

ADENOCARCINOMA-IN-SITU OF THE CERVIX A CASE REPORT

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SYNOPSIS

Adenocarcinoma-in-situ is an uncommon lesion in the cervix. A case of cervical adenocarcinoma-in-situ with questionable invasion diagnosed by colposcopically directed biopsy is described. The pathology of cervical adenocarcinoma-in-situ is discussed and the difficulty of diagnosing early invasion in this lesion is highlighted. The definition of microinvasive carcinoma and the behaviour of early invasive lesions is discussed.

INTRODUCTION

Over 90% of cervical malignancy is of the squamous cell variety only 5-10% being of the adenocarcinoma type. Squamous cell carcinoma-in-situ, a precursor of invasive squamous cell carcinoma of the cervix was first described in 1900, whereas, adenocarcinoma-in-situ in the cervix was first described only in 1953 by Friedell and McKay (1) and is not as widely recognised as squamous cell carcinoma-in-situ. The reasons may be the low incidence of adenocarcinoma of the cervix so that its precursor is less often present; the lesion often involves the deep endocervical glands and the lesion may often be focal, involving only a small portion of the endocervix. We describe a case of adenocarcinoma-in-situ of the cervix with questionable invasion.

CASE REPORT

The patient, L M H, was a 38 year old Chinese woman married for 15 years, gravida 3 para 3, who was referred to our gynaecological clinic because of a Class IIR cervical smear showing mild dyskaryosis. She had had cervical smears repeated at intervals of 6 months to a year since 1976 and these were reported as normal. She had no postcoital bleeding, vaginal discharge or other gynaecological complaints and her menstrual history was normal.

There was no significant past history of note except of tubal sterilisation done in 1978.

Clinically she was a healthy Chinese lady. Heart, lungs, breasts and abdominal examinations were normal. On pelvic examination the vulva and vagina were normal and the cervix appeared clinically healthy. The uterus was anteverted, bulky and mobile. The appendageal regions were normal. A colposcopic examination was performed on 9.1.81 which revealed a wide area of transformation zone on the ectocervix, about half the area of the transformation zone showed features of moderate dysplasia. In this part, there was acetowhite epithelium 2+, fine mosaic vascular pattern, the surface was smooth and the edges clearly defined. Around the external os at 12 to 1 o'clock position, a small area of severe dysplasia/carcinoma-in-situ with more marked colposcopic changes was identified. In this area, the acetowhite epithelium was graded 3+, the surface noted to be slightly irregular, and the edges clearly defined from the area of moderate dysplasia. The abnormal transformation zone was limited only to the cervix without extension to the adjacent vagina. Three colposcopically directed punch biopsies of the lesion were obtained, one each from the areas of moderate dysplasia on the anterior and posterior lip and another from the area of severe dysplasia/carcinoma-in-situ around the external os. Since the entire transformation zone was not visualised, the colposcopic examination was deemed unsatisfactory and a cervical cone biopsy was planned.

Microscopic sections of the directed biopsy from the area of severe dysplasia/carcinoma-in-situ showed severe dysplasia of cervical squamous epithelium with glandular epidermidization. The endocervical epithelium at the squamocolumnar junction showed an abrupt transition from normal tall "picket-fence" type of columnar epithelium with basal nuclei to glandular epithelium with severe cytologic atypia. This area showed loss of nuclear polarity, cellular pleomorphism, nuclear hyperchromatism, mitoses and increased nuclear-cytoplasmic ratio. The "basement membrane" is however intact. These are features of an endocervical adenocarcinoma-in-situ (Figure 1, 2). In addition, there was a small superficial papillary fragment of endocervical tissue showing proliferation and crowding of glands which were lined by epithelium with malignant cytologic features. The "basement membrane" surrounding these glands was not discernible, suggesting the possibility of invasion (Figure 3). Mucin production was not demonstrable. There was no evidence of an endometrial adenocarcinoma. The other 2 pieces of directed biopsy from the areas of moderate dysplasia showed moderate epithelial dysplasia and epidermidization in one and mild epithelial dysplasia and epidermidization in the other. The diagnosis was of a cervical adenocarcinoma-in-situ with questionable invasion.

