COLPOSCOPIC DIAGNOSIS OF CERVICAL NEOPLASIA

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SYNOPSIS

Colposcopy was performed in 326 patients mainly for abnormal cervical smears. In 85% of patients, colposcopic examination was satisfactory. There was a correlation between the colposcopic diagnosis and histology of directed biopsy specimen in 88.1%, directed biopsy histology was less advanced than expected from colposcopy in 4.9% and more advanced in 7.0%. In 86.7% of 98 patients, there was acceptable correlation between the histology of directed biopsy and that of cone biopsy or hysterectomy specimen. In 5.1% the cone biopsy or hysterectomy specimen histology was significantly more advanced and in 8.2% less advanced than directed biopsy. All patients with abnormal cervical smears should have colposcopic assessment to reduce the rate of diagnostic cone biopsies, which was only 8.9% in our study; colposcopy also helps to plan treatment of cervical intraepithelial neoplasia. Colposcopic expertise will allow the adoption of conservative methods of treating cervical intraepithelial neoplasia.

INTRODUCTION

Cervical cytology is an accepted method of screening for cervical cancer but involves a laboratory method of diagnosis, whereas colposcopy is a clinical method of diagnosis. The two methods are not competitive but complementary in the diagnosis and management of cervical neoplasia. In the presence of an abnormal cytological smear, a tissue diagnosis is essential before proceeding with definitive treatment. Colposcopy is used in the evaluation and management of patients with abnormal cytological smears (1). With its use diagnostic cone biopsies can be reduced by 80-90% and there has been a trend towards more conservative treatment of cervical intraepithelial neoplasia (CIN) (2) and even of preclinical invasive cancer of the cervix (3). The conservative methods of treatment depend on a satisfactory colposcopic examination by an expert colposcopist and the accuracy of colposcopically directed biopsies.

We report our experience over a 3 year period with colposcopy in the evaluation of patients with abnormal cytological smears and the accuracy of colposcopy and directed biopsies in the diagnosis of cervical neoplasia.

PATIENTS AND METHODS

From early 1979 to early 1982, colposcopy was performed in 326 who were referred mainly for cervical smears which were doubtful, suspicious or positive. A few others, were referred for a clinically suspicious appearing cervix or for evaluation following cone biopsy or hysterectomy for CIN.

Colposcopy was performed using a Zeiss colposcope on an outpatient basis and, the clinical methods and criteria recommended by Coppleson et al (4) and Kolstad and Stafl (5) were used. The colposcopic features were studied to form a colposcopic impression, which was used to predict the histopathology of the directed biopsies. When the colposcopic features were uncertain, the term indeterminate colposcopic impression was used. Small colposcopically directed biopsies with a Teischler punch biopsy forceps were taken from the most advanced part of any lesion. When the whole transformation zone (TZ) was visualized the examination was considered satisfactory and when the entire TZ could not be seen colposcopy was unsatisfactory. The directed biopsies were processed using routine histological methods.

When the directed biopsy histology was mild or moderate dysplasia, the patients were either followed up or treated with cryosurgery or electrodiathermy. When colposcopy was satisfactory and directed biopsy showed severe dysplasia or carcinoma-in-situ, a cone biopsy was performed for treatment. Diagnostic cone biopsies were done when the smear was Class III or more abnormal and colposcopy was unsatisfactory, when there was significant discrepancy between cytology, colposcopy and directed biopsy histology and in cases showing microinvasion in the directed biopsy.

RESULTS

The patients ages ranged from 16 to 70 years and the mean age was 36 years. The parity of the patients ranged from 0 to 8 with a mean parity of 3.

A total of 326 patients had colposcopy performed. The indications for colposcopy were: doubtful (Class IIR) smear 170, suspicious (Class III) 92 and positive (Class IV and V) in 25. In 39 others, the indications were a clinically suspicious appearing cervix in 17, evaluation following cone biopsy or hysterectomy for CIN in 6 and 1 respectively, and in 15 for a variety of other reasons. such as assessment prior to cryosurgery of the cervix or post-coital bleeding.

Colposcopy was deemed to be satisfactory in 85% (277/326) and unsatisfactory in 15% (49/326). Of the 326 patients, in 79 no directed biopsy was obtained; in 4 others, directed biopsy had been done but the colposcopic impression was indeterminate. In the remaining 243 patients, the colposcopic impression could be correlated with the histology of the directed biopsy (Table 1). The cases in the central lined zone of Table 1, indicate those in whom correlation was clinically accurate (within one histologic degree of neoplasia). The patients in the right zone, represent those in whom the histology of directed biopsy was more advanced than expected from colposcopic impression. Similarly, the cases in the left zone represent patients in whom the histology was less advanced than expected from colposcopic impression.

