CASE REPORT

DOI: 10.5336/caserep.2024-102421

Cervix Adenocarcinoma with Fallopian Tube Mucosa Involvement: An Extremely Rare Case

Dilara AKIN[a], Nil ÇULHACI[a], Niyazi Alper SEYHAN[b], Sinan Can TAŞAN[a]

[a]Aydın Adnan Menderes University Faculty of Medicine, Department of Medical Pathology, Aydın, Türkiye
[b]Aydın Adnan Menderes University Faculty of Medicine, Department of Gynecology and Obstetrics, Division of Gynecological Oncology Surgery, Aydın, Türkiye

ABSTRACT Fallopian tube involvement by cervical carcinoma has rarely been documented. In this case report we present a case of a 56-year-old woman who was diagnosed with human papillomavirus (HPV)-associated endocervical adenocarcinoma in the cervical biopsy and endocervical curettage sample. In examination of hysterectomy material besides the cervical adenocarcinoma, a tumor with the same morphology was also observed in the fallopian tubes. The histopathologic and immunostaining pattern supported the diagnosis of HPV-associated cervical adenocarcinoma with the involvement of the left fallopian tube. As our knowledge about ovarian serous carcinomas increases, we are increasingly encountering larger fallopian tube samples. This will lead to an increase in our knowledge about fallopian tube primary carcinomas and metastases, and we hope that our case report will contribute to the literature in this respect.

Keywords: Uterine cervical neoplasms; adenocarcinoma; fallopian tubes; neoplasm metastasis; human papillomavirus 16

Involvement of the fallopian tubes by cervical cancer has rarely been documented. The application of the sectioning and extensively examining the fimbriated end protocol has allowed us to increase our knowledge about fallopian tube tumors. As primary tumors, we know that approximately 80% of high-grade serous carcinomas of the ovary or peritoneum originate from the fimbrial end of the fallopian tube.[1] Of course, when a tumor is seen in the fallopian tubes, gynecological and non-gynecological metastases must be excluded.

This report outlines the scenario of a 56-year-old female who has been diagnosed with cervical adenocarcinoma linked to human papillomavirus (HPV), demonstrating infiltration into the left fallopian tube. Fallopian tube involvement by cervical adenocarcinoma is extremely rare and yet has unknown effects on patient outcomes. This case may indicate the importance of more comprehensive adnexal sampling and may increase our knowledge and experience on this subject by leading to similar cases.

CASE REPORT

A 56-year-old woman presented with abnormal bleeding to the gynecology outpatient clinic. In physical examination, a nodular lesion was seen in the cervix. Abnormal cells were observed in the Pap smear test. Endocervical adenocarcinoma was diagnosed in the cervical biopsy and endocervical curettage sample. Positron emission tomography/computed tomography revealed a focal hypermetabolic focus in the cervix and no metastatic disease was detected. The patient was informed and an informed consent form was obtained. The patient un-

TO CITE THIS ARTICLE:
Akın D, Çulhacı N, Seyhan NA, Taşan SC. Cervix adenocarcinoma with fallopian tube mucosa involvement: An extremely rare case. Turkiye Klinikleri J Case Rep. 2024;32(4):132-6.

Correspondence: Dilara AKIN
Aydın Adnan Menderes University Faculty of Medicine, Department of Medical Pathology, Aydın, Türkiye
E-mail: md.dilaraotu@gmail.com

Peer review under responsibility of Turkiye Klinikleri Journal of Case Reports.

Received: 26 Feb 2024 ***Accepted:*** 12 Jul 2024 ***Available online:*** 18 Jul 2024

derwent radical hysterectomy, bilateral salpingo-oophorectomy, and bilateral pelvic lymph node dissection and was referred to the pathology clinic for further examination.

Grossly, a gray-white nodular lesion measuring 2.1x1.8 cm was observed on the cervix (Figure 1). The uterine cavity was observed to have a normal appearance with a thickness of 0.3 cm. Bilateral fallopian tubes and ovaries appeared grossly normal. In the thin sections made on the bilateral fallopian tubes, a dirty white area was noticed in the left fallopian tube and sampled.

In histologic examination, well-differentiated, neoplastic gland proliferation was observed with desmoplastic stroma in cervix sections (Figure 2). Lymphovascular invasion was identified, The tumor was evaluated as silva pattern B. The depth of invasion was 16 mm and the horizontal spread was 18 mm. Perinoral invasion was not identified. In situ adenocarcinoma and high-grade squamous intraepithelial lesion were observed around the tumor area. A tumor with the same morphology was also seen in the isthmus and left fallopian tube. With additional sampling performed afterward, all fallopian tubes and endometrium were sampled. In additional samples, a tumor with the same morphology was observed in 1 more microscopic area in the left fallopian tube (Figure 3, Figure 4). There was no tumor in the endometrium, ovaries, parametrium, and 18 regional lymph nodes.