A repeat colposcopic examination on 31.1.81 confirmed the earlier findings and in view of the histology report a cone biopsy was performed on 9.2.81. The cervix was first stained with Lugol's iodine to demarcate the area of unstained epithelium. An incision was made in the ectocervix to include the entire unstained area of the cervix, a cone of cervical tissue excised and curettage performed. Histopathological examination of the cervical cone divided it into 6 blocks. Sections showed some glandular hyperplasia and epidermidiza-

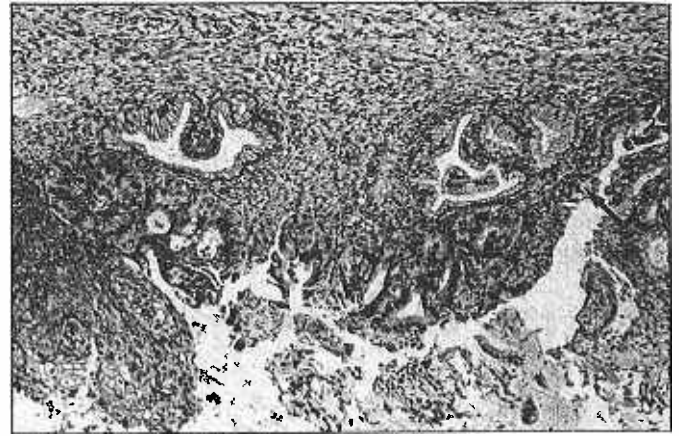


Figure 1
The squamo-columnar junction shows cytologic features of adenocarcinoma-in-situ in the endocervical epithelium. Note the abrupt transition from normal to malignant columnar epithelium (arrow). The deeper endocervical glands are normal. (H & E x 75)

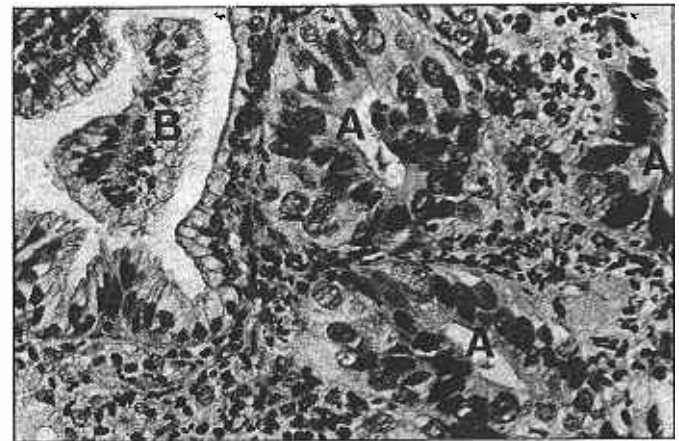


Figure 2
The three glands (A) show adenocarcinoma-in-situ. They are lined by columnar epithelium with loss of nuclear polarity, cellular pleomorphism, hyperchromatism and increased nuclear — cytoplasmic ratio. The basement membrane is however intact. Compare with normal endocervical gland (B). (H & E x 400)

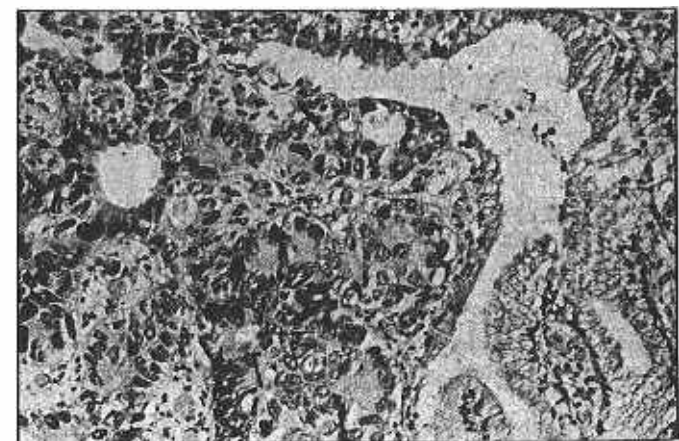


Figure 3
This area shows proliferation and crowding of malignant glands encroaching on to a normal endocervical gland. The basement membrane is not discernible, suggesting the possibility of questionable invasion. (H & E x 250)

tion. There was no residual carcinoma-in-situ. The endometrium was secretory. There was no evidence of hyperplasia or tumor.

