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CASE REPORT

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Synchronous or Metastatic Gastric and Ovarian Malignancies: A Diagnostic Challenge

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Abstract

Primary ovarian carcinoma is the prevailing form of cancer in the female reproductive system, leading to a substantial number of cancer-related fatalities globally. One of the major obstacles encountered in diagnosing this condition is distinguishing between primary gastrointestinal tumors and tumors that have metastasized from the ovaries, since they may exhibit similar histological characteristics. This case report underscores the difficulties involved in determining whether multiple tumors originate primarily or are a result of metastasis. We report a case of a 65-year-old female who presented with abdominal pain and was found to have a large multiloculated cystic mass in the right ovary and a poorly detected left ovary on ultrasound and CT scan. Her serum CA125 level was elevated. She underwent exploratory laparotomy and frozen section analysis of the right ovarian and gastric tumors. The histopathological diagnosis was mucinous cystadenocarcinoma of the ovary and well differentiated adenocarcinoma of the stomach. She also underwent hysterectomy with left salpingo-oophorectomy, which revealed mucinous cystadenocarcinoma of the left ovary. Immunohistochemical staining for specific markers, including CK7, CK20, CDX2, and PAX8, was conducted to identify the origin of the adenocarcinoma. The results revealed that both ovarian and gastric tumors showed a positive expression for CK7, while CK20 was negative in the gastric tumor but positive in the ovarian tumor. Furthermore, both CDX2 and PAX8 were negative in both the gastric and ovarian tumors. These findings provide valuable insights into the differential diagnosis and help to distinguish the possible sources of the adenocarcinoma. This case emphasizes the significance of histopathological examination and immunohistochemistry profiling in accurately diagnosing and determining the primary tumor site. Recognizing the primary tumor and its immunohistochemistry profile aids in guiding treatment strategies and predicting patient prognosis, leading to improved management and outcomes.

Keywords: Ovarian carcinoma; Gastric carcinoma; Immunohistochemistry

Introduction

Primary ovarian carcinoma is the most common malignancy of the female reproductive system and is responsible for a significant number of cancer-related deaths worldwide[1]. The frequency of multiple primary malignancies in the same or different organ systems ranges from 2% to 17%[2]. The presence of multiple malignancies can occur either synchronously, where they are detected simultaneously, or develop over the long-term during follow-up after initial cancer treatment. Recent advancements in immunohistochemistry (IHC) and genetic testing have significantly improved the diagnostic capabilities for identifying multiple primary tumors. IHC plays a crucial role in differentiating between primary tumors and metastatic lesions by assessing the expression patterns of specific markers in tumor cells.

By implementing these strategies, healthcare professionals aim to enhance patient outcomes and reduce the potential impact of additional cancers on their overall health.

Case Report

A 65-year multigravida female presented with complaints of pain abdomen for past 15 days which is intermittent in nature radiating to the back, also had complains of post-menopausal bleeding since 2 days which is not associated with clots and dysmenorrhea. On physical and systemic examination vitals were stable, abdomen is soft, non-tender, pelvic mass reaching up to umbilicus was noted. Per vaginal examination cystocele was present and posterior fornix mass was felt.

USG abdomen & pelvis showed atrophied uterus. Right ovary shows large multiloculated cystic mass which is extending to the umbilicus. Left ovary was poorly detected. Complete blood count and other lab investigations were normal.

CA 125 levels were 47.5 U/ml

CT abdomen & pelvis showed large multiloculated cystic mass lesion with septations likely to arise from pelvis suggestive of malignant etiology.

Endoscopic biopsy was done and showed features of chronic gastritis.

Patient was planned for total abdominal hysterectomy with bilateral salpingo-oophorectomy, then intraoperative frozen was sent for Right adnexal mass which was reported as mucinous cystadenocarcinoma ovary. Later on table tumour was seen extending to abdomen for which extended laparotomy was performed and subtotal gastrectomy with omentectomy was done and on table frozen section was sent and reported as well differentiated adenocarcinoma of stomach.

On examination of both ovaries external surface - capsule was intact, glistening. Cut surface – drained 500 ml of mucoid material, identified multiloculated cysts with focal solid areas measuring 3x1x1cm.

On gross examination of subtotal gastrectomy with omentectomy specimen identified ulcero-proliferative growth in the lesser curvature measuring 6.5x4x2cm.

