Ovarian cancer is the fifth leading cause of cancer-related deaths among US women, with an estimated 21,980 new cases and 14,270 deaths nationwide in 2014.1 Symptoms associated with this disease are typically nonspecific and are often silent before ovarian cancer reaches an advanced stage; more than two-thirds of cases are diagnosed when the disease has progressed to stage III or IV and involves the peritoneal cavity or other organs.2 Primary appendiceal malignant neoplasms may mimic advanced-stage ovarian cancer and can be misdiagnosed because of its presentation as a palpable adnexal mass. The authors describe a 42-year-old woman who was admitted to the department of obstetrics and gynecology to receive treatment for presumed advanced-stage ovarian cancer. She subsequently received a diagnosis of primary pseudomyxoma peritonei metastatic to the ovaries, mimicking a primary ovarian cancer by osteopathic structural examination findings, serum tumor markers, surgical exploration, and histopathologic confirmation.

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Primary appendiceal malignant neoplasms represent 0.5% of all gastrointestinal malignant neoplasms.5 Elevated biomarkers, such as carcinoembryonic antigen and cancer antigen 125, have limited use in diagnosing ovarian cancer. In some situations, however, elevated carcinoembryonic antigen levels can indicate gastrointestinal malignant tumors, including primary appendiceal tumors.5 In addition to conventional means of diagnosing a patient’s medical concerns, osteopathic physicians use palpatory findings from musculoskeletal structural examinations.

We present the case of a woman with primary pseudomyxoma peritonei (PMP) mimicking advanced-stage ovarian cancer.
Report of Case

A 42-year-old woman (gravida 2, para 2) who had no preterm or nonviable deliveries presented to the emergency department with shortness of breath, vague abdominal pain, decreased appetite with early satiety, gastroesophageal reflux disease, night sweats, and a 30-lb weight loss in the past 2 months. She reported that she had tried over-the-counter antacids and proton-pump inhibitors without relief. The patient denied vaginal bleeding, irregular menses, or abnormal discharge. She reported that she did not have regular appointments with a gynecologist or primary care physician. She denied any notable medical or surgical history apart from her previous normal spontaneous vaginal deliveries.

On physical examination, her vital signs were stable, as follows: temperature, 98.4°F; pulse rate, 89/ min; blood pressure, 131/84 mm Hg; and respiratory rate, 18/min. An abdominal examination demonstrated a nontender, grossly distended abdomen with a palpable fluid wave and dullness to percussion in all quadrants. Auscultation of the heart and lungs revealed diminished breath sounds in the right lower lobe. The heart rate was regular and the rhythm was without murmurs, rubs, or gallops. An osteopathic structural examination was performed on the thoracic and lumbar spine, rib cage, chest wall, and sacrum and revealed that T1-9 was neutral, rotated right, sidebent left; T10-12 was flexed, rotated right, sidebent right; L1-2 was flexed, rotated right, sidebent right; L3-5 was flexed, rotated right, sidebent right; and sacrum had a positive seated flexion test on the left and rotated right on a right oblique axis. Because of the prominent ascites, the rib cage and chest wall were not able to be adequately assessed. A posterior Chapman reflex point was found on the right on the outer edge of the 11th intertransverse space.

On hospital admission, radiography, computed tomography, and ultrasonography were ordered. A chest radiograph revealed a right pleural effusion with patchy consolidation in the right lower lobe and lateral segment of the right middle lobe. A computed tomographic scan of the abdomen and pelvis identified a complex right pleural effusion with patchy consolidation at the right lung base, a moderate to large amount of complex and proteinaceous abdominal and pelvic ascites with increased density, nodular densities abutting into the omentum suggestive of omental or peritoneal metastases, and bilateral adnexal cystic masses with the right and left measuring 6.3×5.9 cm and 3.0×3.9 cm, respectively. Indentations were identified along the liver surface in the right hepatic lobe that were suggestive of metastatic lesions. A transvaginal pelvic ultrasonographic image showed bilateral complex ovarian cystic structures with internal septations suggestive of ovarian cancer. The right structure measured 5.68×4.4×5.8 cm, and the left structure measured 2.2×1.8×1.2 cm.

On the same day of presentation and admission, she was transferred to the department of obstetrics and gynecology for further evaluation. On hospital day 1, an interventional radiologist performed a paracentesis and drained 3400 mL of ascetic fluid. Cytologic testing showed more than 1000 red blood cells and 640 white blood cells with a differential of 94% lymphocytes, 3% neutrophils, and 0% mononuclear cells; an albumin level of 3.4 g/dL; a protein level of 6.2 g/dL; and a serum-ascites albumin gradient score of 0.09 g/dL. The initial ascitic fluid from cytologic testing showed isolated atypical mesothelial cells, which were also seen in the cell block (Figure A). A reactive process was favored because of a history of inflammation and a paucity of atypical cells. Tumor markers indicated CEA greater than 1000 μg/L; l-lactate dehydrogenase, 10^3 U/L; cancer antigen 125, 335 U/mL; cancer antigen 19-9, 341 U/mL; and inhibin B, less than 10 pg/mL.

On hospital day 5, the patient remained stable but reported that shortness of breath and abdominal discomfort had returned. Magnetic resonance imaging of the abdomen revealed small lesions at the peripheral surface of the liver, which was suggestive of metastasis. The most prominent lesions were seen adjacent to the gallbladder, corresponding with the previous computed to-
mographic findings. Findings also suggested omental caking and metastases in the omentum associated with a moderate amount of complex ascites. Magnetic resonance imaging of the pelvis revealed a complex cystic mass in the midline lower pelvis posterior to the uterus containing cystic and nodular solid components measuring 5.1×4.9 cm. A 7.5-cm complex cystic mass lesion was observed on the right side of the pelvis, and a complex cystic mass lesion was observed in the right lower abdomen measuring 5.5×3.8 cm. The complex mass lesions at the right side of the pelvis could not be visually separated from the right uterine wall; the possibility of invasion to the right uterine wall was suggested. Large ascites were identified, and the possibility of pelvic adenopathy on the right could not be excluded.