On immunostaining, the tumor cells from the cervix were diffusely positive for CK7, focally posi-

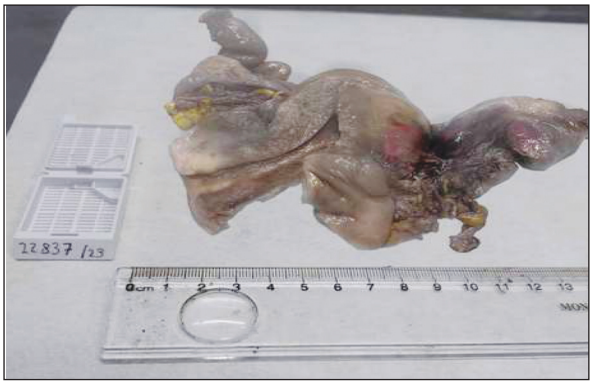

FIGURE 1: Macroscopic appearance of cervical lesion.

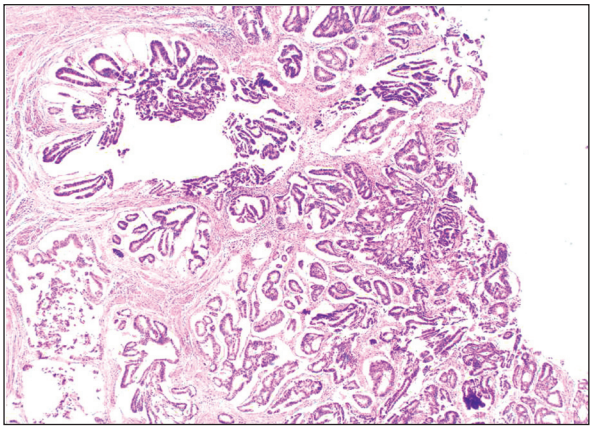

FIGURE 2: Well-differentiated neoplastic gland formation in desmoplastic stroma in cervix (H&E, x20).

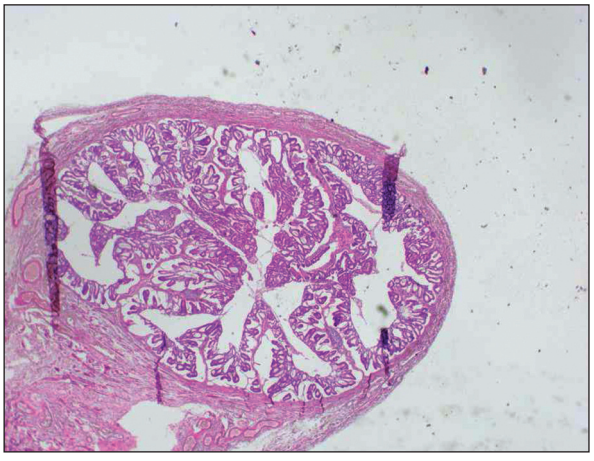

FIGURE 3: The fallopian tube mucosa involvement with cervix adenocarcinoma (H&E, x20).

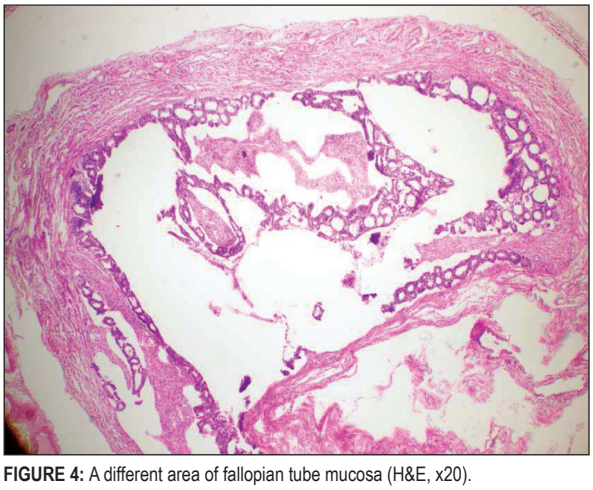

FIGURE 4: A different area of fallopian tube mucosa (H&E, x20).

tive for p16 and CEA, and negative for ER, PR, and p53. The immunohistochemistry from the left fallopian tube was positive for p16, CEA, focally positive for PAX-8 and negative for CK20, CDX2, Gata-3, WT-1, Vimentin, ER, and PR. (Figure 5, Figure 6). Cervical and left fallopian tubal tissues were examined using the HPV-DNA molecular method. Eight 10 µm sections were made from paraffin tissue. The sections were sterilely placed in a 2 mL Eppendorf tube, removed from paraffin, and DNA isolation was performed and evaluated using a real time PCR device. HPV DNA 16 positive was detected in both cases. The histopathologic and immunostaining pattern supported the diagnosis of HPV-associated cervical adenocarcinoma with the involvement of the left fallopian tube.

