

CARCINOMA IN SITU OF THE CERVIX

by

D. J. REDDY*, M.D.

and

D. SARADA**, M.B.B.S.

The alarmingly high incidence of carcinoma of the cervix and breast in the female accounts for the leading cause of mortality due to malignant disease in the elderly female throughout the world. This has led to attempts to detect early or incipient stage of carcinoma of the cervix in recent years and millions of dollars are spent each year in mass screening programmes of women above 25 years of age with the aid of Papanicolaou cytological technique in the economically better advanced countries. This has greatly helped to spot in a significant number of women asymptomatic and clinically non-recognisable lesions of the cervix. Both gynaecologists and pathologists are increasingly aware of intraepithelial carcinoma of the cervix and are anxious to follow up these cases through serial biopsy studies, published reports reveal that many of these cases progress to invasive carcinoma from 11 months to 6½ years. Younge et al, in 1949, from a follow-

up study of 6 cases, earlier reported by Smith & Pemberton from Free Hospital for Women, reported invasive carcinoma supervening on carcinoma in situ. Early detection and appropriate therapy would offer greater security and longevity to this group of patients. As such, non-healing ulcers of the cervix, indurated spots over the cervix, unexplainable leucorrhoea and spotting of blood over the examining finger need to be excluded for carcinoma in situ of the cervix by Papanicolaou smear technique and cone biopsy. This has also cautioned specialists in other fields of medicine to look for intraepithelial carcinoma of larynx, oesophagus, skin, mammary gland etc. This is a biological problem related to neoplasms.

Rubin, in 1910, first reported 3 cases of incipient carcinoma of the cervix and in two of his cases extension into the glands of the cervix was observed. Broders in 1932, introduced the term 'carcinoma in situ'. Carcinoma in situ is completely undifferentiated squamous epithelium forming an intact layer of cells covering the portio vaginalis of the cervix. The diagnosis of carcinoma in situ, as of carcinoma in general, is based chiefly on altered cellular characteris-

* Director & Professor, Upgraded Dept. of Pathology, Andhra Medical College, Visakhapatnam.

** Tutor in Pathology, Guntur Medical College, Guntur.

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tics in contradistinction to cellular situation. The nuclei are large and deeply basophilic and may be grouped. Carcinoma in situ should qualify all the morphological changes of malignancy and desquamated cells from such a lesion should manifest cytological evidence of malignancy. Epithelial hyperplasia and anaplasia, as a mark of changes in pregnancy need to be differentiated from malignancy and either excluded or confirmed on repeat biopsy studies.

Broders recognised early malignant lesions of the cervix and grouped them as under:

1. Carcinoma in situ with involvement of surface epithelium.
2. Carcinoma in situ with glandular involvement.
3. Questionable stromal involvement.

The first two are grouped under carcinoma in situ and not the third. According to Younge; in 50% of the cases of carcinoma in situ the lesion extends to the cervical glands. Carcinoma in situ replaces the columnar cells of the endocervix or of the cervical glands as it advances. This is in contrast to the undergrowth which takes place in squamous metaplasia. Younge et al do not regard glandular involvement as evidence of invasion which is contrary to the opinion of TeLinde. Glandular involvement merely indicates a more extensive replacement of the endocervical epithelium.

One could often demonstrate invasive carcinoma and carcinoma in situ and the transition of normal epithelium in the same section. A review of the biopsies of the cervix re-

gistered at the department of Pathology, Guntur Medical College confirm many of the above findings.

Methods and Material

Biopsies of the cervix registered at the department of Pathology, Guntur Medical College, for the period 1955 to October 1962 were reviewed. The senior author while reviewing the slides was not aware of the original diagnosis recorded in the register and the diagnosis independently thus made was compared with those already recorded in the register. There was no occasion to differ from the original diagnosis made. Even minimal stromal invasion was excluded under carcinoma in situ and the criteria stated above were rigidly adhered to. This review revealed 1934 benign lesions of the cervix, grouped under cervicitis, 1021 epitheliomata and 30 cases of carcinoma in situ. Case histories of 7 of these cases of carcinoma in situ and one recently observed by the senior author from the Upgraded Department of Pathology, Andhra Medical College, Visakhapatnam, are recorded below.

Some Features of Carcinoma in Situ Observed in our Series

We find that carcinoma in situ formed 1.5% and 2.9% of cervicitis and epitheliomata respectively recorded at the department of pathology, Guntur Medical College. Twenty-six of the 30 cases of carcinoma in situ in our series were between 20 and 40 years of age (Table 1). Younge et al observed, in their series of 135 cases, 38 years as the average age of incidence.

