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Case Reports & Case Series

Giant cystic brain metastasis from ovarian papillary serous adenocarcinoma: Case report and review of the literature

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ABSTRACT

Background: Ovarian brain metastases represent a very rare occurrence and without treatment, prognosis is very poor, with a median survival of one month. We present a unique case of a patient affected by a giant cystic intracerebral metastasis (> 7 cm) secondary to an ovarian papillary serous adenocarcinoma, along with a review of the literature regarding large cystic ovarian metastases and their management.

Case description: A 49-years-old female patient was admitted to our institution because she presented progressive headache and altered consciousness. Brain computed tomography (CT) scan and magnetic resonance imaging (MRI) revealed the presence of a giant left frontal intracerebral cystic lesion. The patient underwent a surgical removal of an ovarian high-grade papillary serous adenocarcinoma three years before. We performed a left frontal craniotomy and microsurgical removal of the brain lesion, achieving a safe macroscopic total resection, thanks to intraoperative neurophysiological monitoring (IONM). The post-operative period was uneventful with a complete recovery. Post-operative brain MRI showed a complete removal of the lesion.

Conclusions: The presence of a giant cystic metastasis with symptoms of intracranial hypertension needs a radical and safe surgical removal, along with the management of a multidisciplinary oncologic group.

1. Introduction

Brain metastases represent one of the most common causes of intracranial tumors in adults, with an incidence of about 20–40%, and about 170.000 new diagnoses every year in the United States of America alone [1–3], and one of the main causes of death in cancer patients. Ovarian brain metastasis is a rare finding, as the most common sites of metastatic ovarian cancer include spread to the peritoneum, liver and lymph nodes [4–6]. Rarely, distant sites such as lung (38%), bone (4%) and brain (1%) may be involved [7,8]. Five-year overall survival (OS) for distant metastatic disease is 29.2% [9–11]. Prognosis in ovarian cancer patients with brain, bone, and/or lung metastatic disease is poor, whereas it is better if the site of metastasis is the liver [12]. As for other histological types, without treatment, brain metastases have a median survival of just one month [13,14]. A classification based on the size of the brain cystic metastases was not found in literature, therefore we defined as "giant" those equal to or greater than 7 cm. We present a unique case of a patient affected by a giant cystic ovarian metastasis, along with a review of the literature regarding large cystic ovarian metastases and their management.

2. Case report

A 49-years-old female patient was admitted to our institution because she presented progressive headache, emesis, expressive aphasia associated with mild right hemiparesis (4/5 BMRC) and altered consciousness. Head CT scan revealed the presence of a huge left frontal cystic lesion with 15 mm right midline shift, associated with cortical

Abbreviations: OS, overall survival; CT, computed tomography; MRI, magnetic resonance imaging; CEA, carcino-embryonic antigen; AFP, alpha-fetoprotein; Ca 19.9, carbohydrate antigen 19.9; IONM, intraoperative neurophysiological monitoring; iCT, intraoperative computed tomography; CEUS, contrast-enhanced ultrasound

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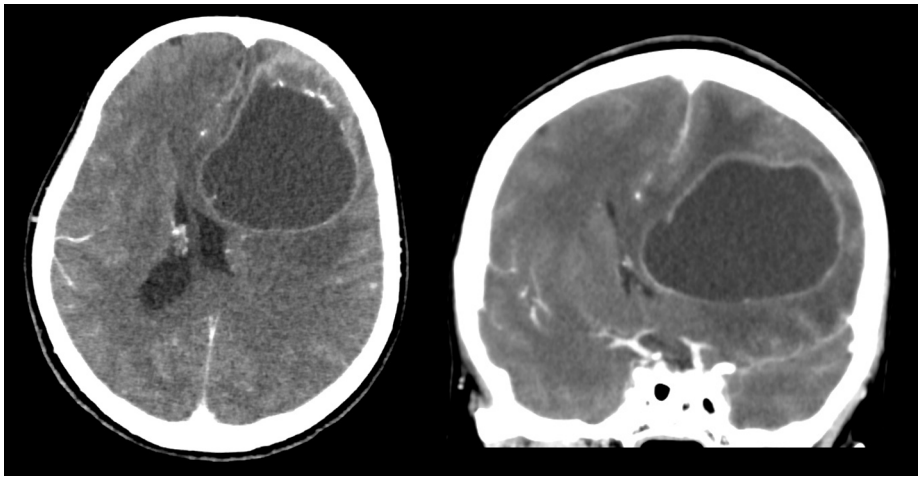

Fig. 1. Preoperative brain CT scan showing the presence of a hypodense large left frontal lesion with 1.5 cm right midline shift characterized by total fluid cystic component, subcortical calcifications and peripheral contrast enhancement.

