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ADNOCARCINOMA OF THE CERVIX (A Report of 363 Cases)

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From 1959 through to May, 1993, 363 patients with adenocarcinoma of uterine cervix were initially treated which accounted for 2.5% of all initially treated cases with cervical carcinoma. Patients' mean age was 50.5 years. 46% of the cases were post-menopausal. The main symptom was irregular vaginal bleeding and/or discharge. Over 88% of the cases were in stage II and III of the disease, they were treated with radiotherapy alone. The overall 5-years survival rate was 51.8%. The recurrence rate was 17.4% with a mean time to recurrence of 33.3 months Thirteen patients recurred beyond 5 years. Recurrence was accompanied with lung metastasis in 17 patients and supraclavicular lymph node metastasis in 11. Among patients whose tumor recurred the 1- and 2- year survival rate were 35.2% and 19.2% respectively. The most significant prognostic factors were the stage of disease, the size of the tumor and the histologic subtypes.

Key words: Cervical carcinoma, Radiotherapy, Adenocarcinoma, Prognosis

The incidence of cervical adnocarcinoma has been increasing past decades.[1] From 1959 through to may, 1993, 14782 patients with primary cervical carcinoma were initially treated in cancer hospital. Chinese academy of Medical sciences. Of these, 363 (2.5%) had cervical adnocarcinoma. The percentage of adenocarcinoma has been increasing: 1.7% between 1959 and 1968, 5.08% between 1979 and 1988, and 8.9% during 1989 to 1993. The epidemiology, biologic behavior and survival appear to differ when adenocarcinoma is compared with squamous cell cancer in literature.[2]

In the current study, we analyzed retrospectively 363 cases with cervical adenocarcinoma treated at cancer institute of CAMS to evaluate the factors influencing on the prognosis.

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PATIENTS AND METHODS

During the period from 1959 to May, 1993, 363 patients with adenocarcinoma of the cervix were initially treated at our hospital. Patients were staged according to FIGO criteria, all slides were reviewed by pathologists. Patients' mean age was 50.5 years (19 to 78), 310 patients had definite records of menstrual and obstetrical histories, the mean number of deliveries was 5.1, 7.7% of these patients were nulliparous or single. The main symptom was irregular vaginal bleeding and/or discharge. In 170 patients, the tumor size was under 4 cm and in 193 it was over 4 cm. 35 patients' uteruses were enlarged over 6 gravid week (GW). The proportion of stages I to IV were 5.23% (19), 43.53%(158), 44.63%(162), 6.61%(24),

respectively. The histologic subtypes were identified as follow; endocervical adnocarcinoma (197 patients), papillary adenocarcinoma (55 patients), mucinous adenocarcinoma(28 patients), clear cell adenocarcinoma (24 patients). endometrioid adenocarcinoma (15 patients) and adeno squamous cancer (44 patients). The degree of differentiation could be estimated in 231 patients, of them 78 well differentiated (Grade I), 118 moderately differentiated (Grade II) and 35 poorly differentiated (Grade III). The main treatment modality was radiotherapy alone which was similar to that of squamous cell carcinoma of the cervix,[3,4] 30 patients received combination therapy (operation plus radiotherapy)> Statistical calculations were done using life-time table method and X^2 test.

RESULTS

Stages and Survival

The overall 5-year survival rate was 51.8% and 5-year survival rates in stages I to IV were 81.9%, 64.9%, 40.0% and 4.2% respectively. The difference was statistically significant ($P<0.05$). Only one patient with stage IV (involved the vulva) survival more than 5 years.

Histologic Subtypes and Survival

The 5-year survival rates in patients with various histologic patterns were: of the endocervical adnocarcinoma it was 53.1%, papillary adnocarcinoma 54.6%, mucinous adenocarcinoma 15.3%, clear cell adenocarcinoma 52.4%, endometrioid adenocarcinoma 58.0%, adenosquamous cancer 59.3%. The difference between patients with mucinous adenocarcinoma and others was statistically significant ($P<0.05$). There were no different in survival among the other subtypes.

Tumor Size And Survival

Patients in grade I to III, the 5-year survival rates were 48.8%, 47.5% and 37.6%, respectively. There was no statistically significant difference in our cases ($P>0.05$).

