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High Grade Serous Papillary Adenocarcinoma of Mullerian Origin

Dr. Monika. P. Patni, Pathology Resident
Dr. Pragati Karmarkar, Associate Professor
Dr. Sadhana Mahore, Professor and HOD
Dr. Kalpana Bothale , Associate Professor
Department of Pathology, NKP Salve Institute of Medical Sciences and Research Centre, Digdoh Hills, Nagpur 440019 Maharashtra.

Correspondence Author: Dr. Monika. P. Patni, Pathology Resident, Department of Pathology, NKP Salve Institute of Medical Sciences and Research Centre, Digdoh Hills, Nagpur 440019 Maharashtra.

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Abstract

Epithelial ovarian, tubal, and peritoneal carcinomas represent a spectrum of disease that originates in the Mullerian compartment, collectively known as adenocarcinoma of Mullerian origin [1], first described by Dr. Swerdlow in 1959 [2]. It was previously known as cancers of unknown primary (CUP). Incidence being 3-5% [3]. It is important to recognize this tumor as it has more favorable prognosis and sensitive to chemotherapy. We report a case of 52 years old female presented with postmenopausal bleeding and was diagnosed with high grade serous papillary carcinoma of bilateral ovaries involving right tube and peritoneal deposits diagnosed after histopathology and immunohistochemistry.

Keywords- Mullerian origin, serous papillary carcinoma, ovary

Introduction

Incident of adenocarcinoma of mullerian origin is approximately 3-5%. Conventionally, epithelial ovarian, tubal, and peritoneal cancers have been considered as separate entities with different origins, pathogenesis, clinical features, and outcomes. But now it has been identified as not distinct entities but a spectrum of disease that originates in the Mullerian compartment[1]. The FIGO staging classification for ovarian, tubal, and peritoneal cancers was revised and includes tubal and peritoneal cancers in the ovarian cancer staging classification[4]. Previously peritoneal and tubal carcinomas have been considered as separate entities from ovarian carcinomas; thus epidemiologic studies have proven difficult [5] . But approximately carcinoma of mullerian origin accounts for 3-5% of malignant epithelial cancers. It is important to recognize the adenocarcinoma of Mullerian origin , because these cancers will typically have a more favourable prognosis and sensitivity to platinum-based chemotherapeutic regimens[6] . Identification of adenocarcinoma of Mullerian origin will guide appropriate treatment options, and provide information regarding prognosis [1,6].

Case Report

A 52 years old female presented with postmenopausal bleeding since 8 months. There was history of bloating of abdomen, breathlessness. On per vaginal examination,

right fix 5X6 cms firm irregular mass and nodularity in pouch of Douglas noted. Hysterectomy with bilateral salphingo-oopherectomy was done. Ultrasound, CECT, histopathology and immunohistochemistry was done.

Ultrasonograghy reveals pelvic solid masses with moderate ascites. Contrast tomography suggestive of ovarian neoplastic lesion, multiple nodularity seen on peritoneal surface. Ascitic fluid tapping cytology suggestive of adenocarcinoma of ovary. Gross- specimen of uterus with cervix with bilateral adnexa along with omentum with multiple nodular areas, largest nodule measuring -1.3 x 0.8x 0.3 cms.

Right ovary measures- 4.5 x 3.5x 1.8 cm and left ovary measures 3.4 x 2.4 x1.5 cm. Both ovaries are greyish brown in color, firm, nodular and shows areas of haemorrhage and necrosis.

Microscopy- Sections from different areas of left and right ovaries show tumor mass having tumor cells arranged in papillary pattern with fibrovascular core, solid sheets and focal glandular pattern. The cells are round to oval with large nuclei with coarsely clumped chromatin and prominent nucleoli. Nuclei shows moderate anisonucleosis and pleomorphism sections from right fallopian tube and nodular mass on omentum shows tumor deposits of similar morphology. Histological features are suggestive of adenocarcinoma involving bilateral ovaries, omentum, right fallopian tube . Immunohistochemistry was positive for Cytokeratin 7, CA 125, Wilms tumor protein and negative for cytokeratin 20 and calretenin Final diagnosis – High grade serous papillary carcinoma of Mullerian origin. Our patient was referred to the oncologist for further management.

