Post Chemotherapy Histopathological Evaluation of Ovarian Carcinoma: A Case Study

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Abstract

Ovarian carcinoma is one of the most common female malignancies worldwide and is the second most common gynecological cancer after cervical cancer. Neoadjuvant chemotherapy is an upcoming treatment modality for ovarian carcinomas. However, the morphological changes after neoadjuvant chemotherapy have not been described in detail. There is a definitive need for the pathologists to understand and assess these histopathological changes as difficulty in tumor typing, grading, and identification of residual tumor arises

Key words: Carcinoma, Chemotherapy, Ovary

INTRODUCTION

Ovarian carcinoma is one of the most common female malignancies worldwide and is the second most common gynecological cancer after cervical cancer.^{1,2} Among women in the United States, ovarian cancer is the eighth most common cancer and the fifth leading cause of cancer deaths.³ However, it causes more deaths than any other cancer of female reproductive system.³ In contrast, ovary is second leading site among gynecological malignancies in India.¹ The conventional treatment modality for advanced ovarian carcinoma is primary cytoreduction surgery followed by chemotherapy. However, the new approach is neoadjuvant platinum-based chemotherapy followed by interval debulking surgery. National Comprehensive Cancer Network guidelines for 2012 recommend the approach as this treatment modality reduces surgical morbidity with equivalent survival times.⁴ Due to this new approach, various morphological changes are seen in the tumor cells and stroma. Various changes seen are nuclear enlargement, hyperchromasia, bizarre nuclei, nuclear clumping, cytoplasmic eosinophilia, vacuolization,

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and foamy cell change. The stromal changes observed are fibrosis, inflammation, necrosis, and dystrophic calcification including the presence of psammoma bodies. Minimal residual disease is defined by the presence of residual tumor ≤1 cm and is one of the best predictive good prognostic factors.⁵⁻⁷ There are two aims of the study. First is to highlight detailed post chemotherapy histopathological parameters, particularly residual tumor, inflammation, necrosis, fibrosis, and psammoma bodies, on hematoxylin and eosin stained sections.^{4,7,8} Second is to stress on the fact that there is need to change reporting formats of ovarian carcinoma incorporating these histopathological changes so that they can provide an extra tool to optimize patient management and care.

CASE REPORTS

Case 1

A 45-year-old female was a known case of carcinoma ovary post-chemotherapy (7 cycles).

Pre-chemotherapy investigations were found as:

- 1. Contrast-enhanced computed tomography (CECT) abdomen Ovary of size $8 \text{ cm} \times 9.5 \text{ cm} \times 10 \text{ cm}$ in the pelvis showing heterogeneous enhancement.
- 5 ml pale yellow fluid from ovarian mass aspirated under ultrasonography (USG) guidance - Cytocentrifuge smear prepared from fluid showed tumor cells arranged in the clusters having pleomorphic nuclei

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and abundant vacuolated cytoplasm, reported as adenocarcinoma of the ovary.

- 3. Serum CA-125 marker was very high (4954.2 U/Ml).
- 4. USG abdomen Round to oval heteroechoic mass lesions showing mild vascularity in bilateral adnexae. Bilateral ovaries are not seen separately. The possibility of neoplastic etiology is likely. Enlarged left iliac lymph node, gross ascitis, and borderline splenomegaly.
- 5. 10 ml ascitic tapping done Cytocentrifuge smear prepared from fluid showed tumor cells arranged in the clusters having pleomorphic nuclei and abundant vacuolated cytoplasm, reported as metastasis of adenocarcinoma from ovary.

Post chemotherapy investigations were found as:

- 1. CECT abdomen In a known case of carcinoma ovary, post chemotherapy status shows huge residual disease of size 4.5 cm × 3.5 cm × 2 cm in the pelvis.
- 2. Histopathological examination:

Gross - Received hysterectomy with bilateral salpingoophorectomy specimen with iliac lymph node and omentum. First container labeled as uterus with cervix with bilateral ovaries and fallopian tubes contain uterus of size 5 cm \times 4 cm \times 2.5 cm, endometrium was 0.2 cm in thickness, myometrium was 2 cm in thickness and endometrial cavity was empty. Cervix of length 3.5 cm. Right fallopian tube of length 5 cm; right ovary of size 3 cm \times 2 cm \times 1.5 cm. On cut-solid, gray-white with some cystic areas. Left fallopian tube of length 5 cm. Left ovary of size 4 cm \times 2 cm \times 1 cm. On cut-solid, gray-white with some cystic areas (Figure 1). Second container labeled as omentum contain fibrofatty tissue of volume 10 cc. altogether, 3 lymph nodes identified.

