	16.7%	.0%	.0%	100.0%
ASC-H	1	1	0	0	1	3
	33.3%	33.3%	.0%	.0%	33.3%	100.0%
LSIL	4	0	1	0	3	8
	50.0%	.0%	12.5%	.0%	37.5%	100.0%
HSIL	2	1	0	1	4	8
	25.0%	12.5%	.0%	12.5%	50.0%	100.0%
SCC	0	0	0	0	5	5
	.0%	.0%	.0%	.0%	100.0%	100.0%
Total	31	6	3	2	13	55
	56.4%	10.9%	5.5%	3.6%	23.6%	100.0%

Table 2: Correlation between cytological and hitopathological finding

Cytological report	Histopathological finding		
	Positive	Negative	Total
Positive	19	11	30
	79.2%	35.5%	10.6%
Negative	5	20	25
	20.8%	64.5%	8.9%
Total	24	31	282
	100.0%	100.0%	100.0%

I on histology. However 2 turned out to be benign by histology.

Lastly all 5 cases of squamous cell carcinoma were confirmed histologically.

Discussion

Our results indicate a moderate degree of agreement between cytolgic abnormalities reported using the Bethesda System for cervicovaginal diagnosis and underlying cervical lesions. We

could not identify a trend towards over estimation or underestimation of disease by cytology.

The proportion of women with negative biopsy results falls with increasing grades of abnormality in cytological smear. From 66.7% among women with ASC-US to 25% after HSIL and nil after a malignant smear.The risk of cancer in almost certain (100%) among those with malignant smears, 44.4% among women with HSIL and 33.3% among women with ASC-H.

Significantly risk of cancer was low with LSIL and also chances of negative results on biopsy were high (50%). Thus cytologic diagnosis of LSIL has poor histologic correlation. The overall rate of cytolgic–histologic discrepancies in our study was 24%. Jones et al. (1996) in study of 22,439 cyto-histo correlation in 348 laboratories reported 16.5% discrepancies [8].

Viewing the cervicovaginal cytology as a screening test with the primary purpose to identify patients requiring further attention overall sensitivity, specificity and predictive value of a positive cytology were determined. The overall sensitivity of cytologic diagnosis was 79.2% with specificity of 64.5%, positive predictive value of 63.3% and negative predictive value 80%. There was substantial variation in the positive predictive value depending on the specific cytologic diagnosis. Of the positive cytologic diagnosis categories the positive biopsy yield varied from 50% in LSIL, 75% in HSIL and 100% in invasive squamous cell carcinoma.

Soost et al. using a large database of cytologic screening of 277,842 women over a period of 10 year found an overall sensitivity 80% and specificity of 99.4% [9]. The AHCPR report has also demonstrated that conventional smears have a sensitivity of 51% and better specificity of 98% [10]. Massad et al in a study of biopsy correlates of abnormal cervical cytology found a statistically significant but weak agreement between cytologic abnormalities reported using the Bethesda system and histology. They observed an overall sensitivity of 42% and specificity of 83% [11].

Table 3: Percentage of Sensitivity, Specificity and Positive Predictive Value

Author	Sensitivity	Specificity	PPV
Soosts et al [9]	80%	99.4%	73%
The AHCPR report [10]	51%	98%	-
Jones et al [8]	61.5%	92%	88.9%
Massad et al [11]	42%	83%	85%
Present Study	79.2%	64.5%	63.3%

It has been shown that the sensitivity of the Pap test is lower. The accuracy of conventional cytology is increased when the goal in detection of higher grade lesions. Higher disease prevalence is also associated with greater sensitivity induced specificity.

The positive predictive value in Soost et al study was 73%. The PPV in this study range from 79% for initial cytologic diagnosis of CIN I to 100% for squamous cell carcinoma. The PPV ranged from 74.1% for histologic diagnosis of LSIL, 77.7% for HSIL and 100% for squamous cell carcinoma, similar findings have been reported in DiBonito study and Soost et al. who found PPV of 73% for mild to moderate dysplasia and 96% for squamous cell carcinoma.

The most common finding on P/V examination was erosion (30.5%) out of which majority (86%) showed NILM on cytology. In 23.4% cases cervicitis was observed and again 83.3% of these showed NILM on cytology. 60% of all cases clinically suspicious for malignancy proved to be SCC on cytology.

Conclusion

Histology co-related with cytology in 55 cases having various grades of SIL and invasive carcinoma. Hundred percent correlation was found in invasive carcinoma, while there is lack of correlation of milder grade of atypia i.e. LSIL and HSIL. 5 cases were diagnosed as false negative. The most common cause of false negative was sample failure where there were no abnormal cells on the slide. This could have been due to non-optimal preparation or non optimal collection.

False positivity was noted in 11 different cytologically diagnosd intraepithelial lesions. Cervicovaginal smears having atypical metaplastic cells and atrophic smears were the frequent cause of false positivity. 15-The sensitivity of Pap smear in detecting squamous intraepithelial lesions and invasive carcinoma of cervix was found to be 79.2%, specificity was 64.5%, positive predictive value was 63.3% and negative predictive value was 80%.

References

1. The 1988 Bethesda System for reporting cervical/vaginal cytological diagnoses. National Cancer Institute Workshop. JAMA. 1989;262:931–4.

2. Broder S. From the National Institutes of Health. Rapid Communication—The Bethesda System for Reporting Cervical/Vaginal Cytologic Diagnoses—Report of the 1991 Bethesda Workshop. JAMA. 1992;267:1892

3. Campion MJ, McCance DJ, Cuzick J, Singer A. Progressive potential of mild cervical atypia: Prospective cytological, colposcopic, and virological study.Lancet. 1986;2:237-40.

4. Lachman MF, Cavallo-Calvanese C. Qualification of atypical squamous cells of undetermined significance in an independent laboratory: is it useful or significant?. Am J Obstet Gynecol. 1998;179:421–9.

5. Kinney WK, Manos M, Hurley LB, Ransley JE. Where's the high-grade cervical neoplasia? The importance of minimally abnormal Papanicolaou diagnoses. Obstet Gynecol. 1998;91(6):973-76.

6. Smith AE, Sherman ME, Scott DR, Tabbara SO, Dworkin L, Olson J, et al. Review of the Bethesda System atlas does not improve reproducibility or accuracy in the classification of atypical squamous cells of undetermined significance smears. Cancer. 2000;90:201–6.

7. Stoler MH, Schiffman M, Atypical Squamous Cells of Undetermined Significance–Low-grade Squamous Intraepithelial Lesion Triage Study (ALTS) Group. Interobserver reproducibility of cervical cytologic and histologic interpretations: realistic estimates for the ASCUS-LSIL Triage Study. JAMA. 2001;285:1500–5.

8. Jones BA, Novis DA. Cervical biopsy-cytology correlation. A College of American Pathologists Q-Probes study or 22,439 correlations in 348 laboratories. Arch Pathol Lab Med. 1996;120:523–31.

9. Soost HJ, Lange HJ, Lehmacher W. The validation of cervical cytologic screening. ActaCytol 1987;31:434-38.

10. Agency for Healthcare Policy and Research: Evidence Report / Technology Assessment, Number S. Evaluation of Cervical Cytology. Maryhand, AHCPR Publication No. 99-E010, February 1999.

11. Massad LS; Collins YC; Meyer PM. Biopsy correlates of abnormal cervical cytology classified using the Bethesda system. Gynecologic Oncology. 2001 Sep;82(3):516-22.