

MANAGEMENT OF DYSPLASIA AND CARCINOMA IN SITU CASES AND THEIR OUTCOME DURING LONG TERM FOLLOW UP

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ABSTRACT

Different treatment modalities were offered to 105 women with different grades of dysplasia and CIS cases. Out of 105 women cryosurgery was offered to 14 persistent dysplasia cases, conisation to 16 persistent dysplasia and 10 carcinoma in situ cases and hysterectomy to 25 persistent dysplasias and 40 carcinomas in situ cases. During follow up period 2 cases progressed to malignancy (1 from moderate dysplasia and other from severe dysplasia) and 1 persisted as moderate dysplasia after cryosurgery. In the conisation group 1 case recurred as severe dysplasia with condyloma after 3 years of follow up. In hysterectomy group one case of mild dysplasia observed after 1 years of follow up. Thus long term follow up is mandatory even after hysterectomy and conservative management should be restricted to the young women with low grade of dysplasia.

INTRODUCTION :

Cytology screening coupled with colposcopic evaluation of lesions detected have revolutionized the early detection of cervical cancer and its management. Adequate management of precancers and early cancers is crucial if the gains of early detection are to be consolidated. For the last two decades the trends for therapeutic approaches are towards conservative management in order to avoid overtreatment and to preserve fertility.

This paper deals with the management of

intraepithelial dysplastic neoplastic lesions and carcinoma in situ among Indian women with different treatment modalities and the problems encountered for the subsequent follow up of these women.

PATIENTS AND METHODS :

a) Patients selection : No organised cytology screening exists in India. Through a hospital based cytology screening-cum-research programme, women attending outdoor clinics of the gynaecology departments of five major hospitals of Delhi are being screened. A total of 105 women with persistent dysplasia (n = 55) and CIS (n = 50) detected through

this programme were recruited in our treatment plan.

b) Diagnostic work up :- At least 3 cytology smears were evaluated for Persistence of dysplasia before a detailed diagnostic work-up was undertaken that included a complete history, pelvic examination, repeat pap smear, colposcopic assessment and a directed biopsy. The colposcopic assessment included a thorough inspection of cervix, vulva and vagina after application of 5% acetic acid. A directed biopsy was taken in the area considered to represent the maximum abnormality. In some cases more than one biopsy was undertaken.

c) Treatment modalities : The different treatment procedures adopted were cryosurgery, conisation, and total hysterectomy, depending on the severity of lesion in histology, age of the patient, parity of the patient including number of live children and the associated gynaecological conditions, if any.

i) Cryosurgery was attempted after securing a tissue diagnosis of dysplasia and where colposcopy was satisfactory with complete visualisation of the Transformation zone (T.Z.) and where the upper margins of the lesions could be demarcated. Cryosurgery was performed using nitrous oxide as the refrigerant. In all cases, single freezing was done. After freezing, another colposcopic examination was performed to ensure destruction of the entire lesion. Patients of persistent dysplasia with an unsatisfactory colposcopic examination and patients with CIS were not treated with cryosurgery.

ii) Conisation was attempted in patients with persistent dysplasias with an unsatisfactory colposcopic evaluation and where an endocervical lesion was suspected. Young patients (mean age 28.6 years) with CIS were also treated

through conisation especially when the women had completed her family (mean parity 2.0).

iii) Hysterectomy: Total hysterectomy was performed for cases of persistent dysplasia associated with other gynaecological problems such as fibroid uteri or dysfunctional uterine bleeding (DUB) that warranted hysterectomy for control of symptoms. Patients with CIS (in histology) who had completed their families were offered simple hysterectomy.

d) Follow-up schedule :- Patients were advised to attend follow up clinics every 6 monthly after initial treatment. At follow up visit, colposcopic examination was done followed by a cytology smear.

RESULTS :

The mean ages of the patients undergoing treatment with cryosurgery, conization and hysterectomy were 27.2, 28.6 and 34.2 years respectively. The mean parity for the 3 treatment classes were 1.8, 2.0 and 3.9 respectively.

PERSISTENT DYSPLASIAS : (Table - 1)

Cryosurgery was offered to 14 cases of persistent dysplasia. In one case dysplasia persisted as moderate dysplasia. Two cases progressed to invasive cancers within the first year of followed up. One of them was a moderate dysplasia and the other a severe dysplasia at the time of treatment.

Conisation was offered to 16 persistent dysplasias of which, 13 regressed during the follow up while one case recurred as severe dysplasia with condylomatous changes after 10 years of follow up. Two cases did not turn up for follow up.

