A RARE CASE OF TWO MALIGNANCIES: CARCINOMA OF THE BREAST AND UTERINE CERVIX

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ABSTRACT

A female patient who had two primary cancers was investigated. Biochemical analysis of patient's serum for different parameters indicated an alteration in the metabolic process. Prognostically, the patient has shown favourable clinical features.

KEY WORDS: Multiple neoplasm, breast cancer, cervical cancer

CASE REPORT

A postmenopausal woman, 55 years old from Aurangabad, Bihar, with the history of breast carcinoma and cervical carcinoma presented in the Department of Radiotherapy, Lok Nayak Hospital, New Delhi, after simple mastectomy operation. In 1995, the patient first noticed a lump in her left breast. The lump was painless and growing slowly. There was no history of any discharge from the nipple. Simple mastectomy was done in December 1997. The preoperative examination revealed non-tender mobile lump (stage II) which was not fixed to deeper structures. There was no involvement of either pectoral muscle or pectoral fascia. The size of the breast tumor was 3x2 cms, and it was situated in the lower-lateral quadrant of breast. The tumor had no fixity to the skin and no ipsilateral or contralateral axillary lymph node was palpable. The tumor was histopathologically diagnosed as infiltrating duct carcinoma of the breast.

The patient experienced watery discharge and bleeding per vaginum since June 1997. Her pelvic examination showed an ulceroproliferative and

necrotic bulky growth on cervix, which was hanging down into vagina. Induration was present in the anterior wall of vagina. Parametrium was thick and infiltration extended up to lateral pelvic walls. Rectal mucosa was free, and there was no malignant invasion of bladder or urethra. Histopathologically the tumor was a moderately differentiated squamous cell carcinoma.

The treatment outline was decided after considering the early stage of the breast malignancy (stage II - T₂ N₀M₀), histopathological diagnosis of infiltrating duct carcinoma with safe margins of resection and no lympho-vascular invasion on simple mastectomy specimen, absence of any axillary involvement pre-operatively or per-operatively, and postmenopausal state of the patient. It was decided to put the patient on tamoxifen therapy (Tab. Tamoxifen 10 mg BD) and irradiate the cervix first as the presenting complaint was carcinoma cervix IIIB (moderately differentiated squamous cell carcinoma). A combination of external beam radiation therapy by telecobalt and intracavitary radiation therapy by remote controlled brachytherapy unit (Selectron) delivering a total dose of 80 Gy at Point A and 60 Gy at Point B was used. A complete response was achieved and the patient was put on close follow-up

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with continuing tamoxifen therapy. At the last follow-up, the patient has been found to be free of disease at both primary sites.

The patient's personal history revealed that she was a non-vegetarian and had habit of taking 'hukkah' (a form of tobacco smoking in rural areas of India). The age at menarche of the patient was 7 years and the age at menopause was 45 years. The patient got married at the age of 7 years. The age at consummation of marriage was 16 years and her age at 1st child birth was 17 years. The history regarding the duration of her menstrual cycle and period of bleeding was normal throughout her reproductive life. The parity of the patient was 11 and there was no history of abortion or death of any child. She gave birth her last child 15 years ago. There was no family history of malignancy.

LABORATORY INVESTIGATION

After an over-night fasting, 6ml. of peripheral venous blood was collected from the patient before initiation of any treatment in the Radiotherapy Department. The serum was separated for different biochemical analyses. The patient's fasting blood glucose level (160 mg/dl) and serum albumin level (6.0 g/dl) were found to have higher than corresponding normal values. Further, serum levels of urea (18 mg/dl), uric acid (3.5 mg/dl), creatinine (1.4 mg/dl) and protein (6.8 g/dl) were in the physiological range. Also, normal levels were observed in cases of serum total bilirubin (0.4 mg/dl), aspartate aminotransferase [AST/SGOT] (5.2 IU/L) and alanine aminotransferase [ALT/SGPT] (2.5 IU/L). Patient's inorganic phosphorus (11.5 mg/dl) and total acid phosphatase (94.0 IU/L) values of the blood were found to be higher; but her alkaline phosphatase level (254 IU/L) was within normal limit. Regarding blood lipids and lipoproteins of the patient, triglycerides or triacylglycerol was 190.9 mg/dl, whereas high-density lipoprotein (HDL) cholesterol level was low (16 mg/dl)

in comparison with the normal range. The levels of serum cholesterol and low density lipoprotein (LDL) cholesterol were 212 mg/dl and 138 mg/dl respectively. Amongst sex-steroid hormones, serum testosterone concentration was 1.55 n mol/L and estradiol-17 β was 35 p mol/L. The sex-hormone binding globulin (SHBG) present in the patient's serum was 26 n mol/L.

