OVARIAN CANCER AFTER BREAST CANCER: A CASE REPORT AND LITERATURE REVIEW

Kagema S[1], Maingi I[1], Inyangala D[2], Kosgei R.J[3], Maranga I.S.O[3]

Affiliation

1. Department of Obstetrics and Gynaecology, University of Nairobi.
2. Department of Human Pathology, University of Nairobi.
3. Department of Obstetrics and Gynaecology, Kenyatta National Hospital.

Correspondence: sammiekagz@gmail.com

ABSTRACT

Objective: We report a case of a 41-year-old, Para 4+0 who presented at the Kenyatta National Hospital, referred from a level V hospital where she had been diagnosed with breast cancer and managed with chemotherapy.

Findings and Management: The patient gave a history of lower abdominal pain radiating to the back. Magnetic Resonance Imaging (MRI) revealed bilateral cystic ovarian masses. Exploratory laparotomy was done, and both ovaries were noted to be cystic with intact capsules, and bilateral high-grade serous carcinoma was reported on histological investigation. A total abdominal hysterectomy and bilateral salpingo-oophorectomy, infracolic omentectomy, and peritoneal washing were done. The patient was then started on chemotherapy scheduled for six cycles.

Conclusion: Ovarian cancer can occur after or before breast cancer. However, these two primary cancers can occur concurrently. Due to the high risk of breast cancer in individuals with Breast Cancer (BRCA-1/BRCA-2), gene mutations, chemoprevention, and prophylactic surgery are recommended. Pelvic examination, Transvaginal Ultrasound (TVU), Human Epididymis Protein 4 (HE4), and Cancer Antigen 125 (CA-125) assays should be considered to routinely screen for cervical cancer.

Keywords: Breast cancer, Ovarian cancer, BRCA1/2 mutations, HBOC

INTRODUCTION

Breast cancer is the second most common cancer after lung cancer. It is the most common cancer affecting women, with an estimated 2.09 million cases in 2018 (1). In contrast, ovarian cancer accounts for 239 000 new cases and 152 000 deaths annually. It is considered to have the highest mortality rate of all genital malignancies, attributed to its insidious onset and 'silent' progression with patients presenting with advanced disease (2). According to the World Health Organization (WHO), the incidence rates of breast cancer vary regionally. Western Europe reported an incidence rate of 89.7 per 100,000 women compared to 19.3 per 100,000 in Eastern Africa in 2016. Survival rates also vary significantly across regions, with over 80% in developed nations and less than 40% in developing ones, attributed to inadequate screening, diagnosis, and treatment (3).

The aetiology of breast and ovarian cancers is linked to genetics, lifestyle, and environmental factors. Hereditary Breast Ovarian Cancer syndrome (HBOC) should be suspected in cases below 45 years, presenting with the two primary tumours. HBOC is linked to germline mutations in the Breast Cancer (BRCA1 and -2) genes and has a strong familial inheritance link (4). Ovarian cancer can result in breast cancer as metastatic disease or as a second primary cancer. Rare cases of ovarian Metastasis to the breast have been reported with a 1% incidence rate (5). Metastasis of breast cancer to the ovary have also been identified in ductal

carcinoma of the breast (6).

Epithelial ovarian cancers are the most common reported ovarian cancer types and are a significant concern in gynaecologic oncology. Epithelial ovarian tumours are difficult to screen, with only 20% diagnosed at stage 1. The rest of the cases present having advanced disease, hence an overall mortality at 75% (7). According to the Center for Disease Control and Prevention (CDC), HBOC is mainly related to BRCA1 and BRCA2 gene mutations accounting for an estimated 3% of breast cancers and 10% of ovarian cancers annually. BRCA mutations are inherited in an autosomal dominant pattern (8) and can be maternal or paternal in origin (9). BRCA1 and BRCA2 gene mutations screening are recommended for those whose relatives are known to have BRCA gene mutations. Genetic counselling, testing, and risk-reducing bilateral salpingo-oophorectomy can be offered to BRCA1/2 gene mutations carriers based on the patient's preference. This surgery is associated with reducing breast cancer by 37-100% and ovarian cancer by 69-100% and lowering mortality by 55-100% (9).

