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Single Case

Primary Peritoneal Clear Cell Carcinoma Presenting with Nonspecific Gastrointestinal Symptoms in a 39-Year-Old Woman: A Case Report

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Keywords
Primary peritoneal clear cell carcinoma · Peritoneal neoplasms · Clear cell adenocarcinoma

Abstract

Introduction: Primary peritoneal clear cell carcinoma (PPCCC) is a rare abdominal tumor, affecting 7 out of every million people. Its vague presenting signs and symptoms often lead to delayed diagnosis and poor prognosis. We present a case involving a young woman with anemia and abdominal discomfort who on further investigation had a 26-cm abdominal tumor identified to be PPCCC. Multimodal therapy with tumor debulking and chemotherapy was pursued. Given the aggressive nature of PPCCC, any clinical suspicion of peritoneal carcinoma should prompt thorough diagnostic evaluation. ***Case Presentation:*** A 39-year-old woman with menorrhagia and peptic ulcer disease presented with abdominal discomfort of 2 days duration. She initially had headaches managed with ibuprofen. Following this, she had generalized abdominal pain with bloating that worsened with food and had no relief with use of stool softeners. She had associated dizziness with palpitations, chest pressure, and exertional dyspnea. In the emergency department, the patient was mildly tachycardic but otherwise stable. On exam, she had a distended abdomen with generalized tenderness and normoactive bowel sounds. Labs showed normocytic anemia with a hemoglobin of 5.2 mg/dL. Electrocardiogram and abdominal and chest X-rays were normal. A non-contrast computed tomography of the abdomen and pelvis showed a fibroid uterus and posterior displacement of multiple bowel loops by a large septate cystic mass (13.5 × 26.0 × 26.7 cm) occupying the entire abdominal cavity. Elevated CA 125 and CA 19-9 were also noted. She underwent exploratory laparotomy with mass resection, partial omentectomy, left colectomy (given extension into transverse colon), appendectomy, and total abdominal hysterectomy with

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bilateral salpingectomy. Biopsy and immunohistochemical staining (positive for PAX-8, ER, P53, P16, Napsin A and negative for PR and WT-1) confirmed mass as stage IIIB PPCCC. There was no evidence of malignancy in other tissue samples. The patient was discharged with a plan for outpatient chemotherapy and genetic counseling. ***Conclusion:*** Given the rarity of PPCCC, our case highlights how increased clinical vigilance and prompt multidisciplinary efforts are essential for an accurate diagnosis, especially in younger patients to not delay management. Currently, there are no established management guidelines; however, initial treatment with surgical debulking followed by chemotherapy is often practiced.

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Introduction

Primary peritoneal clear cell carcinoma (PPCCC) originates from the Müllerian system and is typically found as a large cystic mass in the abdominal cavity [1, 2]. The average age of diagnosis is 61 years, with a higher incidence in white females who have endometriosis [2]. BRCA-1 mutations are involved in 5–10% of cases. PPCCC manifests through nonspecific symptoms, including abdominal bloating, constipation, early satiety, nausea, and vomiting, which can mimic benign gastrointestinal conditions, particularly in younger patients [3]. Herein, we discuss a case of PPCCC presenting with vague gastrointestinal symptoms in a 39-year-old woman.

Case Report

A 39-year-old woman with a history of peptic ulcer disease and menorrhagia presented to the hospital with persistent abdominal discomfort. About 1 week prior to the presentation, she initially developed intermittent headaches managed with ibuprofen. Two days later, she developed generalized abdominal pain associated with bloating. She had worsening discomfort with food intake and had no relief despite the use of stool softeners. Three days prior to presentation, she also endorsed an episode of lightheadedness and dizziness with palpitations, chest pressure, and shortness of breath on exertion. She denied unusual blood loss, including ongoing menorrhagia, melena, hematochezia, or hematuria. Family history was negative for bleeding disorders and cancer. She had no prescribed medications but reported use of ibuprofen as needed for pain relief (1–2 times per month).

In the emergency department, the patient was mildly tachycardic but otherwise vitally stable. Physical exam was remarkable for systolic murmur at the left upper sternal border and a distended abdomen with mild generalized tenderness and normoactive bowel sounds.