DISCUSSION

Amongst Indian women, carcinoma of the uterine cervix ranks first while breast cancer is the second commonest malignancy. Women with higher socio-economic status, low parity or nulliparity, late age at first pregnancy and obesity are more susceptible to develop breast cancer. Both clinical and laboratory studies indicate that estrogenic steroids play an important role in the etiology of breast cancer. Cervical cancer patients generally belong to the low socio-economic class. Multiparity, early age at consummation of marriage, promiscuity and poor genital hygiene are related with the pathogenesis of cervical cancer. Numerous studies have implicated the human papillomavirus (predominantly HPV 16) in carcinoma of the uterine cervix (1).

Multiple primary malignancies in patients with cancer are uncommon, but have been known for a long time. Gastrointestinal tract is the common site which has been involved in the multiple neoplasms (2, 3). Swaroop et. al. (3) reported a case of multiple primary malignant tumors affecting ovary, cervix, breast, bile duct and colon. Also Biswal et.al. (4) reported a case with carcinomas of the breast and cervix.

The significance of this case is due to the fact that risk factors for cervical cancer and breast cancer are usually conflicting to each other; and these two cancers are the most prevalent among Indian women. The patient's habit of smoking, her early age at

consummation of marriage and pregnancy as well as multiparity might be important for cervical cancer(5).

The patient's early menarche reflects an increased duration of exposure to endogenous ovarian hormones. However, we have observed a low level of serum SHBG in this patient. Many investigators(6,7) noticed that breast cancer risk has been related with decreased level of circulating SHBG. The metabolism of sex -steroid hormones is closely associated with the lipid metabolism. We have observed a low level of HDL-cholesterol in the serum of the patient, which might reflect a disturbance in lipid metabolism. Knapp

et. al. (8) and Hoyer & Engholm (9) found a decrease in serum HDL-cholesterol in patients with breast cancer.

Higher levels of blood glucose, acid phosphatase, inorganic phosphorus etc., and lower levels of HDL-cholesterol or SHBG could be a result of an altered metabolic activity associated with the pathogenesis of double malignancy. Also, the occurrence of two malignancies involving breast and uterine cervix is a special phenomenon; and the investigation in these cases may lead to a better understanding of the pathological process.

REFERENCES

1. Ray, A., Sharma, B.K., Bahadur, A.K., Pasha, S.T., Bhadola, P. and Murthy, N.S. (1997) Serum lipid profile and its relationship with host immunity in carcinomas of the breast and uterine cervix. *Tumori* 83, 943-947.
2. Arnot, R.S. and Borges, A.(1979) Multiple intestinal malignancy. *Clin. Oncol.*5, 267-269.
3. Swaroop, V.S., Winawer, S.J., Lightdale, C.J. and Lipkin, M. (1988) Six primary cancers in individuals: Report of four cases. *Cancer* 61, 1253-1254.
4. Biswal, B.M., Rathi, A.K., Mallik, S. and Rathi, G.K. (1994) Carcinoma of the breast and carcinoma of the uterine cervix: A rare form of double malignancy. *Indian J. Pathol.Microbiol.*37 (Suppl.), S6-7.
5. Cuzick, J., Singer, A., De-Stavola, B.L. and Chomet, J.(1990) Case-control study of risk factors for cervical intra-epithelial neoplasia in young women. *Eur. J. Cancer* 26, 684-690.
6. Schapira, D.V., Kumar, N.B. and Lyman, G.H.(1991) Obesity, body fat distribution, and sex hormones in breast cancer patients. *Cancer* 67, 2215-2218.
7. Kaaks, R. (1996) Nutrition, hormones and breast: is insulin the missing link? *Cancer Causes Control* 7, 605-625.
8. Knapp, M. L., Al-Sheibani, S. and Riches, P.G. (1991) Alterations of serum lipids in breast cancer : effects of disease activity, treatment and hormonal factors. *Clin. Chem.* 37, 2093-2101.
9. Hoyer, A.P. and Engholm, G. (1992) Serum lipids and breast cancer risk: a cohort study on 5207 Danish women. *Cancer Causes Control* 3, 403-408.