Case Report

DOI: 10.7860/JCDR/2023/64747.18482

Pathology Section

A Rare Case of Synchronous Cervical Squamous Cell Carcinoma and Ovarian Brenner Tumour in a Postmenopausal Female: A Histological Surprise

RIDDHI JAISWAL[1], DEVAL BRAJESH DUBEY[2], PRASHANT VERMA[3]

ABSTRACT

Synchronous Tumours (ST) are defined as two or more neoplasms originating within six months of diagnosing the first neoplasm. Due to the rarity of synchronous cervical Squamous Cell Carcinoma (SCC) and ovarian Brenner tumours, their pathology has been poorly understood. These patients usually present with symptoms related to cervical cancer and are often diagnosed early. Since many synchronous tumours are incidentally discovered postoperatively, it is important to conduct thorough grossing and histopathological examinations. The primary differential diagnosis for synchronous tumours is multiple metastases from a single primary tumour. The management of multiple tumours is not well-defined and depends on various factors. In the present case, authors present a rare occurrence of synchronous neoplasms: cervical SCC and preoperatively undiagnosed benign Brenner tumour of the left ovary in a 52-year-old postmenopausal female. Immunohistochemistry helped rule out metastasis from a single primary and metastasis from cervical cancer to the ovary. The ovarian tumour showed immunoreactivity for GATA Binding Protein 3 (GATA) but was negative for Carcinoembryonic Antigen (CEA). The cervical SCC was immunopositive for CEA and p40, while no immunoreactivity was observed with GATA 3.

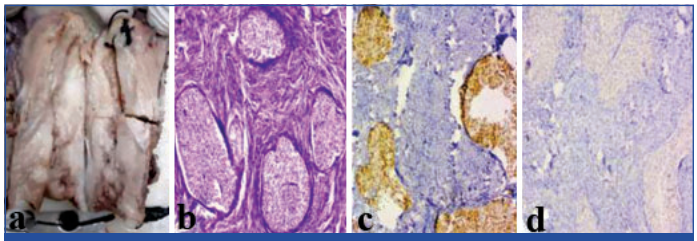
Keywords: Dual tumours, Epithelial tumour ovary, Squamous cell carcinoma cervix

CASE REPORT

A 52-year-old para 3, postmenopausal female presented in February 2022 with intermittent vaginal bleeding and lower abdominal pain for the past five months. She had no significant medical or surgical history and no family history of breast or Female Genital Tract (FGT) cancer. Serum biochemical and haematological parameters, including tumour markers CA-19.9, CA-125, and Human Chorionic Gonadotropin (HCG), were within normal limits. Contrast-enhanced Magnetic Resonance Imaging (MRI) of the pelvis in April 2022 revealed a heterogeneously enhancing lesion in the endocervical canal, cervix, and extending to the lower uterine segment, along with a fibroid in the left parauterine region. Both ovaries were atrophic, and the right internal iliac lymph node was slightly enlarged. Biopsy showed high-grade squamous intraepithelial neoplasia of the cervix. The patient was provisionally diagnosed with metastatic cervical SCC and underwent Wertheim Hysterectomy (WH) with Bilateral Salpingo-Oophorectomy (BSO) and a bilateral pelvic lymphadenectomy in August 2022. The postoperative period was uneventful.

The WH specimen measured 5.5×5.5×4.0 cm, and the cut surface revealed a slit-like endometrial cavity with a suspicious yellow, firm area measuring 1.5×1.0 cm on the lower uterine surface. The cervical lips were entirely involved by the tumour and, therefore, not separately visualised.[Table/Fig-1a]. The right ovary measured 1.8×1.5×1.5 cm and showed unremarkable parenchyma grossly. The cut surface of the bilateral fallopian tubes showed a patent lumen. The left adnexal mass measured 4.5×3.5×2.5 cm, with a bosselated outer surface. The cut surface showed the entire ovarian parenchyma replaced by a homogenous gray-white solid area. A total of 11 bilateral common iliac lymph nodes were isolated. Sections from the left adnexal mass showed a benign tumour arranged in smooth contoured nests and lobules of bland transitional epithelium with surrounding fibromatous stroma [Table/Fig-1b].

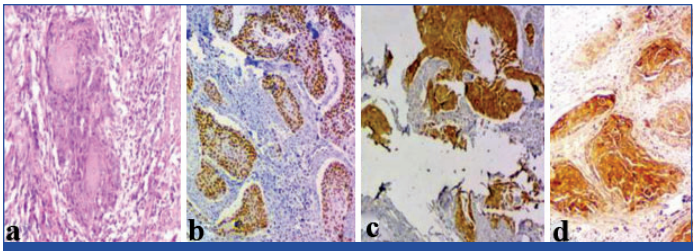
The transitional cells had uniform nuclei and clear to vesicular cytoplasm, with some cells showing nuclear grooves. Immunohistochemistry was also performed to rule out malignant Brenner tumour or metastasis from primary SCC. The ovarian tumour was immunoreactive for Cytokeratin, GATA 3,[Table/Fig-1c], while p16 was positive in epithelial nests and negative for CEA. [Table/Fig-1d]. Ki67 was less than 1% in tumour cells.