The size of uterus did also not correlate with the survival, when the uterus size < 6 Gws, the 5-year survival rate was 52.6%, when uterus > 6 Gws it was 42.5% ($P> 0.05$).

Sixty-three patients recurred or metastasized (17.4%) in our cases, mean time to recurrence was 33.3 months (median, 13 months), 46 patients recurred within 3 years, 13 patients recurred beyond 5 years, one patient developed recurrent disease 25 years after initial treatment. The most common sites of recurrence were the pelvis and regional lymph nodes (52.4%). Patients accompanied with lung metastasis and surpraclavicular lymph node metastasis were 27.0% and 17.5% respectively. 8 patients (12.6%) had metastasis to bones and 3 patients (4.7%) had metastasis to ovaries. Among patients whose tumor relapsed, the 1- and 2-year survival rates were 35.2% and 19.2% respectively.

Complications

Nineteen patients (5.5%) experienced radiation rectitis, 2 of these had rectovaginal fistula, mean time to discover was 2.2 years, 10 patients (2.8%) experienced cystitis with mean time of 8.5 years. No patient had vesicovaginal fistula. Besides, 15 patients experienced pyometrium during the course of radiotherapy, all patients were relief or recovered by conservation management.

DISCUSSION

The management for cervical adenocarcinoma needs to be individualized depending on the stage and clinical presentation. In early stage, the proper treatment is radical hysterectomy, bilateral salpingo-oophorectomy and pelvic lymph node dissection. adjuvant therapy after surgery may be adopted according to various factors such as lymph node status, depth of invasion, etc. Some authors suggested that patients with large tumor size should be given combination therapy (radiation plus surgery), but conflicting opinions also existed.[2,5,6] Radiotherapy is the major treatment modality for those who can not be operated.

In current group the major treatment modality was radiotherapy alone, the overall 5-year survival rate was 51.8%. Factors influencing on survival were:

1. Clinic stage: Our study agrees with other reports,[7] the stage of disease is a critical factor influencing survival. The 5-year survival rate were decreased corresponding the stage increased, the difference between I-IV stages were statistically

significant.

2. Histologic subtypes: adenosquamous carcinoma had been reported to have a poorer prognosis whereas papillary adenocarcinoma has a favourable prognosis when they compared with the other subtypes.[8,9] In our series, the prognosis of mucinous adnocarcinoma was the worst, its 5-year survival rate was only 15.3%, but the difference among other subtypes were not statistically significant.

3. The primary tumor size: Reports from many center showed that tumor size is a well-known prognostic factor.[10] In our study, patients with tumor size < 4 cm had excellent survival than those of tumor size > 4 cm ($P< 0.05$).

In our series, the 5-year survival rate in patients with uterus enlarged was lower than that of patients with normal uterus (42.5% VS 52.6%), although the difference was not statistically significant as the numbers of former group was small, but it is worth to pay attention to this. Tumor grade did not correlate with the survival. Because of radiotherapy, we could not estimated the lymph node status impacting on the survival.

The recurrence rate was 17.4%, mean time to recurrence was later than those of other reports,[10,11,12] 20% of recurrence patients relapsed beyond 5 years, the latest one developed recurrent disease in 25 years after initial treatment. It suggests that adenocarcinoma of the cervix has the potential of late recurrence.[1] The high risk for metatase to lung and/or supraclavicular lymph node is similar to other reports.[8,12] In this study, the proportion of metastases to ovarians and bones were 4.7% and 12.6% respectively, the risk for metastasis to ovarian may be higher than that of squamous cell carcinoma of the cervix. Patients with recurrence had a poorly prognosis, the 2-year survival rate was only 19.1% Adenocarcinoma of the cervix appears to be not sensitive to radiation and the prognosis has been reported worse than that for squamous cell carcinoma.[2,7] It might be proper to increase the dosage in radiotherapy. Patients with poor prognostic factors such as large tumor size, advanced disease, mucinous adenocarcinoma, etc. should be managed by combination methods. We are now trying to adopt chemotherapy combining with radiotherapy and thermotherapy plus radiotherapy to improve the prognosis of this kind of disease.

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