

# Bilateral breast metastasis of ovarian carcinoma

P. Dursun, F.B. Yanik, E. Kuscü, M. Gultekin, A. Ayhan

Department of Obstetrics and Gynecology, Başkent University, School of Medicine, Ankara (Turkey)

## Summary

Primary breast carcinoma is the most common malignancy in women, however, metastatic breast carcinoma is rarely seen in clinical practice. It has been reported that lymphoma-leukemia, melanoma and sarcomas, the most common primary malignancies, can metastasize to the breast. On the other hand, ovarian carcinoma and other gynecologic cancers rarely develop into breast metastasis. However, the incidence of breast metastasis arising from ovarian carcinoma might be increasing as a result of prolongation in survival and improvement in treatment modalities. Bilateral breast metastasis originating from an ovarian carcinoma is an extremely rare clinico-pathological situation. In our literature review we found just nine cases of bilateral breast metastasis from primary ovarian carcinoma. In this study, the mean age was 46 years (range 16-68). Mean interval from initial diagnosis of ovarian carcinoma to bilateral breast metastases was 22 months (range 11-24) and mean survival was 12 (range 5-27) months after the diagnosis of breast metastasis. Serous papillary adenocarcinoma was the predominant histological subtype. Interestingly, five of the nine (56%) cases reported were from Turkey. This interesting observation can be explained by a genetic predisposition, but it requires further research. In conclusion, although it is a rare entity, breast metastasis should not be ruled out in patients with a history of ovarian carcinoma, if patients present with any symptoms of breast diseases.

**Key words:** Ovarian carcinoma; Breast metastasis; Bilateral breast metastasis; Distance metastasis.

## Introduction

Primary breast cancer is the most frequent malignancy in women. However, metastatic breast carcinoma is rarely seen. It is well known that the breast is an unusual site of metastasis for an extra-mammalian malignancy. Approximately 300 cases have been reported, and breast metastasis accounts about for 0.5-6.6% of all breast malignancies [1-4]. The exact cause for the rarity of metastatic breast disease is not known. In 1863, Virchow suggested that tissues with a high frequency of primary malignancy are rarely exposed to metastasis [5, 6].

The first case of breast metastasis from an ovarian carcinoma was reported nearly 100 years ago by Sitzentfrey [7]. The incidence of breast metastasis arising from ovarian carcinoma might be increasing secondary to prolongation in survival and improvement in treatment modalities [8]. However, up to now, less than 50 cases of unilateral and only a few cases of bilateral metastatic breast cancer from an ovarian carcinoma have been reported. We have summarized the clinico-pathological features and management strategies of patients with ovarian carcinoma who developed bilateral breast metastasis with a review of the literature.

## Search Criteria

Data for this review were identified by searches of PubMed, and references from relevant articles using the search terms "ovarian carcinoma" and "breast metastasis", and "bilateral breast metastasis". References of the identified articles were also used for this article.

## Results

We found just nine cases which are detailed in Table 1. The mean age was 46 years (range 16-68), and mean interval from initial diagnosis of ovarian carcinoma to bilateral breast metastases was 22 months (range 11-24). Mean survival was 12 months (range 5-27) after the diagnosis of bilateral breast metastasis. Serous papillary adenocarcinoma was the predominant histological subtype. Interestingly, 56% (5/9) of the reported cases with bilateral breast metastasis from ovarian carcinoma were from our country. Two had an inflammatory appearance. All patients were in high stage (III/IV) at initial diagnosis and also all had malignant findings at mammography.

## Discussion

Primary breast carcinoma is the most common malignancy in women. In this century, about one in ten women will develop breast cancer during her lifetime, and breast carcinoma will cause 20% of cancer-related deaths among women. However, metastatic involvement of the breast is very rare [1, 4]. Nonprimary breast malignancy incidence has been reported as between 1.7 to 6.6% [1, 9]. Abrams *et al.* reported 50 cases of metastatic breast cancer in 1,000 consecutive autopsy cases with epithelial malignancy. Among these, two had metastatic breast cancer originating from an ovarian tumor [10]. In contrast, clinically observed metastatic breast carcinoma only ranges from 0.5-1.3% of all cases of breast cancer [2, 11]. Sandison reported seven (0.4%) metastatic breast tumors in 1,723 cases of clinical breast tumors [12]. Also, Hadju and Urban reported 51 (1.2%) cases with secondary breast cancer in 4,051 patients for suspected breast cancer [11].

