CASE REPORT – OPEN ACCESS

International Journal of Surgery Case Reports 31 (2017) 106–108

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.casereports.com

An ovarian mass after breast cancer: Metachronous carcinoma or metastasis? A case report

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ARTICLE INFO

Article history:
Received 20 November 2016
Accepted 28 December 2016
Available online 30 December 2016

Keywords:
Breast cancer
Triple negative
Ovarian mass
Metastasis
Differential diagnosis

ABSTRACT

INTRODUCTION: Differentiating between primary and secondary ovarian cancer can be a difficult task. In hereditary conditions breast malignancies and primary ovarian cancer often coexist.
PRESENTATION OF CASE: We present a 45-year-old patient with an ovarian mass two years after the diagnosis of a lobular, triple negative breast carcinoma. There was concern whether the lesion represented a metachronous ovarian cancer or a metastasis of the lobular carcinoma. The final histological examination showed a metastatic lesion, deriving from the lobular breast carcinoma, as evidenced by the immunohistochemical profile; nevertheless, there were changes in hormonal receptor expression in the metastatic lesion compared to the primary, triple negative tumor. The patient underwent genetic testing for BRCA1 and BRCA2 mutations and was negative. In the adjuvant setting the patient received 6 cycles of chemotherapy with carboplatin and paclitaxel; eighteen months later, the patient remains without disease recurrence.
DISCUSSION AND CONCLUSION: This case report highlights the role of imaging, histology and predominantly immunohistochemistry as valuable tools in the assessment of ambiguous ovarian lesions after breast cancer.

1. Introduction

Differentiating between primary and secondary ovarian cancer can be a difficult task; histological verification is often necessary. In hereditary conditions breast malignancies and primary ovarian cancer often coexist. BRCA1 and BRCA2 mutations are responsible for the concomitant occurrence of these two cancer types. Specifically, women with BRCA1 alterations have a high risk of developing breast (85%) and ovarian (40–60%) cancer, whilst women with BRCA2 mutations have a similar risk of breast cancer as with BRCA1 mutations and 15–30% probability of developing ovarian cancer [1,2]. Another hereditary syndrome that involves ovarian cancer is Lynch II syndrome, a type of hereditary nonpolyposis colorectal cancer syndrome (HNPCC). Patients with Lynch II syndrome have a higher risk of developing ovarian cancer alongside with other types of cancer such as breast, colon and endometrial cancer. Women with BRCA mutations are at high risk of breast cancer so it is recommended that they follow more intense surveillance programs [3]. For those women two options are available: prophylactic bilateral mastectomy, or intensive surveillance, with the first option substantially decreasing the possibility of cancer [4].

This case report presents a 45-year-old patient with an ovarian mass two years after the diagnosis of breast cancer. The considerations differentiating a metachronous ovarian cancer from a metastasis in the ovary are critically discussed.

2. Case presentation

A nulligravida 45 year old female presented with a mammographic BIRADS V finding in the upper lateral quadrant of her left breast. She was operated with lumpectomy and lymph node excision, 6/13 lymph nodes tested positive for malignancy. The histopathological examination revealed a triple negative, lobular, pT2N1M0 tumor. Adjuvantly the patient received 6 cycles of chemotherapy with TAC (docetaxel, doxorubicin and cyclophosphamide) and radiotherapy.

In February 2015, two years after the initial cancer diagnosis and during the programmed follow up visit, an ovarian mass was revealed at clinical examination. During the preoperative workout a 5 cm left ovarian mass with mixed cystic and solid components was revealed; the Doppler transvaginal

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http://dx.doi.org/10.1016/j.ijscr.2016.12.022

ultrasonography showed increased vascularization of the mass. Serum Ca-125 level was 78 IU/ml. An explorative laparotomy was performed and the frozen section of the left adnexa was positive for malignancy. Intraoperatively cytological washing, hysterectomy, contralateral adnexectomy, infracolic omentectomy and peritoneal biopsies were performed. The cytological washing was positive for cancer cells. There was concern whether the lesion represented a metachronous ovarian cancer or a metastasis of the lobular carcinoma in the ovary.