Laboratory diagnostics demonstrated significant normocytic anemia with a hemoglobin of 5.2 mg/dL (reference range: 11–14.5 mg/dL) and an elevated red cell distribution width of 17.1% (reference range: 11.5–15.5%). Fecal occult blood test was negative. Diagnostic imaging included an abdominal X-ray and chest X-ray that demonstrated no evidence of bowel obstruction or pulmonary infiltrates, respectively. Electrocardiogram demonstrated sinus tachycardia with no evidence of ischemia. The patient was admitted for management of symptomatic anemia thought to be related to upper gastrointestinal bleeding from use of nonsteroidal anti-inflammatory agents in patient with chronic menorrhagia. She received 2 units of packed red blood cell units and proton pump inhibitor therapy was initiated. Despite these efforts, the patient continued to experience worsening abdominal pain, prompting immediate imaging with non-contrast

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computed tomography of the abdomen and pelvis prior to performing endoscopy. Imaging demonstrated a fibroid uterus and posterior displacement of multiple bowel loops by a large septate cystic mass (13.5 × 26.0 × 26.7 cm) occupying the entire abdominal cavity (shown in Fig. 1a). There was no evidence of connection of mass to the ovaries or any distant metastasis. Elevated CA 125 (139.9 IU/mL; reference range: 0–35 IU/mL) and CA 19-9 (102.2 IU/mL; reference range: 0–35 IU/mL) were also noted. An endoscopy was never done given imaging findings, and she underwent exploratory laparotomy with resection of the mass, partial omentectomy, left colectomy (given extension into transverse colon), appendectomy, and total abdominal hysterectomy with bilateral salpingectomy. Biopsy and immunohistochemical staining (positive for PAX-8, ER, P53, P16, Napsin A and negative for PR and WT-1) confirmed the mass to be a stage IIIB PPCCC (shown in Fig. 1b, c). Pathology also identified a left ovarian dermoid cyst. There was an atypical glandular proliferation present in association with the clear cell carcinoma that was identified as polypoid endometriosis, an unusual variant of endometriosis. The patient was discharged and started by outpatient oncology on paclitaxel/carboplatin regimen every 3 weeks for 6 cycles with a plan to introduce bevacizumab (anti-vascular endothelial growth factor) from cycle 2. She underwent genetic and molecular tumor biomarker testing, which was negative for BRCA but positive for ER and programmed death ligand-1 (PDL-1) and showed intact mismatch repair proteins. The patient was followed up with tumor markers and CT scan at 3 months posttreatment and remains without any evidence of residual tumor or disease.

Discussion

PPCCCs are rare, high-grade tumors associated with a poor prognosis [4]. The Society of Gynecologic Oncology has established the following diagnostic criteria for PPCCC: (a) both the ovaries are normal in size or enlarged due to a benign process; (b) the involvement in extraovarian sites is greater than the involvement on the surface of either ovary; (c) microscopically, the ovaries are not involved by the tumor or exhibit only serosal or cortical invasion with dimensions smaller than 5.0 × 5.0 mm; (d) the histopathological characteristics of the tumor are predominantly of the serous type [5]. We present a case of PPCCC, without concomitant disease in the ovaries, fallopian tubes, or other adjacent tissues, meeting the criteria for a primary peritoneal malignancy [3]. Patients with PPCCC typically exhibit nonspecific signs and symptoms related to tumor mass effect, such as progressive abdominal pain and distention. Initially, our patient's subacute abdominal pain suggested benign gastrointestinal causes and was managed conservatively. However, persistent abdominal discomfort necessitated imaging to exclude obstructive causes, leading to the identification of the mass. On computed tomography, PPCCC commonly appears as a single large cystic mass, averaging 7 cm in size, with solid and/or papillary components [4]. The diagnosis is further based on key morphological features, including a solid, papillary, or more commonly, a tubulocystic growth pattern with a clear or eosinophilic cytoplasm, and an immunohistochemical profile consisting of a combination of HNF1B-positive, Napsin A-positive, and p53-wild-type staining increases specificity [4].

Indeed, in our patient, pathology confirmed a papillary architecture with positivity for PAX-8, ER, P53, P16, and Napsin A stains (shown in Fig. 1c). On differentiating from clear cell carcinoma of renal origin which frequently shows distinctive nested alveolar pattern with interalveolar stromal vascularity, patients with PPCCC show tubulocystic patterns, small, rounded papillae, and hobnail cells that are very characteristic. Additionally, Napsin A is less frequently expressed in clear cell renal carcinoma. The pathogenesis of PPCCC is poorly understood [4]. Metaplastic transformation of Müllerian embryonic remnants and endometriosis-directed malignant transformation are two leading theories [6]. While concurrent endometriosis in extraovarian sites accounts for less than 2% of known cases, a component of polypoid

