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Case report

Rare leptomeningeal recurrence of mucinous ovarian carcinoma

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ABSTRACT

Ovarian cancer is the fifth most common cause of cancer death in women and represents the deadliest of the gynecologic cancers. Despite treatment, 80 % of patients diagnosed with ovarian cancer will experience recurrence of disease within 18 months. Mucinous ovarian carcinoma represents an exceptionally rare subtype of ovarian cancer, comprising only 1–3 % of cases. Roughly 65–80 % of cases are diagnosed early at FIGO stage I with an excellent prognosis. However, for those diagnosed with advanced stage III-IV primary or recurrent disease, prognosis is extremely poor secondary to aggressive tumor biology and poor response to traditional platinum-based chemotherapy. Ovarian cancer recurrence most commonly arises secondary to transperitoneal and lymphatic spread of neoplastic cells. Central nervous system seeding, particularly leptomeningeal metastasis, is exceptionally rare with only palliative treatment options. Here, we describe a 44-year-old female with leptomeningeal recurrence remote from surgical treatment of stage IA mucinous ovarian carcinoma.

1. Introduction

According to the American Cancer Society, roughly 20,890 women will be newly diagnosed with ovarian cancer in the United States in 2025. Unfortunately, ovarian cancer remains the leading cause of death from gynecologic cancer, with the projected number of deaths for 2025 at 12,730 in the United States (Heinzelmann-Schwarz et al., 2006; Ovarian Cancer Statistics, 2025). Ovarian cancers comprise a diverse group of neoplasms that can be separated into two main subtypes. Type I ovarian tumors originate from clearly described precursor lesions in the ovary and include clear cell, mucinous, endometrioid, low grade serous, and transitional cell carcinomas. Type II ovarian tumors originate from lesions not clearly described and may develop *de novo* from the tubal or ovarian surface epithelium. This group of tumors include high grade serous carcinomas, undifferentiated carcinomas, and carcinosarcomas.

Mucinous ovarian carcinoma (MOC) is an exceptionally rare histologic subtype of ovarian cancer, and is estimated to represent only 1–3 % of ovarian cancer cases (Borella et al., 2023; Hollis et al., 2021). In contrast to other forms of ovarian cancer, 65–80 % of cases are diagnosed at Stage I (Hollis et al., 2021; Wang et al., 2023). At this stage of diagnosis, the estimated 5-year overall survival rate approaches 90 %. However, for patients with more advanced (stage III-IV) disease, prognosis is very poor with median overall survival times of 12–33 months (Wang et al., 2023; Kurnit and Frumovitz, 2022). This poor prognosis is largely secondary to aggressive tumor biology and resistance of MOCs to traditional platinum-based chemotherapeutic regimens; as such, treatment of primary advanced and recurrent disease is extremely challenging.

Within MOC, there are two subtypes characterized by the tumor's histologic pattern of invasion: expansile and infiltrative. Expansile tumors are characterized by confluent glandular growth, with minimal to no invasion of the ovarian stroma. These tumors are generally less aggressive with lower metastatic potential and improved prognosis. In contrast, infiltrative tumors are comprised of clusters of malignant cells with destructive stromal invasion. This contributes to a greater likelihood for metastasis, both locally to the peritoneum and distally via lymphatic spread, as well as later stage at diagnosis and poorer prognosis (Borella et al., 2023). In addition, expansile patterns are more often associated with ovarian primary tumors, while infiltrative patterns can be indicative of metastasis from another primary source.

Abbreviations: ED, Emergency Department; MOC, Mucinous Ovarian Cancer; CNS, Central Nervous System; CSF, Cerebrospinal Fluid; VPS, Ventriculoperitoneal Shunt; IIH, Idiopathic Intracranial Hypertension; LP, Lumbar Puncture; LMC, Leptomeningeal Carcinomatosis; IT, Intrathecal.

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Ovarian cancer metastasis and recurrence is most commonly secondary to locoregional spread of neoplastic cells through peritoneal fluid and lymphatic drainage. The most common site for recurrent disease is within the peritoneal cavity (Thomakos et al., 2019). In contrast, seeding of the central nervous system (CNS) from ovarian cancer is thought to occur in less than 2 % of cases. Isolated leptomeningeal spread is even rarer, with reports in the literature limited only to cases reports (Borella et al., 2020; Patel et al., 2018).

In this study, we describe a case of leptomeningeal recurrence of mucinous ovarian carcinoma approximately three years after initial surgical management for stage IA disease.