Since directed biopsy showed adenocarcinoma-in-situ with questionable invasion and cone biopsy showed no evidence of residual carcinoma-in-situ, it was probable that the only focus of a very early invasive cancer had been removed by the directed biopsy. As the patient had already completed childbearing, it was decided to perform a simple hysterectomy and on 13.4.81 a vaginal hysterectomy was performed. The post-operative period was uneventful and the patient was discharged home on the seventh post-operative day. Microscopic examination of the uterus and cervix showed no residual tumour.

At the follow-up visit 6 weeks later, the vaginal vault had healed. A vaginal smear was reported as Class IIR showing mild dyskaryosis. She was given an appointment to return in 3 months. It was decided to follow-up the patient with further cytological examinations. These were done on 3 subsequent occasions, at an interval of 3 months initially and then twice at 6 monthly intervals. The 3 subsequent cytological reports were Class I showing no malignant cells. She has remained asymptomatic and was last seen on 16.10.82.

DISCUSSION

The concept that the majority of invasive squamous carcinomas of the cervix are preceded by squamous cell carcinoma-in-situ is well accepted (2, 3). Cervical adenocarcinoma-in-situ as a precursor of the adenocarcinoma variety, however is a lesser known entity which was first described only about 30 years ago. Friedell and McKay (1) recognised the resemblance of the lesion to carcinoma except for demonstrable absence of invasion and the presence of similar morphological changes at the periphery of an invasive adenocarcinoma of the cervix. Adenocarcinoma-in-situ is characterised by a pronounced atypia of the columnar epithelium, lining either cervical glands or the surface of the cervix. This epithelium is comparable in detail with changes seen in the epithelium of a highly differentiated invasive cervical adenocarcinoma. The carcinomatous epithelium is found in individual glands or groups of glands, lining them entirely or only in part and the borders between carcinomatous and unchanged epithelium are usually sharply defined.

In 27 out of 28 cases of adenocarcinoma-in-situ from the Graz clinic (4), there was a coincidence with squamous dysplasia or squamous carcinoma-in-situ and this has also been the experience of others (5, 6). The question, whether both components of such combined lesions have the same origin is not settled. One view holds that both glandular and squamous cancer have a common cell of origin, the subcolumnar reserve cell which has been subjected to a neoplastic stimulus (7). In our case there was also co-existence of adenocarcinoma-in-situ with areas of mild, moderate and severe squamous epithelial dysplasia. Concerning localisation, glands with adenocarcinoma-in-situ, are mainly distributed around the external os being part of the endocervical glandular field. The location of adenocarcinoma-in-situ in our case was at the cervical os where the columnar epithelium is in continuity with that of the endocervical canal.

Colposcopically directed biopsy in our case showed adenocarcinoma-in-situ with a focus of questionable invasion. In Burghart's (4) material nearly all cases of adenocarcinoma-in-situ and microinvasive adenocarcinoma were found by chance in meticulously sectioned cone biopsies done to evaluate an atypia of the squamous epithelium first suspected by cytology, colposcopy and subsequent punch biopsy. In other cases, such changes have been noted in areas adjacent to an invasive adenocarcinoma. The transition from adenocarcinoma-in-situ to invasive growth in the cervix is not easy to recognise since "cervical glands" are not true glands in the ordinary sense but actually represent folds and clefts of the surface lining epithelium. They lack a definite glandular structure and their course is quite irregular and inconsistently branching. The formation of abundant intraglandular papillae, filling an entire gland, points to an excessive proliferation. In such cases a question remains whether a folding or papillae formation directed towards the stroma invariably represents invasion. The behaviour of the stroma around such suspicious formations assumes importance in the evaluation of the case. A loosened and rarified stroma with round cell infiltration around the suspicious areas strongly points to invasive growth, while well-preserved stromal texture most likely indicates a non-invasive formation.

