SYNCHRONOUS VERSUS METACHRONOUS MALIGNANCIES OF BREAST AND OVARY

Parul Gupta[1], Anil Kumar Dhull[2], Vivek Kaushal[3]

[1]Third Year Postgraduate Student, Department of Radiation Oncology, Pt. B. D. Sharma University of Health Sciences, Regional Cancer Center, Rohtak.
[2]Senior Medical Officer, Department of Radiation Oncology, Pt. B. D. Sharma University of Health Sciences, Regional Cancer Center, Rohtak.
[3]Senior Professor and HOD, Department of Radiation Oncology, Pt. B. D. Sharma University of Health Sciences, Regional Cancer Center, Rohtak.

ABSTRACT

BACKGROUND

Coexisting ovarian and breast carcinomas in a single patient are very rare with only infinitesimal cases reported in literature. The two cancers are either detected at the same time (synchronous) or one may follow the other after a period of time (metachronous). Although, breast and ovarian cancers are one of the commonest tumours in females, yet a coexisting primary involving both organs in a single patient is a rarity in medical literature prompting us to publish this article.

KEYWORDS

Synchronous, Metachronous, Double Malignancies, Ovarian Cancer, Breast Cancer.

HOW TO CITE THIS ARTICLE: Gupta P, Dhull AK, Kaushal V. Synchronous versus metachronous malignancies of breast and ovary. J. Evid. Based Med. Healthc. 2017; 4(25), 1486-1488. DOI: 10.18410/jebmh/2017/288

BACKGROUND

Breast cancer is the most frequently diagnosed cancer in women, whereas ovarian cancer is the second most common gynaecological malignancy in the United States after endometrial cancer. Coexisting breast and ovarian tumours in a single patient are very rare, however, can be explained in syndromes that heighten a woman's risk for both cancers. Through this article, we are presenting two such rare cases of synchronous and metachronous ovarian and breast malignancy and also tried to explore the related literature.

CASE REPORT 1

A 60-year-old female presented with history of abdominal pain for one and a half months. Pain was dull aching, moderate in intensity and was associated with a heavy "dragging" sensation. She had lower back pain without neurological deficit. Pain was intermittent and progressive in nature, which was relieved on taking oral analgesics. Patient had medically-controlled hypothyroidism for 3 years. There was no history evident of any chronic illness in the family. Ultrasonography of abdomen and pelvis with transvaginal sonography revealed multiple intramural and subserosal fibroids in anterior and posterior uterine walls with well-defined multiseptated cystic lesion of 18 × 11 cm with nonvascular solid component in right abdominopelvic region. CA-125 level was 0.6 U/mL. With these complaints, patient underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy with infracolic omentectomy including peritoneal biopsy. Histopathological examination of surgical specimen revealed papillary adenocarcinoma. Considering the clinical and pathological workup, the diagnosis of ovarian carcinoma FIGO stage IA was confirmed and she received two cycles of injection paclitaxel 260 mg IV and injection carboplatin 450 mg IV 3 weeks apart. After that, she incidentally noticed a breast lump of lemon size. On clinical examination, the lump was 4 × 4 cm located in outer lower quadrant and was painless, fixed and without any associated discharge or bleeding via nipple. Keeping in view, the present symptomatology, she was further investigated with mammography, which revealed a well-defined irregular and speculated margin lesion in outer lower quadrant of right breast (Figure 1) along with enlarged subcentimetric right axillary node. This lesion was of BIRADS-V grade, i.e. highly suspicious of malignancy. Subsequently, she underwent fine needle aspiration cytology of the breast lesion and the diagnosis of carcinoma breast was confirmed. Clinicoradiological stage of breast lesion was T_1N_1. Subsequently, patient underwent modified radical mastectomy and histopathologically confirmed the carcinoma breast. Further, sporadic mutations for BRCA1 and BRCA2 genes was detected positive.

CASE REPORT 2

A 73-year-old woman presented with a history of breast cancer 4 years prior, infiltrating ductal carcinoma with apocrine differentiation, MBR grade II, NPI score 3.3 with good prognosis, ER-positive and PR-positive, Her2/neu negative with no lymphovascular invasion and no lymph node involvement. It was treated with left MRM followed by 6 courses of chemotherapy. She took tamoxifen for 5 years and had no evidence of recurrence in the ipsilateral or contralateral breasts and was apparently alright for 5 years. She then presented with complaints of abdominal distension and breathlessness for 3 months. Abdominal distension was

Financial or Other, Competing Interest: None.
Submission 23-02-2017, Peer Review 02-03-2017,
Acceptance 16-03-2017, Published 27-03-2017.
Corresponding Author:
Dr. Parul Gupta,
Room No. 115, Block II,
Girls Hostel, PGIMS, Rohtak.
E-mail: parulg1531989@gmail.com
DOI: 10.18410/jebmh/2017/288

insidious in onset and gradually progressive. She had past history of hysterectomy 25 years back. There was no history of associated medical illness of any kind. She underwent contrast-enhanced computerised tomography scan, which revealed 5.2 × 4 cm in right adnexa, solid component showing enhancement with fat stranding to surrounded omentum, right ovary not visualised separate from the lesion and left ovarian cystic lesion of size 8.5 × 5 cm with soft mural nodule along wall showing enhancement with omental thickening and gross ascites. CA-125 was >600 U/mL. Ascitic fluid cytology revealed deposits of adenocarcinoma. Above investigations confirmed adenocarcinoma of ovary FIGO stage IIIc. She then received 6 courses of palliative chemotherapy with injection paclitaxel 260 mg and injection carboplatin 450 mg three weekly.