TABLE I
Age Incidence of Carcinoma in Situ

Age group in years	20-30	31-40	41-50	Unknown	Total
Number in each	12	14	3	1	30

We found nothing grossly pathognomonic of carcinoma in situ. Most of our patients sought advice for leucorrhoea or bloodstained discharge or pain over lower abdomen. The gynaecologist in these cases found evidence of ulceration of the cervix, or induration, blood spotting over the examining finger, clinically suspected cervicitis or tuberculosis of the cervix. Younge et al recorded leucorrhoea in 24%, abnormal bleeding in 30%, and in 6% of 135 cases of carcinoma in situ observed lesions suspicious of malignancy. They found erosion as the frequent physical appearance of the cervix in their series.

Case Report 1

Female, aged 30 years, was seen in the gynaecological clinic for white discharge of 4 months' duration. The cervix was hypertrophied and ulcerated. Biopsy was done.

Biopsy Report. (1182/62), shows changes typical of carcinoma in situ. The basement membrane is intact.

Case Report 2

Hindu female, aged 23 years, sought medical aid of a private medical practitioner for pain in the lower abdomen, leucorrhoea and spotting of blood. Cervix was hard and there was bleeding on the examining finger.

Biopsy Report (1272/62). There is epithelial hyperplasia, with basophilia of the nuclei and change of polarity of the cells, all typifying malignancy. The basement membrane is not penetrated. These changes are characteristic of carcinoma in situ (Fig. 1).



Fig. 1

Case 2—Photomicrograph illustrates carcinoma in situ, the basement membrane is intact; cellular unrest is well depicted. (H & EX 160).

Case Report 3

Hindu female, aged 48 years, attended the gynaecological clinic for postmenopausal bleeding.

Biopsy Report (583/61). Carcinoma in situ. (Fig. 2).



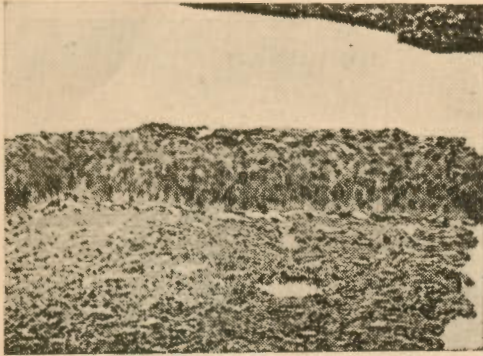
Fig. 2

Case 3—Photomicrograph illustrates carcinoma in situ, intact basement membrane and pleomorphism in the morphology of epithelial cells are seen. (H & EX 160).

Case Report 4

Hindu female, aged 45 years, attended the gynaecological clinic for pain in the lower abdomen. Vaginal examination disclosed nothing abnormal.

Biopsy Report (510/60). The changes in the epithelium observed are consistent with intra-epithelial carcinoma. (Fig. 3).

**Fig. 3**

Case 4—Photomicrograph illustrates carcinoma in situ, intact basement membrane, anaplasia and loss of polarity of epithelial cells are well seen. (H & EX 160).

Case Report 5

Hindu female, aged 50 years, attended the gynaecological clinic for white discharge. Vaginal examination showed cervix flush with the vaginal wall and uterus small. Rectal examination showed parametrium was free. Speculum examination showed ulceration of the cervix.

Biopsy Report (1378/60). Epithelial changes are typical of carcinoma in situ. (Fig. 4).

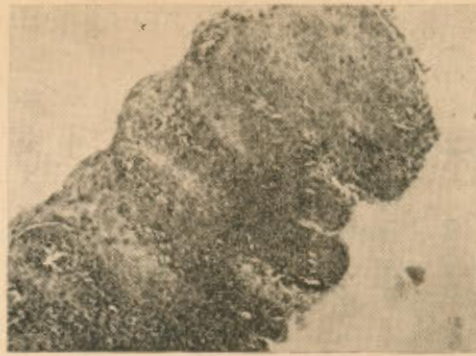
Case Report 6

Hindu female, aged 35 years, attended the gynaecological clinic for blood-stained discharge per vaginam of 2 years' duration. Vaginal examination showed evidence of chronic cervicitis, and cervix on speculum examination appeared unhealthy.

Biopsy Report (1449/60). The epithelial changes observed typify carcinoma in situ. (Fig. 5).

Case Report 7

Hindu female, said to be aged 20 years,

**Fig. 4**

Case 5—Photomicrograph illustrates carcinoma in situ, the basement membrane is not penetrated. (H & EX 120).

**Fig. 5**

Case 6—Photomicrograph illustrates carcinoma in situ, cellular pleomorphism and aggressive features and intact basement membrane are well depicted. (H & EX 140).

attended the gynaecological clinic for leucorrhoea. Speculum examination suggested cervicitis.

Biopsy Report (1333/62). Epithelial hyperplasia with anaplasia limited to the basement membrane is seen. Extension of this into the cervical glands and not into the stroma is observed. These changes characterise carcinoma in situ with extension to the glands of the cervix. (Fig. 6).

