GMR
The Original

HIGH GRADE SEROUS CARCINOMA OF THE FALLOPIAN TUBE PRESENTING AS A CERVICAL MASS: A DIAGNOSTIC CHALLENGE

Dr. S Gowtham[1], Dr Meethu Rappai[2], Dr C D Anand[3*], Dr Muthu S[4]

[1]Post graduate student, Department of pathology, SRM Medical college Hospital and research institute, Kattankulathur, Chengalpattu, Tamil Nadu, India Email id: mathwog.s@gmail.com, Orchid id: https://orcid.org/0009-0001-5479-3646
[2]Assistant professor, Department of pathology, SRM Medical college Hospital and research institute, Kattankulathur, Chengalpattu, Tamil Nadu, India Email id; drmeethurappai@gmail.com, Orchid id: 0009-0006-7681-3413
[3*]Professor, Department of pathology, SRM Medical college Hospital and research institute, Kattankulathur, Chengalpattu, Tamil Nadu, India, Email id: anandd@srmist.edu.in, Orchid id: https://orchid.org/0009-0005-9736-7750
[4]Professor and Head of the department, Department of pathology, SRM Medical college Hospital and research institute, Kattankulathur, Chengalpattu, Tamil Nadu, India, Email id; drmuthus@gmail.com, Orchid id: https://orchid.org/0000-0003-0364-8243
*Corresponding Author: Dr C D Anand, anandd@srmist.edu.in

ABSTRACT

Background: High grade serous carcinoma (HGSC) is a highly aggressive Müllerian neoplasm that most commonly arises from the fallopian tube fimbriae or ovary and spreads to the peritoneum. Secondary metastasis to the uterine cervix presenting as a clinically apparent cervical mass is an exceptionally rare occurrence that can mimic primary cervical carcinoma both clinically and histologically, posing significant diagnostic difficulty.

Case Presentation: We report a case of a 50-year-old postmenopausal woman who presented with per-vaginal bleeding. Per speculum examination revealed an exophytic cervical growth. Initial biopsy of the cervical lesion was interpreted as poorly differentiated squamous cell carcinoma. Radical hysterectomy was subsequently performed. Gross examination revealed a greyish-white exophytic cervical mass with concurrent involvement of the right fallopian tube. Histopathology demonstrated pleomorphic tumour cells arranged in clusters, nests, and micropapillary formations with abundant mitotic figures and necrosis. Immunohistochemical staining showed strong diffuse positivity for WT-1, PAX8, and CK7 in both the cervical and fallopian tube lesions, confirming Müllerian serous origin and supporting the fallopian tube as the primary site.

Conclusion: This case illustrates a rare phenomenon: primary fallopian tube HGSC presenting with clinically dominant cervical metastasis, initially misdiagnosed as squamous cell carcinoma of the cervix. It underscores the critical importance of an expanded immunohistochemical panel and comprehensive specimen evaluation in cases where tumour morphology appears inconsistent with a primary site diagnosis.

KEYWORDS: High grade serous carcinoma; Fallopian tube carcinoma; Cervical metastasis; Immunohistochemistry; WT-1; PAX8; Serous tubal intraepithelial carcinoma (STIC)

1. INTRODUCTION

High grade serous carcinoma (HGSC) is the most common and lethal histological subtype of epithelial ovarian cancer, accounting for approximately 70–80% of all ovarian cancer-related deaths [1]. Over the past two decades, compelling molecular and morphological evidence has shifted the understanding of its origin, with the majority of HGSCs now recognized as arising not from the ovarian surface epithelium, but from the secretory cells of the distal fallopian tube fimbriae often through a recognizable precursor lesion termed serous tubal intraepithelial carcinoma (STIC) [2,3].

STIC represents the earliest morphologically identifiable neoplastic lesion in the carcinogenic sequence leading to invasive HGSC. It harbours universal TP53 mutations and shares identical mutational profiles with concurrent invasive carcinomas, providing strong evidence of clonal origin [4,5]. The average lag time between STIC formation and development of invasive carcinoma is estimated at approximately 6.5 years [6].

Despite the well-characterised peritoneal, omental, and lymph nodal spread of HGSC, metastasis to the uterine cervix presenting as a clinically dominant exophytic cervical mass is exceptionally rare. The vast majority of cervical malignancies encountered in clinical practice are squamous cell carcinomas or adenocarcinomas of primary cervical origin, and this assumption can create a significant diagnostic pitfall. Cases of HGSC exhibiting superficial spread along mucosal surfaces to the cervix mimicking a primary cervical neoplasm have been increasingly recognised but remain infrequently reported in the literature [7,8].

We present a diagnostically challenging case of primary fallopian tube HGSC in a 50-year-old woman, in whom the presenting clinical picture, per speculum findings, and initial biopsy all suggested primary cervical carcinoma. The correct diagnosis was established only on comprehensive evaluation of the radical hysterectomy specimen combined with an extended immunohistochemical panel.

2. CASE REPORT

2.1 Clinical Presentation and Initial Workup

A 50-year-old postmenopausal woman presented to the gynaecology outpatient department with a history of abnormal per-

vaginal bleeding of three months' duration. She had no significant past medical or family history of gynaecologic malignancies. General examination was unremarkable. Per speculum examination revealed an exophytic, friable growth arising from the cervix with contact bleeding. The clinical impression at the time of initial assessment was primary carcinoma of the cervix.

Punch biopsy of the cervical growth was performed. Histopathological examination of the biopsy material revealed sheets and nests of pleomorphic cells with high nuclear-to-cytoplasmic ratio and brisk mitotic activity. The tumour was reported as poorly differentiated squamous cell carcinoma based on conventional haematoxylin and eosin (H&E) morphology. Immunohistochemistry was not performed at the time of initial biopsy.

Magnetic resonance imaging (MRI) of the abdomen and pelvis, along with a whole-body positron emission tomography-computed tomography (PET-CT) scan, were performed for locoregional staging and systemic evaluation. Imaging demonstrated an ill-defined, metabolically active mass involving the cervix and extending into the upper vagina, without overt evidence of discrete adnexal masses or peritoneal dissemination on initial review.