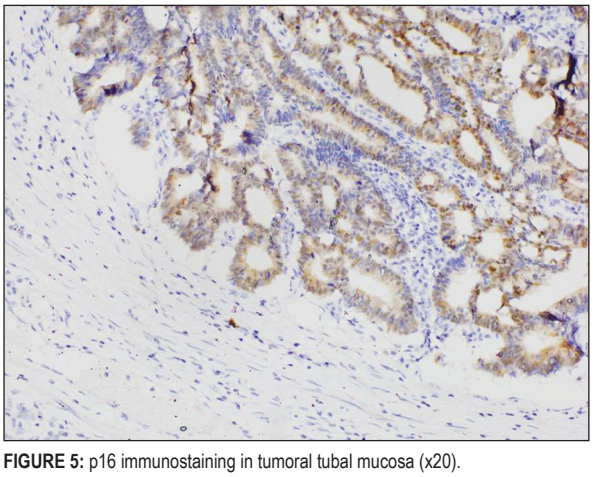

FIGURE 5: p16 immunostaining in tumoral tubal mucosa (x20).

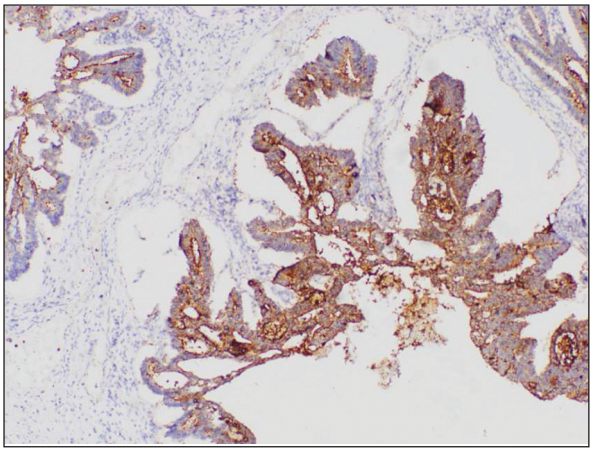

FIGURE 6: CEA immunostaining in tumoral tubal mucosa (x20).

DISCUSSION

Although the rate of cervical cancer is declining, the global burden remains high with over 600,000 new diagnoses every year.[2] Despite of decreasing incidence of the most common subtype, squamous cell carcinoma (SCC), the second most common subtype, cervical adenocarcinoma continues to rise, accounting for 20% to 25% of all cases.[3] In the last years, there have been significant changes to the histopathologic classification of cervical adenocarcinoma. In 2018, the classification of endocervical adenocarcinoma was revised to include 2 major subtypes: HPV-associated and non-HPV-associated or HPV-independent and this classification system was adopted by the World Health Organization in 2020.[4] Another new development is the Silva pattern. The Silva classification is based on the presence or absence of destructive stromal infiltration, the extent of destructive stromal infiltration (if present), the presence or absence of LVI, and the grading of cytologic atypia.[5] Studies have found that this classification is important in detecting lymph node metastases and recurrences. While no recurrence or lymph node metastasis was observed in Silva Pattern A, patterns B and C also found lymph node metastases and recurrences at different rates.[5]

Only a few cases of cervical cancer involving the upper genital tract have been reported in the literature. We know that cervical cancer affects the ovaries beyond just the fallopian tubes. Reyes et al. analyzed 20 cases of cervical cancer with secondary involvement, SCC involved the ovary and fallopian tube in 4 and 6 cases, whereas adenocarcinoma involved the ovary in 4 and the fallopian tube in 8 cases (In their analysis, adenocarcinomas in the ovary grew from small nodules) to confluent, expansile growth, whereas in the fallopian tubes, adenocarcinomas frequently showed mucosal colonization, with all microscopic dimensions ranging from 0.1 to 0.4 cm, mimicking the primary Sexual fallopian tube process.[6]

Deel et al. presented a case of a 50 year old woman who was diagnosed with stage IB1 well differentiated endocervical adenocarcinoma with surface extension to the endometrium and fallopian

tube.[7] But differently, in our case, tumoral involvement was not observed even though the whole endometrium was sampled.

To avoid pitfalls, analysis of histological and immunohistochemical features is crucial to distinguish endocervical cancer metastases from primary fallopian tube malignancies. Immunohistochemistry and molecular analysis of HPV DNA can help identify the primary source of malignancy. While wild-type p53 staining is expected in endocervical adenocarcinomas, serous fallopian tube intraepithelial carcinoma (STIC) exhibits a Mutant-type p53 expression (With aberrant or null pattern).

