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Case Report

Colorectal Carcinoma Presenting as Ovarian Metastasis: A Case Report

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Abstract

There is a common occurrence of colorectal adenocarcinoma metastasis to the ovary and in rare circumstances, these cases may present clinically as primary ovarian cancer and histologically as primary endometrioid carcinoma of the ovary. Approximately 3.6% to 7.4% of patients with colon cancer have ovarian metastasis at the time of initial presentation, of which, 45% are mistaken for primary ovarian tumors. The author reports the case of a 60-year-old female presenting with fatigue and pelvic pain secondary to a pelvic mass. Computed tomography (CT) revealed a lobulated, heterogeneous pelvic mass measuring 11.1 × 10.5 × 9.8 cm, and ultrasound (US) showed complex 13.8 × 8.2 × 12.3 cm mass posterior to the uterus. Upon examination of the specimen following debulking procedure, endometrioid carcinoma of the ovaries was initially considered. However, immunohistochemical stains were performed and showed malignant cells positive for cytokeratin (CK) 20, caudal type homeobox (CDX) 2, and specific AT-rich sequence binding (SATB) protein 2, consistent with metastatic colorectal carcinoma. This report highlights the diagnostic challenges arising with differentiation between primary endometrioid ovarian carcinoma and metastatic colorectal adenocarcinoma to the ovary and the potential clinical consequences of misdiagnosis.

Keywords: Carcinoma; Ovarian metastasis; Immunohistochemical

1. Introduction

The ovaries are a common site of metastases from several locations, a primary one being of colorectal origin [1]. At the time of initial presentation, about 3.6% to 7.4% of patients diagnosed with colon cancer have ovarian metastasis,

of which 45% are mistaken for primary ovarian tumors [2]. The purpose of this report is to identify the clinical and immunohistochemical similarities between endometrioid ovarian carcinoma and primary colorectal cancer, highlight the differences that allow us to distinguish them, and discuss the implications of misdiagnosis due to these features. This case is a 60-year-old female presenting with pelvic mass and pain. Initial pathologic examination showed findings consistent with endometrioid ovarian carcinoma. After reevaluation of pathology and immunostaining, final diagnosis was metastatic colorectal carcinoma to the ovary.

2. Case Report

Our patient is a 60-year-old female who presented to the emergency room (ER) for direct admission due to pelvic pain secondary to pelvic mass. Patient reported feeling of abdominal pressure/fullness, abdominal bloating, and fatigue approximately 4 weeks prior to visit. She reported home management of pain with over-the-counter (OTC) medication. One week prior to the ER visit, the patient was taken via ambulance to a nearby hospital to be evaluated for severe abdominal pain refractory to OTC medications. At that time, computed tomography (CT) scan was performed and showed a lobulated, heterogeneous right pelvic mass measuring 11.1 × 10.5 × 9.8 cm immediately posterior to the uterus and anterior to the spine. The mass was primarily solid with some cystic components. Significant lab results at the time of visit included normal cancer antigen (CA) 125 levels and elevated carcinoembryogenic antigen (CEA). Physical exam at the time of visit showed a frail appearing female in no apparent distress. Abdominal exam showed a distended but firm and globular abdomen. Speculum exam was not done due to a narrow and atrophic vagina. Bimanual exam showed firm right and left adnexa and posterior cervix. Patient reported significant discomfort upon palpation. The patient has no significant past medical history due to lack of primary and gynecologic health care. Family and social history include maternal breast cancer and 23 pack year smoking history. Obstetric history includes non-surgical vaginal delivery x 7.

Gynecology oncology attending was consulted at this time for concerns of possible malignancy and patient was scheduled for examination under anesthesia (EUA) and robotic assisted total laparoscopic hysterectomy and bilateral salpingo-oophorectomy (RATLH/BSO) for possible staging. At the time of the procedure, infracolic omentectomy and complete pelvic tumor debulking was performed. Gross findings included a large right ovarian mass invading and adhesed to the posterior aspect of the uterus and posterior cul-de-sac with the rectosigmoid mesentery. The mass was measuring around 20 cm and appeared very friable. Additionally, there was a left ovarian mass measuring 3-4cm and a normal-appearing uterus. Patient required 2 units of packed red blood cells intraoperatively, but otherwise did well and was ready for discharge on postoperative day 2.