2.2 Surgical and Gross Pathological Findings

Based on the clinical staging and imaging findings, the patient underwent a radical hysterectomy with bilateral salpingo-oophorectomy and pelvic lymph node dissection. The surgical specimen was received fresh and subjected to comprehensive gross examination.

Gross examination of the uterus revealed a greyish-white, exophytic mass measuring 4 × 3 cm involving the cervix, with areas of haemorrhage and necrosis. The endometrium and myometrium appeared grossly unremarkable. The right fallopian tube was noted to be diffusely thickened and distorted, measuring 6 cm in length, with a similar greyish-white infiltrating lesion filling the tubal lumen. The left fallopian tube appeared grossly unremarkable. Both ovaries showed no gross abnormality.

2.3 Histopathological Findings

Representative sections were taken from the cervical mass, bilateral fallopian tubes, ovaries, endometrium, parametria, and the pelvic lymph nodes. All sections were processed by standard paraffin-embedding and stained with haematoxylin and eosin.

Microscopically, both the cervical mass and the right fallopian tube lesion demonstrated an identical morphological pattern. The tumour was composed of large, pleomorphic epithelial cells arranged in clusters, solid nests, papillary formations, and micropapillary architecture. Individual tumour cells exhibited markedly increased nuclear-to-cytoplasmic ratios, irregular nuclear contours, prominent nucleoli, and abundant eosinophilic cytoplasm. The mitotic rate was high, with 10–20 mitotic figures per 10 high-power fields, including atypical mitoses. Extensive areas of geographic necrosis were present. Lympho-vascular invasion was identified.

The right fallopian tube showed diffuse transmural involvement with tumour extending from the mucosal surface through the muscularis. The left fallopian tube showed only mild dysplastic epithelial changes without evident of invasive carcinoma. Both ovaries were free of tumour involvement on histological sampling. The endometrium showed no evidence of neoplasia. Pelvic lymph nodes did not show metastatic deposits in the sampled nodes.

2.4 Immunohistochemical Evaluation

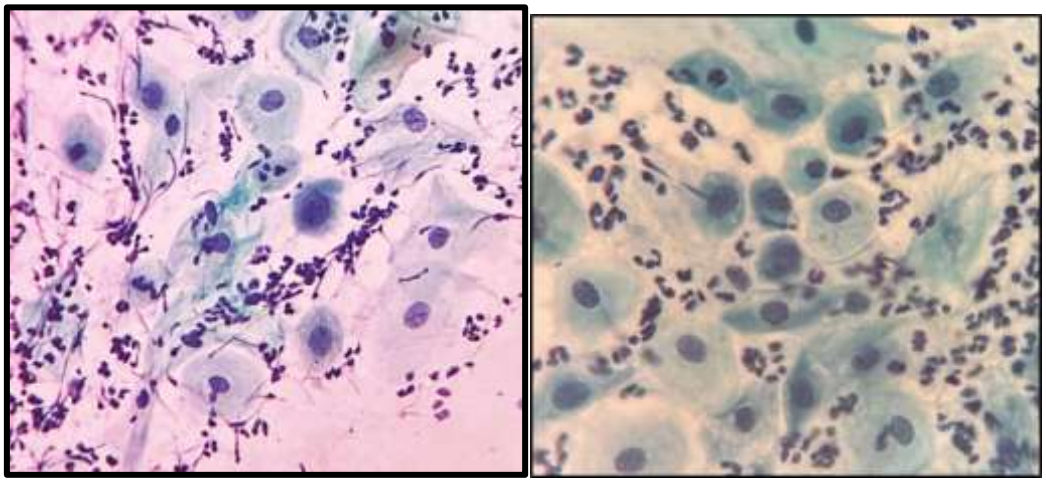
Given the unexpected morphological similarity between the cervical and fallopian tube lesions, and recognising that the microscopic appearance was not consistent with a primary squamous cell carcinoma of the cervix, an immunohistochemical panel was performed on representative sections from both sites.

The tumour cells at both the cervical and fallopian tube sites demonstrated strong and diffuse nuclear positivity for WT-1 and PAX8, and strong cytoplasmic positivity for CK7. Staining for CK20, p40, and p63 was negative in both lesions. High-risk HPV in situ hybridisation (HR-HPV ISH) was negative. Aberrant p53 expression was noted (strong diffuse overexpression pattern), consistent with a missense TP53 mutation characteristic of HGSC.

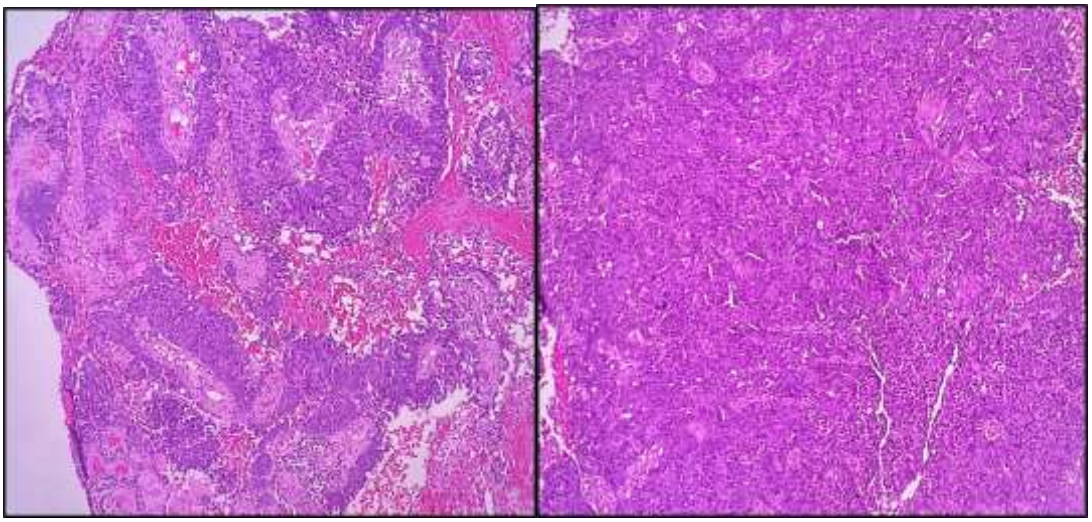
The immune-histochemical profile shows WT-1 positive, PAX8 positive, CK7 positive, p40/p63 negative, HPV negative, aberrant p53 was in keeping with a Müllerian high grade serous carcinoma and seems strongly against a primary cervical squamous cell carcinoma or a primary cervical adenocarcinoma of the usual type.

