Glandular abnormalities on cervical smear: a study to compare the accuracy of cytological diagnosis with underlying pathology

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Summary

The interpretation of glandular abnormalities detected by cervical smear provides a diagnostic dilemma. This study aims to compare the accuracy of cytological diagnosis with underlying pathology so that guidelines for the investigation and management of abnormal glandular smears may be formulated. A retrospective review of 150 women with glandular abnormalities reported on cervical smear collected over 12 months from 1996 in a University hospital was performed. Smears were graded by the initial report into 3 groups, dependent on the severity of abnormality. Investigation, treatment and subsequent 3-year follow-up were recorded.

The accuracy of prediction for a significant neoplastic or preneoplastic glandular pathology only was 0% with mild, 9% (3/35) with moderate, and 24% (9/38) with severe abnormalities. When squamous lesions were included, the chance of finding any dysplastic squamous or glandular abnormality was 16% (12/77), 51% (18/35) and 82% (31/38), respectively, following a smear showing a suspected glandular abnormality only. Our results highlight the poor specificity of predicting glandular neoplasia or preneoplasia from cervical smears, with a final diagnosis of high grade CIN in 35% (17/49) of patients with dyskaryotic glandular cytological changes only and 83% (20/24) where concomitant squamous dyskaryosis was reported. The reporting of reactive or minor changes in endocervical cells was of no diagnostic value. Management protocols for moderate and severe glandular abnormalities should include visualisation and biopsy of the uterine cavity to exclude endometrial neoplasia.

Introduction

The correct identification of glandular cell abnormalities found on cervical smear provides a diagnostic dilemma for the cytologist and as a consequence the clinician in deciding on management. The use of endocervical sampling devices has increased in order to obtain satisfactory sampling of the transformation zone and has significantly improved adequacy rates but frequently provides cells from the upper endocervical canal which may be difficult to characterise [1].

While the sensitivity of glandular dyskaryosis as a predictor of cervical glandular intraepithelial neoplasia (CGIN) has been reported to approach that of squamous lesions at over 80% [2], the specificity is below 20% [3]. On the cervical smear, squamous abnormalities may appear to be glandular, particularly when the endocervical glands are involved by cervical intraepithelial neoplasia (CIN). Furthermore, atypical glandular cells can be confused with tubo-endometrioid metaplasia, microglandular hyperplasia and endometriosis.

With increasing awareness and experience in the characterisation of glandular cells, this study aimed to assess the accuracy of cytological diagnosis in a university cytology laboratory so that guideliness for the investigation and management of abnormal glandular smears may be formulated.

Methods

During the study period of August 1995 to August 1996, 37,460 cervical smears were reported by the Department of Cytopathology and Histopathology at Southampton General Hospital; 160 women were identified with a presentation smear showing a variety of glandular cytological abnormalities during this period. The majority of smears were taken with the Ayres spatula. In addition to glandular dyskaryosis, smears with minor glandular changes interpreted as reactive, those with coexistent squamous abnormalities and those where it was unclear whether the dyskaryotic cells were squamous or glandular in origin were included in the study. These were graded by initial report into 3 groups using the method of DiTomasso *et al.* [4]. The first group included those with minor or reactive changes, an intermediate group with abnormal glandular cells of uncertain significance and a third group in which unequivocal highly atypical glandular abnormalities were seen. In all cases the presence of coexisting squamous dyskaryosis was recognised and recorded (Tables 1, 2 and 3). Detailed records were available for 150 of the 160 women and these formed the study group. For those who underwent colposcopic assessment, adequate visualisation of the squamocolumnar junction and endocervical canal was recorded together with the findings from subsequent histological specimens. Follow-up cervical cytology was also available from computerised records for 3 years after completion of the study period.

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The colposcopy service at Southampton General Hospital is provided by four clinicians. At the time of the study, there was no uniform protocol for the management of cervical smears showing suspected glandular dyskaryosis. During the study LLETZ was used in preference to cold coagulation of the cervix, therefore allowing comprehensive histological sampling.

Results

Of the 150 cases, 62 were managed with cytological follow-up only. Twelve patients underwent dilatation and curettage. The remainder underwent colposcopic assessment and after evaluation 44 patients underwent LLETZ and 7 ablative procedures following biopsy.