The correlation between colposcopic impression and histologic diagnosis of the directed biopsy was clinically accurate in 88.1% (214/243) of patients. Histology was less advanced than expected from colposcopic impression in 4.9% (12/243) and more advanced than expected in 7.0% (17/243). The details of cases that fell outside the central zone are given in footnote to Table 1.

There were 89 patients in whom cone biopsies were done; in 60 colposcopy was satisfactory and directed biopsy histology severe dysplasia/carcinoma-in-situ, and cone biopsy was done for treatment of CIN. Twenty-nine cone biopsies were diagnostic; colposcopy was unsatisfactory in 20, there was microinvasion in directed biopsy in 3, invasion suspected at colposcopy was not confirmed by directed biopsy in 3 and there was significant discrepancy between cytology, colposcopy and directed biopsy histology in 3 cases. The rate of diagnostic cone biopsy was therefore, 8.9% (29/326). There were 31 patients who had hysterectomy done; 21 were simple hysterectomies of which in 2 a cuff of vagina was removed and 10 had radical hysterectomies with pelvic lymphadenectomies for invasive cervical cancer.

The correlation between the histologic diagnosis of the directed biopsy and that of the definitive (cone or hysterectomy) specimen is shown in Table 2. Of the 326 patients, in 67 no tissue was obtained for histopathologic diagnosis; in 12 patients a cone or hysterectomy was performed without a directed biopsy and 149 had only directed biopsy without a definitive surgical specimen available for histology. This left 98 patients, in whom both histology of directed biopsy and of the definitive surgical specimen were available for comparison. There was acceptable correlation between the two biopsies (within one histologic degree) in 86.7% (85/98). In 5.1% (5/98) of patients the definitive specimen histologic diagnosis was more advanced by greater than one histologic degree; in 3 it was carcinoma-in-situ and in 2, invasive cancer. In 8.2% (8/98) of patients, the definitive specimen histologic diagnosis was less advanced than of the directed biopsy. The details of cases with histology of the definitive specimen significantly different from that of directed biopsy are given in footnote to Table 2.

Of the 326 patients who had colposcopy, 259 (79%) had tissue for histopathologic evaluation. The most advanced histologic findings in the directed biopsy, cone or hysterectomy specimen are shown in Table 3.

DISCUSSION

The accuracy of colposcopy in the clinical diagnosis of cervical neoplasia is limited by the clinical skill and expertise of the colposcopist, the ability to visualise the entire transformation zone and accurate identification of the most advanced area for directed biopsy. We found that the colposcopic prediction of histology of the directed biopsy was clinically accurate in 88% of patients which agrees well with the 85% correlation found by Stafl and Mattingly (6). Our present rate is much higher than the 78% correlation that we had in the first 110 cases that we studied and is obviously an effect of improved skill in the technique. The histology of directed

TABLE 1

CORRELATION BETWEEN THE COLPOSCOPIC IMPRESSION AND HISTOLOGY OF DIRECTED BIOPSY

COLPOSCOPIC IMPRESSION	n	HISTOLOGY OF DIRECTED BIOPSY						
		Not Done	Negative	Mild Dysplasia	Moderate Dysplasia	Severe Dysplasia/ Carcinoma-in-situ	Microinvasion	Invasive Carcinoma
Negative	100	55	41	3	1[a]	0	0	0
Mild Dysplasia	75	11	34	12	6	14[b]	0	0
Moderate Dysplasia	73	6	7[c]	6	22	31	1[d]	0
Severe Dysplasia/ Carcinoma-in-situ	41	2	3[e]	2[f]	1	30	2	1[g]
Microinvasion	4	0	0	0	0	3	1	0
Invasive Carcinoma	23	1	0	0	0	0	1	21
Indeterminate	8	4	2	0	1	1	0	0
Total	326	79	87	23	31	79	5	22

a : A tiny area of acetowhite epithelium with punctation which resolved without treatment.
b : 5 cases of severe dysplasia in biopsy; in 1 a repeat colposcopy gave a colposcopic impression of severe dysplasia; 4 cases were underdiagnosed. 9 cases of carcinoma-in-situ on biopsy; all underdiagnosed, of which 4 were early in the study.
c : In 3 the punctation of severe trichomonad vaginocervicitis gave impression of CIN; in 4 the presence of acetowhite epithelium and punctation contributed to overdiagnosis.
d : A small traumatised biopsy suggested microinvasion, cone biopsy only showed moderate dysplasia
f : Severe cervicitis in all led to overdiagnosis
f : Cone biopsy in 1 case confirmed carcinoma-in-situ; in the other repeat directed biopsy showed only cervicitis.
g : Case seen very early in study when early invasion was not recognised colposcopically.