2.5 Final Diagnosis

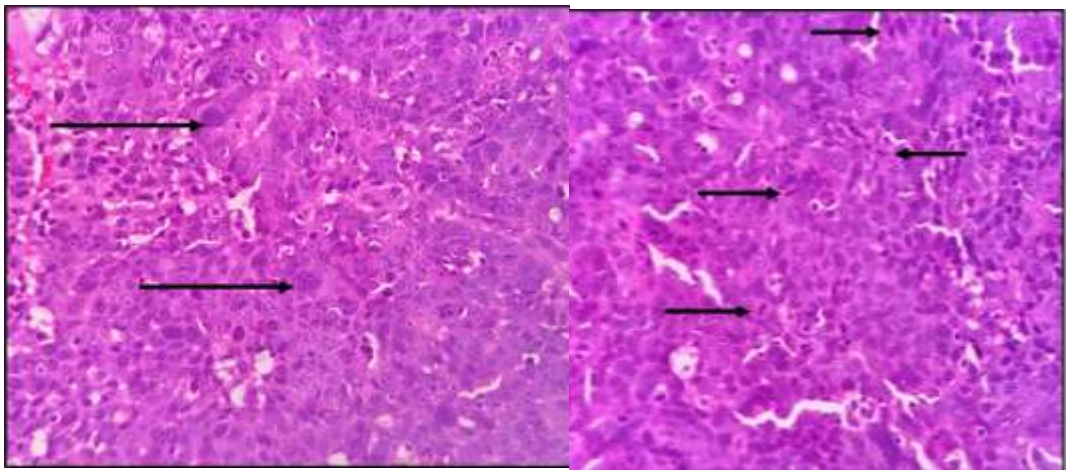
Integration of the clinical, gross, histopathological, and immunohistochemical findings led to the final diagnosis of: High Grade Serous Carcinoma of the Right Fallopian Tube with Secondary Metastasis to the Cervix (FIGO Stage IIIC1). The primary site was designated as the fallopian tube based on (a) the extent and distribution of tubal involvement, (b) dysplastic changes in the adjacent left fallopian tube consistent with a field effect, (c) absence of ovarian or endometrial primary involvement, and (d) characteristic immunophenotype of Müllerian serous lineage.



PAP SMEAR INTERPRETATION: **ASC-H – Atypical squamous cells, cannot exclude high grade squamous intraepithelial lesion. Comments**: Few squamous metaplastic squamous cells seen. Advised follow up smears.



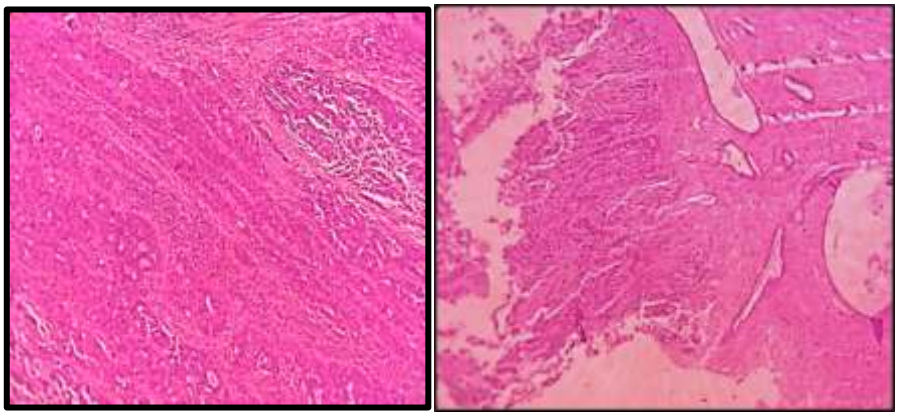
Invasive tumor cells arranged in papillary pattern with central fibrovascular core (left) and sheets (right)



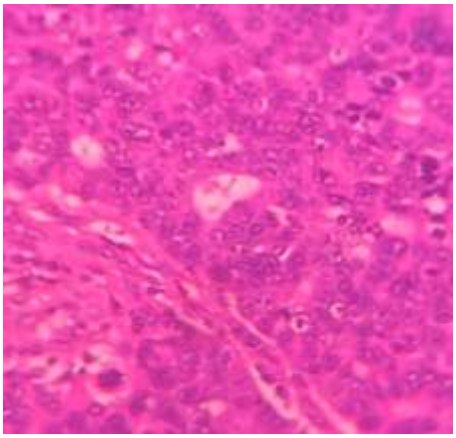
The tumor cells are round to polygonal with hyperchromatic nuclei with irregular nuclear membrane, marked nuclear pleomorphism, prominent nucleoli and scant cytoplasm. Mitotic activity: 30-34/10HPF

GROSSLY: An exophytic tumor of size **2x2x1.5cm** noted protruding through the opening of the cervical canal **(white arrow)**. The cut surface of the tumor was **grey white, homogenous, friable, firm in consistency (red arrow)**. The tumor appeared to infiltrate less than one third of the cervical stroma and did not extend into the endometrium grossly.

