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Case Report
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Mucinous Differentiation in a High Grade Serous Epithelial Ovarian Carcinoma: A Case Report

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Abstract

The most common histological type of epithelial ovarian carcinoma is high grade serous carcinoma. Immunohistochemistry analysis with p53 helps to differentiate high grade serous carcinomas from low grade serous carcinomas and the other type I histologies. However in recent years, there has been much speculation about variants of HGSC. These are characterized by high-grade ovarian carcinoma with unusual morphologies, including the Solid, Pseudo-Endometrioid and Transitional cell carcinoma-like (SET) pattern, exhibiting typical p53 molecular aberration of type II carcinoma and this transformation can also be extended to mucinous feature. Here in we report a case of advanced high grade epithelial ovarian carcinoma with a mucinous differentiation in a 33 year old multiparous, premenopausal lady.

Abbreviations

HGSC: High-Grade Serous Carcinoma; LGSC: Low-Grade Serous Carcinoma; SET: Solid, Pseudo-Endometrioid and Transitional-like; STE-M: Solid, Pseudo-Endometrioid and Transitional-like- Mucinous; FIGO: The International Federation of Gynecology and Obstetrics; WHO: World Health Organization; PCI: Peritoneal Carcinomatosis Index

Introduction

Epithelial ovarian carcinoma is the commonest type of ovarian cancer accounting for 90% of all cases [1,2]. Traditionally, epithelial ovarian carcinoma has been classified into two broad types, type 1, comprising of low grade serous, endometrioid, mucinous and the clear cell variants. Type 2 comprising of High Grade Serous Epithelial Ovarian Carcinoma (HGSC) [3,4]. The prognosis, clinicopathological features of the two types are distinct, however the treatment in general remains the same [5].

The most common histological type is, however HGSC accounting for 70% of all ovarian cancers. The histological features and the molecular profile of HGSC is quite distinct and immunohistochemistry plays an important role in differentiating the types of epithelial ovarian carcinoma. Immunohistochemistry analysis with p53 helps to differentiate high grade serous carcinomas from low grade serous carcinomas and the other type I histologies [6,7]. HGSC is the most aggressive variant and almost always harbors a *TP53* mutation (type II carcinoma), whereas low grade serous carcinoma and the other ovarian cancer histological types, are more indolent and develop through a multi-step carcinogenesis process (type I carcinoma) [4,8].

In recent years, there has been much speculation about variants of HGSC in addition to the conventional morphological variant of HGSC. These unusual variants are characterized by high-grade ovarian carcinoma with unusual morphologies, including the Solid, Pseudo-Endometrioid and Transitional cell carcinoma-like (SET) pattern, and exhibiting typical p53 molecular aberration of type II carcinoma [9]. A few studies in literature have reported the possibility of an additional mucinous differentiation in a HGSC [10]. It is important to differentiate a type 1 and type 2 cancer as it may have clinical implications in terms of prognosis and response to therapy. Herein we report a case of advanced high grade epithelial ovarian carcinoma with a mucinous differentiation in a 33 year old multiparous, premenopausal lady.

Case History

Clinical details

A 33 year old lady in good performance status, ECOG1, premenopausal and multiparous

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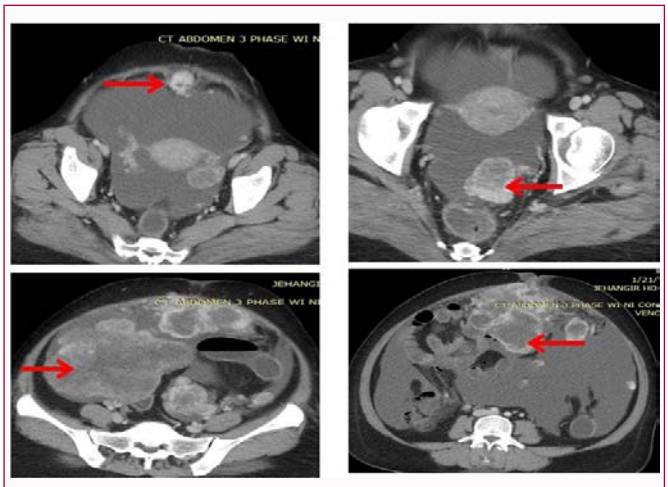

Figure 1: Prechemotherapy CECT showing pelvic, omental, umbilical and peritoneal deposits (Bold Red Arrows).