Seventy-seven patients had reactive or minor changes in endocervical cells of which 26 had coexistent squamous dyskaryosis as shown in Table 1. Histology of the 9 patients who underwent LLETZ showed CIN in accordance with the presence of squamous dyskaryosis on the presenting smears. There were no cases of CGIN.

Thirty-five patients had intermediate abnormalities in endocervical cells and only 6 patients had coexistent squamous dyskaryosis (Table 2). Of the 29 patients with intermediate endocervical gland changes, 9 had squamous CIN, only 1 had CGIN and 2 had endometrial carcinoma. The remaining 9 were either not referred for further investigation or subsequently managed by cytological surveillance and no further abnormality reported. All 6 with squamous dyskaryosis in association with abnormal endocervical changes had squamous CIN but no CGIN.

The 38 cases of high grade glandular abnormalities were subdivided into 3 groups. The first comprised those in which highly atypical glandular cells were present but their precise origin was in doubt, ie endocervical or from elsewhere in the female genital tract. A second subgroup

Table 1. — *Correlation between minor glandular abnormalies on cervical smear and underlying histological diagnosis in those undergoing further investigation (ca.: endocervical cells, sq dys: squamous dyskaryosis)*

	Investigation				Diagnosis					
Presenting smear	No	Colposcopy & directed biopsy	D & C	LLETZ	Low grade CIN	High grade CIN	CGIN	Benign endometrial pathology		Negative investigation or cytological follow-up
Reactive ec	51	7	2	1	1	1		Endometriosis polyps	1 2	46
+ low grade sq dys	19	8		2	2	2				15
+ high grade sq dys	2	2		2		2				0
? grade sq dys	5	5		4	1	3				1
Total	77	22	2	9	4	8	0		3	62

Table 2. — *Correlation between intermediate glandular abnormality on cervical smear and underlying histological diagnosis. (ca.: endocervical cells, sq dys: squamous dyskaryosis, tem: tuboendometrioid metaplasia)*

	Investigation				Diagnosis					
Presenting smear	No	Colposcopy and directed biopsy	LLETZ	D & C	Low grade CIN	High grade CIN	High grade CGIN	Endometrial cancer	Benign endometrial pathology	Negative investigation or cytological follow-up
Atypical ? dyskaryotic ec	29	14	9	6	3	6	1	2	Polyps 3	13
+ high grade sq dys	4	4			2	2			Tem 2	
? grade sq dys	2	2			–	2				
Total	35	20	9	6	5	10	1	2	5	13

Table 3. — *Correlation between presenting smear showing high grade glandular abnormalities and histological diagnosis. (ca.: carcinoma, sq dys: squamous dyskaryosis, AEH: atypical endometrial hyperplasia, em: endometriosis, NI: negative investigation)*

	Investigation				Diagnosis							
Presenting smear	No	Colposcopy and directed biopsy	LLETZ	D & C	Low grade CIN	High grade CIN	CGIN	AEH	Endometrial ca	Adenoca cervix	Benign pathology	NI
Highly abnormal glandular cells ? origin	4			4				1	3			0
Severe dyskaryosis endocervical cells	16	16	13		2	6	1	1		2	em 1	3
+ high grade sq dys	3	3	3			3						
Dyskaryosis ? glandular vs squamous	15	15	10		3	8	1				em 1	2
Total	38	34	26	4	5	17	2	2	3	2	2	5

included those in which endocervical cells showed unequivocal high grade dyskaryosis and a third showed high grade dyskaryosis of either glandular or squamous type. In the first group all 4 cases of highly abnormal glandular cells of unknown origin proved on D&C to have an endometrial abnormality (Table 3). Of the 16 women with unequivocal endocervical dyskaryosis, all 16 were investigated and 13 underwent LLETZ. Of these, 8 had squamous dyskaryosis and only 3 had cervical glandular neoplasia. Despite investigation, in 4 out of 16 (25%) no histological abnormality was identified. The 3 cases of combined endocervical and squamous dyskaryosis all showed high grade CIN only.

All those patients in the third subgroup of high grade dyskaryosis of uncertain type were investigated. Eleven had CIN, only one had CGIN and one endometriosis. Two of the 15 cases in this group showed no histological abnormality.