The final histological examination showed a metastatic lesion, deriving from the lobular breast carcinoma, as evidenced by the immunohistochemical profile of the lesion (positivity for CK7, mammaglobin, ER and PR). The lesion was also positive for Ki-67 in 40% of tumor cells, while it was HER2 negative. No other malignant lesions were revealed. In the adjuvant setting the patient received 6 cycles of chemotherapy with carboplatin and paclitaxel. The patient underwent genetic testing for BRCA1 and BRCA2 mutations and was negative. Eighteen months later, the patient remains without disease recurrence.

3. Discussion

Ovarian cancer is the fifth most common malignancy in women and the most lethal gynecological malignancy [5,6]. Metastatic ovarian cancer is estimated to account for 10% of the total malignant ovarian tumors and originates from various sites, such as the stomach, breast, or colon [6–9]. The profile of neoplasms metastasizing to the ovaries has been described by Kondi-Pafiti et al.; nearly 63% of tumors are metastatic from extragenital organs, with breast cancer taking the second position after gastric cancer, representing 15.5% of metastases [6].

In our case, the metastasis stemmed from the lobular breast cancer diagnosed two years before the ascertainment of the metastatic lesion. It seems interesting to note that the immunohistochemical profile of the primary tumor was triple negative, whereas the metastasis was proven positive for ER and PR. This discrepancy between primary and metastatic lesion may not seem surprising, as such patterns have been reported in the literature [10,11].

Immunohistochemistry has a pivotal role in differentiating primary and secondary ovarian adenocarcinoma. In our case, apart from ER and PR, the lesion was positive for CK7 and mammaglobin. It has been reported that differential cytokeratin (CK7 and CK20) staining can distinguish primary and secondary ovarian adenocarcinoma and to ascertain the likely site of origin of a disseminated peritoneal tumor [12]. Metastatic breast carcinoma is usually positive for CK7 and negative for CK20. Estrogen receptor (ER) and progesterone receptor (PR) are often positive. Hormone receptor positivity is, of course, not specific for a metastatic breast cancer since many primary ovarian and other gynaecological malignancies are commonly positive. Gross cystic disease fluid protein-15 is also commonly positive, but again this is not specific for a breast primary [12]. A study on risk-reducing salpingo-oophorectomies performed on women with BRCA mutations, examined the differential diagnosis between occult primary and metastatic ovarian carcinoma; occult primary ovarian carcinoma was differentiated from ovarian metastases due to breast cancer by WT-1+, p53+, mammaglobin-, GCDPF-immunohistochemical profile [13].

There is often a known history of a primary tumor; sometimes symptoms from the ovarian tumor may arise. These symptoms may include low abdominal pain, pelvic pressure and symptoms from the gastrointestinal tract such as nausea, anorexia, indigestion. Other symptoms include dysuria, urinary frequency and bloating. Ascites is a sign of advanced disease, sometimes accompanied by pleural effusion [14]. Patients with metastatic cancer to the ovaries may present with non-specific pelvic or abdominal symptoms, such as abdominal mass or increased abdominal girth and abdominal/pelvic discomfort. Abnormal uterine bleeding may also be present [15].

Serum tumor markers can be detected in primary and secondary ovarian malignancies. Patients with metastatic ovarian cancer may have high CA 15-3 serum levels (higher than patients with primary ovarian cancer) and high CA 125 serum levels (but lower than patients with primary ovarian cancer) [16]. Furthermore, Antila et al. observed that the serum levels of tumor-associated trypsin inhibitor (TATI) and carcinoembryonic antigen (CEA) are higher in more than half of the patients with metastatic disease [17].

As far as imaging is concerned, Gadolinium enhanced MRI is reportedly slightly superior to both contrast-enhanced CT and Doppler sonography in the differential diagnosis of adnexal masses [18]. The Gadolinium administration provides a better distinction between solid and cystic compartments of a tumor. Primary ovarian tumors are predominantly cystic, while necrotic areas are also commonly present [18,19]. Metastatic ovarian tumors may be mainly solid or consist of both cystic and solid components [18]. Regarding ultrasound, Brown et al. [18] concluded that the resistance index of the blood flow of the tumors had no difference between primary and metastatic tumors; however, Antila et al., suggested that there was a tendency for the primary tumors to show lower resistance index [17]. Also a PET/CT scan can be a helpful aid for tracking the primary tumor.

