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5

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22 **Short Running Title:** Bilious Pleural Effusion from Ovarian Cancer

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32 a case report

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34 **ABSTRACT**

35

36 **Introduction**

37 The pleural cavity is the most common extra abdominal site for ovarian cancer
38 metastasis. It can, however, be difficult to diagnose ovarian malignancy from the
39 presence of a pleural effusion alone.

40

41 **Case Report**

42 We report a 50 year-old premenopausal woman who presented with a large, right-
43 sided, bilious pleural effusion subsequently diagnosed with advanced ovarian
44 cancer.

45

46 **Conclusion**

47 Metastatic ovarian carcinoma should be considered in appropriate populations when
48 another, more obvious source of the pleural effusion is not evident. In bilious
49 effusions, an overt tract may not be visualized despite appropriate diagnostic
50 imaging and gastrointestinal studies. In these cases, video assisted thoracoscopic
51 surgery (VATS) can provide a definitive diagnosis and potential therapeutic
52 interventions by selecting patients who could benefit from surgical and
53 chemotherapeutic interventions.

54

55 **Keywords:** Malignant pleural effusion, Bilious Pleural Effusion, Metastatic effusion,
56 advanced ovarian cancer

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61 **TITLE:** Bilious pleural effusion from metastatic serous adenocarcinoma of the ovary:
62 a case report

63

64 INTRODUCTION

65 The pleural cavity is the most common extra abdominal site for metastatic ovarian
66 cancer [1]. Pleural effusions may be the initial presentation of malignancies, with
67 common origins including carcinomas of the lung, breast or ovary, or lymphomas.
68 Malignant pleural effusions are associated with poor prognosis, the most common
69 histologic subtype being metastatic adenocarcinoma, [2,3]. Our case is that of a 50
70 year-old premenopausal woman who presented with a large, bilious pleural effusion.
71 After extensive workup, she was found to have malignant serous adenocarcinoma of
72 the ovary that had metastasized to the pleural space. We review the diagnostic
73 challenges, considerations and subsequent tools for the diagnosis and management
74 of malignant pleural effusion from advanced ovarian cancer.

75

76 CASE REPORT

77 A 50 year-old pre-menopausal female with a history of laparoscopic cholecystectomy
78 for chronic cholecystitis presented with an 8-month history of cough and shortness of
79 breath. She had undergone several outpatient treatments for suspected asthma and
80 bronchitis with inhaled bronchodilators, corticosteroids and azithromycin that failed to
81 improve her symptoms. Just prior to presentation, she had an outpatient chest x-ray
82 performed which demonstrated a large right-sided pleural effusion. She had a
83 history of tuberculosis exposure, but subsequent PPD tests were negative. Patient
84 denied fever, chills, recent weight loss, and lymphadenopathy.

85 On exam, the patient was afebrile, normotensive, without tachypnea or tachycardia.

86 Oxygen saturation was 100% on room air. There were markedly decreased breath
87 sounds in the right lung with dullness to percussion. There were no rhonchi, rales, or
88 wheezing. The remainder of the physical exam was unremarkable. Chest x-ray
89 demonstrated complete opacification of the right hemithorax, indicative of a pleural
90 effusion (Figure 1). Routine labs including a complete blood count and complete
91 metabolic panel were within normal limits. Serum CA-125 was 699 U/ml (normal 0-
92 35 U/ml). Serum rheumatoid factor was < 20.0 IU/ml (significant if >150 IU/ml).

93 A thoracentesis yielded 650cc of opaque, green-tinged pleural fluid. Pleural fluid
94 analysis demonstrated an exudative process. The pH was 7.53, glucose 2 mg/dl,
95 protein 9.0 g/dl and protein ratio of 0.8, cholesterol 152 mg/dl, triglycerides 76 mg/dl,
96 bilirubin 3.1 mg/dl, LDH 1433 U/L, and amylase 439 U/L. Serum alkaline
97 phosphatase was 62 U/L (range 35-126 U/L), LDH 200 U/L (range 98-192 U/L).
98 Pleural fluid cell counts were elevated with RBC 17000 (range <10,000 cells/cumm)
99 and WBC 1128 (normal range <200 cells/cumm), with a 89% neutrophil
100 predominance. Cultures and stains were negative for bacteria, fungus, and
101 tuberculosis.