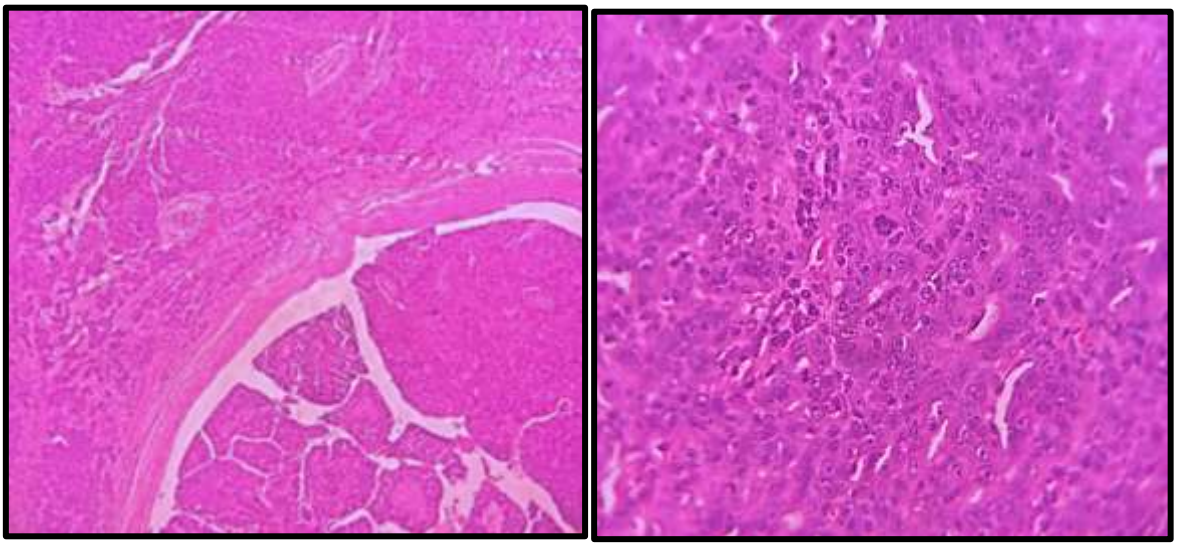
Right fallopian tube: External surface of the right fallopian tube (FT) appeared **grey white, dilated and enlarged**. The cut surface of the FT showed **dilated lumen along with grey white, homogenous and firm to hard lesion in the adjacent stroma** which appeared to reach up to the subserosa grossly (Black and red arrows).



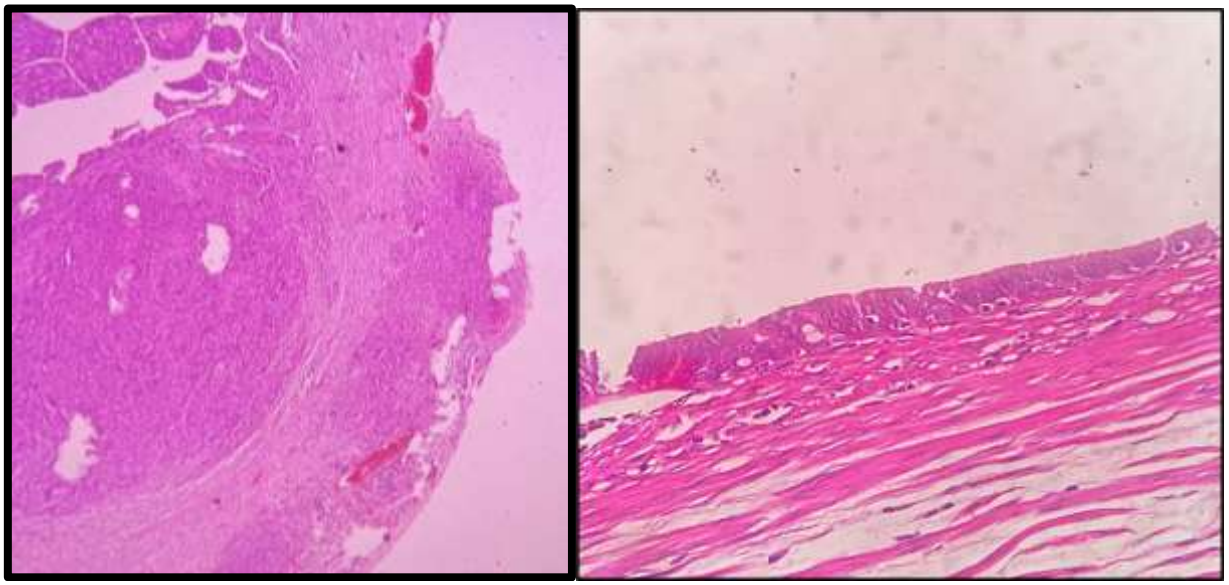
Tumour cells arranged in cords, sheets, nests (Left) and papillary pattern (Right)



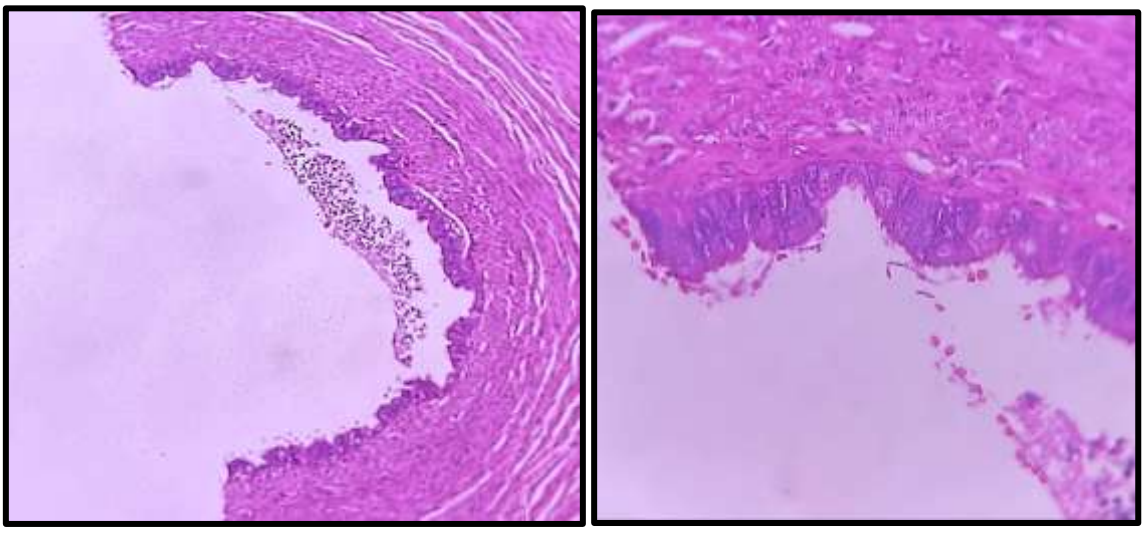
The tumor cells show increased nuclear cytoplasmic ratio, irregular nuclear membrane, prominent nucleoli. Many atypical mitotic figures are also noted (3-5/10HPF)



