

Axillary metastases from ovarian cancer

Nicolae BACALBASA^{1,2,3}, Irina BALESU⁴, Mihaela VILCU^{1,5}, Claudia STOICA^{6,7},
Tarig MASSAWI⁸, Sorin PETREA^{1,4}, Cristina MARTAC⁹, Adriana CIUVICA^{10,11},
Andrei VOICHITOIU^{10,11}, Iulian BREZEAN^{1,4}, Victor CAUNI¹², Bogdan GASPAR^{1,13}

¹Department of Surgery, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

²"Dan Setlacec" Center of Visceral Surgery and Liver Transplantation, Fundeni Clinical Institute, Bucharest, Romania

³Center of Excellence in Translational Medicine, Fundeni Clinical Institute, Bucharest, Romania

⁴PhD student at "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

⁵Department of Surgery, "Ion Cantacuzino" Clinical Hospital, Bucharest, Romania

⁶Department of Anatomy, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

⁷Department of Surgery, Ilfov County Emergency Hospital, Bucharest, Romania

⁸Department of Obstetrics and Gynecology, Ilfov County Emergency Hospital, Bucharest, Romania

⁹Department of Anesthesiology, Fundeni Clinical Institute, Bucharest, Romania

¹⁰Department of Obstetrics and Gynecology, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

¹¹Department of Obstetrics and Gynecology National Institute of Mother and Child Care "Alessandrescu-Rusescu", Bucharest, Romania

¹²Department of Urology, Colentina Clinical Hospital, Bucharest, Romania

¹³Department of Visceral Surgery, Floreasca Clinical Emergency Hospital, Bucharest, Romania

ABSTRACT

Ovarian cancer remains one of the most aggressive gynecological malignancies after cervical and endometrial cancer especially due to the multiple patterns of spread cited so far. Although it has been stated that the peritoneal route is the most dangerous pattern of spread leading to the apparition of disseminated intraabdominal lesions, other pathways such as hematogenous or lymphatic route can be also important, leading to the apparition of abdominal and extra-abdominal metastases. The aim of the current paper is to discuss about the risk of developing axillary metastases from ovarian cancer primaries.

Keywords: axillary metastases, ovarian cancer, extra-abdominal disease, prognosis

INTRODUCTION

Although cytoreductive surgery in association with platinum based chemotherapy has been widely accepted as golden standard in advanced stage ovarian cancer, in certain cases debulking to no residual disease is not feasible especially due to the presence of disseminated, extra-abdominal metastases developed via hematogenous and lymphatic route, the most commonly

incriminated sites being represented by bone, lungs, brain or lymph nodes.

Differential diagnosis of axillary metastases in patients with ovarian cancer

The presence of enlarged lymph nodes at distant sites such as axillary or supraclavicular lymph nodes represent another significant issue, in such cases the presence of a synchronous neoplasia such as advanced stage breast cancer being needed. In such cases the

Corresponding author:

Nicolae Bacalbasa

E-mail: nicolaebacalbasa@gmail.com

Article History:

Received: 30 August 2023

Accepted: 7 September 2023

first step should be to obtain imagistic studies of breasts in order to exclude synchronous malignancies and to conduct immunohistopathological studies such as determining whether GCDFP-15, CA12-5, WT-A or PAX-8 markers are present. Meanwhile, serum determination of CA 125 levels and CA 15-3 levels might orientate the diagnosis; however, it should not be omitted the fact that increased levels of both markers might be found in both ovarian and breast cancer [1,2].

A very interesting situation is the one in which ovarian cancer presents with both breast and axillary metastases, in such cases the differential diagnosis being even harder to be explained [3-6]. Therefore, in such cases the presence of a breast lesion is even more confusing and might be misdiagnosed as a primary neoplasia of the breast while the presence of enlarged axillary lymph nodes might be considered as breast cancer metastases. In order to establish the final diagnosis, a biopsy of both lesions is mandatory. An interesting such case was reported by Raffaele Longo et al. in 2020; in their paper the authors described the case of a 70 years old woman diagnosed with a right ovarian mass highly suggestive for malignancy, multiple adenopathies including at the level of the axilla and a hyper-metabolic lesion at the level of the right breast. The biopsies retrieved from the level of the right axillary adenopathies and from the right breast demonstrated the presence of a high grade serous papillary ovarian adenocarcinoma with axillary and breast metastases and therefore the patient was submitted to carboplatin and paclitaxel regimen combined with bevacizumab with rapid induced response.