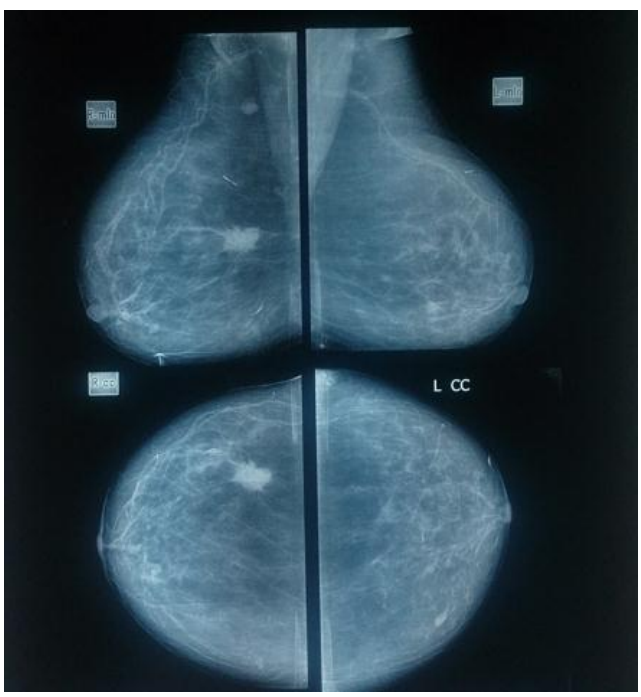

Figure 1. Initial Imaging of the Breast Lump. Right MLO and Right CC Projection Mammogram Showing a Speculated Mass in the Lower Outer Quadrant (BIRADS-V)

DISCUSSION

Breast cancer is the most frequently diagnosed cancer in women worldwide and while ovarian cancer is the second most common gynaecological malignancy in the United States after endometrial cancer.[1,2] Coexisting breast and ovarian cancer is a very rare entity. This presentation in the same individual raises the suspicion of a hereditary process. Patients with either BRCA1 or BRCA2 germline mutations have an average risk of ovarian cancer in the range of 16-60% and the risk of breast cancer is estimated to be in the range of 28-87%.[3,4] Double primary breast and ovarian tumours can appear even in those without prior relevant clinical or family histories as present in our present case in view of the fact that sporadic mutations of the BRCA1 and BRCA2 genes.

Despite the known genetic association and molecular link to the BRCA1 and BRCA2 genes, the occurrence of breast and ovarian carcinoma in same patient is remarkably rare. The approach to these patients differs with respect to consideration of several clinical possibilities as the patient with ovarian cancer presenting with a breast lump, the subtype of breast cancer is an important factor. The biggest question in patients with both cancers at same time is that whether they truly have synchronous primary carcinomas or metastases from one site to the other and another big question is what should be the optimal intervention and follow-up in such cases. Invasive Lobular Carcinoma (ILC) of the breast has the potential to mimic a second primary cancer by virtue of its ability to spread to serosal surfaces and involve gynaecological organs. Therefore, the abdominal pathology could easily be related to either metastatic spread from the breast and/or from the ovary. Although, both invasive lobular carcinoma and Invasive Ductal Carcinoma (IDC) have been reported to metastasise to the ovary. There is evidence to suggest that ILC is more likely to do so than IDC.

An autopsy study revealed that 36% versus 2.6% patients of ILC and IDC respectively had ovarian metastases.[5] Furthermore, in a report of 29 cases of ovarian metastases from breast cancer, 12 of 29 patients (43.5%) were found to have lobular carcinoma (compared to the reported incidence of lobular carcinoma in the entire breast cancer population of about 15%).[6] Therefore, in a patient with a history of ILC, a new malignant ovarian mass is more suspicious for metastatic disease than in the patient with IDC.

There are only 37 cases reported in the English literature as ovarian cancer metastasising to breast conversely the frequency of breast metastasis of ovarian carcinoma varies from 0.5% to 1.2% in the clinical setting.[7-15] These ovarian cancers are widespread ones and it is critical to pursue an accurate diagnosis when evaluating a patient with an ovarian mass who is also presenting with a breast mass or who has a history of breast cancer. The most common sites of metastasis for breast cancer are the bones, lung and liver. However, metastases to the peritoneum, stomach and ovaries are well described in patients with breast cancer. The majority of these metastases will be bilateral and are associated with poor prognosis. In our case, because of unilateral abdominopelvic mass, there is increased probability of synchronous distinct primaries. Using IHC staining solely as is common in daily practice to support the histological findings may not be helpful and sometimes may lead to a false diagnosis and an ineffective treatment strategy.