Discussion

The most recent proposed division of epithelial ovarian carcinoma [EOC] includes two distinct histologic groups: type I and type II cancers. It should be noted that the type I and type II which is generally used to broadly classify ovarian neoplasms for research purposes based on their unique clinical and molecular genetic features and was not meant to be used for clinical purposes[7].

Type I tumours include low-grade serous, low-grade endometrioid cancers, Mucinous, clear cell, and transitional cell carcinomas. This category of tumours arise from atypical proliferative borderline tumours, benign cystic lesions, or endometriosis. . Generally, this tumours are more indolent, present at an earlier stage, and are confined to the ovary, are often large and have worse prognosis[1].

Type II cancers account for 75% of EOC and are responsible for vast majority of ovarian cancer deaths. These include high-grade serous and high-grade endometrioid carcinomas. These cancers are typically aggressive and diagnosed at a later stage[7,8,9] .Many high grade serous carcinomas arise as a result of their precursor lesions, serous tubal intraepithelial carcinomas, in the fallopian tube fimbriated end. An observation by Piek et al. would eventually revolutionize hypotheses regarding the origin of high- grade serous carcinoma (HGSC)[1]. In 2001, Piek and colleagues examined specimens from women who had undergone bilateral salpingo-oophorectomy. At least half of the specimens had pre invasive dysplastic lesions (later coined “serous tubal intraepithelial carcinoma” (STIC)) that resembled HGSC and almost all specimens had high levels of p53 protein accumulation [10]. HGSCs of the ovary, fallopian tube, and peritoneum are almost identical in histopathology.

Microscopically, the architecture could vary from complex papillary to solid pattern or glandular pattern.. The papillae are usually large, irregularly branching, and highly cellular. The marked cytologic atypia and frequent mitotic figures characterize HGSC. The tumour cells are enlarged, with high nuclear/cytoplasmic ratio and great

variation in size. The nuclei are of high-grade with vesicular chromatin and prominent nucleoli [11]. Serum biomarkers are useful for the detection, response assessment, and prognosis in a adenocarcinomas of Mullerian origin. Cancer antigen 125 (CA125) is the only biomarker commonly used for monitoring treatment response and cancer progression in EOC , as well as tubal and peritoneal cancers [1]. Immunophenotypically, ovarian and tubal HGSCs strongly and diffusely express p16, and CK7; express WT-1, PAX-8, estrogen receptor, CA125 and E-cadherin in most cases; do not express Her-2, calretinin, or CK20; and have a high Ki67 proliferative index. [11,12]. Overall, peritoneal serous carcinomas almost always demonstrate the same immunohistochemistry pattern as ovarian and tubal HGSCs, with minor and inconsistent differences in WT-1, b-catenin, vimentin and CK20 expression [12].

Conclusion

Adenocarcinoma of Mullerian origin histologically resembles primary ovarian cystadenocarcinoma. It is important to recognise this tumour as it has more favourable prognosis and sensitive to chemotherapy. Currently, the standard treatment of adenocarcinomas of Mullerian origin includes cytoreductive surgery and chemotherapy. The advances made in understanding the underlying molecular determinants of adenocarcinomas of Mullerian origin, as well as development of targeted therapeutics, will enable the implementation of genomic-driven treatment decisions in the future, elucidation of novel targets that can be used in preventive strategies, and better identification of precursor lesions that will yield improved survival outcomes.

Figure 1 : GROSS- Uterus with bilateral adnexa showing multiple nodularity. Omentum also shows multiple nodularity.

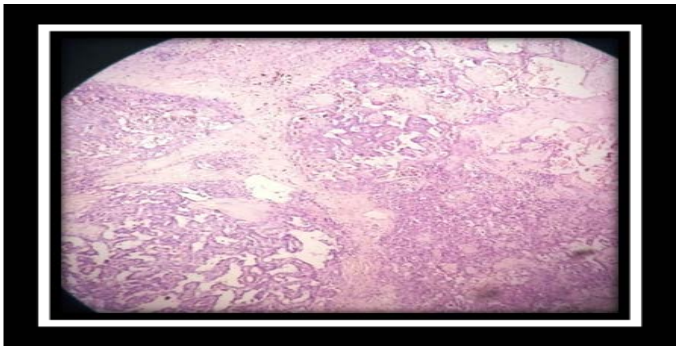

Figure 2 : MICROSCOPY- [low power 10X]- section shows tumour cells arranged in papillary pattern and in solid sheets pattern with adjacent stroma.