Hysterectomy was performed in 25 cases of persistent dysplasia associated with fibroid uterus or Dysfunctional uterine bleeding. Two patients were lost to follow up immediately after hysterectomy. All other cases regressed to normalcy

TABLE - I

Management of precancerous lesions - Outcome of different treatment Modalities

	Dysplasia		CIS		
	Cryosurgery	CONE	Hyst	Cone	Hyst
No. treated (n)	14	16	25	10	40
Patients followed up (no.)	14	14	23	10	19
OUTCOME					
— Persistence	1*	0	0	0	0
— Recurrence	0	1***	0	1****	1****
— Prog. to Carcinoma	2**	0	0	0	0
— Regression	11	13	13	9	18

* Persistent moderate dysplasia

** Progressed to cancer (1 CIN + 1 Inv.) one from moderate dysplasia other from severe dysplasia

*** Recurred as severe dysplasia with condyloma after 10 years of follow up.

**** Recurred as carcinoma in situ after 3 years of follow up.

**** Recurred as mild dysplasia with condyloma after six months of follow up.

Carcinoma in Situ.

during follow up.

Of the 50 CIS cases 10 were treated with cone and remaining 40 by simple hysterectomy. Of the 10 CIS patients treated by conization, 1 showed recurrence after 3 years of follow up as CIS while others regressed to normal. 40 CIS cases treated through hysterectomy, 21 were lost to follow up after treatment while of the remaining 19 patients, one showed fresh lesions of mild dysplasia with condyloma after 6 months of follow up and other didn't show any abnormality.

The overall loss to follow up was 23.8% (25 cases). CIS had significantly higher loss of follow up compared to dysplasia (42%, 21 cases vs 7.3%, 4 cases). Among the treatment categories, there was no loss for those treated through cryosurgery. The loss to follow up was significantly higher for those undergoing hysterectomy

(33.4%; 23 cases) as compared to those undergoing conisation (7.7%, 2 cases). The details of the follow up are given in table - 2.

DISCUSSION :**Management of Persistent dysplasia :**

Cryosurgery was done in 14 cases. In one case, dysplasia persisted as moderate dysplasia. It indicates the primary treatment failure in literature (Parkin et al, 1978). Main reasons ascribed to the treatment failure have been due to the lesions extending into endocervical canal or an extensive lesion. In this particular case, the upper margin of the lesion was well demarcated. In fact no case was managed with cryosurgery where T.Z was not fully visualized or where an endocervical lesion was suspected.

TABLE - II

Follow up of patients according to the severity of lesions and mode of treatment

	Overall n = 105	Dysplasia n = 55	CIS n = 50	Cryo n = 14	Cone n = 26	Hyst n = 56
Loss of F.U.	25(23.8%)	4(7.3%)	21(42.0%)	0	2(7.7%)	23
One F.U. only	27 (25.7%)	17(12.7%)	10(20.0%)	3(21.5%)	10(38.5%)	14
F.U. for more than one year	53(51.5%)	34(80.0%)	19(38.0%)	11(78.5%)	14(53.8%)	28
Mean F.U.	2.6	2.4	2.9	2.4	2.8	1.4
Median F.U.	2.5	2.3	3.0	2.3	2.7	1.6

The failure rate of cryosurgery for the primary lesion in the present series (7.1%) fall within the range of 6-29% described through series of work conducted under controlled conditions in cancer centres, with strict protocols for the pre-treatment work up and post-treatment follow up (Sevin et al, 1979). Even in the hands of experienced colposcopist and cryotherapists, a residual disease of 10-15% after cryotherapy has been described.

Two of the 14 persistent dysplasia treated with cryosurgery progressed to malignancy within the first year of follow-up; one from moderate dysplasia and the other from severe dysplasia. A short interval after treatment for progression indicates that at the time of pre-treatment assessment a higher lesion was missed. Invasive cancers have been described shortly after cryosurgery (Sevin et al, 1979). The main reasons described for such cases have been initial false ve cytology, incomplete colposcopic evaluation, flaws in the cryosurgical technique and ineffective post cryosurgical follow up. In the present series of patients, at least 3 cytology smears were obtained before instituting the treatment. Likewise cryosurgery was attempted only in those cases where colposcopy was satisfactory and the upper margins of the lesions were well outside the

endocervical canal and the biopsy was taken from most advanced lesion; multiple biopsies were attempted as and when indicated. The only reason why we could have missed a higher lesion might have been due to the fact we did not perform an endo-cervical curettage. Moreover, microinvasive carcinoma can be missed when colposcopic directed biopsies rather than conisation is attempted. Alternatively, these two invasive cancers might represent the progression from the residual lesion because of the impaired immune response of the patients following cryosurgery (Sevin et al, 1979).

