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ORIGINAL ARTICLE

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Study of recurrences during cytological follow up in radiation treated carcinoma cervix

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OBJECTIVE(S) : To evaluate the role of cervicovaginal cytology in detection of postradiation dysplasia and recurrent carcinoma in women treated with radiation for carcinoma cervix.

METHOD(S) : The study comprised of 786 women attending gynecological outpatient clinic between January 1992 to December 2004 in whom cervical cancer in different stages was diagnosed clinically and confirmed on histological examination. These women were treated with radiation and had cytological follow up for periods ranging from 6 months upto 12 years.

RESULTS : The incidence of postradiation dysplasia and recurrent carcinoma was found to be 8.5% and 7.1% respectively. Nineteen cases of small cell carcinoma were also observed. Only 28.3% of the recurrent carcinomas were found to be symptomatic or had clinical signs of any growth. Recurrence of both cytopathologies was seen upto 8 years after radiation and was maximum in women beyond 40 years of age. Both cytopathologies showed tendency to appear late with increasing age and showed rise with increasing stage of cancer.

CONCLUSION(S) :Cytology appears to be valuable tool in detecting postraditiation dysplasia and recurrent carcinoma even when there is no clinical sign or symptom. It alerts the clinicians beforehand for the recurrence and facilitates better chances of survival for the patients.

Key words : postradiation dysplasia, recurrent carcinoma, radiation

Introduction

Cervicovaginal cytology has been established as an indispensable tool in differentiating radiation changes from the recurrence in the first few months after treatment and also for detecting recurrence of carcinoma even when there are no clinical signs or symptoms [1,2]. It also helps in detecting cases of postradiation dysplasia originating in the altered mucosa of the irradiated cervix. Since 1992 it has been our practice to call the patients treated with radiation for 3 monthly cervical cytology follow up irrespective of whether they have any symptoms or not. This has helped in detecting recurrences of both cervical dysplasia and carcinoma to provide early treatment and increase the longevity of the patients. Till December 2004, a total of 876 irradiated women have been followed for periods ranging from 6 months to 12 years and the present communication embodies the details of 67 cases of recurrent carcinoma and 75 cases of cervical dysplasia encountered during the study.

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Methods

Between January 1992 and December 2004, a total of 876 women have been registered at our center, and have been treated with radiation for carcinoma of cervix. Cervical cytology was performed in all cases after completion of treatment to rule out presence of malignant cells. Since majority of the treated patients came from remote places a planned follow up was not possible and the patients were advised to come after every 3 months for repeat Pap smear. Only 741 of them returned for follow up 6 months to 1 year after receiving radiation. Follow up after 2 years was available in 357 and after 3 years in 193, and the number substantially reduced beyond this period.

The cervical smears received from the irradiated women were stained by Papanicalou's technique and cytopathological grading of the smears was made according to WHO classification of 1973 [3].

Results

The incidence of postradiation cervical dysplasia and recurrent carcinoma during the follow up was 8.5% (75/876) and 7.1% (67/876). Of the 75 cases of dysplasia 36 had mild displasia and 39 moderate dysplasia. Of the 67 women with recurrence of carcinoma only 19 (28.3%) were symptomatic or had any growth on the cervix while 48 (71.7%) had no symptoms or clinical signs of any growth. This signifies a great utility of cytological follow up in detecting the silent recurrences even when there is no symptom or clinical sign.

Follow up cytology revealed 19 cases of small cell carcinoma 1-6 years after radiation. Since these carcinomas are known to be persistent type even after full exposure of radiation, they have not been included as recurrent carcinoma in the analysis. Majority of these small cell carcinomas were seen above the age of 40 years (68.4%), in stage-I cases (52.6%), and within one year of observation (73.6%).

The incidence of postradiation dysplasia and recurrent carcinoma in relation to clinical stage of cervical cancer is shown in Table 1. The incidence of both cytopathologies was found to be higher in stage I and III cases and was very low in stage II cases. The difference was statistically highly significant ($P<0.01$). However the difference between stage I and stage III cases was insignificant ($P>0.05$)

The periods when 75 cases of postradiation dysplasia and 67 cases of recurrent carcinoma were encountered are shown in Table 2. Maximum number of dysplasia was detected between 6 months to 1 year after radiation (46 cases) after which the incidence declined till 4 years but showed steep rise at 5 years and remained high till 8 years. However, no dysplasia was seen in smears examined beyond 8 years. As

Table 1. Incidence of postradiation dysplasia and recurrent carcinoma in relation to clinical stage of cancer.