Accurate differentiation of metastatic type from primary tumours is important because the treatment and prognosis differ significantly, whereas on the other hand, when patients present with a subsequent ovarian mass like in our case report 2, one has to be more suspicious of a primary ovarian malignancy.

Despite the availability of multimodality treatment options, synchronous breast and ovarian carcinoma carries a poor prognosis. For management, treatment recommendations would have to take into account the

characteristics and treatment practices of both breast and ovarian malignancies. Literature review has shown that neoadjuvant chemotherapy has an established role in both breast and ovarian cancer, which can help decrease the volume of disease. Chemotherapeutic agents, which are active in both diseases, such as platinum drugs, taxanes and anthracyclines can be used. Systemic therapy should include both an anthracycline and a taxane, both drugs are active against both breast and ovarian cancer. Data suggest that BRCA1/2-related breast and ovarian cancers maybe more sensitive to platinum agents (carboplatin and cisplatin). Although, not considered standard of care for the treatment of breast cancer, the use of platinum agents in this setting would be a very reasonable approach to cytoreduction prior to surgical excision, but our case was T_1N_1,therefore, modified radical mastectomy was done after two courses of platinum-based chemotherapy. Finally, the addition of endocrine therapy with tamoxifen or an aromatase inhibitor should be considered standard treatment in this patient population. For metachronous malignancy as in case 2 reported here due to rarity of such condition, the standard guidelines for management have not been formulated yet, but as far as this case is concerned because of the time gap and distinct pathological features of the two malignancies, both are treated as new primary tumours as opposed to metastases from breast cancer to ovary.

CONCLUSION

Although, malignant ovarian masses in patients with breast cancer are more often primary ovarian malignancies than breast cancer metastases. It is important to understand, which primary breast cancer patients are most likely to present with ovarian metastases. The main emphasis should be to differentiate breast metastases from primary ovarian malignancies and vice versa for subsequent best management of these patients to decide curative or palliative approach. BRCA testing of the patient is indispensable in both cases. Systemic therapy should include both an anthracycline and a taxane, both drugs are active against both breast and ovarian cancer. The more controversial issue would be inclusion of a platinum agent. Accumulating data support, chemotherapy selection guided by mutation and receptor status with some indication that BRCA1/2-associated and ER-/PR-/HER2-negative cancers are sensitive to platinum-based therapy.

REFERENCES

[1] Siegel R, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J Clin 2015;65(1):5-29.
[2] Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA Cancer J Clin 2012;62(1):10-29.
[3] Risch HA, McLaughlin JR, Cole DE, et al. Prevalence and penetrance of germline BRCA1 and BRCA2 mutations in a population series of 649 women with ovarian cancer. Am J Hum Genet 2001;68(3):700-710.
[4] Ford D, Easton DF, Bishop DT, et al. Risks of cancer in BRCA1-mutation carriers. Breast Cancer Linkage Consortium. Lancet 1994;343(8899):692-695.
[5] Harris M, Howell A, Chrissohou M, et al. A comparison of the metastatic pattern of infiltrating lobular carcinoma and infiltrating duct carcinoma of the breast. Br J Cancer 1984;50(1):23-30.
[6] Li CI, Anderson BO, Daling JR, et al. Trends in incidence rates of invasive lobular and ductal breast carcinoma. JAMA 2003;289(11):1421-1424.
[7] Yamasaki H, Saw D, Zdanowitz J, et al. Ovarian carcinoma metastasis to the breast case report and review of the literature. Am J Surg Pathol 1993;17(2):193-197.
[8] Manini C, Pietribiasi F, Sapino A, et al. Serous cystadenocarcinoma of the ovary with simultaneous breast metastases. Description of a case. Pathologica 1998;90(2):152-155.
[9] Orris BG, Geisler JP, Geisler HE. Ovarian carcinoma metastatic to bilateral axillary lymph nodes. A case report. Eur J Gynaecol Oncol 1999;20(3):189-190.
[10] Fondrinier E, Gamelin E, Verriele V. Inflammatory breast metastasis from primary ovarian cancer: case report. Eur J Gynaecol Oncol 1999;20(1):16-17.
[11] Petersen BL, Hogdall E, Kryger- Baggesen N. Metastasis to the breast from an ovarian carcinoma. Acta Obstet Gynecol Scand 1999;78(9):826-867.
[12] Wadhwa J, Dawar R, Kumar L. Ovarian carcinoma metastatic to the breast. Clin Oncol (R Coll Radiol) 1999;11(6):419-421.
[13] Cormio G, di Vagno G, Melilli GA, et al. Ovarian carcinoma metastatic to the breast. Gynecol Obstet Invest 2001;52(1):73-74.
[14] Kayikcioglu F, Boran N, Ayhan A, et al. Inflammatory breast metastases of ovarian cancer: a case report. Gynecol Oncol 2001;83(3):613-616.
[15] Hajdu SI, Urban JA. Cancers metastatic to the breast. Cancer 1972;29(6):1691-1696.