OBSERVATIONS WITH ADENOCARCINOMA OF UTERINE CERVIX

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ABSTRACT

BACKGROUND

Adenocarcinoma comprises of about 10% of cancer cervix. Late presentation, infiltrative growth, larger tumour bulk, poor radiosensitivity and quick recurrence makes this disease a field of special concern. Very low number of cases are reported in literature. Therefore, a standard protocol for management of adenocarcinoma has not yet been clearly established.

This study is an observational study from the pool of total number of early invasive cancer cervix who had undergone radical surgery in our institute and compare them with squamous cell carcinomas of cervix with regard to several parameters like incidence, age, parity, histopathology, morphology, response to treatment and recurrence patterns.

MATERIALS AND METHODS

A total number of 541 patients of early invasive cancer cervix who underwent radical hysterectomy during the period January 2006 to January 2016 in A.H. Regional Cancer Centre, Cuttack, and followed upto 5 years or more were studied. A retrospective analysis was done to study the incidence and observe and compare the epidemiological parameters, histopathological grade, morphology, nodal involvement and survival statistics of adenocarcinoma with that of squamous cell carcinoma of cervix.

RESULTS

Adenocarcinoma comprised 9.1% of total number of cases. Majority were 50-59 years and in para 3-4 group. Infiltrative lesion was seen in 44% of cases, 40% of the growth were more than 5 cm in diameter and 92% were well-differentiated. Though nodal involvement didn't show much difference from squamous cell cancer, 36% of adenocarcinomas needed adjuvant radiotherapy. The 5 years disease-free survival was better with squamous carcinoma (88.4%) than adenocarcinoma (84%).

CONCLUSION

Though, potentially a different tumour compared to squamous cell carcinoma, for adenocarcinomas of cervix surgery is the mainstay of treatment. The role of radiotherapy, being controversial, judicious postoperative radiotherapy has to be given as and when required.

KEYWORDS

Adenocarcinoma, Cervix, Radical Surgery, Radiotherapy, Survival, Recurrence.

HOW TO CITE THIS ARTICLE: Mohapatra J, Parija J. Observations with adenocarcinoma of uterine cervix. J. Evid. Based Med. Healthc. 2017; 4(75), 4408-4411. DOI: 10.18410/jebmh/2017/878

BACKGROUND

The adenocarcinoma of cervix comprises of 10% of all cases of carcinoma cervix (Kilgore et al).[1] Yet, it generates many controversies in the management. Early age, late detection, infiltrative nature of the growth and poor radiosensitivity, keeps this disease as a separate entity than squamous cell carcinoma of cervix. Prognostically, adenocarcinoma is potentially eruptive than matching groups of squamous cell carcinoma. Due to low incidence of adenocarcinoma, the prognostic features are less clearly defined in literature. As it stands today, no definitely different policy to manage adenocarcinoma of the cervix has been defined. An attempt has been made to study the comparison of adenocarcinoma of the cervix with that of squamous cell carcinoma in relation to histopathology, prognostic variables, treatment methods and outcome.

Aims and Objectives- Our objective was to analyse adenocarcinomas of cervix from the total number of early invasive cancer cervix who had undergone radical surgery in our institute and compare them with squamous cell carcinomas of cervix with regard to several parameters like incidence, age, parity, histopathology, morphology, response to treatment and recurrence patterns.

MATERIALS AND METHODS

A total number of 541 cases of early invasive carcinoma of the cervix who underwent radical hysterectomy at Acharya Harihar Regional Cancer Centre, Cuttack, during the period January 2006 - January 2012 were retrospectively analysed. All cases were followed up for 5 years or more. The adenocarcinomas and squamous cell carcinomas were compared in relation to risk factors, presentation,

Financial or Other, Competing Interest: None.
Submission 26-08-2017, Peer Review 04-09-2017,
Acceptance 13-09-2017, Published 15-09-2017.
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DOI: 10.18410/jebmh/2017/878

pathological differentiation, nodal status, treatment and results keeping in mind the erratic behaviour of adenocarcinoma and its intrinsic problem.

RESULTS

Histopathology	No. of Cases	%
Adenocarcinoma	49	9.1
Squamous cell carcinoma	492	90.9
Total	**541**	**100**
Table 1. Distribution of Cases According to Histopathology		

Sl. No.	Adenoca No.	Adenoca %	SCC No.	SCC %
Stage IB	20	40	357	72.5
Stage IIA	22	44	94	19.2
Stage IIB	7	16	41	8.3
Table 2. Distribution of Cases Stage Wise				

Chi-square test of association. Chi-square statistic is 22.0491. The p-value is 0.000016. The result is significant at p <0.05.