CASE PRESENTATION

A 41-year-old para 4+0 presented at Kenyatta National Hospital referred from a County Referral Hospital, with a diagnosis of stage 4 breast cancer and managed by chemotherapy in 2017. The surgical history of the patient was positive for a right breast lumpectomy nine years ago. However, she was not put on any treatment, and no histology report was available to ascertain the lump's histological diagnosis. Diagnostic tests, right breast biopsy for histology and immunohistochemistry, and Computed Tomography (CT) were done to guide chemotherapy. The histological investigation reported an adenocarcinoma, likely invasive ductal carcinoma, and the immunohistochemistry result was estrogen and progesterone receptor-positive in 60-70% cells, HER-2 negative and Ki-67 >20%. Chest CT scan showed ipsilateral axillary lymphadenopathy, bilateral sub-pleural lower lobe opacities, and multiple sclerotic foci in several thoracic vertebrae. She was then commenced on six cycles of palliative chemotherapy, docetaxel (118.5mg), doxorubicin (79mg), and cyclophosphamide (79mg). Additionally, she was put on tamoxifen (20mg) once daily, but which she defaulted in the first month of treatment out of fear of the side effects that she read.

The patient presented at our institution in February 2019, two years since referral. She reported a three-month history of lower abdominal pain radiating to the back. The patient's gross examination showed the right breast to be shrunken onto the chest wall, with areas of scarring and nodules noted and positive axillary lymphadenopathy. The left breast appeared normal on gross examination. The abdomen had a mass equivalent to 18 weeks fundal height that was mobile and tender. Tumour marker assays were requested in May 2019; Cancer Antigen (CA-19-9) 115.28 U/ml (Normal <37), Carcinoembryonic Antigen (CEA) 8.31 (within normal range), CA-125 1.2U/ml (within normal range). BRCA1 and BRCA2 gene mutations test and the Paired-Box gene 8 (PAX8) expression assay, essential in differentiating primary epithelial and metastatic ovarian cancer tumours, were not done due to their unavailability locally.

On Magnetic Resonance Imaging (MRI), bilateral adnexal multiloculated, septated cystic lesions on the right (12 x 6 x 12 cm), left (9 x 10 x 7 cm) were demonstrated. The patient was then scheduled for an exploratory laparotomy. Intraoperatively, the right ovarian cyst was seen to have undergone torsion without gangrene and measured 10 x 8 cm. The left ovary measured about 18 x 10 cm with multiple cysts. Both ovarian capsules were intact. The omentum, liver, peritoneum, and gut had no visible tumour seeding. Ovarian cancer was surgically staged at 1B. A total abdominal hysterectomy, bilateral salpingo-oophorectomy/cystectomy, infracolic omentectomy, and aspiration of peritoneal washings were done. The resection of the tumours was considered optimal. The tissue specimen and peritoneal washings were submitted for histopathological and cytological analysis, respectively. Bilateral high grade ovarian serous carcinoma was reported histologically, and the peritoneal washing cytology was negative for malignancy. The patient was then scheduled for six cycles of chemotherapy with cisplatin (83mg) and paclitaxel (249mg); unfortunately, she defaulted after the first cycle due to financial constraints.