State of cancer	No. of cases	Dysplasia		Carcinoma	
Stage I a and b	305	32	(10.4%)	22	(7.2%)
Stage II a and b	318	18	(5.1%)	19	(5.9%)
Stage III a and b	252	25	(9.9%)	26	(10.3%)

Figures in pareuthesis indicate percentages.

Table 2. Incidence of postradiation dysplasia and recurrent carcinoma in relation to duration of follow up.

Duration of follow up at the time of cytology smear	No. of cases	Incidence	
		Dysplasia (n=75)	Carcinoma cervix (n=67)
6 months to 1 year	741	46 (6.2%)	37 (4.9%)
2 years	357	15 (4.2%)	14 (3.9%)
3 years	193	6 (3.1%)	8 (4.1%)
4 years	67	2 (2.9%)	4 (5.9%)
5 years	29	2 (6.8%)	2 (6.8%)
6 years	27	2 (7.4%)	1 (3.7%)
7-8 years	35	2 (5.7%)	1 (2.8%)
9-10 years	22	- -	
11-12	6	- -	
Mean period		1.8 years	1.9 years

Figures in parenthesis indicate percentage.

Table 3. Relation between period of occurrence of dysplasia and carcinoma cervix and clinical stage of cancer.

Period of occurrence detection	Grade I			Grade II			Grade III		
	No.	Dysplasia	Carcinoma cervix	No.	Dysplasia	Carcinoma cervix	No.	Dysplasia	Carcinoma cervix
6 months to 1 year	268	18 (6.7%)	12 (4.4%)	252	15 (5.9%)	12 (4.1%)	221	13 (5.8%)	13 (5.8%)
2 years	135	8 (5.9%)	4 (2.9%)	92	2 (2.1%)	3 (3.2%)	130	5 (3.7%)	7 (5.1%)
3 years	55	3 (5.4%)	3 (5.4%)	74	1 (1.1%)	2 (2.2%)	64	2 (3.6%)	3 (4.6%)
4 years	15	1 (6.6%)	1 (6.6%)	20	-	2 (10%)	32	1 (3.1%)	1 (3.1%)
5 years	12	-	1 (8.2%)	9	-	-	8	2 (25%)	1 (12.5%)
6 years	12	-	1 (8.3%)	8	-	-	7	2 (28)	-
7-8 years	10	2 (20%)	-	16	-	-	9	-	1 (11.1%)
9-10 years	6	-	-	10	-	-	6	-	-
11-12 years	1	-	-	2	-	-	3	-	-
Man period		1.9 years	1.9 years		1.2 years	1.6 years		2.4 years	2.1 years

Figures in parenthesis indicate percentages

Table 4. Relation between postradiation dysplasia and recurrent carcinoma and age.

Age group	No. of cases	Dysplasia		Carcinoma cervix	
		Incidence	Mean period of occurrence	Incidence	Mean period of occurrence
< 30 years	62	4 (6.4%)	1.0 year	3 (4.8%)	1.5 years
31-40 years	195	15 (7.6%)	1.8 years	13 (6.6%)	1.8 years
>40 years	619	56 (9.1%)	1.9 years	51 (8.2%)	2.0 years

Figures in parenthesis indicate percentages

Table 5. Relation between age and clinical stage of cancer

Age group	Grade I			Grade II			Grade III		
	No.	Dysplasia	Carcinoma cervix	No.	Dysplasia	Carcinoma cervix	No.	Dysplasia	Carcinoma cervix
<30 years	24	4 (16.6%)	2 (8.3%)	23	-	-	15	-	1 (6.1%)
31-40 years	84	9 (10.7%)	9 (10.7%)	67	3 (4.4%)	2 (2.2%)	44	3 (6.8%)	2 (4.5%)
>40 years	193	19 (9.8%)	11 (5.6%)	217	15 (6.9%)	17 (7.8%)	184	22 (11.9%)	23 (18.4%)
Mean age		44.3 years	43.8 years		49.7 years	48.1 years		47.9 years	47.3 years

regards carcinoma cervix, although the maximum recurrence was seen between 6 months to 1 year (37 cases), the incidence remained almost identical till 5 years after which it declined till 8 years and no recurrence was observed beyond 8 years.

