

Post Irradiation Cytopathology of Cervical Cancer Patients

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Abstract

Introduction: Pap smear from uterine cervix or vaginal vault (in hysterectomised) patient is an important tool for follow up after completion of radiation therapy. It is quick, simple and cost effective. It can be used for monitoring and early detection of residual/recurrent neoplasm. In this study we report the cytopathological changes in patients undergoing radiation therapy for carcinoma cervix. **Aim and Objectives:** This study aims at awaring about cellular changes resulting from irradiation and varied composition of post irradiation smear which may lead to more accurate interpretation of cytological findings. **Material and Methods:** This is a descriptive study of 42 cases presented in cytological section of department of Pathology, PMCH, Patna from January 2020 to March 2021. Pap-smear was collected from vaginal vault in hysterectomised patient and from endocervix/ectocervix in patient who retained uterus due to one or another reason. Pap-smear was collected on three occasion i.e. on 1st follow up at one month of completion of radiotherapy, 2nd follow up at four month after completion of radiotherapy and 3rd follow up at ten month after completion of radiotherapy. **Observations:** Out of 42 carcinoma cervix patients participating in this study, youngest patient was a 26 years old married female coming from a rural area and was having well differentiated squamous cell carcinoma. Another female was 30 years old with a history of early marriage and having three children. Peak incidence in this study was observed in age group 41-50 years with all grades of squamous cell carcinoma i.e well, moderately and poorly differentiated SCC and one case of adenocarcinoma of endocervix. In age group greater than 61 years, five cases were seen of which one was diagnosed as poorly differentiated SCC. Rest four were well differentiated SCC. **Conclusion:** Cytology is a valuable tool for the detection of local recurrence of carcinoma cervix. It is simple and economical to perform at the time of follow up examination of the patients of carcinoma cervix after completion of radiotherapy. Awareness of cellular changes resulting from irradiation and varied composition of post irradiation smear led to more accurate interpretation of cytological finding. However cytological features of post irradiation dysplasia are difficult to distinguish from recurrent carcinoma cervix and owing to its higher progression rate of colposcopic examination and biopsy are recommended.

Keywords: Squamous cell carcinoma of cervix, post radiotherapy, pap smear, benign reactive changes

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Introduction

Carcinoma cervix is one of the most common neoplasm of Indian female other being carcinoma breast and oral neoplasm. According to ICMR reports in India carcinoma cervix has increased from 0.11 million in year 2000 to 0.16 million in year 2010. The proportion ranged from 15-55% of female cancer from different parts of country. Over 80% of the cervical cancer presents at a fairly advanced stage and annually around 80,000 deaths are reported in India. The mainstay treatment for carcinoma cervix comprises of hysterectomy and radiotherapy combined with chemotherapy. Patients undergo surgery, external beam radiotherapy, concurrent chemotherapy, Brachytherapy etc according to the recommendation for their stage of the carcinoma cervix. Patients who successfully completed the planned treatment were called for follow at completion of 1 month, 4 months and 10 months. At the time of follow up clinical examinations including PR and PV, routine blood examinations, USG of Whole abdomen and pelvis and Pap-smear were performed. The presence of nodularity of the cervix, vagina or rectum should prompt biopsies. In carcinoma cervix patients following radiotherapy there are anatomical and tissue

changes which may compromise cervicovaginal cytology. Collection of representative samples may be difficult and benign radiation changes, post irradiation dysplasia and frequent occurrence of repair cells and active stomal cells in post irradiation smear may cause diagnostic problems[1].

Material and Methods

This is a descriptive study of 42 cases presented in cytological section of department of Pathology, PMCH, Patna from January 2020 to March 2021. All the female patients of any age group who were having HPE confirmed carcinoma cervix and who underwent radiotherapy in department of Radiotherapy, PMCH, Patna, were taken in account. Informed consent was taken from the patients who showed willingness to participate in this study. Pap-smear was collected from vaginal vault in hysterectomised patient and from endocervix/ectocervix in patient who retained uterus due to one or another reason. Pap-smear was collected on three occasion i.e. on 1st follow up at one month of completion of radiotherapy, 2nd follow up at four month after completion of radiotherapy and 3rd follow up at ten month after completion of radiotherapy, was collected on clean slide, wet fixed and stained with Papanicolaou stain and then examined under microscope.

Observations

Histopathological findings, treatment and cytopathological finding in follow up patients of carcinoma cervix.