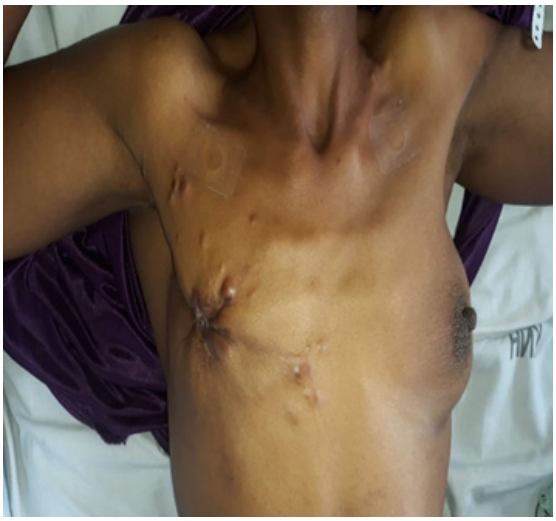

Figure 1: Shrunken right breast with nodules

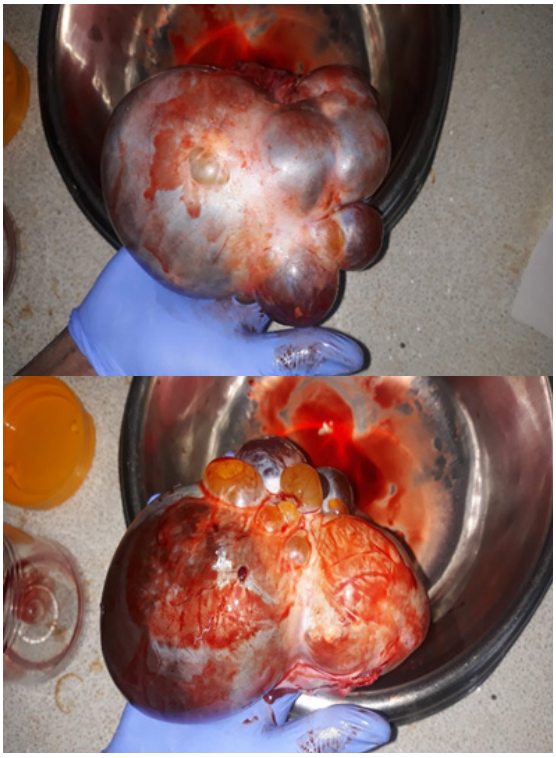

Figure 2: Left Ovarian mass with multiple cysts

Figure 3: Right ovarian mass

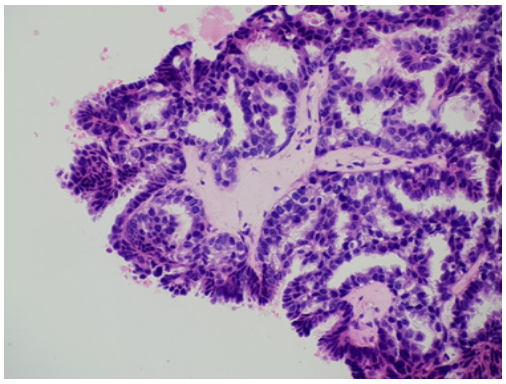

Figure. 4: Branching papillary fronds (H/E stain X40 magnification)

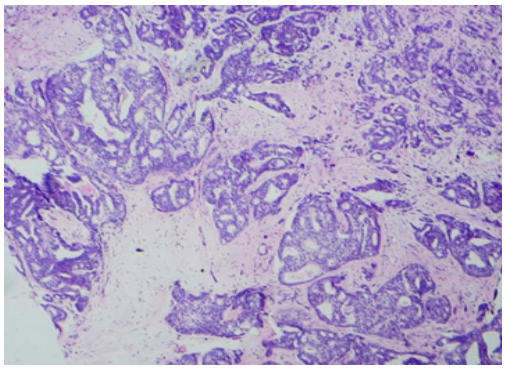

Figure. 5: Glandular complexity (H/E stain X400 magnification)