Right Fallopian tube – Infiltrating tumor cells arranged in papillary, tubopapillary, fused glands and sheets. Individual cells are markedly pleomorphic with vesicular nucleus. Prominent nucleoli (2-3) noted. The cytoplasm is moderate to abundant and eosinophilic. Frequent mitosis (2-3/10 HPF) noted

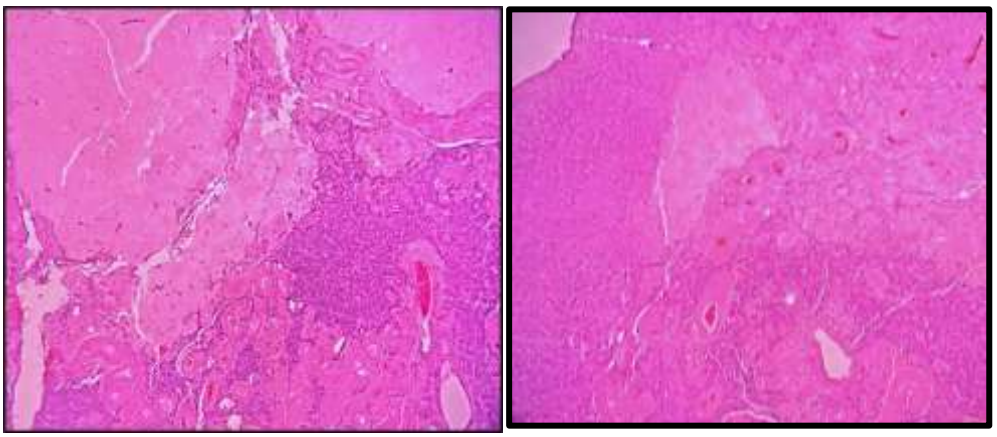


Intraluminal growth of right fallopian tube is infiltrating into the muscular wall focally involving serosal margin Adjacent distal area of Right fallopian tube also shows mild to moderate dysplastic changes in the lining epithelium



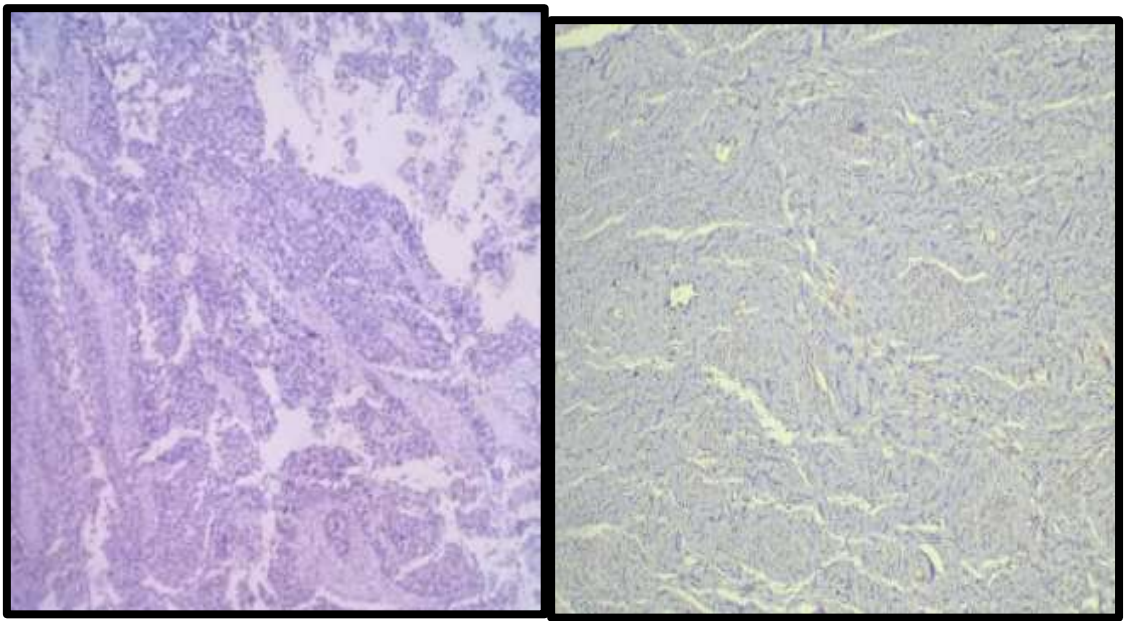
Left Fallopian tube showed dysplastic appearing lining epithelium with atypical cells with mid pleomorphism with loss of polarity and loss of plical structures

The lining epithelium showing dysplastic cells with mild pleomorphism and loss of polarity. The normal plical structures are not seen here.