Post-operative pathology report discussed gross and immunohistochemical findings. Sections of the right and left ovaries demonstrated bilateral adenocarcinomas with multi nodularity and “dirty”, segmental necrosis. The resected omentum showed fragments of poorly preserved adenocarcinoma with necrotic debris, which were likely contaminants. The rest of the specimen resected was negative for malignancy. Immunostaining of the malignant

cells of the ovaries was performed due to uncertainty of diagnosis from gross pathology alone. The specimen was positive for CK20, CDX2, and SATB2 and negative for CK7 and PAX8. Additionally, KRAS and BRAF gene mutation identification was performed via PCR-SNAPSHOT analysis with no evidence of mutations. Endometrioid carcinoma of the ovaries was initially considered, but morphology and immunohistochemical staining pattern was consistent with metastatic carcinoma of gastrointestinal origin or colorectal carcinoma. Chemotherapy teaching and initiation of therapy was scheduled to begin with FOLFOX regimen- Leucovorin, Fluorouracil, and Oxaliplatin.

3. Discussion

Ovarian cancer is the second most common gynecological malignancy and the leading cause of gynecologic deaths in the United States [3]. Epithelial cell derived ovarian carcinomas are the most common and malignant type. These account for 85-90% of all ovarian cancers [4]. Endometrioid carcinoma, a subtype of epithelial tumors, is the second most common malignant ovarian neoplasm [1]. They are typically low-grade tumors and are found at an early stage, conferring a better prognosis than other types of ovarian neoplasms. Approximately 1.2-14% of women diagnosed with primary colorectal adenocarcinoma have ovarian involvement at some point. Metastatic colon cancer to the ovary (MCCO) are predominantly distal lesions that originate from the rectosigmoid colon. Spread to the ovary is thought to be through lymphatics, blood routes, or direct overgrowth through adjacent tissue. While the majority of these cases have the diagnosis of primary colorectal carcinoma prior to discovery of ovarian spread, a small percentage have ovarian tumor as the initial manifestation of disease [4].

Clinical features of MCCO and endometrioid carcinoma can present similarly and are therefore not diagnostically reliable. As in the case of this patient, symptoms can be non-specific: pelvic pain, presence of a pelvic mass, and constitutional symptoms such as weight loss and fatigue. Other potential overlapping symptoms include changes in bowel habits, early satiety, and younger aged patients [5]. Of note, one characteristic found primarily in MCCO is increased steroid hormone production and therefore, patients may present with more endocrine manifestations [6].

Gross and histological features of the ovaries may be more helpful than clinical presentation for accurate diagnosis. MCCO commonly resembles primary ovarian endometrioid adenocarcinoma [4]. These tumors are usually characterized on imaging as complex, solid-cystic masses; however, in some cases they may appear as completely solid [5, 7, 12]. Examination of the ovarian surface typically shows fibrous plaques with infiltrating carcinoma, and nodular growth pattern with hilar involvement is highly associated with MCCO [8]. Bilateralism is very common in MCCO (approximately 80% of cases), whereas unilateral masses are typically features of primary ovarian cancer. All bilateral mucinous and any unilateral tumor < 10 cm are metastatic carcinomas, while any unilateral tumor ≥ 10 cm are classified as primary ovarian carcinomas according to an algorithm developed to aid with diagnosis [9]. Histological examination of MCCO will reveal a glandular pseudoendometrioid, infiltrative invasion pattern. Characteristics of these metastases include garland and cribriform growth patterns and segmental necrosis of the walls [5]. This pattern appears as multiple, large, cystic glandular structures with coarse granular necrotic debris consisting of sloughed carcinoma cells (“dirty necrosis”) [5, 8, 10, 11]. Other helpful cytological features include

marked atypia (2+ or 3+) and high mitotic index [12]. Primary ovarian carcinoma has some overlapping features, including necrosis and intraluminal cellular debris [8]. However, this debris consists primarily of thin secretions and degenerating neutrophils [13]. Other characteristics supporting diagnosis of primary ovarian carcinoma include the expansive pattern of invasion, the presence of complex papillary pattern and Mullerian features [5, 14].