Histology plays a crucial role in the diagnostic process. Among metastatic ovarian tumors, mucinous carcinoma is the most common type, followed by signet-ring cell carcinoma, endometroid carcinoma and adenocarcinoma not otherwise specified. For signet-ring cell carcinomas, the primary site is most often unknown, followed by stomach, colon, and appendix. According to Bruls et al., ductal and lobular carcinomas were responsible for respectively and 6.7% (n = 156) of all metastases to the ovary [9]. It is not uncommon for microscopic metastases originating from the breast to be found; this usually occurs during prophylactic oopherectomy in patients with known history of breast cancer.

Patients with bilateral disease, a known history of malignancy, young age, tumor <9 cm, solid structure of the malignancy, absence of ascites and elevated serum CEA and TATI levels are more likely to have metastatic disease [17]. Regarding prognosis, patients' menopausal status, laterality, size of the ovarian metastases, pre-operation serum CA125, CEA and LDH level do not seem to independently correlate with survival in ovarian metastases from extragenital primary sites [20].

Breast cancer is the most common malignancy in women and one of the leading causes of death among women [21,22]. The most common metastatic sites of breast cancer are bones, brain, liver and lungs. Breast cancer metastatic to the ovary may be of ductal or lobular type [23,24] Although ductal carcinoma is the most common type of ovarian metastasis, lobular carcinoma is proportionally more likely to spread to the ovary [12]. According to our case, the patient had breast cancer metastatic to the ovaries but was negative for BRCA1 or BRCA2 mutation. In general, BRCA1 mutation-associated breast cancers are more aggressive, as they are often characterized by high grade and triple-negative phenotype; on the other hand, BRCA2 mutation-associated breast carcinomas seem rather similar to sporadic breast cancer [25].

In conclusion, regular follow-up of women with breast cancer is necessary; clinical assessment should not neglect gynecological examination. The evaluation of an ovarian lesion years after breast cancer may represent a diagnostic challenge. The possibility of a metastatic lesion should always be taken into account; imaging, histology and predominantly immunohistochemistry may provide valuable tools in the assessment of ambiguous cases.

Conflict of interest

None.

Funding

None.

Ethical approval

Approval for the publication of this case report has been given the Institutional Review Board of "Attikon" Hospital.

Consent

Patient's approval is given for this study.

Author contribution

George-Marios Makris: study concept and design, data collection, writing the paper.

Aexandros Marinelis: data collection and writing the paper.

Marco-Johannes Battista: study design, writing the paper.

Charalampos Chrelias: study concept, data interpretation, supervision.

Nikolaos Papantoniou: data interpretation, supervision.

