BACKGROUND: Serous carcinoma is the most prevalent form of ovarian cancer (OC) and has been extensively studied and reviewed. Despite significant research, this aggressive gynecologic neoplasm continues to have a high fatality rate. While dissemination to the brain is rare, metastasis to the cerebellum are the most common. To the best of our knowledge, intraventricular metastasis remains unreported.

CASE PRESENTATION: We present a compelling case study involving a 48-year-old female patient with a previous medical history of ovarian cancer, who was treated with bilateral salpingo-oophorectomy and adjuvant chemotherapy. Remarkably, 48 months following her initial treatment, she developed an intraventricular metastasis. Imaging revealed the presence of a multi lobulated mass within the left occipital horn. Despite undergoing a radical surgical resection, her clinical course remained highly aggressive, highlighting the challenging nature of this particular case.

CONCLUSION: Radical surgical resection stands out as the primary treatment option for patients with unique metastasis to the ventricular system. This case contributes to the existing body of literature regarding the unfavourable prognosis associated with serous ovarian carcinoma, further emphasizing the importance of early detection and diagnosis awareness.

KEYWORDS: Brain metastasis, Case report, Choroid plexus, Ovarian cancer, Serous carcinoma.

INTRODUCTION

Ovarian cancer (OC) continues to be the leading cause of mortality among gynecologic neoplasms. It is characterized by high metastatic potential, with the peritoneum, liver, and lymph nodes being the most commonly affected sites. Brain dissemination, albeit rare, is associated with an unfavorable prognosis, accounting for only 0.29 to 5% of cases and frequently occurring concurrently with extracranial metastasis. While several cases of intraventricular metastasis have been documented in the literature, none have been reported specifically from ovarian serous carcinoma.

We present an exceptional case of solitary choroid plexus metastasis originating from a high-grade serous ovarian carcinoma, which unfortunately, had a poor clinical outcome.

CASE PRESENTATION

A 48-year-old female patient was referred to our department for detection of a suspicious brain metastasis (BM). The patient had previously undergone successful treatment for high-grade serous ovarian carcinoma, including bilateral salpingo-oophorectomy and platinum-based chemotherapy, resulting in four years of progression-free survival. However, she began experiencing mild headache that persisted for two months, followed by symptoms of constant dizziness and blurry vision, prompting her oncologist to initiate further investigations. Physical examination revealed decreased visual acuity, bilateral papilledema grade 3, and left homonymous hemianopia, while no motor or sensory deficits were observed.

Subsequent brain magnetic resonance imaging (MRI) revealed the presence of a polylodbed deep-seated mass located in the posterior horn of the left lateral ventricle, measuring 38 x 61 x 45.6 mm. The mass was surrounded by edema and exhibited significant mass effect, leading to midline shift and dilation of the posterior left lateral ventricle. T1-weighted images exhibited prominent heterogeneous enhancement (Fig. 1). Additionally, decreased diffusion observed on apparent diffusion coefficient mapping at the periphery of the solid portion indicated high cellularity. Spectroscopy analysis revealed an increase in lipids and a decrease in other metabolites, providing additional support for the diagnosis. Based on the MRI features, we considered the potential diagnosis of choroid plexus carcinoma as a differential diagnosis for the intraventricular metastasis, taking into account the patient’s history.

Following the initiation of high doses of intravenous steroids (1mg/kg/day of methyl prednisolone), the patient underwent a successful total tumor resection using a parietal transcortical approach, after obtaining

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an informed consent. During the surgical procedure, two distinct components of the mass were identified; a cystic portion and a solid portion characterized by a fibrous and hemorrhagic appearance. Further examination confirmed that the lesion originated from the choroid plexus (CP). Her postoperative recovery was uneventful. Subsequent imaging revealed no evidence of residual tumor.

Pathological examination (Fig. 2), supported by immunohistochemistry (Fig. 3), confirmed the presence of metastatic high-grade serous ovarian carcinoma, consistent with the characteristics of her primary tumor. Further systematic restaging of the patient revealed metastasis in the liver, lungs, and peritoneum. Based on this extensive metastatic spread, the ovarian carcinoma was classified as stage IV B according to the International Federation of Gynecology and Obstetrics (FIGO) staging system. The patient was then referred to the oncology department for platinum-based systemic therapy and cranial radiation. Unfortunately, despite the treatment, her clinical condition continued to worsen, and she passed away seven months later due to the aggressive nature of the disease.