[Table/Fig-1]: (a) Gross image of specimen; (b) Brenner tumour of ovary (H&E, 10x) showing smooth contoured nests and lobules of bland transitional epithelium with surrounding fibromatous stroma; (c) GATA 3 immunopositivity in Brenner tumour of ovary (10x); (d) CEA immunoreactivity in Brenner tumour of ovary (10x).

Haematoxylin and Eosin (H&E) sections from the lower uterine segment showed SCC displaying islands, nests, and sheets of tumour cells [Table/Fig-2a]. The individual tumour cells were pleomorphic and had a moderate amount of cytoplasm, a high nucleo-cytoplasmic ratio, round to oval hyperchromatic nuclei, and inconspicuous nucleoli. Tumour-infiltrating lymphocytes were moderate, and lymphovascular invasion, perineural invasion, and necrosis were not evident.

The cervical SCC showed immunopositivity for cytokeratin, CEA [Table/Fig-2b], p40 [Table/Fig-2c], and p16 [Table/Fig-2d], while no immunoreactivity was observed with GATA 3. Ki67 showed 40% proliferation in tumour cells. The final diagnosis was moderately-differentiated SCC of the cervix with a benign BT of the left ovary. Pathological staging was assigned as pT1b1N0M according to the Cancer of American Pathologists protocol, 2022 [1]. The uterus, bilateral fallopian tubes, right ovary, five left common iliac lymph nodes, and six right common iliac lymph nodes were free from



[Table/Fig-2]: (a) Squamous Cell Carcinoma (SCC) of cervix (H&E, 20x) nests of tumour cells having moderate amount of cytoplasm, high nucleo-cytoplasmic ratio, round to oval hyperchromatic nuclei and inconspicuous nucleoli; (b) p40 immunopositivity in SCC of cervix (10x); (c) p16 immunopositivity in SCC of cervix (10x); (d) CEA immunopositivity in SCC of cervix (10x).

tumour invasion. The patient is currently under close follow-up and remains disease-free at the time of writing this report.

DISCUSSION

De Luca A et al., mentioned in their literature review that ST are defined as multiple independent primary neoplasms in the same or different organs, where the second (or third, etc.) neoplasms arise within six months of the diagnosis of the first neoplasm [2]. The incidence of synchronous gynaecologic neoplasms ranges from 0.7% to 1.8%, with synchronous ovarian and endometrial adenocarcinoma being the most frequent, possibly due to the hormonally active nature of these tumours [3]. Although the association of SCC of the cervix with Brenner Tumours of the ovary (BT) has rarely been reported, this occurrence may be due to the shared origin of the ovarian surface epithelium and uterine cervix (the coelomic epithelium) [2]. To the best of authors knowledge, this is the third report of such an occurrence [Table/Fig-3] [4,5].

S. No.	Author and year of publication	Age of patient	Status of menopause	Organs	Synchronous neoplasms of Female Genital Tract (FGT)
1.	Pekin T et al., (2007) [4]	62 years	Menopausal	Cervix right ovary left ovary endometrium	Cervical SCC, benign Brenner tumour, granulosa tumour, endometrial polyps
2.	Adhya AK et al., (2019) [5]	48 years	Menopausal	Cervix right ovary left ovary	Cervical SCC, dermoid cyst, benign Brenner tumour
3.	Present case	52 years	Menopausal	Cervix left ovary	Cervical SCC, benign Brenner tumour

[Table/Fig-3]: Case reports with similar synchronous tumours [4,5].

The concept of synchronous primary neoplasms of the female genital tract (particularly cervix and ovary) is a well-recognised yet uncommon phenomenon. It may result from a carcinogenic process affecting tissues with similar embryological origins [5]. Patients with such tumours usually present with abnormal vaginal bleeding in the early stages, as was the case with the patient [6].

It has been postulated that the extended Mullerian system, comprising ovarian epithelium, fallopian tube, uterine corpus, and cervix, shares the same embryological origin and genetic structure. Consequently, they may respond similarly to environmental exposures and produce concurrent primary carcinomas in multiple sites [7]. However, this theory fails to explain the simultaneous occurrence of neoplasms of varying cell lines, such as epithelial and germ cell lines [5].

The ST is also common in hereditary mutation syndromes such as non polyposis colon cancer syndrome, breast ovarian cancer syndrome, Li-Fraumeni syndrome, etc. The present case showed no clinical evidence of any syndromic association [8].

Several clinicopathologic criteria have been proposed for accurate differentiation of these distinct cancers. Gertsch P et al., have suggested that the best way to differentiate these two entities is by confirming: 1) the absence of direct continuity between the two neoplasms, 2) the characteristic pattern of growth of the primary tumours, and 3) clear histologic differences between the two tumours [9].

In the present case, the neoplasms are not continuous, as each growth pattern is typical of the respective cancers, and there are clear histomorphological differences between the two tumours. No evidence of local extension was found. Extensive sampling of the ovarian mass, histopathology, and immunohistochemistry ruled out the presence of any mixed components and the possibility of cervical SCC metastassing to the ovary. Synchronous tumours of the female genital tract generally have better prognoses compared to tumours with single metastatic lesions, as they tend to be diagnosed at early stages and low grades [10].