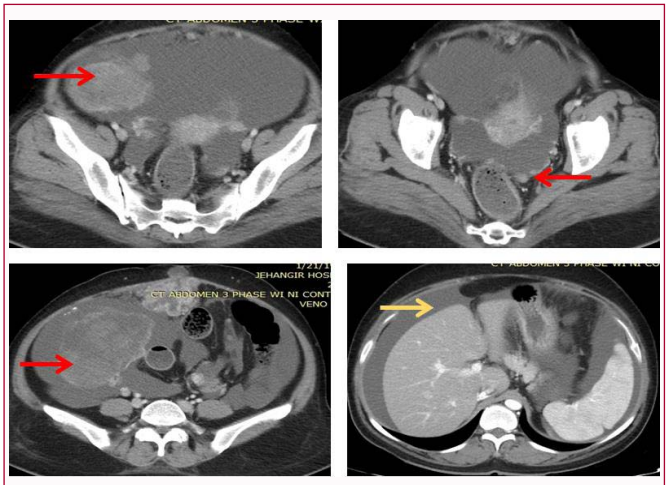

Figure 2: Postchemotherapy CECT showing partial decrease in pelvic, omental, umbilical and peritoneal deposits (Bold Red Arrows), and persistent ascites (Yellow Arrow).

presented to us in October 2020, with complaints of abdominal distention and weight loss. On clinical examination she was found to have gross ascites and Contrast Enhanced Computed Tomography (CECT) of the abdomen, thorax and pelvis revealed, bilateral ovarian masses, multiple omental, umbilical and peritoneal deposits and moderate to gross ascites (Figure 1). Her laboratory investigations revealed an elevated CA125-583 IU/ml. The other tumor markers, CA19.9, CEA, AFP and Inhibin were within normal limits. She underwent an ascitic fluid tapping and an USG guided biopsy of omental deposit. The biopsy report was suggestive of poorly differentiated serous carcinoma of ovary. In view of the above findings she was planned for Neoadjuvant Chemotherapy (NACT) and was started on platinum doublet chemotherapy with carboplatin and paclitaxel. Targeted therapy with bevacizumab, though ideal in the presence of ascites, was not considered due to financial constraints of the patient which is a very common scenario in clinical practice in a resource driven country such as ours. However, after 3 cycles of NACT there was no significant clinical response to chemotherapy (Figure 2). It was then decided, to change the chemotherapeutic agent to Gemcitabine and oxaliplatin. She received, 3 cycles of the same. Interim CECT scan showed a partial response and hence the patient was planned for a cytoreductive surgery. Intraoperative Peritoneal

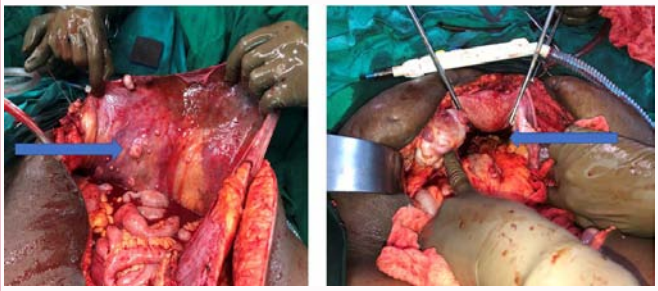

Figure 3: Intraoperative pelvic and peritoneal deposits (Blue Arrow).

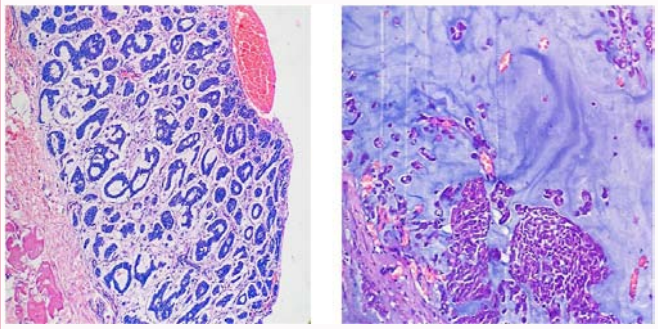

Figure 4: A) Tumour cells in acini in fibrous stroma, H&E, 20x. B) Tumour cells in glands & clusters in mucin pools, H&E, 20x.

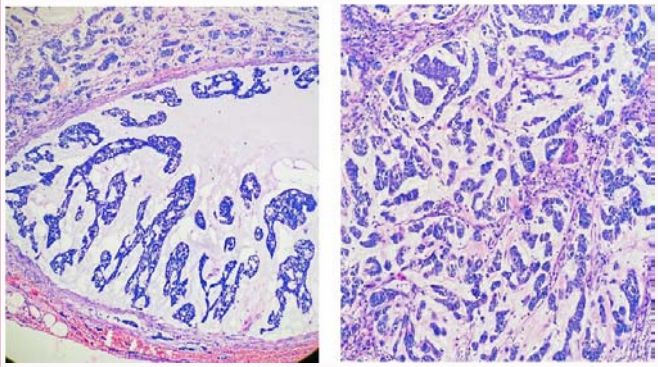

Figure 5: A, B) Tumour cells in floating clusters in mucin pools, H&E, 20x.

Carcinomatosis score (PCI) score was 30 [11]. The cytoreductive surgery was extensive and entailed resection of the total parietal peritoneum, splenectomy, anterior resection, total omentectomy, abdominal hysterectomy with bilateral salphingo oophorectomy with retroperitoneal and pelvic lymph nodal dissection (Figure 3).