The institution has approved the study and the patient was consented for publication.

Fig 1: (A & B) MRI axial and coronal post contrast T1 weighted images demonstrating multilobulated mass with heterogeneous enhancement within the left occipital horn. (C) Coronal T2 weighted image demonstrating the surrounding vasogenic edema and mass effect with midline shift.

Fig 2: (A) Microscopic picture showing tumor proliferation with papillary and micro-papillary architecture with large necrosis (Hematoxylin & Eosin stain x 4). (B) Microscopic picture focusing on the tumor, at medium magnification (Hematoxylin & Eosin stain x 10), with better delineation of the papillary architecture with multiple papillary epithelial tufts. (C) At high magnification (Hematoxylin & Eosin stain x 40), the papillary structures are lined with cubo-cylindrical cells with an amphophilic cytoplasm, marked nuclear atypia and multiple mitoses (at least 4 mitoses are seen).
DISCUSSION

The most common intraventricular tumor in adults is meningoima, whereas CP papillomas, carcinomas, and ependymomas tend to appear in children and young adults (3% of all intracranial tumors in children and 0.5% in adults).4 Intraventricular metastasis accounts for only 3% of intraventricular tumors, with the incidence of lateral ventricle metastasis estimated at 0.75% of all cerebral metastasis.5,6 Metastasis to the choroid plexus are extremely rare and may be misdiagnosed as the more prevalent central neurocytoma. The intraventricular environment is typically considered unfavorable, which raises the question of how certain extracranial carcinomas acquire adaptations that enable them to flourish within the acellular cerebrospinal fluid.7,8

A study conducted by Farnia et al. revealed that the majority of cases involving intraventricular metastasis originated from renal cell carcinoma, followed by breast adenocarcinoma, lung cancer, esophageal adenocarcinoma and papillary thyroid carcinoma.9 Notably, to the best of our knowledge, there have been no previously reported cases of intraventricular metastasis originating from ovarian carcinoma in the existing global literature. The primary mode of dissemination from the genital tract to the brain is through hematogenous spread, wherein tumor cells travel to the lungs and subsequently reach the brain via the pulmonary vasculature.10

According to a study conducted by Pakneshan et al., the median age of patients at the time of diagnosis of brain metastasis from ovarian cancer is 54.3 years, with a range of 20 to 81 years. The median interval between the initial diagnosis of ovarian tumor and the development of brain metastasis is reported to be 24 months, ranging from 0 to 133 months.11 In the case of our patient, the interval time between the initial diagnosis and the occurrence of brain metastasis was 48 months, which falls within the reported range. These findings emphasize the importance of long-term surveillance and follow-up in ovarian cancer patients, as brain metastasis can occur even several years after the initial diagnosis.12,13 Although, the stage of the disease has little effect on the time to BM, in most cases intraventricular metastasis were one of multiple systemic metastatic lesions.14

Clinical symptoms associated with intraventricular metastasis are primarily caused by the localized effects of the tumor, which can vary depending on factors such as the number, size, and location of the metastasis. These symptoms tend to develop gradually, consistent with the typically slow-growing nature of this type of neoplasm. Among the most commonly reported symptoms of intraventricular metastasis are headaches and vision disturbances, often resulting from the size of the tumor mass, peritumoral edema, or the presence of hydrocephalus.6 However, BM may be asymptomatic in 26% of cases at time of diagnosis.13 An active follow-up protocol of OC must be established to allow early detection of BM.

Imaging of brain metastasis in ovarian cancer reveals a spectrum of radiological presentations, encompassing calcification, intratumoral hemorrhage, multiple metastatic nodules and leptomeningeal involvement. The tumor can be solid, cystic or a mixed form.15 At time of diagnosis, BM from OC is usually present as multifocal intra-parenchymal lesions. The occurrence of solitary lesions is usually less common.11,16,17 According to a study conducted by Pakneshan et al. the most common location is the cerebellum (33%) followed by the frontal lobe (20%).11

Given the low frequency of intraventricular brain metastasis, there is limited literature that describes its management in detail. However, surgical excision is considered the most viable option for treatment. Surgical intervention serves multiple purposes including the control of intracranial hypertension and the radical removal of the tumor. Following surgical excision, histological examination of the tumor confirms the diagnosis and provides valuable information for further treatment planning. Although the management of intraventricular BM requires further investigation and standardization, surgical intervention remains crucial for achieving tumor control and alleviating intracranial pressure.