Another aspect which seems to be important in distinguishing between the two entities – axillary metastases from ovarian cancer or association of ovarian cancer and metachronous breast cancer and axillary metastases is the stage at diagnostic of the ovarian tumor; therefore it seems that cases diagnosed with advanced stage ovarian tumors are more likely to develop distant metastases via lymphatic route, including axillary metastases while cases diagnosed with stage I-II ovarian tumors are more likely to be diagnosed with metachronous breast cancer [6]. As expected, patients with metachronous breast cancer usually originate from families with heavy cancer history, a BRCA test in such cases being mandatory [7-10].

THERAPEUTIC STRATEGIES IN PATIENTS WITH AXILLARY METASTASES FROM OVARIAN PRIMARIES

Due to the extremely low number of cases diagnosed with axillary metastases from ovarian cancer, a standard therapeutic management strategy is still missing. Therefore, each case should be discussed sepa-

rately in multidisciplinary teams [2,11,12]. Moreover, special attention should be given to the time of diagnosis in order to differentiate between synchronous and metachronous metastases. As expected, cases diagnosed with synchronous lesions are rather candidates for systemic therapy while cases diagnosed with metachronous lesions might be submitted to surgery if isolated axillary lesions are present or to systemic chemotherapy if disseminated lesions are encountered [3]. Therefore in the paper conducted by Ozmen et al. the authors presented two cases diagnosed with axillary metastases from ovarian cancer. The first one was the case of a 74 year old patient previously diagnosed with stage IIIA ovarian cancer and diagnosed at the four year follow up with a right axillary mass and a right lateral wall involvement of the rectum and was submitted to axillary lymph node dissection and low anterior rectal resection, the histopathological studies confirming the metastatic origin of the lesions. The second case was the one of a 38 year old patient diagnosed with stage IIIA epithelial ovarian cancer two years previously and was further submitted to systemic chemotherapy; at the time when writing the paper the patient was diagnosed with enlarged axillary lymph nodes, the histopathological findings being of metastatic ovarian cancer [3].

Maybe the largest study conducted on the issue of breast and axillary masses in ovarian cancer patients has been published in 2008 by Karam et al and included 29 patients. Among these cases there were 10 patients diagnosed with axillary or breast metastases from ovarian primaries and 19 patients with epithelial ovarian cancer and a metachronous breast neoplastic tumor. The mean interval between the diagnostic of epithelial ovarian cancer and the apparition of breast and axillary lesions was of 14,9 months in cases in which the breast and axillary lesions proved to be metastatic tumors from ovaries and respectively 77,4 months in cases diagnosed with metachronous breast cancer; as expected, cases diagnosed with axillary and breast metastases from ovarian cancer reported an overall survival significantly poorer when compared to cases diagnosed with metachronous breast cancer. Meanwhile, cases diagnosed with metachronous breast malignancies were more likely to have a familial history of breast cancer. Depending on the extent of the disease patients diagnosed with axillary recurrences from ovarian cancer were submitted to axillary lymph node dissection alone or in association with lumpectomy if no other distant metastases were found or to systemic therapies if disseminated lesions were already present. At the end of the study, five patients were dead of disease, four patients were alive with other recurrences from ovarian cancer while the status of the tenth patient was unknown [5].

Data reported by Karam et al come to underline once again the necessity of continuing to perform breast screening in ovarian cancer survivors.

Oppositely, Nomoto et al reported another type of unexpected situation: axillary metastases from ovarian cancer in a patient with previous history of breast cancers therefore the authors reported the case of a patient initially submitted to surgery for a left breast malignant tumor, at that moment a left mastectomy followed by chemotherapy being performed. Six years later she was diagnosed with an isolated lung metastasis for which she was submitted to an atypical lung resection, the immunohistochemical studies demonstrating the breast cancer origin of the lesion. Thirteen years later she was diagnosed with a left adenopathic mass which was biopsied and considered at that moment as a recurrence of her previously known breast cancers computed tomography and positron emission computed tomography demonstrated the presence of multiple lymphatic, peritoneal and liver metastases. In this respect she was submitted to epirubicin, cyclophosphamide and fluorouracil chemotherapy; however, she reported a poor response to chemotherapy and six months later she complained about abdominal disten-

sion while the abdominal ultrasound revealed the presence of a large amount of ascites. The histopathological and immunohistochemical studies of the ascites cells revealed certain features of primary serous papillary carcinoma with axillary lymph node metastases; in this respect she was submitted to debulking surgery followed by carboplatin and paclitaxel based chemotherapy with positive response. However the long term outcomes of this patient are not reported [8].