102 Differential diagnosis of green pleural exudate in our patient included bilious effusion
103 secondary to previous cholecystectomy, tuberculosis, metastatic gastrointestinal
104 malignancy, metastatic ovarian malignancy, and rheumatoid pleurisy [1]. Given the
105 bilious effusion and elevated amylase, there was concern for biliary leak. HIDA and
106 ERCP were unrevealing. An MRI of the abdomen did not show any abnormalities of
107 the liver or biliary ducts. MRI of the pelvis showed mild ascites and enlargement of
108 the ovaries with soft tissue enhancement (Figure 2). This, in conjunction with
109 elevated CA-125, raised concern for ovarian malignancy. Gynecology-oncology,
110 pulmonology, cardiothoracic surgery, general surgery, and gastroenterology were
111 consulted.

112 The patient underwent video-assisted thoracoscopy (VATS) of the right lung with
113 evacuation and subsequent biopsy of the right pleura. Histological exam showed
114 metastatic serous adenocarcinoma consistent with a primary ovarian tumor. The
115 tumor cells stained positive for CK7, CA-125 and D2-40. Following diagnosis, the
116 patient was discharged in stable condition with plans to follow up with gynecology-
117 oncology and pulmonology as an outpatient for further staging and treatment. She
118 elected to follow up elsewhere, and the details of her ongoing care are unknown.

119

120 **DISCUSSION**

121 Diagnosing metastatic cancer on the basis of pleural effusion alone can be
122 challenging. As in our case, pleural effusion can be one of the only presenting signs
123 of a malignancy. In a retrospective study of 123 women with malignant pleurisy,
124 effusion was the presenting manifestation of cancer in 29% (36) [3]. Another

125 retrospective study reviewed 742 malignant pleural effusions [4]. Top etiologies were
126 lung (273 patients, 37%), breast (127, 17%), hematologic (74, 10%), and ovarian
127 cancer (50, 7%). More than two-thirds of effusions were large, occupying half or
128 more of the hemithorax. Part of the diagnostic challenge of such cases is that the
129 differential diagnosis for pleural effusions is vast. It includes, but is not limited to,
130 cirrhosis, heart failure, tuberculosis and other infectious etiologies, constrictive
131 pericarditis, endometriosis, and malignancy [1].

132 Of interest, our patient presented with an exudative bilious effusion. This led to
133 procedures and imaging looking for a biliary tract fistula— workup included a HIDA,
134 abdominal CT and MRI, and ERCP, none of which showed an identifiable tract. With
135 no biliary source, rheumatoid factor was ordered. Green-yellow effusions can be
136 seen with rheumatoid pleurisy and occur in about 2-3% of patients with rheumatoid
137 arthritis (RA) [5]. This effusion is typically exudative with a high RF titer; rarely,
138 rheumatoid effusions can have features of a sterile empyematous exudate with high
139 lipids and lactate dehydrogenase, and very low glucose and pH levels.

140 Approximately 75% of patients with ovarian cancer are diagnosed at advanced
141 stages, either Stage III or Stage IV [6]. Stage IV ovarian cancer, diagnosed in our
142 patient, occurs when cancer has spread to the liver parenchyma or outside the
143 abdomen. The most common extra-abdominal site of disease is the pleural surface,
144 with effusions present in greater than one-third of stage IV diagnoses [7]. Malignant
145 pleural effusions in ovarian cancer result from pleural invasion from nearby
146 structures, such as the diaphragm or other pleuroperitoneal communications [8].
147 These can be difficult to detect with standard lab and imaging modalities, as
148 mentioned above. Certain radiological findings are more predictive of a malignant
149 effusion in those with known ovarian cancer. The predictors of malignant pleuritis are
150 effusions of moderate to large size (81% versus 9% of those studied), supra-
151 diaphragmatic lymph node enlargement of ≥ 1 centimeter (75% versus 9%) and
152 pleural nodules of ≥ 3 millimeters (50% versus 0%) [9].

153 Making diagnosis more challenging, effusion cytology did not provide us with a
154 definitive diagnosis. About 30% of malignant pleural effusions from ovarian cancer
155 exhibit false-negative cytological pleural fluid results [1]. In these circumstances,
156 exploratory video assisted thoracoscopic surgery (VATS) can be used as a

157 diagnostic, staging, and therapeutic modality. A retrospective case review by Diaz et
158 al. reviewed patients with untreated ovarian cancer and moderate to large pleural
159 effusion who underwent VATS. In these patients, VATS revealed macroscopic
160 pleural disease in 29 (69%), the majority (18 patients) having nodules greater than 1
161 centimeter [10].

