Primary Mucinous Adenocarcinoma of the Ovary with Pulmonary Recurrence: A Case Report

Sarah Y. He1*, Teuta Shemshedini2, Ester Yoon3, Amrita Arneja4, and Tana S. Pradhan1,2

1Department of Gynecologic Oncology, New York Medical College, USA
2Department of Gynecologic Oncology, Westchester Medical Center, USA
3Department of Pathology, Westchester Medical Center, USA
4Department of Radiology, Westchester Medical Center, USA

Abstract

A 35-year-old Caucasian female presented with worsening pelvic pain, pressure and bloating was found to have a large 22 cm mass arising from the left ovary, determined to be a stage IA primary mucinous adenocarcinoma. After excision with negative margins, she was treated with four cycles of carboplatin and paclitaxel. Initial surveillance revealed no evidence of disease and to date, tumors markers have been normal. Repeat PET/CT were performed seventeen months after initial surgery and noted to have enlargement of a left lower lung nodule. A robotic assisted wedge resection of the left lower lobe lung lesion showed metastatic ovarian mucinous carcinoma with tumor necrosis. Endoscopic ultrasound guided fine needle aspiration (FNA) of a large celiac lymph node revealed clusters of intermediate to large malignant cells with high N:C ratio, irregular nuclear contour in the background of mucin. The patient finally underwent intensity-modulated radiation therapy. Her follow-up MRI shows stable nodal disease at this point. She is remains asymptomatic with no significant physical exam findings.

ABBREVIATIONS

PET: Positron Emission Tomography; CT: Computed Tomography; SUV: Standardized Uptake Value; N:C ratio: Nuclear: Cytoplasmic Ratio

INTRODUCTION

Ovarian cancer remains the leading cause of gynecologic cancer-related deaths in the US. Annually 22,000 new cases are found and 15,500 deaths occur [1]. Most commonly, ovarian cancer is epithelial in origin, and presents in the sixth decade. Invasive mucinous carcinomas, however, are infrequent primary tumors of the ovary, accounting for only 6-10% of all primary ovarian carcinomas [2]. Generally patients with invasive mucinous carcinoma range from 14-87 years, present with large tumors occasionally in excess of 40 cm in greatest dimension [3-5]. In this review, we present one such case of metastatic stage 1A invasive mucinous carcinoma of the ovary.

CASE PRESENTATION

A 35 year old Caucasian female presented with worsening pelvic pain, pressure and bloating was found to have a left adnexal mass with solid and cystic components on ultrasound. Her physical exam revealed a palpable large mass about 5 cm above and the left of the umbilicus. Her CA 19-9 was 2100 U/mL (normal 0-37 U/mL) and CA 125 was 220 U/mL (normal 0-35 U/mL). On CT imaging, there was a large heterogeneous multi-septated peripherally enhancing cystic lesion measuring approximately 11.6 x 15.9 x 22 cm (Figure 1).

She subsequently underwent an exploratory laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymph node dissection and appendectomy with optimal debulking. Intraoperative findings revealed a large 22 cm mass was found arising from the left ovary with smooth-
walls, multilobulated and solid and cystic in nature. There was no evidence of gross disease at the end of the procedure.

On pathology, the 25 x 20 x 10 cm left ovary showed mucinous adenocarcinoma, intestinal type, moderately differentiated, stage IA with expansile growth and a large area of necrosis. The tumor was confined to the ovary without capsular penetration (Figure 2); the fallopian tube, omentum and surrounding tissue were negative for malignancy, and subsequent tumor markers returned to normal range. She recovered post operatively without complications and was promptly treated with four cycles of carboplatin and paclitaxel.

Initial surveillance physical exam and imaging revealed her to have no evidence of disease; however, upon repeat imaging three months post operatively, three lung opacities were noted, measuring 4 x 4mm (left lower lobe), 2 x 2 mm (left lower lobe) and 4 x 3 mm (right middle lobe). Mediastinal and abdominal lymph nodes increased in size and number including one larger celiac lymph node which was biopsied and was negative for malignancy. Interestingly, non-necrotizing granulomas were identified and confirmed with review of previous pathology, suggesting a diagnosis of sarcoidosis.