Guarantor

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References

[1] C.B. Begg, R.W. Haile, A. Borg, K.E. Malone, P. Concannon, D.C. Thomas, et al., Variation of breast cancer risk among BRCA1/2 carriers, JAMA 299 (2008) 194–201.
[2] J.D. Fackenthal, L. Cartegni, A.R. Krainer, O.I. Olopade, BRCA2 T2722R is a deleterious allele that causes exon skipping, Am. J. Hum. Genet. 71 (2002) 625–631.
[3] H.F. Vasen, N.E. Haites, D.G. Evans, C.M. Steel, P. Moller, S. Hodgson, et al., Current policies for surveillance and management in women at risk of breast and ovarian cancer: a survey among 16 European family cancer clinics. European Familial Breast Cancer Collaborative Group, Eur. J. Cancer 34 (1998) 1922–1926.
[4] H.F. Vasen, E. Tesfay, H. Boonstra, M.J. Mourits, E. Rutgers, R. Verheyen, et al., Early detection of breast and ovarian cancer in families with BRCA mutations, Eur. J. Cancer 41 (2005) 549–554.
[5] A. Jemal, R. Siegel, E. Ward, Y. Hao, J. Xu, M.J. Thun, Cancer statistics, 2009, CA. Cancer J. Clin. 59 (2009) 225–249.
[6] A. Kondi-Pafiti, E. Kairi-Vasilatou, C. Iavazzo, C. Dastamani, K. Bakalianou, A. Liapis, et al., Metastatic neoplasms of the ovaries: a clinicopathological study of 97 cases, Arch. Gynecol. Obstet. 284 (2011) 1283–1288.
[7] F. Holtz, W.R. Hart, Krukenberg tumors of the ovary: a clinicopathologic analysis of 27 cases, Cancer 50 (1982) 2438–2447.
[8] N.A. Janovski, T.L. Paramanandhan, Ovarian tumors. Tumors and tumor-like conditions of the ovaries, fallopian tubes and ligaments of the uterus, Major Probl. Obstet. Gynecol. 4 (1973) 1–245.
[9] J. Bruls, M. Simons, L.I. Overbeek, J. Bulten, L.F. Massuger, I.D. Nagtegaal, A national population-based study provides insight in the origin of malignancies metastatic to the ovary, Virchows Arch. 467 (2015) 79–86.
[10] S. Kimbung, N. Loman, I. Hedenfalk, Clinical and molecular complexity of breast cancer metastases, Semin. Cancer Biol. 35 (2015) 85–95.
[11] S. Huang, Y. Chen, K. Podsypanina, Y. Li, Comparison of expression profiles of metastatic versus primary mammary tumors in MMTV-Wnt-1 and MMTV-Neu transgenic mice, Neoplasia 10 (2008) 118–124.
[12] W.G. McCluggage, N. Wilkinson, Metastatic neoplasms involving the ovary: a review with an emphasis on morphological and immunohistochemical features, Histopathology 47 (2005) 231–247.
[13] J.T. Rabban, M. Barnes, L.M. Chen, C.B. Powell, B. Crawford, C.J. Zaloudek, Ovarian pathology in risk-reducing salpingo-oophorectomies from women with BRCA mutations, emphasizing the differential diagnosis of occult primary and metastatic carcinoma, Am. J. Surg. Pathol. 33 (2009) 1125–1136.
[14] N. Kawakubo, M. Okido, R. Tanaka, K. Mitsugi, M. Fukuhara, S. Aishima, et al., Pseudo-Meigs' syndrome associated with breast cancer metastasis to both ovaries: report of a case, Surg. Today 40 (2010) 1148–1151.
[15] S. Khunamornpong, P. Suprasert, W.N. Chiangmai, S. Siriaunkgul, Metastatic tumors to the ovaries: a study of 170 cases in northern Thailand, Int. J. Gynecol. Cancer 16 (Suppl. 1) (2006) 132–138.
[16] A. Tserkezoglou, S. Kontou, G. Hadjieleftheriou, N. Apostolikas, M. Vassilomanolakis, K. Sikiotis, et al., Primary and metastatic ovarian cancer in patients with prior breast carcinoma: pre-operative markers and treatment results, Anticancer Res. 26 (2006) 2339–2344.
[17] R. Antila, J. Jalkanen, O. Heikinheimo, Comparison of secondary and primary ovarian malignancies reveals differences in their pre- and perioperative characteristics, Gynecol. Oncol. 101 (2006) 97–101.
[18] D.L. Brown, K.H. Zou, C.M. Tempany, M.C. Frates, S.G. Silverman, B.J. McNeil, et al., Primary versus secondary ovarian malignancy: imaging findings of adnexal masses in the Radiology Diagnostic Oncology Group Study, Radiology 219 (2001) 213–218.
[19] F.F. Souza, A. Katkar, A.D. den Abbeele, P.J. Dipiro, Breast angiosarcoma metastatic to the ovary, Case Rep Med 2009 (2009) 381015.
[20] W. Li, H. Wang, J. Wang, L. VF, X. Zhu, Z. Wang, Ovarian metastases resection from extragenital primary sites: outcome and prognostic factor analysis of 147 patients, BMC Cancer 12 (2012) 278.
[21] A. Jemal, T. Murray, A. Samuels, A. Ghafoor, E. Ward, M.J. Thun, Cancer statistics, 2003, CA. Cancer J. Clin. 53 (2003) 5–26.
[22] S.B. Nandy, L. Gangwani, Z. Nahleh, R. Subramani, A. Arumugam, J.M. de la Rosa, et al., Recurrence and metastasis of breast cancer is influenced by ovarian hormone's effect on breast cancer stem cells, Future Oncol. 11 (2015) 983–995.
[23] Y. Gagnon, B. Tetu, Ovarian metastases of breast carcinoma: a clinicopathologic study of 59 cases, Cancer 64 (1989) 892–898.
[24] R.H. Young, R.W. Carey, S.J. Robboy, Breast carcinoma masquerading as primary ovarian neoplasm, Cancer 48 (1981) 210–212.
[25] K.L. Smith, C. Isaacs, BRCA mutation testing in determining breast cancer therapy, Cancer J. 17 (2011) 429–499.