2. Case description

Our patient is a 44-year-old G2P2002 who originally presented in April 2021 with abdominal pain for several months. Imaging at the time was significant for a large complex cystic mass arising from the right ovary. She was referred to Gynecologic Oncology and underwent exploratory laparotomy with removal of pelvic mass, total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic and *para*-aortic lymphadenectomy, omentectomy, and appendectomy. Pathology was significant for well-differentiated ovarian mucinous carcinoma, predominantly expansile type, with few foci of desmoplastic stromal invasion with disease limited to the ovary (stage IA). No adjuvant therapy was recommended. Following surgical management, the patient was lost to follow-up until presenting to the emergency department in April 2024 with a chief complaint of headaches.

Upon initial presentation, the patient described her headaches as a "head pressure" accompanied by blurred "wavy" vision and chronic floaters. She also endorsed dizziness, pulsatile tinnitus, and shooting pain down her neck and back. She underwent imaging with CTA/CT Head and Neck that was significant for narrowing of the bilateral transverse sinuses, possible papilledema, and a partially empty sella. Findings were suggestive of idiopathic intracranial hypertension (IIH). Lumbar puncture (LP) was recommended but the patient declined and was scheduled for outpatient follow-up.

The patient re-presented to the emergency department days later with worsening headache, visual symptoms, and persistent neck and back pain. An MRI Venogram of the brain was performed which showed stenosis at the bilateral distal transverse sinuses, which in conjunction with a partially empty sella configuration and questionable flattening at the optic nerve papilla (papilledema), can be seen with increased intracranial pressure. There was an ill-defined, non-mass-like enhancement along the bilateral 7th-8th cranial nerve complexes and a subcentimeter focus of ring-like enhancement within the right inferior temporal gyrus versus abnormal leptomeningeal enhancement or vascular loop. For context, a vascular loop refers to a condition where blood vessels form a loop around cranial nerves. These vascular variations can lead to compression of the nerves, resulting in various neurologic symptoms.

During this admission, the patient underwent LP with an elevated opening pressure of 37 cm H2O. Roughly 20 cc of cerebrospinal fluid (CSF) was drained for a final closing pressure of 16 cm H2O. Neurology, neurosurgery, and ophthalmology were consulted. At that time, work up was most consistent with IIH and the patient was eventually discharged on acetazolamide with outpatient neurology and ophthalmology follow up.

The patient represented three days later with constant head pressure and worsening visual changes characterized by blurry vision with transient complete visual blackouts, dizziness, unsteady gait, nausea, vomiting, and worsening neck and back pain. At that time, ophthalmic exam was notable for bilateral optic disc edema and splinter hemorrhages.

The patient was admitted and once again underwent LP with an elevated opening pressure. Initial CSF studies were significant for an elevated white cell count of 92, 98 % mononuclear cells, a low glucose of 37, and an elevated protein of 108. CSF bacterial, fungal, and viral testing was pan-negative. Cytology revealed malignant cells. Immunohistochemical staining was positive for cytokeratin 20, cytokeratin 7, and PAX8. Mucicarmine staining highlighted cytoplasmic mucin of the malignant cells, which confirmed the diagnosis of metastatic mucinous ovarian carcinoma (Fig. 1).

Repeat imaging with MRI/MRA of the brain, cervical, thoracic, and lumbar spine was done. Imaging findings were significant for abnormal enhancement related to 7th and 8th nerve complexes bilaterally, possibly the right trigeminal nerve at its cisternal component, enhancement of the bilateral internal auditory canals, as well as a 6 mm antero-inferior right temporal ring-enhancing lesion (Fig. 2). MRI of the cervical spine showed enhancement of a lesion at the T2 level, as well as vague upper thoracic leptomeningeal enhancement along the periphery of the spinal cord (Fig. 2). MRI lumbar spine was significant for diffuse enhancement of the terminal nerve roots, suggestive of leptomeningeal enhancement. CT C/A/P was also performed which showed no evidence of malignancy.

With findings confirming leptomeningeal carcinomatosis, radiation oncology, neuro-oncology, gynecologic oncology, neurosurgery, and palliative medicine were consulted. The patient was started on intravenous steroids for symptomatic management and her pain was managed with multi-modal analgesia. She then underwent palliative radiation therapy and completed a total of five fractions of 4.0 Gy to the lumbosacral spine as well as 10 fractions of 3.0 Gy to the brain. Neurosurgery was consulted and a ventriculo-peritoneal shunt (VPS) was placed for CSF diversion.

Gynecologic oncology and neuro-oncology considered options for possible treatment while CSF samples were sent for molecular profiling with the hope that specific genetic testing could guide choice for chemotherapy. Multiple intrathecal (IT) agents were originally considered, including methotrexate. However, the patient was a poor candidate for IT chemotherapy secondary to VPS placement, as the shunt disrupts normal CSF fluid dynamics and essentially diverts chemotherapeutic agents out of the intrathecal space, reducing overall effectiveness of IT chemotherapy. Thus, several conventional intravenous regimens were considered.