TABLE 2

HISTOLOGIC COMPARISON OF DIRECTED BIOPSY AND CONE/HYSTERECTOMY SPECIMEN

DIRECTED BIOPSY DIAGNOSIS	n	FINAL HISTOLOGICAL DIAGNOSIS MADE ON CONE OR HYSTERECTOMY SPECIMEN						
		Not Done	Negative	Mild Dysplasia	Moderate Dysplasia	Severe Dysplasia/ Carcinoma-in-situ	Microinvasion	Invasive Carcinoma
Not Done	79	67	1	0	0	10	0	1
Negative	87	85	1	1	0	0	0	0
Mild Dysplasia	23	19	0	1	0	3[a]	0	0
Moderate Dysplasia	31	20	1[b]	0	0	9	0	0
Severe Dysplasia/ Carcinoma-in-situ	79	12	3[b]	2[b]	5	53	2	2[c]
Microinvasion	5	0	1[b]	0	1	2	0	1
Invasive Carcinoma	22	12	0	0	0	0	1	9
Total	326	215	7	4	6	77	3	13

a : Poor directed biopsy specimens in all 3 patients showed mild dysplasia, because cytology abnormal, cone biopsy in 2 showed carcinoma-in-situ and severe dysplasia in the other.
b : Directed biopsy removed the area of most advanced histology.
c : Colposcopic impression of microinvasion in 1 case but directed biopsy showed carcinoma-in-situ only; a diagnostic cone biopsy was done, this showed invasion and patient treated by Wertheims hysterectomy. In the second case seen early in study, an endocervical invasive cancer missed and simple hysterectomy done for prolapse. Radiotherapy given postoperatively and patient well 3 years later.

TABLE 3

FINAL HISTOLOGIC DIAGNOSIS IN DIRECTED BIOPSY, CONE BIOPSY OR HYSTERECTOMY SPECIMEN

HISTOLOGIC DIAGNOSIS	PATIENTS (n)
Negative (Normal/Cervicitis)	89
Mild Dysplsia	21
Moderate Dysplasia	21
Severe Dysplasia/Carcinoma-in-situ	98
Microinvasion	6
Invasive Carcinoma	24
Total	**259**

biopsy was more advanced than expected from colposcopic impression in 7% whereas the corresponding figures of Stafl and Mattingly (6) were 3.3% and Benedet et al (7) were 3.1%. Our higher rate of colposcopic under diagnosis is due to the inclusion of cases that were seen very early in our experience with the method and because 3 individuals performed colposcopy. In 5% the histology was less advanced than expected and, this is due to benign lesions such as papillomas, cervicitis and cervical wart virus infection. In such cases, the colposcopic differentiation from cervical intraepithelial neoplasia can be difficult and at times impossible. In other cases, definite colposcopic lesions may be present without significant histologic changes and these require careful observation for possible development of CIN (8).

Cone biopsy is adequate treatment for all grades of CIN confined to the cervix, which is completely excised in a cone biopsy with margins which are not involved by intraepithelial neoplasia (9). It is our treatment of choice when, with satisfactory colposcopy severe dysplasia/carcinoma-in-situ is the sole abnormality without other gynaecological symptoms or pathology which require hysterectomy. In those with invasive cancer which is not obvious macroscopically, colposcopically directed biopsy which shows invasive carcinoma avoids the need for cone biopsy. Directed biopsy alone confirmed the colposcopic impression of invasive carcinoma in 91% (21/23): in them, hospitalisation and further diagnostic procedures especially cone biopsy was avoided. This facilitated early application of definitive surgical or radiotherapeutic treatment. In only 2 patients in our study, was a cone biopsy necessary to confirm invasion. In one, only the edge of an early endocervical invasive cancer was visible, and, to accurately assess the depth of invasion a cone biopsy was preferred which confirmed invasive cancer. In the other, with a colposcopic impression of invasive cancer the directed biopsy showed only microinvasion, so a cone biopsy was done which confirmed invasion.

There was acceptable correlation of the directed biopsy histology with the definitive histologic diagnosis of the cone/hysterectomy specimen in 87% a figure exactly similar to that of Stafl and Mattingly (6). In 5% of patients who were significantly underdiagnosed in the directed biopsy, only in a single patient did it lead to an error in management. This case had carcinoma-in-situ in directed biopsy because the invasive growth which was endocervical was missed and a simple hysterectomy was performed. Underdiagnosis is a more real and clinically important error than overdiagnosis, and, the overdiagnosis rate in the directed biopsy of 8% was due to the most advanced foacl lesion being removed by directed biopsy. It is also known, that a biopsy may induce regressive changes in the remaining lesion (10). Our directed biopsy overdiagnosis rate of 8% matches the 8% of Benedet et al (7).