162 The standard treatment of advanced epithelial ovarian cancer includes surgery
163 followed by adjuvant systemic chemotherapy [11]. Complete resection in stage IV
164 patients taken to primary surgery is about 10%. The goal of surgical cytoreduction is
165 to have no visible residual disease in any location. Based on the retrospective study
166 above, in those with VATS findings, management plans were changed in 18 (43%)
167 patients— 6 underwent intrathoracic cytoreduction first followed by abdominal
168 surgery on the same or a later day; and 12 received neoadjuvant chemotherapy for
169 unresectable pleural tumors followed by interval debulking [10]. The former shows
170 the importance of VATS in influencing the primary management choice in patients
171 with newly diagnosed advanced ovarian cancer that has spread to the pleural space.

172

173 CONCLUSION

174 It can be difficult to diagnose metastatic ovarian cancer from a presentation of
175 pleural effusion alone. A high degree of suspicion must be maintained and a
176 combination of diagnostic tools may be employed, including labs like CA-125,
177 abdominal and pelvic MRI, and VATS. In bilious effusions, an overt tract may not be
178 visualized even with extensive imaging and GI studies. VATS can provide more
179 definitive tissue diagnosis with potential for therapeutic interventions by selecting
180 patients who can benefit from intrathoracic cytoreduction or neoadjuvant
181 chemotherapy before primary surgery in the abdomen and pelvis.

182

183 CONFLICT OF INTEREST

184 None

185

186 AUTHOR CONTRIBUTIONS

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188 Group 1- Conception and design, Acquisition of data

189 Group 2- Drafting the article, Critical revision of the article

190 Group 3- Final approval of the version to be published

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195 Group 3- Final approval of the version to be published

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199 Group 2 - Critical revision of the article

200 Group 3 -Final approval of the version to be published

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206 **REFERENCES**

207 1. Porcel J, Diaz J, Chi D. Clinical implications of pleural effusions in ovarian
208 cancer. *Respirology*. 2012;17(7):1060-1067.

209 2. Heffner JE. Diagnosis and management of malignant pleural effusions.
210 *Respirology*. 2008;13(1):5-20.

211 3. Cellerin L, Marcq M, Sagan C, Chailleux E. Malignant pleural effusion as the
212 presenting site of cancer: comparison with metastatic pleural effusions from
213 known cancers. *Rev Mal Respir*. 2008; 25: 1104–9.

214 4. Rodríguez-Panadero F. Medical Thoracoscopy. *Respiration*. 2008;76(4):363-372.

215 5. Balbir-Gurman A, Yigla M, Nahir A, Braun-Moscovici Y. Rheumatoid Pleural
216 Effusion. *Seminars in Arthritis and Rheumatism*. 2006;35(6):368-378.

217 6. Jelovac D, Armstrong D. Recent progress in the diagnosis and treatment of
218 ovarian cancer. *CA: A Cancer Journal for Clinicians*. 2011;61(3):183-203.

- 219 7. Wimberger P, Wehling M, Lehmann N, Kimmig R, Schmalfeldt B, Burges A et al.
220 Influence of Residual Tumor on Outcome in Ovarian Cancer Patients With FIGO
221 Stage IV Disease. *Annals of Surgical Oncology*. 2010;17(6):1642-1648.
- 222 8. Porcel J, Rodríguez-Panadero F. Malignant effusions. In: Maskell N, Millar A
223 Oxford Desk Reference: Respiratory Medicine. Oxford University Press, Oxford.
224 2009;342–345.
- 225 9. Kim K, Choi H, Kang S, Park S, Jung D, Cho J et al. The utility of multi-detector
226 computed tomography in the diagnosis of malignant pleural effusion in the
227 patients with ovarian cancer. *European Journal of Radiology*. 2010;75(2):230-
228 235.
- 229 10. Diaz J, Abu-Rustum N, Sonoda Y, Downey R, Park B, Flores R et al. Video-
230 assisted thoracic surgery (VATS) evaluation of pleural effusions in patients with
231 newly diagnosed advanced ovarian carcinoma can influence the primary
232 management choice for these patients. *Gynecologic Oncology*. 2010;116(3):483-
233 488.
- 234 11. Schorge J, Garrett L, Goodman A. Cytoreductive surgery for advanced ovarian
235 cancer: Quo Vadis? *Oncology*. 2011;25:928–934.

237 **FIGURE LEGENDS**

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239 Figure 1: Chest x-ray PA View. Complete opacification of the right hemithorax.

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241 Figure 2: MRI Pelvis with Contrast, Sagittal. Enlarged left ovary with small cysts and
242 some enhancing solid tissue.

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251 **FIGURES**

252



253

254 Figure 1: Chest x-ray, PA view. Complete opacification of the right hemithorax.