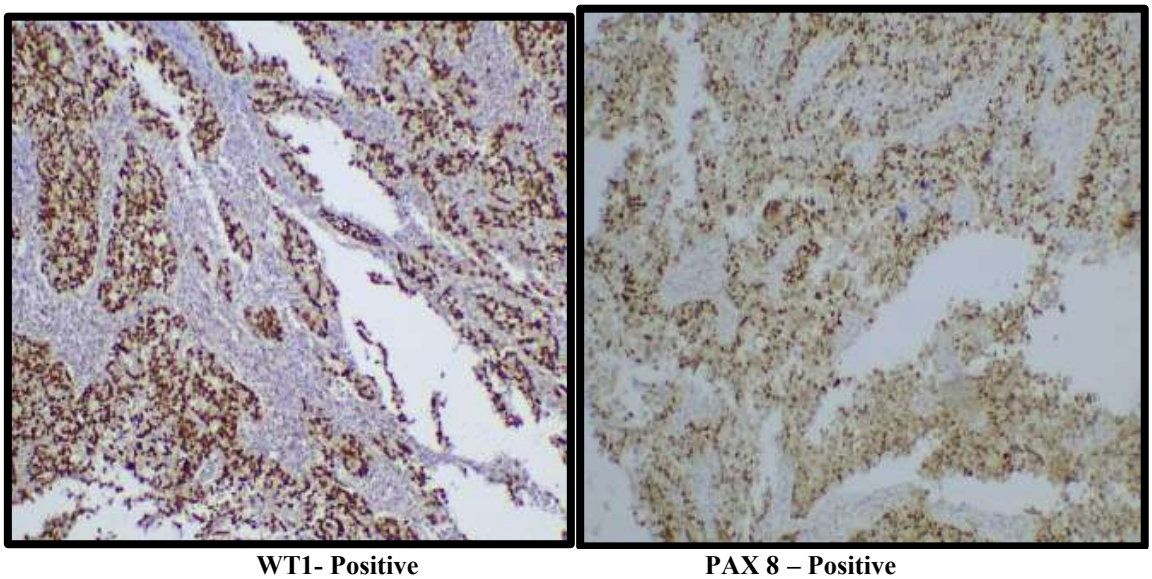


Left ovary showed unremarkable histology with corpus albicans and dilated blood vessels
Right ovary showed unremarkable histology with corpus albicans and dilated blood vessel