In our case, the histopathological diagnosis relied
on the presence of normal brain tissue along with a papillary carcinoma proliferation with large necrosis. The immunohistochemistry affirmed the diagnosis by a diffuse positivity for paired-box gene 8 (PAX8); showing origin from female genital tract, and a diffuse positivity for Wilms’ tumor-1 (WT-1); showing serous histotype. As ovarian metastasis can be confused with colorectal ones, cytokeratin 7 (CK7) and CK20 were also checked and supported the ovarian origin, with a diffuse and intense expression of CK7 and not CK20.

Chemotherapy plays a pivotal role in the standard treatment of ovarian cancer, including its extracranial recurrence. However, its effectiveness in managing ovarian carcinoma brain metastasis remains a subject of debate. This uncertainty is attributed to the blood-brain barrier, which restricts the delivery of large hydrophilic drugs to the brain, influencing the choice of agents and dosages. Several studies suggested better tumor control with surgery combined with radiotherapy; whole brain radiotherapy or Gamma knife radiosurgery. Stereotactic radiosurgery is typically recommended for patients with up to three cerebral lesions, allowing for high-dose radiation treatment in a single high dose radiation fraction. However, it is worth noting that the trimodal approach, which combines surgery, radiotherapy, and chemotherapy, has been shown to achieve the best survival outcomes for patients with BM from OC. Considering our patient’s multiple metastatic locations at the time of BM diagnosis, she received platinum-based chemotherapy as part of a trimodal approach, aiming to achieve optimal treatment outcomes.

Despite receiving post-hysterectomy chemotherapy, our patient experienced the development of cerebral metastasis. Notably, Borella et al., in their review, reported that 79% of patients who developed brain metastasis had originally been diagnosed with high-grade serous OC. This observation raises the possibility that platinum-based chemotherapy, commonly used in the treatment of ovarian cancer, may have an impact on the blood-brain barrier, potentially increasing its vulnerability and permissiveness for the occurrence of brain metastasis. However, the relationship between platinum-based chemotherapy and the development of brain metastasis remains controversial and necessitates further investigation.

Despite the available therapeutic options, the prognosis for BM originating from OC remains unfavorable. The median overall survival reported in the existing literature varies significantly, ranging from 3 to 38.9 months, with several factors influencing the outcomes. Factors associated with a more favorable impact on survival, as documented in the literature, include the presence of a solitary lesion, younger age at the time of diagnosis, higher Karnofsky performance scale (>70), trimodal therapy (Combining surgery, radiation, and systemic treatment), and the absence of extracranial metastasis. These factors highlight the importance of early detection, comprehensive treatment approaches, and disease control beyond the central nervous system for improved outcomes in patients with BM from OC. Furthermore, patients who had undergone multiple prior treatment regimens and experienced a longer interval between their primary diagnosis and the diagnosis of BM exhibited shorter survival rates.

CONCLUSION

Brain metastasis originating from epithelial ovarian carcinoma is a rare occurrence, and intraventricular location has not been previously reported in the existing literature. The prognosis for patients with CP metastatic lesions remains poor, primarily due to the challenges associated with late-stage diagnosis. It is noteworthy that patients with high-grade serous OC are at a higher risk of developing BM, emphasizing the importance of implementing a targeted follow-up strategy for this patient population. However, due to the rarity of intraventricular metastasis from ovarian cancer, larger-scale studies are needed to provide further insights into the prognosis and management options specifically for this unique anatomical location.

List of Abbreviations:

BM: Brain metastasis.
CK: Cytokeratin.
CP: Choroid plexus.
FIGO: International federation of gynecology and obstetrics.
MREI: Magnetic resonance imaging.
OC: Ovarian cancer.
PAX8: Paired-box gene 8.
WT-1: Wilms’ tumor-1.

Disclosure

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