Combining the subgroups (Table 3), all cases were investigated with 22 out of 38 cases (58%) found to be CIN and only 4 cases (10.5%) representing endocervical neoplasia. In addition, 5 cases of endometrial neoplasia and preneoplasia were identified. Despite high grade cytological abnormalities on cervical smear, 5 cases (13%) had no demonstrable histological abnormality.

The accuracy of prediction for a significant neoplastic or preneoplastic glandular abnormality was 0% in group 1, 9% (3/35) in group 2, and 28% (9/38) in group 3. When squamous lesions are included, the chance of finding any dysplastic squamous or glandular abnormality was 16% (12/77), 51% (18/35) and 82% (31/38), respectively.

The final diagnosis was CIN in 35% (17/49) of patients with dyskaryotic glandular cytological changes only (groups 2 and 3).

Discussion

This study supports the findings of other studies which show that a report of glandular abnormalities in cervical smear has relatively poor specificity. In the presence of a negative colposcopy, other benign findings included endometriosis, endometrial polyps and tuboendometrioid metaplasia. No significant glandular pathology was detected in those women whose smears were reported as reactive or who had minor changes in endocervical cells, which on review were regarded as within normal limits. In those who had a report showing concomitant squamous dyskaryosis, CIN was found.

In contrast, squamous abnormalities have the capacity to mimic glandular dyskaryosis and the final diagnosis was CIN in 35% of patients with dyskaryotic glandular cytological changes only. Reporting of minor changes in endocervical cells is not of any proven value and the specificity of detecting a high grade glandular or squamous abnormality increases if these minor changes are ignored.

Jackson *et al.* [5] reported a 45% probability of a glandular neoplastic or preneoplastic lesion in the presence of severely atypical glandular cells on smear and our results show a 24% probability of a such a glandular lesion (group 3), but with 5/9 (56%) of these proving to have endometrial cancer or atypical hyperplasia. Our results highlight that high grade CGIN in isolation is rare, with 3 cases presenting over 1 year compared with over 200 cases of CIN 3.

Contreras-Melendez *et al.* [5] from the same institution in 1992 reported 5 cases of glandular neoplasia from 20 cervical smears showing abnormal glandular changes, obtaining the histological diagnosis using colposcopy and punch biopsy. Colposcopic findings in the presence of high grade CGIN are relatively non-specific. It can present focally within the endocervix distant from the transformation zone and punch biopsy only may therefore be insufficient for identification of CGIN [6]. In the presence of a cervical smear reporting glandular neoplasia, cone biopsy has been advocated [1] for full histological evaluation of the endocervical canal. However while this approach is justifiable when there is a high correlation between cytological reporting and underlying pathology, on the basis of our study this would result in significant overtreatment. Units have a responsibility to undertake a critical audit before introducing such a procedure.

Despite the introduction of LLETZ for assessment and/or treatment since the study by Contreras-Melendez *et al.* [4], the overall sensitivity and specificity in our unit has not risen as we would have hoped. Based on these findings, all cases of intermediate (group 2) and high grade glandular cytological abnormality (group 3) were referred for colposcopy and those cases of squamous CIN identified and treated. In addition those patients with abnormal glandular cells of unknown origin were investigated with hysteroscopy and curettage, as were those cases in groups 2 and 3 where neither a squamous or glandular abnormality was detected on colposcopy. If there is no endometrial pathology, LLETZ should be undertaken, particularly in those with highly abnormal glandular cells on the smear to exclude a high occult endocervical tumour.

Those cases of high grade glandular cytology in whom no histological diagnosis was made at colposcopy/LLETZ and endometrial curettage should undergo pelvic ultrasound and CA125 estimation and be followed-up very closely at 6 months with repeat colposcopy and endometrial biopsy.

In the presence of unequivocal neoplastic glandular cells on cervical smear and negative investigation, where fertility is not an issue, pelvic clearance should be considered to exclude occult cervical, uterine and fallopian tube carcinomas.

We believe that such a rationalisation of reporting abnormalities in glandular cells with subsequent standardised management protocols will aid diagnostic and treatment planning. The study highlights the limitations of accurately predicting glandular abnormalities from cervical smears but such patients should undergo colposcopic assessment to exclude CIN.

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