Table 1. — *Bilateral breast metastasis from primary ovarian carcinomas.*

Author	Age (years)	Stage*	Histological subtype	Interval (months)**	Survival (months)***
Brown & O'Keefe <sup>†</sup>	16	IV	Ovarian lymphosarcoma	Concurrent	13 days
Krishnan [29]	60	NA	Well differentiated papillary adenocarcinoma	11	5
Hughes [30]	48	IV	Poorly differentiated papillary adenocarcinoma	29	5
Özgüroğlu [28]	55	IIIc	Serous papillary cystadenocarcinoma	24	3
Wadhwa [18]	45	IV	Papillary serous adenocarcinoma	Concurrent	27 <sup>+</sup>
Özsaran [17]	41	IV	Serous papillary cystadenocarcinoma	Concurrent	NA
Oksuzoglu [31]	NA	IIIc	Papillary cystadenocarcinoma	24	NA
Kayıkçıoğlu [27]	35	IIIc	Serous papillary adenocarcinoma	24	18
Gokaslan <i>et al.</i> [32]	68	IV	Papillary serous cystadenocarcinoma	Concurrent	NA

\*Time of initial diagnosis of ovarian carcinoma. \*\*From diagnosis of ovarian carcinoma to breast metastasis. \*\*\*Diagnosis from breast metastasis to death. +: Lost to follow-up. NA: Not available. †: Cited by Krishnan *et al.*

The most common extra-mammalian primary tumors metastasizing to the breast are, in descending order of frequency, leukemia-lymphoma, malignant melanoma, lung cancer, soft tissue sarcomas, gastrointestinal and genitourinary cancers (Table 2) [1, 4]. The most common presentation of breast metastasis is a solitary lesion in the upper outer quadrant of the breast. Diffuse involvement of the breast has been seen in 4% of cases. Metastatic tumors tend to cause multiple and superficial lesions in the breast. The left breast is more frequently (53%) involved by metastatic disease than the right breast (39%) [6]. Also, 26 (26%) patients had bilateral involvement at first presentation [14]. The diagnosis of metastatic breast disease has been accomplished by incisional or excisional biopsy, lumpectomy, or fine-needle biopsy [4, 9, 15]. Mammography might be helpful in the diagnosis of metastatic breast carcinoma. Well-defined, non-calcified dense masses are accepted as classic mammographic findings. Microcalcification and spiculations are rarely seen in metastatic breast carcinomas [6, 15, 16].

The overall incidence of gynecologic malignancies metastatic to the breast has been reported as 0.17-5% [12, 16]. Ovarian carcinoma is the most common gynecologic malignancy metastasizing to the breast. Epithelial ovarian carcinoma (EOC) usually spreads by the trancolemic or lymphatic route. The exact mechanism of breast metastasis

from EOC is not known but it is thought to be a result of hematogeneous dissemination [17]. However, breast metastasis in ovarian carcinoma is strongly associated with widespread metastasis of the disease [8]. Papillary serous adenocarcinoma is the most common histologic subtype associated with breast metastasis from ovarian carcinomas [18] but sporadically, dysgerminoma, endometrioid-type ovarian carcinoma, ovarian lymphosarcoma, granulosa cell tumor, ovarian choriocarcinoma, carcinoid tumor of the ovary and borderline ovarian tumors have been reported [19-22]. Sporadically, other gynecologic malignancies including cervical and fallopian tube carcinomas metastasizing to the breast have been reported [6, 23, 24].