Unfortunately, despite palliative radiation therapy, the patient continued to decline. She became increasingly encephalopathic and weak, prohibiting her from pursuing further cancer-directed therapy. Shortly after, the patient was transitioned to hospice care and died approximately two months following initial admission to the hospital.

3. Discussion

Leptomeningeal carcinomatosis (LMC) is defined as metastatic involvement of the meningeal layers including the arachnoid mater, subarachnoid space, and pia mater. Leptomeningeal metastasis is uncommon and occurs as a late complication in 5–8 % of solid tumors, most commonly seen in melanoma, brain, lung, and breast cancers (Batool and Kasi, 2024). Leptomeningeal metastasis carries substantial morbidity and mortality and, without treatment, results in a median survival of only 4–6 weeks (Grossman and Krabak, 1999).

CNS metastasis is atypical in ovarian cancer, occurring in only 2 % of cases. Specifically, leptomeningeal metastasis is exceedingly rare, having been described in the literature only in case reports (Thomakos et al., 2019; Patel et al., 2018). It is common for LMC to present with headache, altered mental status, back and radicular pain, weakness, sensory abnormalities, cranial nerve palsies, and seizures. With this constellation of non-specific symptoms, diagnosis of LMC is largely dependent on imaging studies, specifically T1-weighted MRI with gadolinium contrast, and CSF analysis demonstrating malignant cells. Generally, sensitivity and specificity of LMC diagnosis following CSF cytology ranges from 50-60 % and 75–80 % respectively with first and second CSF aspirations, therefore, it may be necessary to conduct multiple LPs if LMC is suspected (Nguyen et al., 2023).

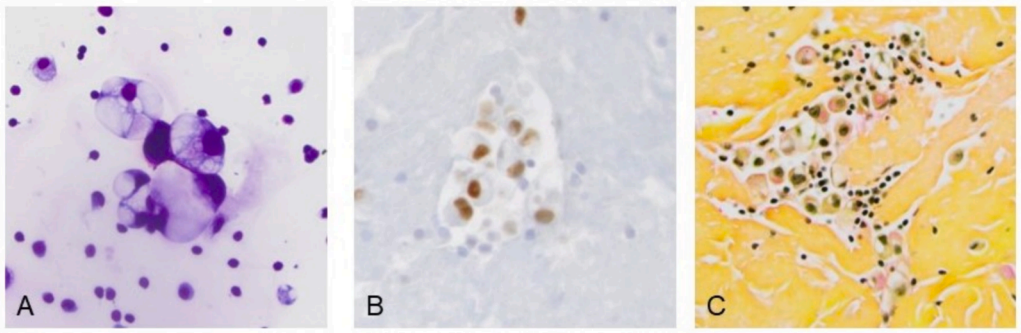

Fig. 1. Cytology exam of the CSF showed malignant cells (A. Diff-Quik, 400x). Immunohistochemical staining for PAX8 shows nuclear positivity (B. PAX8 IHC, 400x). A mucicarmine stain highlights cytoplasmic mucin in the malignant cells (C. Mucicarmine, 400x).