Age in Yrs.	Adenoca No.	Adenoca %	SCC No	SCC %
20-29	2	4	11	2.3
30-39	8	16	104	21.1
40-49	14	28	177	36
50-59	23	48	161	32.7
60+	2	4	39	7.9
Table 3. Age Distribution				

Chi-square test of association. The Chi-square statistic is 5.3391. The p-value is 0.254236. The result is not significant at p <0.05.

Parity	Adenoca Number	Adenoca Percentage	SCC No.	SCC %
0	2	4	6	1.2
1-2	6	12	27	5.5
3-4	21	44	202	41.1
5+	20	40	257	52.2
Table 4. Parity Relationship				

Chi-square test of association. The Chi-square statistic is 6.9741. The p-value is 0.072728. The result is not significant at p <0.05.

Tumour Diameter in cms	Adenoca No.	Adenoca %	SCC No.	SCC %
<2	17	34.7	248	50.4
2-4	12	24.5	155	31.6
>4	20	40.8	89	18
Table 5. Tumour Size				

Chi-square test of association. The Chi-square statistic is 14.3802. The p-value is 0.000754. The result is significant at p <0.05.

Type	Adenoca No.	Adenoca %	SCC No.	SCC %
Exophytic	17	34.7	408	82.8
Infiltrative	22	44.9	84	17.2
Endocervical	10	20.4	-	-
Table 6. Morphology				

Chi-square test of association. The Chi-square statistic is 120.7043. The p-value is <0.00001. The result is significant at p <0.05.

Differentiation	Adenoca No	Adenoca %	SCC No.	SCC %
Well differentiated	45	92	70	14.2
Moderately differentiated	-	-	66	13.4
Poorly differentiated	-	-	355	72.4
Adenoacanthoma	4	8	-	-
Table 7. Tumour Differentiation				

Chi-square test of association. The Chi-square static is 183.4305. The p-value is <0.00001. The result is significant at p <0.05.

Stage	Total Number Adenoca	Number of Node + Adenoca	Percentage Node + Adenoca	Total Number of SCC	Number of Node + SCC	Percentage of Node + SCC
IB	20	2	10	357	91	23.2
IIA	22	3	13.6	94	43	41.3
IIIB	7	4	57.1	41	26	57.8
Total	49	9	18.37	492	160	32.52
Table 8. Nodal Status						

Chi-square test of association. The Chi-square statistic is 22.1259. The p-value is 0.000016. The result is significant at p <0.05.

Histopathology	Total	5 Year DFS-No.	5 Year DFS-%	Mean Time for Recurrence
Adenocarcinoma	49	41	84%	373 days
Tt (S_X-64%)				
Tt (S_X + RT-36%)				
Squamous cell carcinoma	492	435	88.4%	337.7 days
Tt (S_X-72.5%)				
Tt (S_X+RT-27.5%)				
Total	**541**	**476**	**87.9%**	

Table 9. 5 Years Disease-Free Survival

DISCUSSION

Adenocarcinoma comprised 9.1% of cases in this series in comparison to 90.9% of squamous cell carcinoma (Table 1). This observation is in this series of consecutive cases and compares well with the 10% incidence of Kilgore et al.[1]

Majority of the cases belonged to stage IB in the squamous cell carcinoma group, whereas 44% of adenocarcinomas were in stage IIA. Late presentation of adenocarcinomas is well documented by Kline et al (Table 2).[2]

Adenocarcinoma was more commonly seen in the elderly age group of 50-59 years, whereas squamous cell carcinoma was more common in the 40-49 years age group (Table 3). According to a study by John O. Schorge, Lynne M. Knowles,[3] there also appears to be a recent shift in the epidemiology of the disease process with younger women being diagnosed more frequently.

High parity was associated more with squamous cell carcinoma (52.2%) than adenocarcinoma (Table 4).

Tumours of more than 4 cms in diameter was seen in 40% cases of adenocarcinoma in contrast to 17.9% of squamous cell carcinoma (Table 5). May late presentation is a factor influencing the size of the lesion in the format.