Microscopic findings - First container labeled as uterus with cervix with bilateral ovaries and fallopian tubes: Cervix showed chronic cervicitis with nabothian cyst, endometrial glands are in proliferative phase, myometrium showed adenomyosis, right ovary showed features of residual tumor (Figure 2), right fallopian tube showed no specific pathology, left ovary showed features of hemorrhagic cyst, left fallopian tube showed features of acute salpingitis. Second container labeled as omentum showed fibrofatty tissue free from tumor, vial labeled as right iliac lymph node showed 3/3 lymph nodes free from tumor.

Case 2

A 52-year-old female known case of carcinoma ovary post chemotherapy.

Pre-chemotherapy investigations:

1. Computed tomography (CT) abdomen - Right ovarian mass with ascitis, bilateral pleural effusion,

fatty liver, omental caking, and degenerative changes in spine.

2. USG-guided fine needle aspiration cytology from ovarian mass-smears showed clusters of large pleomorphic malignant cells with high N: C ratio. Cells are arranged in an acinar pattern, good number of mononucleated giant cells are also present, reported as ovarian adenocarcinoma (Figure 3).



Figure 1: Both ovaries shows debulking



Figure 2: Residual tumor (1), fibrosis (2). (H and E, ×10)



Figure 3: Smear made by centrifuged deposit of fluid from ovarian mass showing features of adenocarcinoma. (MGG, ×10)

Post-chemotherapy investigations:

Histopathological examination:

Gross - Received hysterectomy with bilateral salpingo-ophorectomy specimen with bilateral pelvic lymph node, peritoneal tissue, and omentum. First container labeled as uterus with cervix with bilateral ovaries and fallopian tube contain uterus of size $6 \text{ cm} \times 7 \text{ cm} \times 3.5 \text{ cm}$, endometrium was 0.5 cm in thickness, myometrium was 1.2 cm in thickness, a globular mass of diameter 2.5 cm present showed the whorled pattern on cut. The endometrial cavity was empty. Cervix of length 4 cm. Right fallopian tube of length 4 cm; right ovary of diameter 2 cm. On cut-solid, gray-white. Left fallopian tube of length 5 cm. Left ovary of diameter 1.5 cm. On cut-solid, gray-white (Figure 4). Second container labeled as omentum contain fibrofatty tissue of volume 15 cc altogether. No lymph node identified. First vial labeled as peritoneal tissue contain tissue piece of size $0.3 \text{ cm} \times 0.2 \text{ cm} \times 0.1 \text{ cm}$. Second vial labeled as bilateral pelvic lymph node contain fibrofatty tissue of volume 5 cc altogether. 2 lymph nodes identified.

Microscopic findings - First container labeled as uterus with cervix with bilateral ovaries and fallopian tube: Cervix showed chronic cervicitis, endometrial glands showed atrophic changes, myometrium showed intramural leiomyoma both fallopian tubes showed acute salpingitis, both ovaries showed features of residual tumor (Figure 5). Second container labeled as omentum shows fibrofatty tissue free from tumor, first vial labeled as peritoneal tissue showed fibrocollagenous tissue only, second vial labeled as bilateral pelvic lymph node showed 2/2 lymph nodes free from tumor.

DISCUSSION

Neoadjuvant chemotherapy is an upcoming treatment modality for ovarian carcinomas.⁹ However, the morphological changes after neoadjuvant chemotherapy have not been described in detail. There is a definitive need for the pathologists to understand and assess these histopathological changes as difficulty in tumor typing, grading, and identification of residual tumor arises.¹⁰ There have been very few studies done to address this issue. Only one study carried out by Samrao *et al.* has objectively evaluated these morphological parameters.⁴ They had chemotherapy research and practice 3 largest series of 67 patients and the histological parameters chosen were easily reproducible, whereas in comparison the other studies had smaller case series of 18 patients



Figure 4: Both ovaries shows debulking



Figure 5: Residual tumor (1), necrosis (2), fibrosis (3), proliferated blood vessels (4), calcification (inset)

and the parameters chosen included volume percentage of epithelium, mean nuclear area, and clinical response to chemotherapy which were difficult to reproduce.¹¹ This study had comparatively larger number of patients and in comparison to Samrao *et al.* number of parameters was increased to five by the inclusion of psammoma bodies.⁴ According to a study carried out by McCluggage *et al.* presence of psammoma bodies without residual tumor was considered a good response to chemotherapy.¹⁰

Neoadjuvant therapy is an upcoming treatment modality and various studies have documented morphological changes induced by therapy in sites such as colon, breast, esophagus, and lungs.¹²⁻¹⁴ However, not much literature is available on neoadjuvant chemotherapy-induced histopathological changes of ovarian cancer. This leads to erroneous diagnosis particularly when the history of chemotherapy is not clearly stated.¹⁵ On the basis of guidelines published by College of American Pathologists recent American Joint Committee on Cancer staging manual has recommended change in reporting format with stress on morphological changes induced by chemotherapy in colorectal carcinoma.¹⁶ Authors want to stress upon the fact that such changes should be done in ovarian carcinoma formats. In the present study, the tumor grading and subtyping were not done. Both are considered of prognostic value. Authors want to stress on the fact that neoadjuvant chemotherapy-induced changes make such evaluation impossible which has been confirmed by various studies.^{10,11} All prognostic markers become insignificant after chemotherapy so there is need to change reporting formats and our study wants to stress on post chemotherapy changes and make pathologists aware of such morphological changes. All the parameters considered in this study are easily reproducible and do not require much expertise on the part of pathologists, and their inclusion in the final histopathological report would help in patient management.