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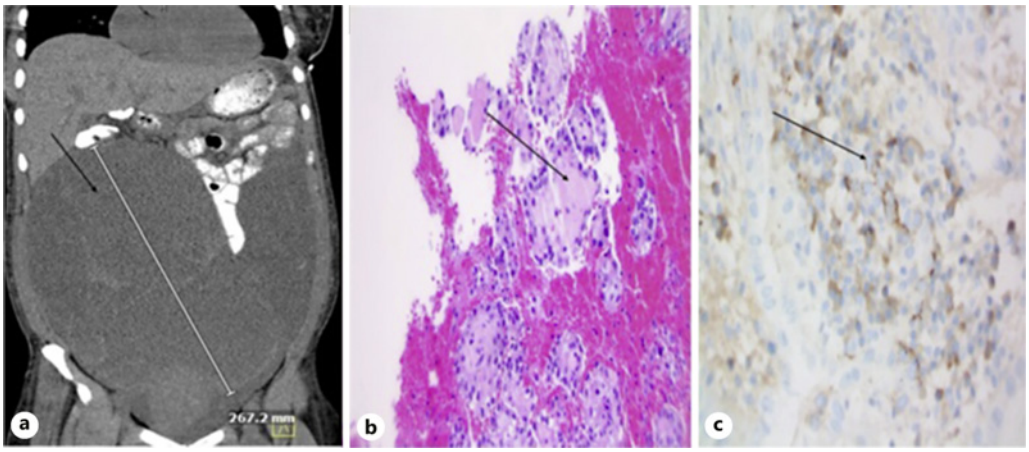

Fig. 1. a Non-contrast CT depicting a 26.7-cm peritoneal mass [1]. **b** H&E stain at ×400 magnification showing papillary growth lined by clear cell with some hobnail features [1]. **c** Positive Napsin A immunohistochemical staining specific for peritoneal clear cell carcinoma [1].

endometriosis was identified in this case [7]. Recent studies also highlight immune system dysregulation in ovarian and endometrial clear cell carcinoma [8]. Currently, no established management guidelines exist; however, treatment has initially involved surgical debulking [9]. In patients who undergo surgery, the presence of residual primary tumor is associated with increased mortality compared to those without residual tumor, who typically achieve a median disease-free interval of 13.5 months [4]. Surgery is typically followed by six cycles of platinum-based chemotherapy and bevacizumab administered every 3 weeks [9]. In patients with inoperable or recurrent disease, radiation therapy has been demonstrated to reduce tumor size without notable morbidity [10]. Moreover, limited evidence from case series has shown a potential role for immunotherapy, particularly activity against the immune checkpoint PD-1, in modulating tumorigenesis and tumor clearance [11]. Prior reported cases of PPCCC involved older, postmenopausal women [6, 12, 13]. Our case highlights a younger, premenopausal patient with a significantly larger mass with subacute vague gastrointestinal symptoms at presentation, leading to a diagnostic conundrum. The objective of our case report was to emphasize the importance of avoiding anchoring bias among clinicians. It underscores the need to maintain a broad differential diagnosis, even in younger patients who present with seemingly benign gastrointestinal symptoms and lack significant risk factors for malignancy. Given the rarity of PPCCC, increased clinical vigilance and prompt, coordinated multidisciplinary efforts are essential for an accurate diagnosis and management. Insights from additional case studies and genetic analyses may aid in developing targeted screening and management strategies.

The CARE Checklist has been completed by the authors for this case report, attached as online supplementary Figure 1 (for all online suppl. material, see https://doi.org/10.1159/000544883).

Statement of Ethics

This study protocol was reviewed by the MedStar Health Ethics Committee and approval was not required. Written informed consent was obtained for this case report from the patient for publication of the details of their medical case and accompanying images. Additionally, permission was received from Wolters Kluwer Health Inc. to republish author's original abstract and figures within this original manuscript.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

R.V. and T.D. were involved in review of literature, data interpretation, and manuscript writing. G.G. and C.J.H. were involved with manuscript editing and review. B.S. was involved with direct patient care and manuscript review. J.I. was responsible for pathological analysis and interpretation and manuscript review. All authors have approved the final version for submission. C.J.H. is the article guarantor.

Data Availability Statement

The data supporting the findings of this case report are available upon reasonable request from the corresponding author. Due to privacy and confidentiality concerns, patient-specific data will not be made publicly available. All identifying information has been anonymized in accordance with ethical guidelines to protect patient confidentiality.

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