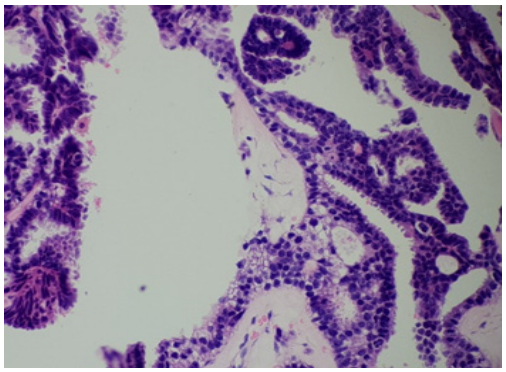

Figure. 6: Nuclear pleomorphism (H/E stain X400 magnification)

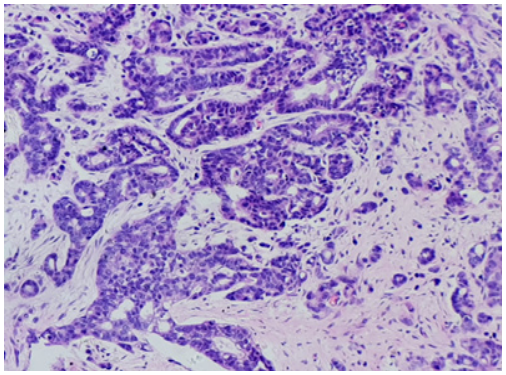

Figure. 6: Atypical glands with desmoplastic stroma (H/E stain X400 magnification)

DISCUSSION

Inherited gene mutations account for 5-10% of cancer of the ovary and breast (10). These mutations are often linked to the HBOC if it is of early-onset (below 50 years), has a strong familial link in a first-degree relative, breast cancer involving both breasts, ovarian and breast cancer in the same individual, as well as cancer of the breast in the male. Metastasis of breast cancer to ovaries or ovarian cancer to the breast can be ascertained on histology and histological comparison of tissues from both sites (10,11).

The exact incidence of HBOC is difficult to ascertain due to the restrictively high cost of genetic laboratory testing. BRCA1 mutation carriers have a lifetime risk of breast cancer of 36-85% and ovarian cancer of 28-54%. BRCA1 gene mutations increase the risk of developing cancer of the stomach, gall bladder, and colon. In contrast, BRCA2 gene mutations increase the risk of development of cancers of the breast, ovary, fallopian tube, and peritoneum. Male breast cancer is seen in 7% of carriers of both gene mutations (10).

Following genetic counselling and identifying high-risk individuals, testing for BRCA1 and BRCA2 gene mutations may be done. If positive, risk-reducing surgery or close clinical and laboratory-based disease surveillance is recommended (9). Prophylactic chemotherapy and use of oral contraceptives for at least six years, reduces the risk of ovarian cancer by up to 60% (10). Furthermore, prophylactic salpingo-oophorectomy reduces the risk of ovarian cancer by upto 100%. However, both methods will still require lifelong surveillance. A combination of a pelvic examination, Transvaginal Ultrasound (TVU), and CA-125 serum assay are recommended every six months, beginning at 35 years to those who may not opt for surgical prophylaxis (9,10).

Paired-Box 8 (PAX8) tumour marker has been shown to help differentiate primary epithelial from metastatic ovarian cancers with high sensitivity and specificity, and may have a possible role in determining prognosis (12).

CONCLUSION

Ovarian cancer can occur after or before breast cancer; however, these two primary cancers may occur concurrently. There exists a high risk of breast and ovarian cancer in women with BRCA1 and BRCA2 gene mutations, and thus genetic counselling and screening are recommended. Chemoprevention and surgical prophylaxis, (bilateral mastectomy, and salpingo-oophorectomy) can be considered in high-risk individuals. Pelvic examination, Transvaginal Ultrasound (TVU), Human Epididymis Protein 4 (HE4), and Cancer Antigen 125 (CA-125) assays should be considered to routinely screen for cervical cancer. Furthermore, patient education by the care team on treatment protocols and health financing schemes should be done to ensure patient compliance.

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Conflict of interest: None to declare

Author Contribution: All authors contributed towards the development of this scientific work.

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