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Original Research Paper

Oncology

SYNCHRONOUS CARCINOMA OF BREAST AND OVARY IN INDIAN POPULATION WITH BRCA-1/BRCA-2 POSITIVITY: AN INSTITUTIONAL STUDY

Dr Mahesh Rewadkar Assistant Professor, Dept of Radiotherapy and Oncology, Cama & Albless Hospital, Mumbai.

ABSTRACT Synchronous malignancies of breast and ovary are a rare clinical presentation .in this retrospective study we present case series of synchronous malignancies of carcinoma breast and carcinoma ovary who were found to be BRCA -1/BRCA-2 positive.

KEYWORDS : Synchronous, BRCA, Breast Carcinoma, Carcinoma Ovary.

INTRODUCTION

According to Globocon 2012 Breast cancer is the second most common cancer in the world and the most frequent cause of cancer death in women in less developed regions. Ovarian cancer is a heterogenous group of disease associated with high morbidity and mortality. Synchronous malignancy of breast with ovary is extremely rare. Most cases of synchronous malignancy are found to be either BRCA 1 or BRCA 2 positive. BRCA-1 and BRCA-2 associated breast and ovarian cancer syndrome are mostly hereditary.BRCA-1 and BRCA-2 are tumor suppressor genes which act in DNA repair processes1. Individuals with mutations in these two genes are at an increased risk of developing breast, ovarian, and other cancers. The lifetime risk of breast cancer among BRCA mutation carriers is 45-80% and for ovarian cancer, 45-60%2. Ovarian cancer patients with BRCA mutations are known to have better outcomes as compared to non-carriers.

Methodology

We collected data from the 2013-2018 of patients having synchronous malignancy of cancer breast and cancer ovary.9 patients were found to have synchronous cancer breast and cancer ovary .all the patients were in the age group of 27-50 yrs. The patients had undergone all routine blood examinations, Mammography, Biopsy, PET CT, CA -125, ER, PR, HER-2 & BRCA-1/BRCA-2testing. After completion of treatment the patients were followed up at every 6 months with History physical examination USG abdomen and CA-125 Levels.

RESULTS

The mean age at presentation was found to be 31 yrs. The most common symptoms reported by patients were lump in the breast with distention of abdomen.

On clinical examination in these 9 patients the largest tumor size was of 5 cm and 4 out of these 9 patients had clinically palpable axillary lymph node disease. On per abdomen examination a hard lump in abdomen was felt. These patients underwent simultaneous MRM with axillary lymph node dissection of the affected side with Total abdominal hysterectomy with B/L Salphingo-oophrectomy with pelvic lymph node dissection.

In these cases the pathological staging was suggestive of high grade serous carcinoma of the ovarian specimen and invasive ductal carcinoma from the breast specimen. On Immunohistochemistry testing out of 9 breast samples 4 were found to ne ER / PR +, HER -2 negative and 5 were found to be TNBC. Ovarian samples were found positive for PAX-8 markers confirming the presence of synchronous malignancies. All the patients were subjected to BRCA-1/BRCA-2 Testing. Patients were administered 6 cycles of Paclitaxel with Carboplatin followed by local Radiotherapy to affected breast & hormonal therapy in the form of Tablet Tamoxifen 20mg/day for premenopausal and Tablet Letrozole 2.5mg/day for postmenopausal women.

TABLE1: Characteristics of the patients

S. NO	Age of patent	Site of breast cancer	Breast cancer staging	ER/PR/HER-2	Ovarian cancer site & laterality
1	28	RT UOQ	T2 N1MO	+/+/-	RT OVARY
2	26	LT UIQ	T1N1MO	+/+/-	B/L OVARY
3	34	LT UOQ	T2N0MO	+/+/-	B/L OVARY
4	24	LT UOQ	T3N0MO	+/+/-	B/LOVARY
5	37	RT UOQ	T1N0MO	TNBC	B/L OVARY
6	43	RT UOQ	T2N1MO	TNBC	LT OVARY
7	32	LT UOQ	T1NOMO	TNBC	B/L OVARY
8	48	LT UOQ	T2NO MO	TNBC	B/L OVARY
9	29	LT UOQ	T1NOMO	TNBC	B/L OVARY

Table2: shows Immuno-histochemical marker differentiating breast cancer from ovarian cancer

Marker	Ovarian Cancer		Breast Cancer
	Mucinous	Serous	
GATA 3	–	–	ER-pos: ++, ER-neg: +
Mammoglobin	–	–	+++
GCDFP-15	–	–	+
MUCSAC	+++	–	–
CA 19-9	+++	–	–
CK20	+++	–	–
WT1	–	+++	–
PAX8	–	+++	–

DISCUSSION

Synchronous Breast cancer and epithelial ovarian cancer are associated with familial cancer syndromes with mutations in the BRCA-1 and BRCA-2 genes [3-5]. The BRCA-1 gene is located on chromosome 17ql2-21. BRCA-1 is not associated with sporadic breast or ovarian cancers, or breast cancer in males. BRCA-2 gene is located on chromosome 13ql2-13 [4] and is associated with both sporadic and familial breast cancers.

Lobular carcinoma of the breast spreads to serosal surfaces and can involve gynecological organs mimicking a second primary cancer [6-8]. Histopathological assessment of tumor from both the pelvis and the breast is mandatory. It can be achieved by doing fine needle aspiration or core biopsy[9]. Stromal tumors of the ovary, associated with hyperestrogenism, can be associated with estrogen dependant malignancies such as breast cancer and endometrial cancer. In an epidemiological study of granulosa cell tumors of 172 cases accumulated over 15 years, 6.4% of patients presented with associated breast cancers and 11% with associated endometrial cancers[10]. The most common sites of metastasis for breast cancer are the bones, lung, and liver and metastases to the peritoneum, stomach, and ovaries are seen rarely[11].A retrospective analysis of 7,166 cases of breast cancer and 1,758 cases of ovarian cancer identified through the Duke University Medical Center and University of North Carolina Hospitals identified only 50 cases of multiple primary cancers of the breast and ovary. Only four of these were cases of synchronously diagnosed breast and ovarian cancer[12]. Since breast cancer can metastasize to the ovaries and to a lesser extent ovarian cancer can metastasize to the breast a careful

histological confirmation of both malignancies is important In cases where these two malignancies are diagnosed in an individual, the possibility of a BRCA1/2 germline mutation should be raised.

The vast majority of breast cancers, both metastatic and primary, show positive expression for GATA3, and mammaglobin, while ovarian malignancies are negative for these markers.12–17 Gross cystic disease fluid protein 15 (GCDFP-15), another marker of breast origin, is a useful addition to the panel because, although sensitivity is lower than mammaglobin and GATA3, the specificity for breast is high. Markers with positive expression in ovarian tumors that have shown clinical utility in differentiating between primary ovarian cancer and metastatic breast cancer include: WT-1, Pax8, MUC5AC, CA19-9, and Ck20[11].

Chemotherapeutic agents which are active in both diseases, such as platinum drugs, taxanes, and anthracyclines, can be used. Data suggest that BRCA1/2-related breast and ovarian cancers may be more sensitive to platinum agents (Carboplatin and cisplatin) [12].

Appendix:

BRCA: Breast Carcinoma gene
UOQ: Upper Outer Quadrant
UIQ: Upper Inner Quadrant
TNBC: Triple Negative Breast Carcinoma
RT: Right
LT: Left
B/L: Bilateral
MRM: Modified Radical Mastectomy
ER: Estrogen Receptor
PR: Progesterone Receptor

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