CONCLUSIONS

Axillary metastases from ovarian cancer represent a very scarce eventuality, isolated cases being reported so far; in such cases establishing the right pathological diagnosis remains the key for an adequate management of these cases. As for the therapeutic strategy, although it is not well standardized due to the very low number of cases, it seems that patients presenting disseminated lesions are rather candidates for systemic chemotherapy while in cases presenting isolated axillary lymph node metastases, a local surgical approach might bring a benefit in terms of survival.

Conflict of interest: none declared

Financial support: none declared

REFERENCES

- Ilhan B, Kılıç B, Karanlık H. Ovarian cancer presenting as an axillary mass: Case series and literature review. *Curr Res Transl Med*. 2016 Jul-Sep;64[3]:161-163. PMID: 27765277. doi: 10.1016/j.retram.2016.04.002
- Zuhdy M, Alghandour R, Abdelazeem G, Saleh GA, Saleh MM, Hamdy M et al. Axillary nodal metastasis in ovarian cancer: a report of three cases and review of literature. *J Egypt Natl Canc Inst*. 2019 Dec 23;31[1]:9. PMID: 32372131. doi: 10.1186/s43046-019-0008-x
- Skagias L, Ntinis A, Vasou O, Kondi-Pafiti A, Politi E. Ovarian carcinoma presenting with axillary lymph node metastasis: a case diagnosed by fine-needle aspiration and brief review of the literature. *Diagn Cytopathol*. 2008;36[12]:891-3. PMID: 18925569. doi: 10.1002/dc.20945
- Azmen V, Asoglu O, Karanlık H, Cabioglu N, Kecer M, Bakkaloglu H. Primary ovarian cancer presenting with axillary lymph node metastases: a report of two cases. *Acta Chir Belg*. 2007 Jan-Feb;107[1]:75-7. PMID: 17405606. doi: 10.1080/00015458.2007.11680018
- Longo R, Bastien C, Campitiello M, Plastino F, Rozzi A. Breast and Axillary Lymph Node Metastasis from Ovarian Cancer: A Case Report. *Am J Case Rep*. 2020 Aug 4;21:e925089. PMID: 32750046. doi: 10.12659/AJCR.925089
- Karam AK, Stempel M, Barakat RR, Morrow M, Gemignani ML. Patients with a history of epithelial ovarian cancer presenting with a breast and/or axillary mass. *Gynecol Oncol*. 2009 Mar;112[3]:490-5. PMID: 19101713. doi: 10.1016/j.ygyno.2008.11.006
- Recine MA, Deavers MT, Middleton LP, Silva EG, Malpica A. Serous carcinoma of the ovary and peritoneum with metastases to the breast and axillary lymph nodes: a potential pitfall. *Am J Surg Pathol*. 2004 [Dec;28[12]:1646-51. PMID: 15577686. doi: 10.1097/0000478-200412000-00015
- Williams SA, Ehlers RA 2nd, Hunt KK, Yi M, Kuerer HM, Singletary SE et al. Metastases to the breast from nonbreast solid neoplasms: presentation and determinants of survival. *Cancer*. 2007 Aug 15;110[4]:731-7. PMID: 17582626. doi: 10.1002/cncr.22835
- Nomoto K, Nakajima T, Miwa S, Hayashi S, Tsuneyama K. Primary peritoneal serous papillary carcinoma that metastasized to an axillary lymph node in a woman with a history of breast cancer: A case report and diagnostic pitfalls. *Human Pathology: Case Reports*. 2015;2:90-93. <https://doi.org/10.1016/j.ehpc.2015.03.003>
- Patel TS, Shah C, Shah MC, Shah MJ. Axillary node metastasis from primary ovarian carcinoma. *J Cytol*. 2014 Oct-Dec;31[4]:202-4. PMID: 25745286. doi: 10.4103/0970-9371.151132
- Aydin Ç, Ünalp HR, Baloğlu A, İnci AG, Yiğit S, Yavuzcan A. Axillary lymph node metastasis from serous ovarian cancer: a case report and review of the literature. *Arch Gynecol Obstet*. 2009;279[2]:203-7. PMID: 18470522. doi: 10.1007/s00404-008-0669-5
- Orris B, Geisler J, Geisler H. Ovarian carcinoma metastatic to bilateral axillary lymph nodes. A case report. *Eur J Gynaecol Oncol*. 1999;20[3]:189-90. PMID: 10410882