Adenocarcinomas were mainly infiltrative in nature (Table 6). Exophytic growth was seen in 82.8% of squamous cell carcinomas in comparison to 36% in the adenocarcinoma group.

Differentiation of the lesion influences the prognosis according to Shingleton et al.[4] Adenocarcinoma was most commonly well differentiated (92%); whereas 72.1% of squamous cell carcinomas were poorly differentiated (Table 7).

Nodal infiltration with stage matching is shown in Table 8. It was observed that more advanced the stage, more was the node infiltration. Squamous cell carcinoma showed a higher incidence of nodal infiltration. This proved beyond doubt that adenocarcinoma stays localised for a fairly longer period.

Surgery was supplemented with radiotherapy in 36% of adenocarcinomas and 27.5% of squamous cell carcinomas, respectively. Adjuvant therapy was decided on the amount of node infiltration and any specific dissection problem that was encountered during surgery. With this modality of treatment, the 5-year disease-free survival was 84% with adenocarcinomas. The squamous cell carcinoma showed a better disease-free survival of 88.4%. The mean recurrence period was 373 days with adenocarcinoma and 337.7 days with squamous cell carcinomas (Table 9). After the end of 1 year of treatment; recurrence was virtually absent. Radiotherapy administered postoperatively does not improve the salvage rate, rather it adds to morbidity (Cuecia et al). In the present series, there is marginally better result in adenocarcinoma with a little higher postoperative radiotherapy use than in the squamous cell carcinoma group.

Harriet O, Smith MD, et al 2000[5] observed that survival rates for adenocarcinoma vs. squamous cell carcinoma were poorer for regional (P = 0.04), but not localised or distant disease. Takashu Nakano, Tatsuo Arai et al[6] in their study showed that the survival rate and local control rate for large tumours were significantly lower than those for small and medium tumours. Multiple regression analysis indicated that stage and tumour volume were independently variables for survival and local control, respectively. The data of PW Grisby, CA Perez et al[7] indicate that adenocarcinoma of the uterine cervix does not confer a worse prognosis than does epidermoid carcinoma when all other factors are equal. Those factors most significant for survival are size of the primary lesion and the presence of positive lymph nodes. A Baalberger, PC Ewing et al[8] in their retrospective analysis to determine the prognostic factors for adenocarcinoma cervix found that, for patients with stages I and IIA disease, survival was significantly better where the primary treatment was surgical as opposed to primary radiotherapy (P = 0.002). Longest survival was for patients with early stage disease, younger patients and after primary surgery. They found FIGO stage, grade and lymph node metastases of significant prognostic value for survival in cervical adenocarcinoma.

CONCLUSION

A series of 541 cases of early invasive carcinoma cervix who underwent radical hysterectomy were retrospectively analysed. The adenocarcinomas, which comprised 9.1% of the series were compared with squamous cell carcinoma for its different behaviour and poor radiosensitivity. Adenocarcinomas mostly present a decade later than squamous cell carcinomas and are seen in the lower parity group. The tumour mass stays infiltrative in nature (44%) in adenocarcinomas, so larger tumours, more than 4 cms, came for treatment in 40% of cases. The exophytic variety in squamous cell carcinoma was 82.8% and almost half (49.5%) of the cases were less than 2 cms in diameter. Adenocarcinomas were mostly well differentiated (92%) in contrast to 71.2% of the poorly-differentiated variety in squamous cell carcinomas. Differentiation in this series has contributed a lot for survival in adenocarcinomas, which almost matched the squamous cell carcinomas in spite of the

large growth encountered in adenocarcinomas. More nodes were affected in squamous cell cancer than adenocarcinomas in all stages, which is an important factor for prognosis in this series of adenocarcinomas. It was observed that, beyond one year of treatment, the chance of recurrence was extremely rare. Disease-free survival of patients through five year or more follow-up showed a good prognosis of 84% in adenocarcinoma with a 36% adjuvant radiotherapy rate. In squamous cell carcinomas, the postoperative radiotherapy rate was 27.5%. The five year disease-free survival was 88.4%. The number of cases of adenocarcinomas in this series and also in other reports are so small that no definite difference from squamous cell carcinoma can arrived at. Late detection of adenocarcinomas and misleading staging due to infiltrative lesions is a big problem. Surgery is the mainstay of treatment because of poor radiosensitivity and when judicious combined with postoperative radiotherapy yields optimum results.

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