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Table 1: Histopathological findings, treatment and cytopathological finding in follow up patients of carcinoma cervix

Age group	No. of Patient	Diag. on HPE	Cytopathological findings (months)		
			1 st	4 th	10 th
20-30 yrs	2	WD SCC	BRC+NILM	NILM+LB	NILM
31-40yrs	12	WD+MD SCC and ADCA	BRC+IC+C	BRC+IC+LB	BRC+NILM
41-50 yrs	14	WD+MD+PD SCC	BRC+AC	BRC+ NILM+C	BRC+NILM
51-60 yrs	9	WD+MD SCC	BRC	BRC+SCC (1 case)	BRC+NILM
≥61	5	WD+PD SCC	AC+C	BRC+AC+C	SCC (1 case)

SCC – Squamous cell carcinoma, WD – Well differentiated, MD – Moderately differentiated, PD – Poorly differentiated, BRC – Benign reactive changes, IC – Inflammatory changes, AC – Atrophic changes, LB – Lactobacillus, C – Candidiasis, NILM - Intra epithelial Lesion or Malignancy

Out of 42 carcinoma cervix patients participating in this study, youngest patient was a 26 years old married female coming from a rural area and was having well differentiated squamous cell carcinoma. Another female was 30 years old with a history of early marriage and having three children. Peak incidence in this study was observed in age group 41-50 years with all grades of squamous cell carcinoma i.e well, moderately and poorly differentiated SCC and one case of adenocarcinoma of endocervix. In age group greater than 61 years, five cases were seen of which one was diagnosed as poorly differentiated SCC. Rest four were well differentiated SCC. In history taking it was found that 29 patients out of 42 belonged to lower-to-lower middle class with rural background and 26 patients were having 3 or more children.

Discussion

In present study benign reactive morphological changes are the most common finding obtained on cytological examination of post radiation carcinoma of cervix in first follow up. Radiation associated changes includes marked cellular and nuclear enlargement with reservation of nucleus - to -cytoplasmic ratio, cytoplasmic vacuolation and cytoplasmic polychromasia (two-tone cytoplasm). Some large bizarre cells may also be seen. Even though the cells are large, the N:C ratio is maintained. Nucleus have fine granular chromatin and there can be nucleus as well as cytoplasmic vacuolation. Cells are isolated or arranged in groups and multinucleation is common[2]. In our study in first month Karyomegaly and anisokaryosis were seen in 51% cases. Cytoplasmic vacuolation and polychromasia was seen 17% cases and multinucleation and cellular gigantism was seen in 9% cases. Radiation can cause morphological and molecular changes in neoplastic and non-neoplastic cells due to interference in mRNA synthesis, decrease in protein production, inhibition of DNA synthesis and mitotic activity as well as cytochemical changes, with protein denaturation and enzyme release with the subsequent destruction of cytoplasmic organelles. In first month follow up 16% patients shows inflammatory with atrophic pattern which is described the literature as a finding induced by ionising radiation, since it promotes DNA changes preventing the maturation process[3]. These changes appears once the reparative changes resolve and may persists for several years. In rest 7% NILM with reparative changes was observed. Typical repair is composed of flat sheet of cells that have an enlarged nucleus, a prominent nucleolus and occasional mitosis. Polarity is uniformly maintained giving rise to streaming effect [4]. The features that favour repair over malignant lesions are – Flat sheet arrangements of cells, rather than syncytia or three-dimensional clusters. The lack of nuclear overlapping; The lack or rarity of single cells; The lack of tumour diathesis. The fact that all the nuclear in the same sheet exhibit similar features- i.e size, shape, chromatin pattern and nuclear status[5]. These reparative changes result from injury to the cervical epithelium and the proliferation of reserve cells which grow to reepithelialise a focus of ulceration[4]. Zannoni and Vellone (2008) evaluated the diagnostic accuracy of cytopathology in patients with cervical cancer after radiotherapy, finding 46% of smears with benign alterations

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produced by radiochemotherapy, 20% with atrophy and 9% with inflammation. The authors reported that cytoplasmic and nuclear enlargement, multinucleation, cytoplasmic vacuolation, and bizarre cells forms such as fibroblasts and tadpole were among common morphological changes in post irradiation pap smear. Collaborating much of the morphological changes found in the present study. Candida was seen in 20% of cases in the 2nd follow up at 4 months of radiotherapy only 34 patients turned up. Among them in 60% patients' benign reactive changes persist. In 1 patient the smear was cellular as against the scattered radiation cells. Cells show significant atypia i.e markedly decreased N:C ratio. Cellular enlargement with nuclear margin and marked hyperchromasia, coarse chromatin with few spindle cells and tadpole cells were also present. So, this was labelled as recurrent Squamous cell carcinoma. In 6 patients atrophic changes with NILM seen. In 7 patients NILM with inflammation was observed. Lactobacillus was seen 4 patients. Candida was present in 2 smears. In 3rd follow up at 10 months only 28 patients turned up, among them NILM with inflammatory changes was present in 21 cases. In 2 cases benign reactive changes like bizarre cells with multinucleation persisted, in 4 cases atrophic changes were seen whereas in 1 case atypical squamous epithelial cells seen which was labelled as recurrent squamous cell carcinoma. In this case patient was of 62 years, presented with bleeding PV and dysuria on further investigation urinary bladder mucosa was found to be involved so it was labelled as IVa according to FIGO classification.

Conclusion

From above observations and discussion, it is clear that cytology is a valuable tool for the detection of local recurrence of carcinoma cervix. It is simple and economical to perform at the time of follow up examination of the patients of carcinoma cervix after completion of radiotherapy. Awareness of cellular changes resulting from irradiation and varied composition of post irradiation smear led to more accurate interpretation of cytological finding. However cytological features of post irradiation dysplasia are difficult to distinguish from recurrent carcinoma cervix and owing to its higher progression rate of colposcopic examination and biopsy are recommended.

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