

Cervical and Ovarian Cancer with Different Histological Patterns: A Case Report

Hazera Khatun¹, Ferdousi Begum², Khandaker Shehneela Tasmin³, Easmin F⁴

ABSTRACT

A case with dual primary cancer occurring in both ovaries and cervix with different histological features is reported here. In November 2009, a 50-year-old lady presented with lower abdominal pain and dyspareunia for 5 years, foul smelling vaginal discharge for 1 year and difficulty in micturition and constipation for 2 months. On clinical examination and investigation she was found to have a moderately differentiated squamous cell carcinoma (stage III A) of the cervix, while histopathological diagnosis of biopsy material taken from the lump during cytoreduction after laparotomy showed papillary serous cystadenocarcinoma of ovary grade II. But our clinical diagnosis was stage IIIA of ovarian malignancy. She was treated with chemotherapy followed by radiotherapy. We presented this case and compared and contrasted with similar cases reported by other investigators.

Key Words: Cervical Cancer, Ovarian Cancer

INTRODUCTION

Simultaneous or metachronous occurrence of multiple primary cancers in the upper genital tract is well recognized¹⁻⁴ and metastases to the female genital tract occur frequently, the ovary being the most common site.⁵ Simultaneous carcinomas of the uterine corpus and ovary, usually detected as synchronous and less commonly as metachronous tumors, occur in 15 to 20% of ovarian tumors and in approximately 5% of uterine tumors (endometrioid type in the majority of cases).⁶

Uterus may be involved either by direct extension (tubal, ovarian, peritoneal or cervical carcinoma) or by metastatic carcinoma. Extragenital carcinomas that frequently involve the uterus include breast, stomach and colon, with cervix being more commonly involved than the uterine corpus.⁵ Secondary involvement of vulva and vagina occurs from primary tumors in other pelvic sites (cervix, endometrium),⁴ uterine

choriocarcinoma, colon and rectum, ovary, urinary bladder or urethra. Metastases to the ovary account for 6-17% of ovarian cancers,⁷ originating in colorectum, breast, stomach, cervix, pancreas, appendix, biliary tract, lung, and skin.⁵

Correct diagnosis as separate independent primary tumors or as primary tumor associated with its metastasis, and identification of the site of origin in secondary tumors has important prognostic implications and is necessary for appropriate staging and planning treatment. The diagnosis and staging mainly relies on assessment of conventional histopathologic examination.⁶ The present case study is one such case which presented us with a diagnostic riddle.

Case report:

A middle-aged (50 years) woman admitted in the Gynae ward of Shaheed Surwardy Medical College Hospital on November 2009 with the

Authors' Information:

1. **Dr. Hazera Khatun**, Associate Professor, Department of Obstetrics & Gynaecology, Shaheed Suhrawardy Medical College Hospital (SSMCH), Dhaka
2. **Professor Dr. Ferdousi Begum**, Department of Obstetrics & Gynaecology SSMCH, Dhaka
3. **Dr. Khandaker Shehneela Tasmin**, Medical Officer, Department of Obstetrics & Gynaecology SSMCH, Dhaka
4. **Dr. Farida Easmin Shelley**, Associate Professor, School of Science & Technology, Bangladesh Open University, Dhaka.

Address of Correspondance: Dr. Hazera Khatun, Mobile: 01711-529768, E-mail: khatuhazera1234@yahoo.com

complaints of lower abdominal pain and dyspareunia for 5 years, foul smelling vaginal discharge for 1 year and difficulty in micturition and constipation for last 2 months. She was found mildly anaemic with average body-build. The abdomen was distended and mildly tender on superficial palpation while shifting dullness was evident on deep palpation. On pervaginal and perspeculum examination, cervix seemed to be broad and hypertrophied with an ulcerative lesion in the posterior lip of the cervix which bleeds on touch. Uterus seems to be normal in size but mobility restricted. An irregular lump was felt through both the fornices. Similar findings were



FIGURE 1 : Showing Solid, Angry Looking Ovarian Tumour.

obtained on per-rectal examination with free rectal mucosa. Laboratory investigation revealed moderate anaemia (haemoglobin 9.6 g/dl), raised ESR (73 mm in 1st hour) and raised S. CA-125 (135 U/L). Ultrasound of whole abdomen showed both ovaries (each about 10 cm in size) with multiple cystic lesion, the largest one being 6 cm in the right ovary. Pouch of Douglas was clear with moderate amount of free fluid present in the peritoneal cavity. Endometrial curettage was done which revealed proliferative phase of endometrium. Cervical biopsy showed moderately differentiated squamous cell carcinoma (grade-II). On the basis of these findings, the case was provisionally diagnosed as carcinoma of cervix stage II A with ovarian tumour.