The mean latent period for dysplasia and carcinoma cervix was found to be identical (1.8-1.9 years). However, when this was analyzed in relation to clinical stages of cancer, it was found to be 1.6 years for both cytopathologies in stage II cases followed by 1.9 years for stage I cases and 2.1 years for III cases. (Table 3). Maximum number of both cytopathologis were seen upto 1 year in all three stages of cervical cancer. The diferene in mean period of recurrence

of dysplasia and carcinoma cervix was significant between stage I and stage II cases (P<0.0.5) and was highly significant between stage II and stage III cases (P<0.01). While the incidence of both dysplasia and recurrent carcinoma cervix showed increases till 8 years, it showed decline in stage II cases where no cytopathology was observed beyond 4 years.

Relation between the occurrence of the dysplasia and carcinoma cervix in relation to age is depicted in Table 4. The dysplasia was found to appear comparatively at an early age (mean age – 38.1 years) than carcinoma cervix (45.2 years). However, both cytopathologies showed progressive rise with increasing age being maximum in women beyond 50 years of age (9.1% of dysplasia and 8.2% of carcinoma cervix). The mean latent period of both cytopathologies showed rise with increasing age indicating that recurrences of both dysplasia and carcinoma cervix had tendency to appear late with increasing age.

Relation between occurrence of both cytopathologies was also investigated age wise in different clinical stages of cervical cancer (Table 5). The incidence of recurrence of both dysplasia and carcinoma cervix was maximum below 30 years age in grade 1 cases while this was highest in women beyond 40 years in grade 2 and 3 cases. The mean age of recurrent dysplasia and carcinoma cervix was earlier (44 years) in stage I cases and later in stage II (48-50 years) and stage III cases (47-48 years).

Further follow up was available after treatment in 25 of the 75 postradiation dysplasias and in 36 of the 67 recurrent carcinomas. While all 36 cases of carcinoma showed normal cytology on next follow ups, persistence of dysplasia was seen in 2 of the 25 cases.

Discussion

Cytological evaluation of cervical smears in 876 women treated with radiation for cervical carcinoma asserted the immense utility of cytology in detection of recurrences, both of dysplasia and carcinoma cervix even when there was no symptom or clinical sign of the disease. Timely picking up of these silent recurrences by cytology is of considerable help in alerting clinicians for early treatment of the lesion and enhancing the longevity of the patient. The incidence of postradiation dysplasia and carcinoma cervix was found to be 8.5% and 7.6% respectively. More recurrences could have been noticed if a regular follow up after radiation would have been possible. It needs sincere efforts on the part of clinicians for providing proper education and guidance to the patients regarding regular follow up.

Many investigators have also emphasized great accuracy of cytology as useful adjunct to clinical examination in follow up of treated carcinoma cervix cases. Shield and Wright [4] have also found cytological diagnosis of locally recurrent carcinoma to preceed clinical signs in 24.5% and have asserted that cytology is a valuable tool in detection of locally recurrent lesions. Whittaker et al [5], have reported the overall sensitivity of cytology in diagnosing the recurrent carcinoma as 85% with a specificity of 99.5% [5].

In the present series, both postradiation dysplasia and recurrent carcinoma cervix were optimally detected between 6 months to 1 year after radiation therapy; both bite cytopathologies were seen as late as 8 years. Meckenzie et al [2] have reported recurrence of cancer cervix only upto 5 years. Koss et al [6] have reported dysplasia appearing as late as 17 years after radiation. The mean latent period when squamous intracepithelial lesion and carcinoma cervix appeared in our series was identical (1.8 and 1.9 years respectively). However both cytopathologies occurred early in younger women below 30 years (mean latent period being 1.0 year for dysplasia and 1.5 year for carcinoma cervix). The mean period of occurrence was identical for both cytopathologies in women between 31-40 years (1.8 years) and beyond 40 years (2.0 years) (Table 4). On the other hand Pattern et al [7] have found mean latent period of dysplasia as 2.87 years in young women and 5.9 years in older women [7].

Conclusion

The recurrence of dysplasia and carcinoma cervix was found to be higher in stage I and III cases than in stage II cases. The mean latent period of both cytopathologies was also late in stage I and III than in stage II cases. However, the mean age of both dysplasia and carcinoma cervix showed tendency to appear early at an earlier age according to increasing stage of caner.

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