The suitability of cryosurgery for higher CIN lesions have been debated. While in one large series (Richart et al, 1980), the treatment failure has been reported to be the same for mild, moderate and severe dysplasia. Others reported a very high failure rate for severe dysplastic lesions (Sevin et al, 1979). The proponents for cryosurgery for severe dysplasias recommended the destruction of entire transformation zone and not only ablating the local lesion. In the present series, however, cryo application was limited to only the colposcopically visible lesion, using single freezing. Our results are not very favourable for higher grade lesions (severe dysplasia) and now we recommend cryosurgery only to mild or

moderate dysplasia.

Conisation was the mode of treatment in 16 dysplasia cases. Of the 14 patients available for follow up, 13 showed regression. One case that remained cytologically & colposcopically negative for 10 years consisting of 20 follow ups developed severe dysplasia with condylomatous changes. Condyloma was never evident in the pre-treatment cytospin. Considering the time lag of 10 years after conisation, it seems that it was a new lesion. The preceding cytology consistent with mild/moderate dysplasia was never obtained and thus it may be considered as a fast growing lesion that evolved within 6 months of last negative cytology. Earlier, it has been shown that patients with condylomatous lesions tend to show faster growth (Byrne et al, 1986). Alternatively, it may show a recurrence and because of false negativity of cytology due to long conisation, severe dysplasia could not be recognized earlier. Development of severe dysplastic lesions have been described at a rate of 3% following conisation of severe dysplastic lesions in a large series of British Columbia (Boyes et al, 1970). In the present series the recurrence rate was 7.1%. This higher percentage may be due to smaller series of patients. Unlike cryosurgically treated patients, none of the patients treated by conisation progressed to malignancy and there was no treatment failure of the primary lesion. Thus, conisation gave better results than cryosurgery in this series of persistent dysplasia patients. Total hysterectomy was performed in 25 patients of persistent dysplasia associated with D.U.B. or fibroid. The indications for hysterectomy were the associated conditions for symptoms control rather than for dysplasia. Neither any recurrence nor any treatment failure of the primary lesion was recorded, though patients could be followed up for an average 1.4 years; the median length of follow up was only 1.6 years. Generally, excellent results have been described of results of severe dysplasia treated by hysterectomy. In a large series of 2849 patients with severe dysplasia treated by hysterectomy was only 0.7% for

further CIN lesions and 0.25% for invasive cancers (Boyes et al, 1970).

b) Management of carcinoma in situ :

None of the CIS cases was treated by cryosurgery. Of the 50 cases of CIS, 10 were treated by conisation because of their younger age (mean age = 28.6 years) and because these women had not completed their families (mean parity = 2.0 years). One patient had recurrence after 3 years of follow up. 40 cases of CIS were treated by hysterectomy. Twenty one of these were lost to follow-up. Of the remaining 19, one developed mild dysplasia with condylomatous lesion at the first follow up at 6 month following hysterectomy. None of the pre-treatment cytology smear nor colposcopy revealed any condylomatous changes. Thus it appears that it was a newly acquired lesion.

c) Adequacy of follow up :-

In the present series 23.8% (n = 25) patients were lost to follow up. The average follow up of the patients was 2.6 years with a median follow up of 2.5 years. The loss to follow up during post operative period is a serious problem especially with the conservative management. It has been described earlier in one large, well organised screening programme (14) that only 59% had been adequately followed up and of the remainder 28% had only one follow up. Similarly in another study (Elwood et al, 1984) 18% of patients for whom a repeat smear advised had been discharged from the hospitals. These studies indicate that for a successful screening programme an adequate follow up for patients following treatment must be ensured and that communication between laboratory, clinician and the patient must be ensured.

In the present series, persistent dysplasia had significantly better follow up as compared to CIS. Likewise, loss to follow up was significantly more for those undergoing hysterectomy compared to those treated by conisation. Some of these problems arise because of the lack of

continuing organised surveillance programme of treated patients by gynaecologists. In India due to the lack of medical manpower and due to the large burden of infectious diseases as well as maternity services, gynaecologists are not left with much time for the long time surveillance of the treated women.

We thus propose to restrict conservative management for your women, smaller lesions and those could adhere to long term follow up only. Hysterectomy should be performed in older women, high grade lesions and where it is not possible for the women or their physicians to undertake a long term follow up.

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