The most important differential diagnosis in such cases is multiple metastases from a single primary. It is crucial to differentiate between metastatic foci and the primary lesion, as survival significantly differs. Misdiagnosing multiple synchronous tumours as metastatic disease would significantly reduce expected survival [4]. In the present patient, the prognosis is clearly dependent on cervical carcinoma alone, but it may not be true if the BT had malignant features.

The management of multiple synchronous tumours is not well-defined and depends on various factors such as the patient's age, general status, histological type, local aggressiveness of the tumours, surgical resectability, and distant spread [5]. In the present case, treatment was directed towards SCC of the cervix as described above. Since the BT was undiagnosed preoperatively and was found to be benign, surgical resection was sufficient. If the BT was diagnosed as malignant, an omentectomy would be added, followed by adjuvant therapy postoperatively.

However, for multiple synchronous carcinomas, current literature suggests treating each tumour as a primary tumour with tailored treatment and prolonged follow-up.

CONCLUSION(S)

Synchronous tumours of the female genital tract are being observed more frequently in current practice. Therefore, it is important for surgeons, oncologists, radiologists, and surgical pathologists to have a high level of suspicion and awareness of such occurrences for proper and timely diagnosis and management. Synchronous neoplasms pose challenges in terms of tumour staging and treatment, and it is crucial to differentiate them from multiple metastases of a single primary tumour. Meticulous grossing, evaluation of histomorphological features, and immunohistochemistry are helpful in establishing the primary nature of these neoplasms.

Acknowledgement

The authors would like to express their sincere gratitude to all the staff members and technicians working in the Pathology Departments.

REFERENCES

[1] College of American Pathologists. Protocol for the examination of resection specimens from patients with primary carcinoma of the uterine cervix. Version: 5.0.1.3. CAP; 2022.
[2] De Luca A, Frusone F, Vergine M, Cocchiara R, La Torre G, Ballesio L, et al. Breast cancer and multiple primary malignant tumours: Case report and review of the literature. In Vivo. 2019;33(4):1313-24.
[3] Tong SY, Lee YS, Park JS, Bae SN, Lee JM, Namkoong SE. Clinical analysis of synchronous primary neoplasms of the female reproductive tract. European Journal of Obstetrics & Gynecology and Reproductive Biology. 2008;136(1):78-82.
[4] Pekin T, Yoruk P, Yıldızhan R, Yıldızhan B, Ramadan S. Three synchronized neoplasms of the female genital tract: An extraordinary presentation. Arch Gynecol Obstet. 2007;276(5):541-45.
[5] Adhya AK, Mohanty R. Triple synchronous tumour of female genital tract: Cervical squamous cell carcinoma, right ovarian dermoid cyst and left ovarian benign Brenner tumour. BMJ Case Reports CP. 2019;12(7):e230695.
[6] Ree YS, Cho SH, Kim SR, Kim KT, Park MH. Synchronous primary endometrial and ovarian cancer with three different histologic patterns: A case report. Int J Gynecol Cancer. 2003;13(5):678-82.
[7] Phupong V, Khemapech N, Triratanachat S. Triple synchronous primary cervical, endometrial and ovarian cancer with four different histologic patterns. Arch Gynecol Obstet. 2007;276(6):655-58.

[8] Jayalakshmy PS, Kulath FK, Parambil AV, Sideeque NA. Multiple synchronous lesions in the genital tract of a female: A rare combination with unrelated histogenesis. J Menopausal Med. 2018;24(2):133-37.
[9] Gertsch P, Thomas P, Baer H, Lerut J, Zimmermann A, Blumgart LH. Multiple tumours of the biliary tract. Am J Surg.1990;159(4):386-88.
[10] Elishaev E, Gilks CB, Miller D, Srodon M, Kurman RJ, Ronnett BM. Synchronous and metachronous endocervical and ovarian neoplasms: Evidence supporting interpretation of the ovarian neoplasms as metastatic endocervical adenocarcinomas simulating primary ovarian surface epithelial neoplasms. Am J Surg Pathol. 2005;29(3):281-94.

PARTICULARS OF CONTRIBUTORS:
1. Additional Professor, Department of Pathology, King George's Medical University, Lucknow, Uttar Pradesh, India.
2. Resident, Department of Pathology, King George's Medical University, Lucknow, Uttar Pradesh, India.
3. Junior Resident, Department of Pathology, King George's Medical University, Lucknow, Uttar Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Deval Brajesh Dubey,
I/F Kali Mandir, 74, Betiahata, Gorakhpur-273001, Uttar Pradesh, India.
E-mail: deval1992@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Apr 20, 2023
- Manual Googling: May 26, 2023
- iThenticate Software: Jun 22, 2023 (6%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. Yes

Date of Submission: **Apr 15, 2023**
Date of Peer Review: **May 25, 2023**
Date of Acceptance: **Jun 28, 2023**
Date of Publishing: **Sep 01, 2023**