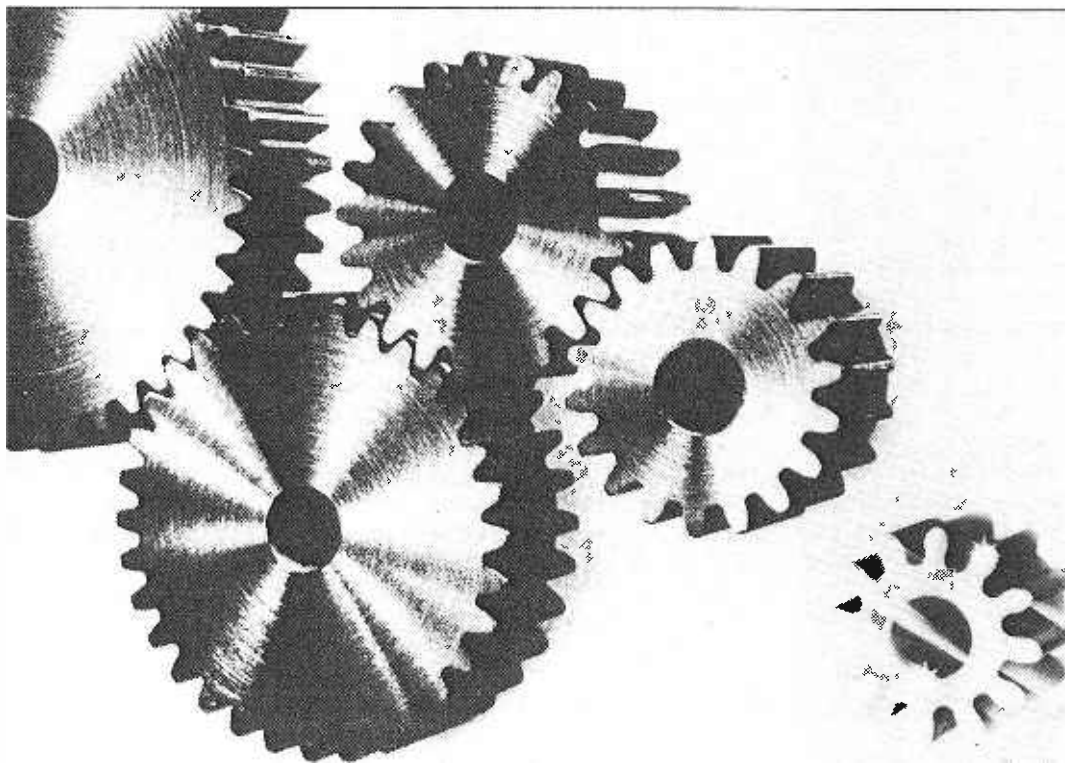
There is no generally accepted definition of microinvasive carcinoma of the cervix. Some authors consider a maximal depth of invasion below the basement membrane of 5 millimetres, while others have suggested depths of 1, 3 to 4 and even 9 millimetres (8). Presently, there is an increasing tendency towards volumetric measurement from mensuration of 2 or even 3 dimensions. For "microcarcinoma" as defined by Burghardt and Holzer (9) a volume of 500 cubic millimetres is suggested as the upper limit. These definitions are generally applied to cervical microinvasive squamous cell carcinoma, but none have been proposed or accepted for the definition of microinvasive adenocarcinoma.

It is believed that the capacity for metastatic spread is higher in invasive cervical adenocarcinoma than in squamous cell cancer. Whether microinvasive adenocarcinoma also has a capacity for earlier and more rapid metastatic spread than microinvasive squamous cell carcinoma is uncertain. In one study (4) of 8 cases of very early invasive adenocarcinoma it appeared that small adenocarcinoma of the cervix do not behave differently from squamous cell cancers of similar size. Further studies of this less commonly recognised condition must be awaited for more definitive evidence.

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