Laparotomy and peroperative findings:

Laparotomy was done followed by bilateral ovariectomy. Peroperative finding demonstrated

huge, straw coloured ascetic fluid. There was bilateral, solid, angry looking ovarian tumour of about 10 × 8 cm (Fig: 1). The tumours were adherent to the gut and adjacent structures with strong band which was resected. Bladder was plastered with uterus and hysterectomy was too difficult to perform. After adhesiolysis bilateral ovariectomy (Fig. 2) was done but the tumour could not be resected totally due to its extensive adhesion with gut. Cytoreduction was done as far as practicable. Seedlings were also observed in the inferior surface of liver and parietal peritoneum.

Conclusive diagnosis and definitive treatment:

Histopathological examination of biopsy material taken from the cervical lesion revealed a moderately differentiated squamous cell carcinoma (stage-II A), while histopathological diagnosis of biopsy material of endometrium did not reveal any evidence of malignancy. Histopathology report of biopsy material taken from lump showed papillary serous cystadenocarcinoma of ovary grade II. The case was referred to an Oncologist who prescribed a course of chemotherapy, Paclitaxel and



FIGURE 2 : Showing Adhesiolysis and Bilateral Ovariectomy.

Carboplatin every 21 days for 6 cycles and suggested that further cytoreduction could be done after improvement. The patient was admitted in the hospital and to receive the course of chemotherapy and symptomatic management till writing this report.

DISCUSSION

Simultaneous occurrence of primary tumors in the ovary and cervix in the present study should not be surprising. Synchronous endometrial and ovarian cancers are the most frequent simultaneously occurring genital malignancies, as the surface epithelium of the ovary has the same embryogenic derivation as the Mullerian duct⁸ and therefore, in adults, a given carcinogenic stimulus may produce similar epithelial proliferations in both structures.⁹ Synchronous and metachronous endometrial and ovarian cancers may be part of familial (hereditary) aggregation of cancers, like mismatch repair genes anomalies, known as Hereditary Non-polyposis colon cancer (HNPCC) and Muir Torre Syndrome and BRCA1 (full meaning) gene mutations resulting in BRCA1 Syndrome.^{4,10} Ovarian tumors may also spread to the contralateral ovary or even to the cervix and cervical tumors may metastasize to the ovary.¹¹

Cancers developing concomitantly in these locations are frequently misdiagnosed as metastatic tumors.¹ However, the overall survival of these patients suggests multifocal rather than metastatic disease, because most of these patients survive without recurrence, a finding compatible with stage I endometrial and ovarian carcinomas,^{2,11,12} about a third of the cases (14-29%) being independent tumors simultaneously involving both sites.^{13,14}

Independent primary tumors of low histologic grade, usually of endometrioid type, and with involvement limited to the endometrium and ovary, are associated with favorable outcome, without additional treatment.¹⁵ Frequently the ovarian cancer is discovered as an incidental finding and diagnosed at an earlier stage because of the symptomatic endometrial tumor. In contrast, tumors that are metastatic from the uterus to ovary, or from the ovary to uterus, usually carry a poor prognosis and require adjuvant therapy. Occasionally ovarian and uterine tumors are similar but of other cell types, and rarely the histologic type of tumor is

different in the two organs.⁴ Grade³ endometrioid carcinoma and malignant mesodermal mixed tumors are generally primary in one organ and metastatic to the other when detected.¹⁶

Conventional macroscopic and microscopic parameters in simultaneous uterine and ovarian endometrioid adenocarcinomas are, to date, the most practical criteria for distinguishing independent primary tumors from a primary tumor with metastasis. The conventional clinicopathologic parameters include the following^{1,6,17} stage, tumor size, histologic type, tumor grade, lymphovascular invasion, fallopian tube involvement, myometrial invasion, unilateral or bilateral ovarian tumor, pattern of ovarian involvement (multinodular growth or ovarian surface implants), presence or absence of coexistent lesions (ovarian endometriosis or a pre-existing adenofibromatous component in the ovarian tumor or atypical endometrial hyperplasia), and follow-up. Generally, in cases of primary carcinomas in an organ associated with metastasis in the other organ, the primary neoplasm is identified by its larger size or more advanced stage, keeping in mind that metastasis from the endometrium to the ovary occurs more often than the reverse.