Our study confirms that colposcopy and directed biopsy is sufficiently accurate to utilize as a method of reaching an accurate and safe diagnosis when the whole transformation zone is visualised in cases with cervical neoplasia. With colposcopy the need for diagnostic cone biopsy is now limited to about 9% of our patients, hence, in about 90% diagnostic cone biopsy is no longer necessary. This is a great advantage because cone biopsy is associated with significant morbidity (11) and may impair fertility and adversely affect future pregnancy outcome (12). Adequate skill in colposcopy also allows the adoption of conservative methods of treating CIN and, excellent results can be achieved with electrodiathermy, cryosurgery or the carbon dioxide laser (2) in carefully selected cases.

All patients with abnormal cervical smears should have colposcopic assessment; ideally no patient with CIN should be treated unless there has been prior colposcopic assessment (13). Colposcopy is a specialised technique that needs training and constant practice. There is therefore, an urgent need to develop further, local expertise in colposcopy and this can be done by referral of all patients with abnormal cytology for colposcopy to experienced individuals so that sufficient cases with significant colposcopic findings can be used for teaching others. Those using colposcopy need to acquire the skill by handling adequate numbers of cases with significant findings and constantly correlating cytologic, colposcopic and histopathologic findings. However, it is extremely important that no changes from conventional methods of diagnosis and management of cervical intraepithelial neoplasia are made or locally destructive methods employed based on colposcopic evalation until ones own accuracy and skill in the technique has been evaluted.

ACKNOWLEDGEMENT

We are grateful to Dr Millicent Mao and the staff of the Cytology Unit at Kandang Kerbau Hospital who read all the cytological smears. We also wish to thank Staff Nurse Foo and Nurses Amy and Sumathi who help to run our colposcopy clinic.

REFERENCES

1. Coppleson M: Colposcopy. In: Stallworthy J and Bourne G, eds. Recent advances in obstetrics and gynaecology, No 12. London, Churchill Livingstone, 1977: 155-87.
2. Jordan J A: The management of premalignant conditions of the cervix. In: Studd J, ed. Progress in obstetrics and gynaecology Vol 2. London, Churchill Livingstone 1982: 153-65.
3. Coppleson M: Preclinical invasive carcinoma of cervix: Clinical features and management. In: Coppleson M, ed. Gynaecologic Oncology: Fundamental principles and

clinical practice Vol 1. London, Churchill Livingstone, 1981: 451-64.
4. Coppleson M, Pixley E and Reid B: Colposcopy: A scientific and practical approach to the cervix and vagina in health and disease. Springfield Illinois, Charles C Thomas, 2nd ed, 1978.
5. Kolstad P and Stafl A: Atlas of colposcopy. Baltimore, University Park Press. 2nd rev ed, 1977.
6. Stafl A and Mattingly R F: Colposcopic diagnosis of cervical neoplasia. Obstet and Gynaec 1973; 41: 168-76.
7. Benedet J L, Boyes D A, Nicholas T M and Millner A: Colposcopic evaluation of patients with abnormal cytology. Br J Obstet and Gynaec 1976; 83: 177-82.
8. Coppleson M: The origin and nature of premalignant lesions of the cervix uteri. Int J Gynaec and Obstet 1970; 8: 539-50.
9. Kolstad P and Klem V: Long term follow-up of 1121 cases of carcinoma-in-situ. Obstet and Gynaec 1976; 48: 125-9.
10. Richart R M: Influence of diagnostic and therapeutic procedures on the distribution of cervical intraepithelial neoplasia. Cancer 1966; 19: 1635-8.
11. Coppleson M: Cervical Intraepithelial Neoplasia: Clinical features and management. In: Coppleson M ed: Gynecologic Oncology: Fundamental Principles and Clinical Practice Vol 1. London, Churchill Livingstone, 1981: 420.
12. Jones J M, Sweetnam P and Hibbard B M: The outcome of pregnancy after cone biopsy of the cervix. A Case Control Study. Br J of Obstet and Gynaec 1979; 86: 913-6.
13. Conclusions. Royal College of Obstetricians and Gynaecologists Study Group on Pre-clinical Neoplasia of the Cervix. In: Jordan J A, Sharp F and Singer A eds. Preclinical neoplasia of the cervix. (London, 1981). London: RCOG, 1982: 299.