Histopathological examination of bilateral ovaries revealed cyst wall lined by mucinous cells. Few areas showing multilayering with nuclear atypia. The tumor is seen involving the stroma.

Histopathological examination of subtotal gastrectomy with omentectomy revealed tumor cells arranged in glandular pattern. Individual tumor cells are round to oval with enlarged, pleomorphic hyperchromatic nuclei and scant amount of cytoplasm. The tumor cells are seen infiltrating the submucosa, muscularis layer and serosa. Stoma shows lymphoplasmacytic infiltration. Lymphovascular invasion seen. No perineural invasion noted. A total of 22 lymph nodes were retrieved out of which 2 lymph nodes

showed tumor deposits without extracapsular extension. Rest 20 lymph nodes are free from tumor involvement.

Final impression was given as

1. Bilateral mucinous cystadenocarcinoma of ovaries
2. Well differentiated adenocarcinoma – Stomach – Grade 1

Immunohistochemical staining was conducted to investigate the origin of the adenocarcinoma. The results revealed that both the ovarian and gastric tumors exhibited positive staining for CK7, indicating a presence of this marker in both types of tumors. However, only the ovarian tumors displayed positive staining for CK20, suggesting that this marker was specific to ovarian tumors. Notably, both tumors tested negative for CDX2 and PAX8.

Based on these findings, it can be concluded that two distinct primary cancers have developed simultaneously: ovarian carcinoma and primary adenocarcinoma of the stomach.

Discussion

Multiple primaries are defined as more than one synchronous or metachronous cancer in the same individual. For epidemiological studies, tumours are considered multiple primary malignancies if arising in different sites and/or are of a different histology or morphology group. This avoids misclassification of multifocal/multi-centric tumours or metastases as multiple primaries[3].

The etiology of multiple primary tumors in different organ systems remains largely unknown. Several factors have been proposed as potential contributors, including genetic predisposition, environmental factors, and shared risk factors. It is possible that certain genetic mutations or alterations may increase the susceptibility to developing multiple malignancies. However, further research is needed to elucidate the underlying mechanisms involved in the co-occurrence of these malignancies[4].

Histopathological examination, along with immunohistochemistry (IHC) analysis, plays a crucial role in distinguishing multiple primary carcinomas origin. The expression patterns of CK7 and CK20 in the presented case offer valuable insights into the differential diagnosis of gastric adenocarcinoma and mucinous cystadenocarcinoma of the ovaries. CK7 is commonly expressed in tumors arising from various glandular epithelia, including gastric adenocarcinoma and ovarian mucinous tumors[3].

The presence of CK20 expression solely in the ovarian tumor suggests a possible metastatic involvement of the ovary by the gastric adenocarcinoma. Previous studies have demonstrated that CK20 expression is typically seen in gastrointestinal malignancies, such as colorectal adenocarcinoma[4]. The absence of CK20 staining in the gastric adenocarcinoma suggests a differential expression pattern compared to the ovarian tumor, supporting the notion of a separate primary malignancy in the ovary.

The negativity of CDX2 and PAX8 staining in both tumors further supports the distinction between gastric adenocarcinoma and ovarian mucinous cystadenocarcinoma. CDX2 is a marker commonly associated with gastrointestinal differentiation and is frequently expressed in colorectal adenocarcinoma. PAX8 is a transcription factor frequently expressed in various gynecologic malignancies, including ovarian tumors. The absence of CDX2 and PAX8 staining in both tumors suggests an alternative origin or differentiation pathway for these neoplasms.

The accurate identification of the primary tumor site and its immunohistochemistry profile is crucial for selecting appropriate treatment strategies. Further research and larger-scale studies are needed to elucidate optimal management strategies and long-term outcomes in cases of multiple primaries. Collaborative efforts between gynecologic oncologists, gastroenterologists, and pathologists are essential for accurate diagnosis, treatment planning, and follow-up care.

Conclusion

This case underscores the importance of histopathological examination and immunohistochemistry profiling for precise diagnosis and identification of the various primary sources of tumors. The positive CK7 expression in both gastric adenocarcinoma and mucinous cystadenocarcinoma of the ovaries, along with differential CK20 expression, provides valuable diagnostic and prognostic information. The absence of CDX2 and PAX8 expression further supports the differential diagnosis and rules out alternative origins. Future studies exploring the molecular mechanisms and therapeutic targets specific to this tumor combination are warranted.

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