On hospital day 13, the patient underwent diagnostic laparoscopy. Exploration of the abdomen and pelvis revealed bilateral adnexal masses; omental caking; diffuse disease with peritoneal involvement, including the diaphragm surface and liver capsule; and an inflamed appendix secreting a mucinous material (Figure B and Figure C). Bowel and peritoneal lesions were biopsied and sent for frozen and permanent section, and the peritoneal fluid was sent for pathologic analysis. The patient tolerated the procedure well, without complications.

Intraoperative pathologic examination of the frozen section of the peritoneal nodule showed low-grade mucinous epithelium in pools of mucin, confirming a diagnosis of mucinous neoplasm. Concurrent, repeat cytologic analysis of the ascitic fluid demonstrated numerous sheets of bland mucinous columnar cells in a background of abundant mucin (Figure D). These characteristics were also seen on cell block analysis. Such findings were suggestive of malignant neoplasm, favoring primary PMP. Permanent sections of the peritoneal nodule and the specimen from the colon nodule correlated with cytologic and frozen section findings: abundant pools of mucin accompanied by acute and chronic inflammation, with granulation tissue formation and strips and clusters of well-differentiated mucinous neoplasm (Figure E). Results of the biopsies predominantly showed a low histologic grade; however, the colon nodule biopsy specimen demonstrated occasional pools of mucin containing clusters of cells with increased nuclear atypia and pleomorphism with focal cribriform glands, compatible with a focus of borderline malignancy (Figure F). All of the findings together were consistent with primary PMP from a mucinous cystadenocarcinoma, with the appendix as the primary site. The coexisting bilateral mucinous ovarian tumors and peritoneal deposits represented metastasis from the appendiceal primary neoplasm.

The patient was discharged home in stable condition on hospital day 16, postoperative day 3. Outpatient care included evaluation for neoadjuvant heated intraperitoneal chemotherapy followed by extensive debulking, total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, and right hemicolectomy.

Discussion

Primary appendiceal malignant neoplasms may mimic advanced-stage ovarian cancer. To our knowledge, preoperative diagnosis has only been reported with the mucinous histologic subtype. Mucinous cystadenocarcinomas are frequently found with intra-abdominal metastases or PMP. A rare disease, PMP is characterized by an extensive mucinous accumulation within the peritoneal cavity associated with a malignant cystic neoplasm arising commonly from the appendix or ovary. Aggressive debulking, oophorectomy, and omentectomy are recommended for the management of mucinous cystadenocarcinomas. Some data suggest that right hemicolecctomy confers a survival benefit vs simple appendectomy even in advanced-stage disease.

The relationship between appendiceal and ovarian low-grade mucinous tumors when accompanied by PMP is controversial. Some authors have proposed metastasis from the ovaries, whereas other authors favor a primary origin from other viscera, such as the appendix. In the
The current case, on the basis of the substantially elevated carcinoembryonic antigen level, appearance of the appendix on surgical exploration, and cytologic and histologic confirmation of the diagnosis, the PMP was determined to have originated from a primary appendiceal source.

This diagnosis was also supported by the osteopathic structural examination findings, which initially suggested a primary appendiceal origin of the patient’s malignant neoplasm: during the initial evaluation, a posterior Chapman point was identified on the right on the outer edge of the 11th intertransverse space that corresponds to inflammation of the appendix without identification of reflex points corresponding to the ovary. Chapman noted in his description of viscerosomatic reflex centers that those of the appendix and ovary are of great value because the lymphatic drainage of the right ovary also drains the appendix and, by comparison of the reflexes of the ovary with those of the appendix, the exact location of the seat of inflammation can be determined.

Because some neoplastic diseases often arise independent of innervations, otherwise notable pathologic characterizations that lack afferent input to the central nervous system may not result in a substantial viscerosomatic reflex response. In these cases, reflex somatic dysfunction may be identified when sufficient inflammation is established in the tissues displaced by the tumor. Nevertheless, given the inflammatory nature of PMP at its origin, osteopathic physicians should consider performing an osteopathic structural examination during the initial patient evaluation.

Figure.
Histopathological analysis. A, atypical mesothelial cells were seen in the cell block (inset). B and C, bilateral adnexal masses (arrow), omental caking, diffuse disease with peritoneal involvement including the diaphragmatic surface and liver capsule, and an inflamed appendix (asterisk) secreting mucinous material (triangles). D, ascitic fluid demonstrates bland mucinous columnar epithelial cells with low-grade nuclei, arranged in strips, sheets, and nests, in the background of abundant mucin, also seen in the cell block (inset). E, low-grade, well-differentiated morphology of the neoplastic mucinous epithelium showing bland nuclei with minimal pleomorphism at the basal aspect of the columnar mucin-producing cells (original magnification ×40). F, increased nuclear atypia with cribriform glands (original magnification ×40).
Conclusion

Primary appendiceal malignant neoplasms may mimic advanced-stage ovarian cancer and, therefore, may be misdiagnosed. In conjunction with serum tumor markers, diagnostic imaging, surgical exploration, and histopathologic confirmation, performing an osteopathic structural examination may aid in the diagnosis of presumed advanced-stage ovarian cancer vs primary appendiceal carcinoma metastatic to the ovaries. Further studies relating viscerosomatic reflexes and various malignant neoplasms are needed to solidify this concept.

References


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