Pathological findings

On gross examination, sections from bilateral ovaries and nodular deposits on the peritoneum showed whitish solid cystic mucinous areas. On microscopic evaluation, sections from both ovarian masses showed high grade adenocarcinoma with tumor cells arranged in tubules, cords, trabecula and few cribriform areas & sheets in fibromyxoid stroma. Floating clusters of tumour cells in mucin pools were noted (Figure 4,5). Individual tumor cells showed round to elongated hyperchromatic pleomorphic nuclei with prominent nucleoli and brisk mitosis. On immunohistochemistry, the tumor cells expressed CK7, PAX8 & WT-1 and were immunonegative for CK20, SF-1, calretinin, Melan A, EMA, SALL4, CA125, ER, PR & chromogranin A. p53 expression was of wild type (Figure 6).

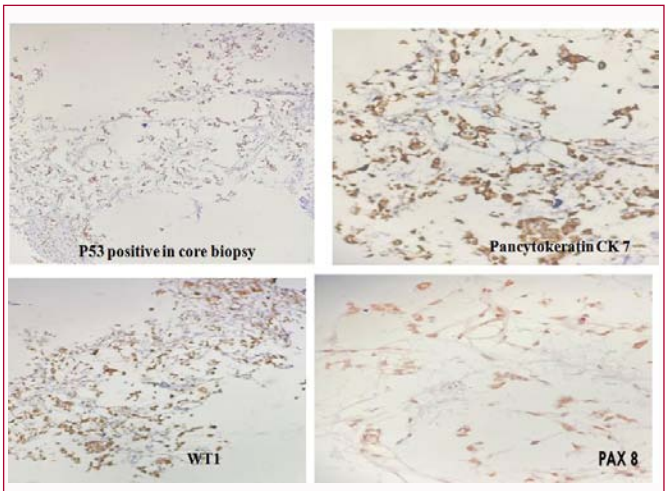

Figure 6: Immunohistochemistry positivity for, p53, CK7, WT1 and PAX8.

Discussion

HGSC consists of the conventional-type and alternative SET-type. Conventional-type HGSC usually shows papillary and slit-like glandular architecture with high-grade nuclear atypia that is derived from fallopian tubal epithelium. SET-type HGSC predominantly contains solid, pseudo-endometrioid, and/or transitional cell carcinoma–like histologic components. Recently, it has been proposed that the mucinous phenotype be included in the SET-type HGSC, thus giving way to a new SET to STE-M nomenclature/classification of HGSC, which includes a mucinous variant [9,10]. According to the WHO tumor classification mucin production may be found in serous tumors, particularly the serous borderline forms, but the mucins are almost entirely extracellular [12]. In our study it was necessary to distinguish between a seromucinous ovarian carcinoma *vs.* a high grade serous carcinoma with a mucinous differentiation. In our case, the cancer cells showed high-grade nuclear atypia and mucin-producing patterns. The high grade serous pattern observed in our study was of the conventional high grade type; however it was interspersed with predominant extracellular and intracellular mucin & myxoid stroma. There was no definite papillary pattern, psammoma bodies or transitional like areas in our case. The closest differential was seromucinous carcinoma. Seromucinous carcinomas are composed of endocervical type mucinous cells and serous carcinoma like morphology, however the mitosis count is low (<5/10 HPF) and they are ER & WT1 positive along with wild-type p53 immunophenotype [12]. Our case showed high mitotic activity with tumour cells arranged in tubules, cords, trabecula and few cribriform areas and sheets in fibromyxoid stroma with floating clusters of tumour cells in mucin pools. The immunohistochemistry profile of our case showed WT1 positivity, p53 expression on the biopsy, PAX8 positivity and CK7 positivity, while tumour was negative for CK20, Inhibin, calretinin, SALL4, ER, PR, CA125, CDX2, Chromogranin, Melan A, and EMA in the radical specimen. All these establish the fact that it was a high grade serous carcinoma with a mucinous differentiation and not a seromucinous carcinoma of ovary. WT1 & PAX8, established the fact that it was a high grade serous carcinoma, although, the prechemotherapy biopsy showed p53 expression; it was lost in post chemotherapy tumor tissue. This phenomenon is not uncommon as in 5% to 10% of cases; there can be a loss of p53 expression in tumor tissue following chemotherapy [13]. It has been postulated that this may be due to, due to deactivation of the mutated p53 gene, spontaneous mutation, selective growth within a heterogeneous population or alteration of p53 protein.

In our case in addition to the conventional morphology of HGSC, there were mucins producing patterns seen with extensive extracellular and intracellular mucin. Therefore, this can be considered as a conventional type HGSC transformation to a mucinous differentiation, dominated by mucin producing patterns.

We understand the limitations of this report and acknowledge the fact that molecular studies are lacking and will further help to classify these tumors effectively. Nevertheless, histological evaluation aided by immunohistochemistry does play an important role in assessing, identifying and classifying such rare variants. Another case study in literature has reported similar mucinous differentiation and confirmed it through molecular studies [2].

Conclusion

Mucinous differentiation in a high grade serous epithelial carcinoma is a rare and unique transformation that must be confirmed with molecular studies. Morphologic variants of high grade serous epithelial ovarian cancer must be acknowledged.

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