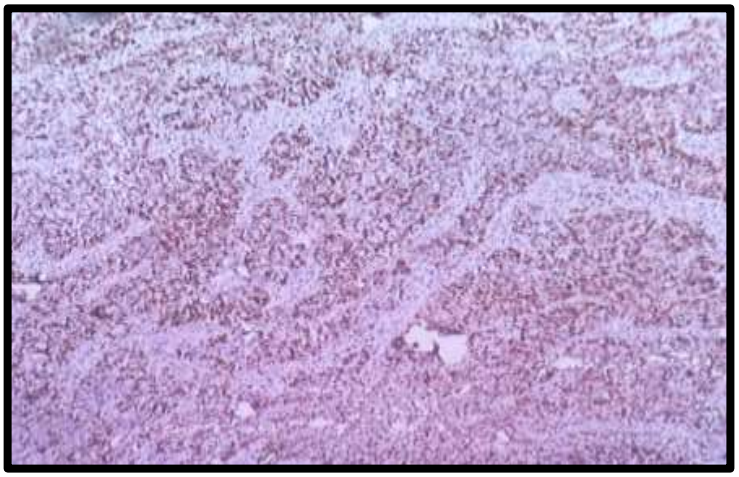
IMMUNOHISTOCHEMISTRY (IHC) – CERVIX



P63 – Negative on cervical tumor cells **CEA - Negative**

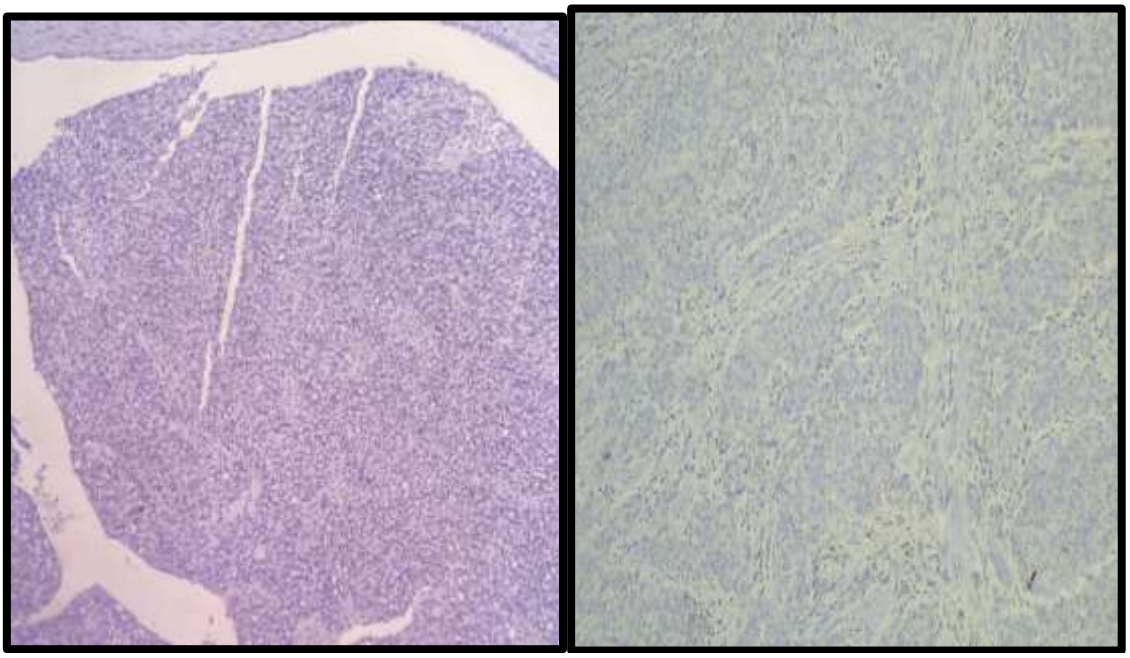


WT1- Positive **PAX 8 – Positive**

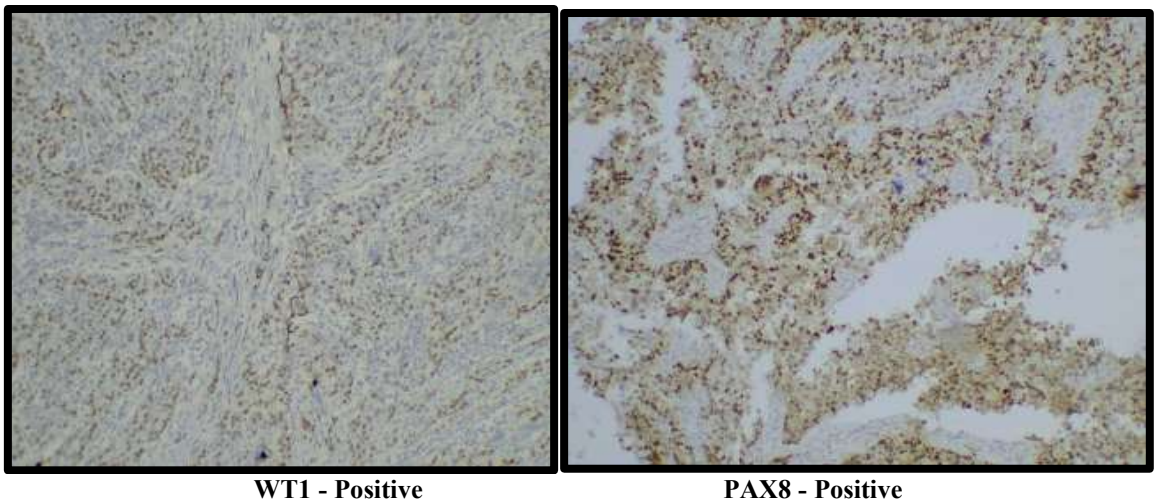


Ki67 – 80-90% positivity on cervical tumor cells

IHC- RIGHT FALLOPIAN TUBE



P63 – Negative on Fallopian tubal stromal neoplastic cells. **CEA – Negative**



WT1 - Positive **PAX8 - Positive**

DISCUSSION

The paradigm shift in understanding the pathogenesis of HGSC has been one of the most significant advances in gynaecologic oncology. Current consensus strongly supports the fallopian tube fimbriae as the predominant site of origin for the majority of pelvic HGSCs, irrespective of whether the carcinoma ultimately presents as ovarian, tubal, or peritoneal disease at the time of diagnosis [2,3,9]. STIC, characterised by a proliferation of atypical secretory-type tubal epithelial cells harbouring TP53 mutations, is now accepted as the immediate precursor lesion for most HGSCs [4,10].

Primary fallopian tube carcinoma (PFTC) has historically been considered rare, with an estimated incidence of 0.41 per 100,000 population [11]. However, this incidence is likely an underestimate, as many fallopian tube primaries have

historically been misattributed to ovarian primary sites. The commonest histological subtype is high grade serous carcinoma, and the tumour typically spreads via peritoneal dissemination, lymphatic routes, and haematogenous spread to the liver and lungs [12].

Metastasis to the uterine cervix from an extra-uterine primary is a well-recognised but infrequent occurrence, with cervical involvement most commonly reported as a consequence of direct extension from endometrial or vaginal carcinomas, or haematogenous/lymphatic seeding from distant primaries such as the breast, colon, or kidney [13]. Metastasis from a primary fallopian tube HGSC manifesting as a clinically dominant exophytic cervical mass is considerably rarer, with only isolated case reports available in the world literature [7,8].

The mechanism of cervical involvement in our case most likely represents direct transmucosal or lymphatic spread from the right fallopian tube primary. An alternative but less probable mechanism is superficial intramucosal spread a pattern that has been described in cases of HGSC of tubal origin extending along the endometrial surface to the endocervix and ectocervix [7]. The exophytic clinical appearance in our case, combined with the HPV-negative status and absence of in-situ squamous or glandular changes in the adjacent cervical epithelium, supports metastatic disease rather than a primary cervical neoplasm.

From a diagnostic standpoint, this case highlights the pivotal role of immunohistochemistry in resolving ambiguous morphology. WT-1 is a transcription factor with strong sensitivity for Müllerian serous carcinomas; it is diffusely positive in HGSCs but typically negative in endocervical adenocarcinomas of the usual type and in cervical squamous cell carcinomas [14,15]. PAX8, a Müllerian lineage marker, demonstrates sensitivity of 79–99% in serous ovarian/tubal carcinomas and is negative in the vast majority of cervical squamous cell carcinomas [16]. CK7 positivity combined with CK20 negativity is consistent with a Müllerian, rather than a gastrointestinal or urothelial, origin. Aberrant p53 expression (overexpression or null pattern) reflects the underlying TP53 mutation that is virtually universal in HGSC, distinguishing it from low-grade serous and other Müllerian carcinoma subtypes [17,18].

The initial erroneous biopsy diagnosis of poorly differentiated squamous cell carcinoma reflects the challenges of evaluating small, poorly differentiated tumours on biopsy material without the benefit of immunohistochemistry. The solid and nested growth pattern of HGSC can closely mimic poorly differentiated squamous cell carcinoma on conventional H&E morphology, particularly in a biopsy that samples the surface of a cervical mass. Routine inclusion of an expanded immunohistochemical panel including at minimum WT-1, PAX8, CK7, CK20, and p40 or p63, with HPV testing where available should be considered in all poorly differentiated cervical tumours where morphology is not definitively squamous, particularly in postmenopausal patients in whom HPV-driven disease is less expected.

Interestingly, the left fallopian tube in our case showed mild dysplastic epithelial changes without invasive carcinoma. This may represent early STIC or a p53 signature, consistent with the field effect described in the carcinogenic sequence of HGSC. The identification of precursor or dysplastic changes in the contralateral tube further supports the fallopian tube as the primary tumourigenic site and has implications for the management of at-risk populations through opportunistic salpingectomy [19].

Clinically, this case also illustrates the importance of radiological-pathological correlation. Although PET-CT detected a metabolically active cervical and upper vaginal lesion, adnexal involvement may not always be conspicuous on imaging in fallopian tube primaries, particularly when the tube is involved diffusely rather than as a discrete mass. Pathologists and clinicians should maintain a high index of suspicion for an unusual primary or metastatic site, particularly in postmenopausal women with poorly differentiated tumours at atypical locations.

CONCLUSION

We report an exceptionally rare presentation of primary high grade serous carcinoma of the fallopian tube with secondary cervical metastasis, which was initially misdiagnosed as a primary poorly differentiated squamous cell carcinoma of the cervix on biopsy. This case underscores several important diagnostic principles: (1) Poorly differentiated tumours involving the cervix in postmenopausal women should always prompt a comprehensive immunohistochemical evaluation before assigning a primary site; (2) The WT-1/PAX8/CK7/p40-p63/HPV panel is highly informative in distinguishing Müllerian serous carcinoma from primary cervical squamous or glandular malignancies; and (3) Thorough gross and histological evaluation of all adnexal structures in hysterectomy specimens is essential, as the clinically dominant mass may represent metastatic rather than primary disease. Recognition of this rare presentation is critical to ensure accurate staging, appropriate systemic treatment, and prognostic counselling for the patient.