Rarely, ovarian spread from an endometrial carcinoma with squamous differentiation takes the form of deposits of keratin or degenerated mature squamous cells associated with a foreign body giant cell response on the ovarian serosal surface. If no viable-appearing tumor cells can be identified in these deposits, this finding does not appear to worsen the prognosis even when the granulomas are also found elsewhere on the peritoneum.¹⁰ Isolated histologic features can be misleading, as the depth of myometrial invasion, as some cases with a minimally invasive, or even non-invasive, primary endometrial carcinoma may spread to the ovary but the absence of lymphovascular invasion in the myometrium suggests the extra-uterine tumor dissemination to the ovary by retrograde transtubal migration⁶. Consequently, at least two histologic criteria need to be associated.¹²

As many as 29% of patients with endometrioid ovarian adenocarcinomas will have associated endometrial cancer.⁶ Frequently in practice, primary ovarian endometrioid carcinomas metastatic to the endometrium may show direct extension of a high grade ovarian tumor to the serosal aspect of the uterus, with prominent myometrial invasion in the outer half of the myometrial wall and less often, anterograde tubal migration may result in tumor implantation in the endometrium.

CONCLUSION

We cannot make any conclusive comment with a single case, particularly when the treatment of the case has not been completed. However, overall survival of patients with simultaneous primary cancers of the ovary and uterus suggests multifocal rather than metastatic disease. Diagnosis relies upon conventional clinicopathological criteria. However, the distinction is important because the prognosis and management are different.

REFERENCE

1. Woodruff JD, Julian CG. Multiple malignancy in the upper genital canal. *Am J Obstet Gynecol* 1969;103(6):810-22.
2. Eifel P, Hendrickson M, Ross J, Ballon S, Martinez A, Kempson R. Simultaneous presentation of carcinoma involving the ovary and the uterine corpus. *Cancer* 1982;50(1):163-70.
3. Young RH, Path FRC, Scully RE. Metastatic tumors of the ovary. In: Kurman J. Blaustein's pathology of the female genital tract, 5th edn., Springer, 2002,1063-101.
4. Amalinei CR, Balan R, Ivan L, Socolov R, Socolov D, Cotutiu C. Multiple primary malignant neoplasms- case report, *Central European Journal of Medicine* 2006;1(1): 87-98.
5. Oliva E. Metastatic tumors to the female genital tract, with emphasis to metastatic tumors to the ovary. IAP Annual Congress, Montreal, 2006. Available at: <http://www.uscap.org/newindex.htmiap2006/sym>.
6. Irving JA. Simultaneous endometrioid adenocarcinomas of the uterine corpus and ovaries. IAP Annual Congress, Montreal, 2006. Available at:
7. Palacios J. Metastatic tumors of the female genital tract, In: European Congress of Pathology, Carrefour Pathologic. Update in Pathology, Paris, 2005,165-7.
8. Amalinei C. Morphogenesis and differentiation of the female genital tract. Genetic determinism and epithelium stromal interactions. 2007. *Rev Med Chir Soc Med Nat Lasi* 2007;111(1):200-09.
9. Matias-Guiu X, Lagarda H, Catusus L, Bussaglia E, Gallardo A, Gras E, Prat J. Clonality analysis in synchronous or metachronous tumors of the female genital tract. *Int J Gynecol Pathol* 2002;21(3):205-21.
10. Tavassoli FA, Devilee P. World Health Organization Classification of Tumors, Pathology and genetics. Tumours of the breast and female genital organs, IARC Press, Lyon, 2003.
11. Prat J, Matias-Guiu X, Barreto J. Simultaneous carcinoma involving the endometrium and the ovary: A clinicopathologic, immunohistochemical, and DNA flow cytometric study of 18 cases. *Cancer* 1991;68(11): 2455-9.
12. Ulbright TM, Roth LM. Metastatic and independent cancers of the endometrium and the ovary: a clinicopathologic study of 34 cases. *Hum Pathol* 1985; 16(1):8-34.
13. Kiemi PJ, Grnroos M. Endometrioid carcinoma of the ovary. A clinicopathologic, histochemical, and electron microscopic study. *Obstet Gynecol* 1979;53(5):572-9.
14. Kline RC, Wharton JT, Atkinson EN, Burke TW, Gershenson DM, Edwards CL. Endometrioid carcinoma of the ovary: retrospective review of 145 cases. *Gynecol Oncol* 1990;39(3):337-46.
15. Zaino RJ, Unger ER, Whitney C. Synchronous carcinomas of the uterine corpus and ovary. *Gynecol Oncol* 1984;19(3):329-35.
16. Amalinei C, Carantu ID, Balan R, Cotutiu C, Badescu M. Carcinosarcoma of the corpus uteri- a case report. *Rev Med Chir Soc Med Nat Lasi* 1997;101(1-2):213-7.
17. Prat J. Simultaneous adenocarcinomas of the uterus and ovaries, European Congress of Pathology, Carrefour Pathologic 2005. Update Pathol 2005;158-62.