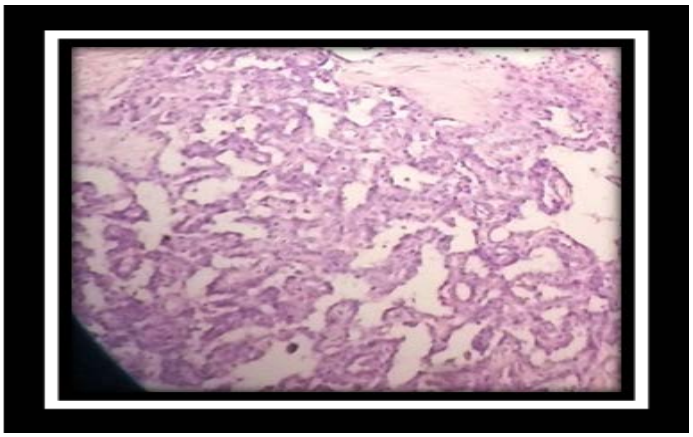

Figure 3 : High power view of same section showing papillary features.

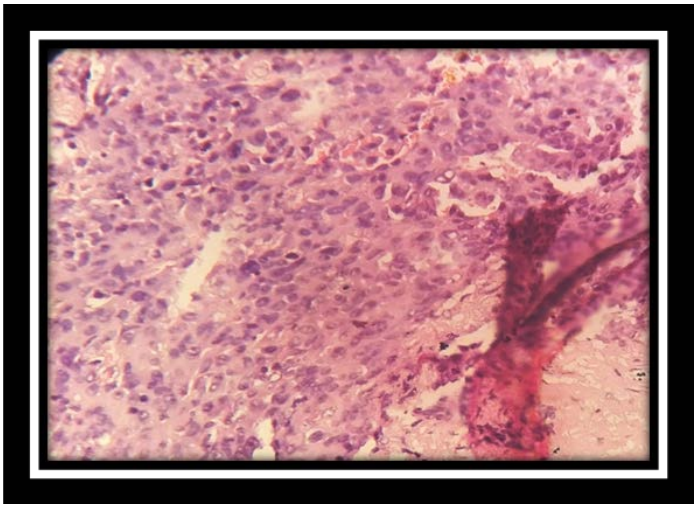

Figure 4 : High power view- 40X- Tumour cells show moderate anisonucleosis and pleomorphism. Nuclei are round to oval and hyperchromatic and moderate cytoplasm.

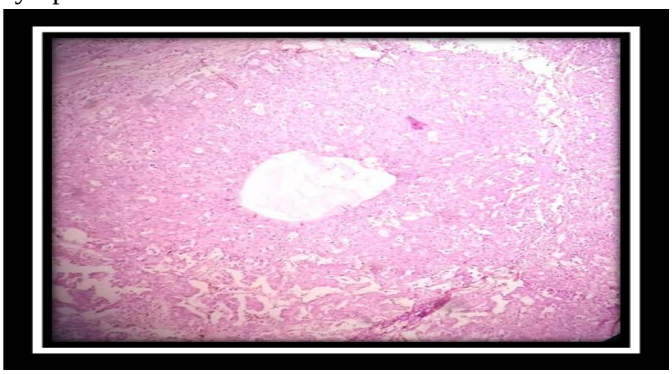

PHOTO-5-Section from fallopian tube shows tumour cells with similar histology(10X)

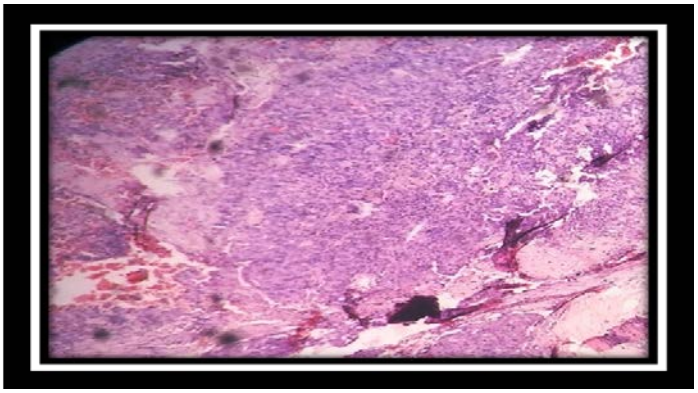

PHOTO-6-Sections from omentum shows similar tumour cells histology

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