SUMMARY

HGSC of the fallopian tube can present with a clinically dominant cervical mass, mimicking primary cervical carcinoma.

Initial biopsy of surface cervical lesions without ancillary immunohistochemistry may result in misclassification of the tumour subtype and primary site.

An immunohistochemical panel including WT-1, PAX8, CK7, p40/p63, and HPV testing is essential for accurate diagnosis of poorly differentiated cervical tumours.

Aberrant p53 expression along with WT-1 and PAX8 positivity strongly supports a diagnosis of HGSC of Müllerian/tubal origin.

Dysplastic changes in the contralateral fallopian tube may serve as an indicator of tubal field effect and support the fallopian tube as the primary neoplastic site.

6. PATIENT CONSENT

Verbal informed consent was obtained from the patient for the submission and publication of this case report. All patient data have been anonymised in accordance with institutional ethical guidelines.

REFERENCES

1. Torre LA, Trabert B, DeSantis CE, et al. Ovarian cancer statistics, 2018. CA Cancer J Clin. 2018;68(4):284–296. https://doi.org/10.3322/caac.21456
2. Kurman RJ, Shih IM. The dualistic model of ovarian carcinogenesis: revisited, revised, and expanded. Am J Pathol. 2016;186(4):733–747. https://doi.org/10.1016/j.ajpath.2015.11.011
3. Piek JM, van Diest PJ, Zweemer RP, et al. Dysplastic changes in prophylactically removed Fallopian tubes of women predisposed to developing ovarian cancer. J Pathol. 2001;195(4):451–456. https://doi.org/10.1002/path.1000
4. Meserve EEK, Brouwer J, Crum CP. Serous tubal intraepithelial neoplasia: the concept and its application. Mod Pathol. 2017;30(5):710–721. https://doi.org/10.1038/modpathol.2016.238
5. Lee Y, Miron A, Drapkin R, et al. A candidate precursor to serous carcinoma that originates in the distal fallopian tube. J Pathol. 2007;211(1):26–35. https://doi.org/10.1002/path.2091
6. Zakhour M, Cohen JG, Touboul C, et al. Serous tubal intraepithelial carcinoma and its clinical implications. Curr Treat Options Oncol. 2016;17(3):15. https://doi.org/10.1007/s11864-015-03850
7. Mohamed I, Elshaikh A. Pap smear as the first clue: fallopian tube high-grade serous carcinoma presenting as atypical glandular cells on cervical cytology. Am J Clin Pathol. 2025;164(Suppl_1):aqaf121.184. https://doi.org/10.1093/ajcp/aqaf121.184
8. Pinto A, Krasinskas AM, Bhatt S, et al. Adenocarcinoma of the cervix involving the fallopian tube mucosa: report of a case. Diagn Pathol. 2016;11:70. https://doi.org/10.1186/s13000-016-0519-3
9. Soong TR, Kolin DL, Teschan NJ, Crum CP. Back to the future? The fallopian tube, precursor escape and a dualistic model of high-grade serous carcinogenesis. Cancers (Basel). 2018;10(12):468. https://doi.org/10.3390/cancers10120468
10. Seidman JD, Zhao P, Yemelyanova A. Primary peritoneal high-grade serous carcinoma is very likely metastatic from serous tubal intraepithelial carcinoma: assessing the new paradigm of ovarian and pelvic serous carcinogenesis and its implications for screening for ovarian cancer. Gynecol Oncol. 2011;120(3):470–473. https://doi.org/10.1016/j.ygyno.2010.10.031
11. Dhakhwa R, Vaidya A, Giri A, Shakya A, Vaidya A. Primary high grade serous carcinoma of the fallopian tube: a case report. J Nepal Med Assoc. 2020;58(232):942–945. https://doi.org/10.31729/jnma.5674
12. Momtahan M, Khosravi G, Naderi A. Primary fallopian tube carcinoma presenting with massive inguinal tumor: a case report and literature review. Medicina (Kaunas). 2022;58(5):581. https://doi.org/10.3390/medicina58050581

13. Mazur MT, Hsueh S, Gersell DJ. Metastases to the female genital tract: analysis of 325 cases. Cancer. 1984;53(9):1978–1984. https://doi.org/10.1002/1097-0142(19840501)53:9<1978::aid-cncr2820530905>3.0.co;2-2
14. Taube ET, Denkert C, Pietzner K, et al. Wilms tumor protein 1 (WT1) — not only a diagnostic but also a prognostic marker in high-grade serous ovarian carcinoma. Gynecol Oncol. 2016;140(3):429–436. https://doi.org/10.1016/j.ygyno.2015.12.019
15. Lilac L, Carcangiu ML, Canevari S, et al. The value of PAX8 and WT1 molecules in ovarian cancer diagnosis. Rom J Morphol Embryol. 2013;54(1):17–27. PMID: 23529305
16. Laury AR, Perets R, Piao H, et al. A comprehensive analysis of PAX8 expression in human epithelial tumors. Am J Surg Pathol. 2011;35(6):816–826. https://doi.org/10.1097/PAS.0b013e318216c112
17. Cole AJ, Dwight T, Gill AJ, et al. Assessing mutant p53 in primary high-grade serous ovarian cancer using immunohistochemistry and massively parallel sequencing. Sci Rep. 2016;6:26191. https://doi.org/10.1038/srep26191
18. Kommoss S, Gilks CB, du Bois A, Kommoss F. Ovarian carcinoma diagnosis: the clinical impact of 15 years of change. Br J Cancer. 2016;115(8):993–999. https://doi.org/10.1038/bjc.2016.273
19. Hanley GE, McAlpine JN, Pearce CL, Miller D. The performance and safety of bilateral salpingectomy for ovarian cancer prevention in the real world: a population-based analysis. BJOG. 2018;125(9):1071–1077. https://doi.org/10.1111/1471-0528.15113