Repeat PET/CT were performed seventeen months after initial surgery and again noted to have enlargement of the left lower lung nodule. On PET, the lung nodule showed a 17mm x 14mm hyper metabolic spiculated lesion with SUV max of 8.7g/mL and an additional 2.2cm x 1.9 cm hypermetabolic paraaortic lymph node near the celiac trunk, with SUV max 3.3g/mL was also present. Based on these findings, metastatic ovarian cancer was suspected in the paraaortic lymph noted; however, primary lung malignancy was suspected over metastatic disease.

To date, tumors markers had been normal (CA 19-9 was 10 U/mL and CA 125 was 15.7 U/mL). Biopsy of the new lung mass was positive for adenocarcinoma with mucinous features consistent with metastatic ovarian mucinous carcinoma (Figure 3). A robotic assisted wedge resection of the left lower lobe lung lesion was performed with negative margins and showed metastatic ovarian mucinous carcinoma with tumor necrosis (Figure 4). The pleural surface of the left upper lobe appeared concerning and was resected; microscopic examination showed multiple foci of granulomatous inflammation but was negative for metastasis. Endoscopic ultrasound guided fine needle aspiration (FNA) of celiac lymph node now revealed clusters of intermediate to large malignant cells with high N:C ratio, irregular nuclear contour in the background of mucin (Figure 5).
DISCUSSION

Mucinous ovarian carcinomas are estimated to be the second most common type of ovarian carcinomas, accounting for approximately 10% [7]. However, the true percentage of primary mucinous ovarian tumors is actually estimated around 2.4%, since many mucinous ovarian tumors are truly sites of metastasis from gastrointestinal sources to the ovary [8].

Differentiating between primary mucinous tumors of the ovary and of the gastrointestinal tract can be difficult; immunohistochemistry has proven to be a useful tool [9]. Cytokeratin 7 (CK7) is a highly sensitive marker for Müllerian or epithelial origin whereas [10] CK20 is a highly sensitive marker for intestinal origins [11,12]. For example, diffuse CK7 positivity with patchy CK20 positivity or CK20 negativity are more suggestive of primary ovarian mucinous tumors compared to metastatic intestinal carcinomas. Unfortunately, in high grade tumor, these markers can be lost [13] so consideration of the complete immunohistochemistry profile must be taken into consideration. In this patient, the biopsy of the new lung mass showed cells positive for CK7, and CK20; while negative for TTF1 and Pax8 which rules out primary lung adenocarcinoma. The immunohistochemistry profile supports the diagnosis of metastatic ovarian carcinoma to the lungs.

The most common metastatic routes are via direct peritoneal seeding and lymphatic spread [14]. Most stage I invasive mucinous carcinomas of the intestinal type with expansile growth pattern, like this patient, do not metastasize [4,5]. Mucinous carcinomas of the infiltrative pattern of stromal invasion are more aggressive in comparison and account for the majority of metastasis [3-5]. In a literature review, metastasis to the mediastinum has been documented in two previous case reports [15] but there have been no previously described cases of primary mucinous ovarian carcinoma with metastatic spread to the lungs. Tumor markers in the presence of invasive mucinous ovarian carcinoma are typically not helpful; CA-125 is usually negative, while CA 19-9 shows a variable range (68-83%) in positivity as reported by one study [16]. Other tumor markers were not considered; however, recent research has suggested the possibility of using new tumor markers such as human epididymis protein 4, and may be more sensitive than CA-125 [17]. This is the first case in the literature which primary ovarian carcinoma with normal CA-125 and CA 19-9 levels which metastasized to the lungs. These markers may not be sensitive enough to have detected the metastasized cancer, indicating a need for further research into more sensitive tumor markers.

The patient finally underwent intensity-modulated radiation therapy of 3500cGy to the celiac node with 3 cycles of cisplatin sensitization since this node was the remaining site of her disease. Her follow up MRI shows stable nodal disease at this point only 2 weeks out from radiation. A follow up PET/CT is scheduled about 6-8 weeks from completion of radiation to assess for response to treatment. She remains asymptomatic with no significant physical exam findings.

REFERENCES