CONCLUSION

Accurate tumor typing and grading of ovarian cancer are impossible when preoperative chemotherapy is used. It can be difficult to confirm the presence of residual tumor, making it imperative that pre-chemotherapy tissue biopsies are obtained.

REFERENCES

- Agarwal S, Malhotra KP, Sinha S, Rajaram S. Profile of gynecologic malignancies reported at a tertiary care center in India over the past decade: Comparative evaluation with international data. Indian J Cancer 2012;49:298-302.
- Momtahen S, Kadivar M, Kazzazi AS, Gholipour F. Assessment of gynecologic malignancies: A multi-center study in Tehran (1995-2005). Indian J Cancer 2009;46:226-30.
- U.S. Cancer Statistics Working Group, Unites States Cancer Statistics: 1999-2011 Incidence and Mortality Web-Based Report. Atlanta, GA, USA: Department of Health and Human Services, Centers for Disease Control and Prevention and National Cancer Institute; 2014.

- Samrao D, Wang D, Ough F, Lin YG, Liu S, Menesses T, *et al.* Histologic parameters predictive of disease outcome in women with advanced stage ovarian carcinoma treated with neoadjuvant chemotherapy. Transl Oncol 2012;5:469-74.
- Winter WE 3rd, Maxwell GL, Tian C, Carlson JW, Ozols RF, Rose PG, *et al.* Prognostic factors for stage III epithelial ovarian cancer: A Gynecologic Oncology Group Study. J Clin Oncol 2007;25:3621-7.
- Skírnisdottir I, Sorbe B. Prognostic factors for surgical outcome and survival in 447 women treated for advanced (FIGO-stages III-IV) epithelial ovarian carcinoma. Int J Oncol 2007;30:727-34.
- Langer R, Ott K, Feith M, Lordick F, Siewert JR, Becker K. Prognostic significance of histopathological tumor 4 Chemotherapy Research and Practice regression after neoadjuvant chemotherapy in esophageal adenocarcinomas. Mod Pathol 2009;22:1555-63.
- Wu TT, Chirieac LR, Abraham SC, Krasinskas AM, Wang H, Rashid A, et al. Excellent interobserver agreement on grading the extent of residual carcinoma after preoperative chemoradiation in esophageal and esophagogastric junction carcinoma: A reliable predictor for patient outcome. Am J Surg Pathol 2007;31:58-64.
- Wang Y, Wang Y, Zheng W. Cytologic changes of ovarian epithelial cancer induced by neoadjuvant chemotherapy. Int J Clin Exp Pathol 2013;6:2121-8.
- McCluggage WG, Lyness RW, Atkinson RJ, Dobbs SP, Harley I, McClelland HR, *et al.* Morphological effects of chemotherapy on ovarian carcinoma. J Clin Pathol 2002;55:27-31.
- Miller K, Price JH, Dobbs SP, McClelland RH, Kennedy K, McCluggage WG. An immunohistochemical and morphological analysis of post-chemotherapy ovarian carcinoma. J Clin Pathol 2008;61:652-7.
- Shimosato Y, Oboshi S, Baba K. Histologic evaluation of effects of radiotherapy and chemotherapy for carcinomas. Jpn J Clin Oncol 1971;1:19-35.
- Junker K, Langner K, Klinke F, Bosse U, Thomas M. Grading of tumor regression in non-small cell lung cancer: Morphology and prognosis. Chest 2001;120:1584-91.
- Shia J, Guillem JG, Moore HG, Tickoo SK, Qin J, Ruo L, *et al.* Patterns of morphologic alteration in residual rectal carcinoma following preoperative chemoradiation and their association with long-term outcome. Am J Surg Pathol 2004;28:215-23.
- 15. Freedman OC, Dodge J, Shaw P, Oza AM, Bernadini M, Klachook S, *et al.* Diagnosis of epithelial ovarian carcinoma prior to neoadjuvant chemotherapy. Gynecol Oncol 2010;119:22-5.
- Jass JR, O'Brien J, Riddell RH, Snover DC; Association of Directors of Anatomic and Surgical Pathology. Recommendations for the reporting of surgically resected specimens of colorectal carcinoma: Association of directors of anatomic and surgical pathology. Am J Clin Pathol 2008;129:13-23.

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