Case Report 8

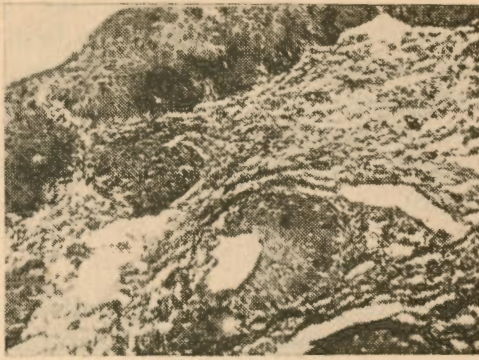


Fig. 6

Case 7—Photomicrograph illustrates carcinoma in situ with extension into the gland. (H & EX 100).

Hindu female, aged 40 years, attended the gynaecological clinic, King George Hospital, Visakhapatnam, on 8-5-63 for leucorrhoea since one year. She has had no menstruation since the birth of her last child a year ago. Vaginal examination revealed retroverted bulky uterus, about 12 weeks in size. Speculum examination showed unhealthy cervix with tears; biopsy was taken from the anterior lip of the cervix.

Biopsy Report (1879/63 dated 10-5-63). Extensive surface and glandular extension of carcinoma of cervix was observed (Fig. 7). In view of the suspicion of pregnancy

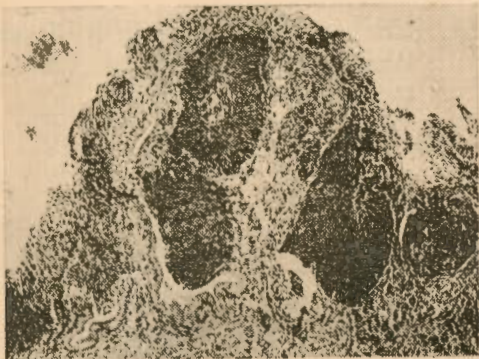


Fig. 7

Case 8—Photomicrograph illustrates carcinoma in situ with extension into the glands—first biopsy. (H & EX 60).

special care was exercised to confirm malignancy in the lesion and the aggressive features of malignancy were observed in the epithelial cells (Fig. 8).

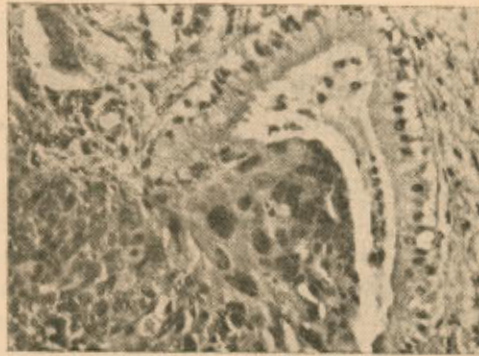


Fig. 8

Case 8—Photomicrograph shows under higher magnification, extension of the neoplastic change into the gland, giant and hyperchromatic nuclei marking malignancy are well seen. (H & E 200).

To exclude hyperplastic changes in the epithelium in pregnancy a second biopsy was done 15 days later.

Biopsy Report (2119163 dated 25-5-63). Similar appearances as observed in the previous biopsy were seen. The extension of the lesion was limited to the glands and no stromal invasion was observed. (Fig. 9). Unequivocal morphological features of

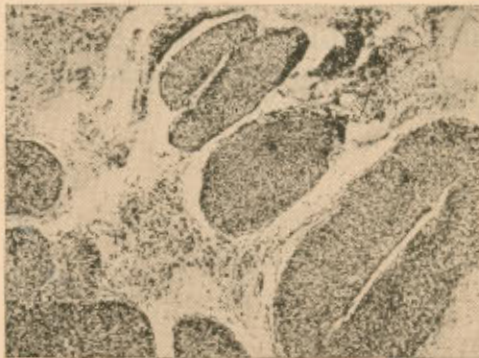


Fig. 9

Case 9—Photomicrograph of repeat biopsy illustrates carcinoma in situ with extension into the glands simulating epidermidisation. (H & EX 60).

malignancy of the surface epithelium were seen, clearly distinguishable from squamous metaplasia.

Comment

In the study of eight cases of carcinoma in situ we observed extension of the lesion into the glands of the cervix. Younge et al observed a higher percentage of incidence of the same in their series. While confirming carcinoma in situ in the last case, included in our report, pseudoepithelial hyperplasia commonly encountered in pregnancy was kept in mind and the true malignant nature of the lesion was confirmed only after repeat biopsy.

Summary

(1) Literature pertaining to carcinoma in situ is briefly reviewed.

(2) Carcinoma in situ formed 1.5% and 2.9% of benign and malignant lesions of cervix respectively as revealed from the registry of Department of Pathology, Guntur Medical College.

(3) Findings in cases of carcinoma in situ are recorded, and glandular extension of the malignant lesion to be viewed as intraepithelial carcinoma is confirmed.

(4) This study emphasises the value of repeat biopsies when first or later biopsy findings are equivocal of malignancy, and commend resorting to cone biopsy technique to exclude or confirm the presence of carcinoma in situ.

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