While molecular HPV-DNA positivity is in favor of HPV-associated endocervical adenocarcinoma, HPV positivity is not an expected finding in serous tubal intraepithelial carcinomas (STIC). Positive WT-1 immunostaining also supports serous fallopian tube tumors.[8] Unfortunately, p16 does not contribute to this differentiation.

Non-gynecological tumor metastases, which can present with mucosal involvement and mimic primary fallopian tube carcinomas, should also be excluded using immunohistochemistry and molecular HPV-DNA method.

Increasingly, we are encountering larger fallopian tube samples that demonstrate the possible fallopian tube origin of high-grade serous ovarian cancer. It is expected that we will see more fallopian tube tumors, both metastatic and primary. Therefore, the distinction between metastases and primary metastases is becoming increasingly important.[9]

Due to recent developments, tumors localized to the cervix involving the fallopian tubes represent stage M1 disease in the AJCC (involving the fallopian tubes and/or ovaries) but are stage I in Figo (organs located in the pelvis itself).[10]

In conclusion, the involvement of the upper genital tract in cervical cancer is still an uncommon occurrence, and more information and a larger number of cases are needed to determine diagnostic value.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Dilara Akın, Nil Çulhacı, Niyazi Alper Seyhan, Sinan Can Taşan;* ***Design:*** *Dilara Akın, Sinan Can Taşan;* ***Control/Supervision:*** *Nil Çulhacı, Niyazi Alper Seyhan;* ***Data Collection and/or Processing:*** *Dilara Akın, Sinan Can Taşan;* ***Analysis and/or Interpretation:*** *Dilara Akın, Nil Çulhacı, Niyazi Alper Seyhan, Sinan Can Taşan;* ***Literature Review:*** *Dilara Akın, Sinan Can Taşan;* ***Writing the Article:*** *Dilara Akın, Nil Çulhacı, Niyazi Alper Seyhan, Sinan Can Taşan;* ***Critical Review:*** *Nil Çulhacı;* ***Materials:*** *Niyazi Alper Seyhan.*

REFERENCES

1. Maeda M, Hisa T, Matsuzaki S, Ohe S, Nagata S, Lee M, et al. Primary fallopian tube carcinoma presenting with a massive inguinal tumor: a case report and literature review. Medicina (Kaunas). 2022;58(5):581. [Crossref] [PubMed] [PMC]
2. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209-49. [Crossref] [PubMed]
3. Smith HO, Tiffany MF, Qualls CR, Key CR. The rising incidence of adenocarcinoma relative to squamous cell carcinoma of the uterine cervix in the United States—a 24-year population-based study. Gynecol Oncol. 2000;78(2):97-105. [Crossref] [PubMed]
4. Salinaro JR, DiSilvestro J, Lokich E. Adenocarcinoma of the uterine cervix. Topics in Obstetrics & Gynecology. 2023;43(16):1-6. [Crossref]
5. Alvarado-Cabrero I, Parra-Herran C, Stolnicu S, Roma A, Oliva E, Malpica A. The silva pattern-based classification for HPV-associated invasive endocervical adenocarcinoma and the distinction between in situ and invasive adenocarcinoma: relevant issues and recommendations from the international society of gynecological pathologists. Int J Gynecol Pathol. 2021;40(Suppl 1):S48-S65. [Crossref] [PubMed] [PMC]
6. Reyes C, Murali R, Park KJ. Secondary involvement of the adnexa and uterine corpus by carcinomas of the uterine cervix: a detailed morphologic description. Int J Gynecol Pathol. 2015;34(6):551-63. [Crossref] [PubMed] [PMC]

7. Deel CD, Allen RA, Holman LL, Zuna RE. Adenocarcinoma of the cervix involving the fallopian tube mucosa: report of a case. Diagn Pathol. 2016;11(1):77. [Crossref] [PubMed] [PMC]

8. Hashi A, Yuminamochi T, Murata S, Iwamoto H, Honda T, Hoshi K. Wilms tumor gene immunoreactivity in primary serous carcinomas of the fallopian tube, ovary, endometrium, and peritoneum. Int J Gynecol Pathol. 2003;22(4):374-7. [Crossref] [PubMed]

9. Singh N, Gilks CB, Wilkinson N, McCluggage WG. Assessment of a new system for primary site assignment in high-grade serous carcinoma of the fallopian tube, ovary, and peritoneum. Histopathology. 2015;67(3):331-7. [Crossref] [PubMed]

10. Krishnamurti UG, Crothers BA, Birdsong GG, Klepeis V, Lankarani SM, Otis CN. Protocol for the Examination of Specimens from Patients with Carcinoma of the Uterine Cervix. College of American Pathologists. [Link]