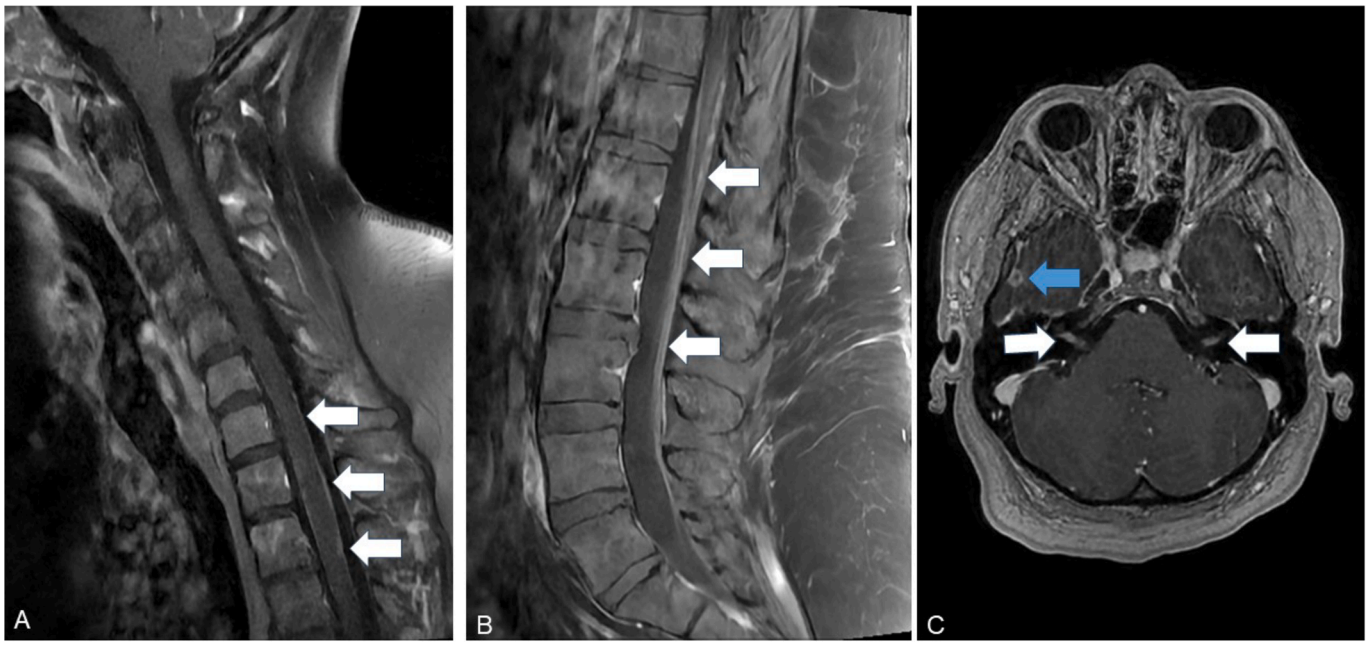

Fig. 2. Sagittal MRI Cervical Spine, postcontrast, T1-weighted demonstrates leptomeningeal enhancement along the periphery of the spinal cord (A, white arrows). Sagittal MRI Lumbar Spine, postcontrast, T1-weighted demonstrates diffuse leptomeningeal enhancement of terminal nerve roots (B, white arrows). Axial MRI Brain, Fast Spoiled Gradient-Echo (FSPGR), postcontrast demonstrates enhancement of the bilateral internal auditory canals (C, white arrows) and a 6 mm anteroinferior right temporal ring-enhancing lesion (C, blue arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

The goals of treatment in patients with LMC include palliation of symptoms and prolonging survival. Because of the rarity of LMC in patients with ovarian cancer, specifically mucinous ovarian cancer, there is no standard approach to treatment. However, mainstay therapies in other cancers with LMC may include a combination of surgery, whole brain radiation therapy, intravenous chemotherapy, and intrathecal chemotherapy (Borella et al., 2020; Dye et al., 2024). LMC has been more extensively studied in breast and lung cancers, with several retrospective studies showing improved overall survival when intrathecal chemotherapy is used (Chamberlain and Kormanik, 1997; Takahara et al., 2022). Few antineoplastic agents are fit for intrathecal administration, though some studies have found methotrexate may be an effective intrathecal agent for LMC from ovarian cancer. A 2022 paper by Takahara et al. reviewed 31 cases of LMC in ovarian cancer patients. Researchers found a median survival of more than seven months in patients who received IT chemotherapy and three weeks in those without IT chemotherapy. Among those who received IT chemotherapy, the median survival was even higher when it was delivered via an Ommaya reservoir, which is an indwelling ventricular catheter placed below the scalp allowing for repetitive intrathecal access, compared with repeated intrathecal injections via lumbar puncture (Takahara et al., 2022). Unfortunately, our patient was not a candidate for IT chemotherapy secondary to VPS placement, which disrupts CSF flow dynamics and shunts chemotherapeutic agents out of the intrathecal space.

This patient's case demonstrates one of the few documented leptomeningeal recurrences of mucinous ovarian carcinoma. As LMC in ovarian cancer is exceptionally rare, there are no uniform treatment protocols. However, multimodal treatment regimens of chemotherapy, radiation, and surgery can aid in palliation of symptoms as well as prolonging life. LMC can present with a constellation of non-specific symptoms and requires early detection via MRI and CSF cytology to minimize decline and preserve quality of life. Overall, this case illustrates the need to maintain a high level of suspicion for CNS metastases in ovarian cancer patients presenting with neurological symptoms. It also highlights the need for further research regarding CNS metastasis of ovarian cancer with the goal of developing standard treatment strategies in addition to enhancing patient quality of life and survival outcomes.

CRediT authorship contribution statement

Gabrielle LeBlanc: Writing – review & editing, Writing – original draft, Conceptualization. **Sarah G. Bell:** Writing – review & editing, Writing – original draft, Investigation, Conceptualization. **William Delfyett:** Writing – review & editing, Writing – original draft. **Brian Enloe:** Writing – review & editing, Writing – original draft. **Madeleine Courtney-Brooks:** Writing – review & editing. **Michelle Boisen:** Writing – review & editing, Supervision.

Informed Consent

Written informed consent was obtained from the patient's spouse for publication of this case report and accompanying images.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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