The mean age of patients with breast metastasis from ovarian carcinoma was 51.8 (range 30-80) years in the series of Moore *et al.* Also, in this series, mean survival was seven months, and mean interval between initial diagnosis of EOC and diagnosis of breast metastasis was 27 months (range 3-75) [6]. In contrast, mean age and mean interval has been reported as 48 years (range 16-69), and 42 months (range 2-120), respectively, in the literature review of Wadhwa *et al.* [18]. These numbers are similar to our findings. Prognosis of metastatic breast carcinoma is usually poor, and more than 80% of the patients with metastatic breast carcinoma die within one year of diagnosis [6, 13]. On the other hand, Matseoane [8] reported that patient age ranged from 16 to 60 years with a median of 38 years in a review of 13 cases with breast metastasis arising from ovarian carcinoma. All these patients presented with a breast mass. The breast mass was single or multiple, occurring in any site of the breast, but usually the upper outer quadrant in metastatic breast diseases. Matseoane also suggested that post-operative follow-up of patients with ovarian carcinoma should include routine breast examination by both patients and physicians. Moreover, he stated that baseline mammography should be obtained at the first visit and repeated semiannually for all patients with ovarian carcinoma.

Because of the rarity of breast metastasis originating from ovarian carcinoma, it is difficult to assess the effectiveness of the different management strategies, and as stated by Matseoane "There is no ideal therapy for these

Table 2. — *Origin of 127 cases of metastatic breast carcinomas.*

Lymphoma-Leukemia	27 (21%)
Melanoma	19 (15%)
RMS	15 (12%)
Lung tumors	11 (9%)
Ovarian tumors	11 (9%)
RCC	7 (6%)
Intestinal carcinoid	4 (3%)
SCC of head and neck	4 (3%)
LMS	3 (2%)
Others*	26 (20%)

Table created by the data from reference 1.

\* Thyroid, uterine cervical, pancreatic and gastric carcinomas, mesotheliomas, plasma cell myelomas. RMS: Rhabdomyosarcoma. RCC: Renal cell carcinoma. LMS: Leiomyosarcoma.

patients". Management strategies involve a combination of surgery (excisional biopsy, lumpectomy or simple mastectomy), chemotherapy and hormonal manipulations. Before starting therapy it is essential to assess other metastatic sites including the thorax, abdominopelvic area and central nervous system by different imaging modalities. Surgery is the cornerstone for the management of metastatic breast lesions in order to achieve local control and to evaluate pathologic features of the tumor. However, the place of aggressive surgery is limited in metastatic breast disease. Chemotherapy can contribute to local and systemic control of the breast disease [8].

Interestingly, more than half of the reported cases (56%) of bilateral breast metastasis arising from ovarian carcinoma have been reported from our country. This observation may arise from a publication bias or it may reflect a genetic predisposition. In contrast, although inflammatory breast carcinoma is a rare clinico-pathological entity in primary breast carcinomas and represents 1% to 4% of all breast cancers, we found that 25% (2/8) of patients with bilateral metastatic breast carcinomas originating from ovarian carcinomas have an inflammatory appearance. Prognosis and survival are worse in these types of breast carcinomas. This observation may also reflect the aggressive clinical behavior of this clinico-pathological situation.

The differential diagnosis of metastatic breast carcinoma from a primary breast cancer can be accomplished by some specific histologic staining, immunohistochemical staining, and DNA flow cytometry. CA-125 immunohistochemical staining may be helpful in diagnosing metastatic breast disease from an ovarian carcinoma. Immunohistochemical staining with tumor markers OC125 and OV632 has a high sensitivity (86%) and specificity (89%) for ovarian carcinomas. On the other hand, GCDFD-15, is a useful immunohistochemical staining to differentiate most metastatic mammary carcinomas of other common primary sites [25-27].

## Conclusion

Ovarian carcinoma rarely metastasizes to the breast. Bilateral breast metastasis from an ovarian metastasis is even more rare. Breast metastasis should be ruled out in patients with a history of ovarian carcinoma, if patients present with any symptoms of breast diseases. Frequent clinical and mammographic screening may be the logical approach for patients with a history of ovarian carcinoma especially in papillary serous-type carcinoma. Genetic predisposition for bilateral metastasis of ovarian carcinoma should be investigated in the Turkish population.

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Address reprint requests to:  
P. DURSUN, M.D.  
Department of Obstetrics and Gynecology  
Baskent University School of Medicine  
Kubilay Sk. No: 36 Maltepe, Ankara (Turkey)  
e-mail: pdursun@yahoo.com