Lastly, it is important to utilize immunohistochemistry in the event that gross and microscopic features fail to distinguish between primary ovarian and MCCO. The malignant cells were positive for CK20, CDX2, and SATB2 and negative for CK7 and PAX8. Endometrioid ovarian adenocarcinomas are typically CK7 positive and CK20 negative. MCCO, however, are mostly positive for CK20 and negative for CK7 [21, 23, 24]. Expression of CDX2 gene is also helpful in identifying MCCO, due to it encoding an intestine specific transcription factor. Therefore, while expression is still observed in up to 70% of primary ovarian tumors, lack of CDX2 presence is strongly indicative of primary ovarian carcinoma [13, 15, 16]. Paired box genes (PAX) are transcription factor genes that are essential for determining cell fate during development of several organs. PAX 8 is also found in high levels in certain tumors, including epithelial ovarian carcinomas. The lack of PAX8 in the patient's tumor sample indicates that the tumor is not of ovarian epithelial cell origin [17]. SATB2, a transcription factor regulating chromatin remodeling and transcription, is also a useful tumor marker due to its isolated expression in colorectal carcinomas [18]. Additionally, other markers not used with our patient such as carcinoembryonic antigen (CEA) and cancer antigen (CA) 125 can be of great utility when used as part of a diagnostic panel, but unreliable as a single test [10, 19-23]. CEA is especially useful when it comes to distinguishing primary endometrioid carcinoma from MCCO with pseudoendometrioid pattern; the latter will stain strongly for CEA [10, 24]. CA 125 is useful diagnostically because it stains strongly for endometrioid ovarian carcinoma, while only 4-15% of colorectal carcinomas are immunoreactive for CA 125 [20, 23].

Failure to consider the possibility of MCCO could result in negative consequences including ineffective clinical management. Additionally, patient expectation and goals will vary based on the different prognosis of MCCO and endometrioid ovarian cancer. A study found five-year survival of patients with endometrioid cancer of the ovary to be 62%, with a mean survival rate of 58 months [25]. This differs from the poor overall five-year survival rate in patients with ovarian metastases from colorectal carcinoma, which is 22 percent [26]. Initial therapy is chosen based on location of primary tumor, patient fitness, KRAS and BRAF mutation status and the goal of therapy. For most patients, treatment will be palliative in order to maintain quality of life and prolong survival. In addition, patients diagnosed with MCCO will undergo BRAF and KRAS mutation analysis, and if present, is associated with worse prognosis and will necessitate more aggressive therapy [27]. This patient was selected to begin FOLFOX regimen, which consists of oxaliplatin plus leucovorin and short term infusional fluorouracil, as this is considered a first line therapy for MCCO [28]. This differs from what treatment would have been initiated if the primary cancer had been of an epithelial ovarian cell source (EOC). Standard approach for therapy of EOC is using a platinum agent (ie. cisplatin) with a taxane (ie. paclitaxel). As in our patient with optimally cytoreduced disease, six cycles of

alternating intravenous and intraperitoneal (IP) chemotherapy combination is preferred [29]. Therefore, initiating therapy for a primary EOC would have been of absent or reduced efficacy in treating her MCCO and possibly resulted in negative outcomes for our patient.

4. Conclusion

Misdiagnosis of a MCCO as a primary ovarian tumor can lead to inappropriate choice of agents (4), and in the case of this patient, would have resulted in an ineffective therapy regimen for her specific type of cancer. It is essential to suspect ovarian metastasis from colorectal cancer when a female patient presents with pelvic mass, especially if she is of premenopausal age. Appropriate workup by utilizing clinical, gross, histological, and immunostaining presentation is essential to make an accurate diagnosis and ensure that the appropriate medical management is initiated for best possible outcome.

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