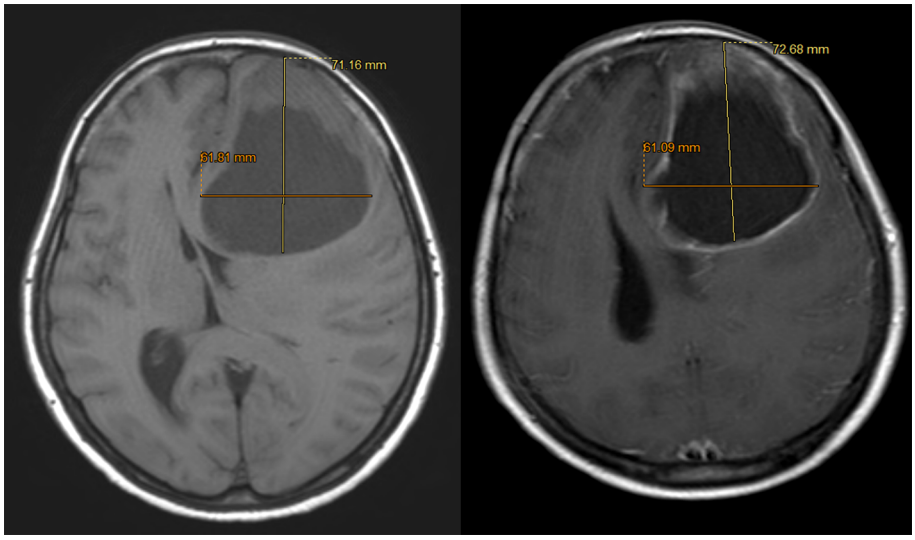

Fig. 2. Preoperative T1 weighted MRI pre- (left) and post- (right) gadolinium contrast agent (Gd) administration, that better characterized the large cystic tumor, presenting peripheral hyperintense post-contrast enhancement and fluid component without internal septa.

calcifications (Fig. 1). A brain MRI confirmed the presence of a left frontal intracerebral lesion, characterized by thin peripheral contrast enhancement, containing fluid, hyperintense in T2 and fluid-attenuated inversion recovery (FLAIR) sequences, with 72 × 55 × 48 mm dimensions (Fig. 2). In view of the positive oncological history, a subsequent total-body CT scan revealed common post-operative findings at the pelvis (relative to a previous surgery), laterocervical lymph nodes (maximum diameter of 15 mm) bilaterally, as well as perigastric lymph nodes (maximum diameter of 10 mm), and it was negative for further tumor spread. The patient's medical history was positive for pelvic surgery 3 years before: total laparoscopic hysterectomy, with bilateral adnexectomy and bilateral removal of lesions of the adnexa, adhesiolysis, bilateral pelvic lymphadenectomy, appendicectomy, omentectomy, lumbosacral lymphadenectomy, removal of juxta-rectal lesions. Abdomen CT scan revealed the presence of a lesion (8 × 10 cm) located at the right adnexa, connected with another 11 cm lesion located at the small pelvis. The pelvic lesions showed calcifications and septa. Specific tumor markers were examined as follow: carcino-embryonic antigen (CEA): 2.25 ng/ml, alpha-fetoprotein (AFP): 0,62 ng/ml, carbohydrate antigen 19.9 (Ca 19.9): 11.93 U/ml. Histological examination of the pelvic lesions documented an ovarian high-grade papillary serous adenocarcinoma (Fig. 3). We performed a left frontal craniotomy and microsurgical removal of the brain lesion, achieving a safe macroscopic total resection, thanks to intraoperative neurophysiological monitoring (IONM). A characteristic intraoperative finding was represented by a cleavable tumor with a thick capsule in the deepest and posterior portions, with cortical calcifications and a thinner capsule medially, adherent to the left lateral ventricle, which was impinged and repaired. The internal cystic component contained a citrine fluid with whitish whips. Histological examination of the brain lesion showed high-grade epithelioid neoplasia, highly necrotic, with solid/trabecular growth pattern, marked cytonuclear pleomorphism, and high mitotic index with the presence of atypical mitoses. The immunohistochemical investigations performed on vital neoplastic tissue gave the following results: CKAE1/AE3+, CK7+, EMA+, WT1+, PAX8+, GFAP-, CD56-, Chromogranin A−, synaptophysin−, calretinin-, CK5/6−, ER−, CD99−, p40−, TTR1−, CK20−, CDX2−, CK34be12−, S100−, Melan A−. The morpho-immunophenotypic analysis pointed to brain metastasis from poorly differentiated carcinoma, with large areas of necrosis, most probably originally from the female genital tract of serous histotype. (Figs. 4 and 5). The post-operative period was uneventful: post-operative brain MRI showed a complete removal of the lesion with the return of the midline structures to the axis (Fig. 6). The patient recovered completely and was

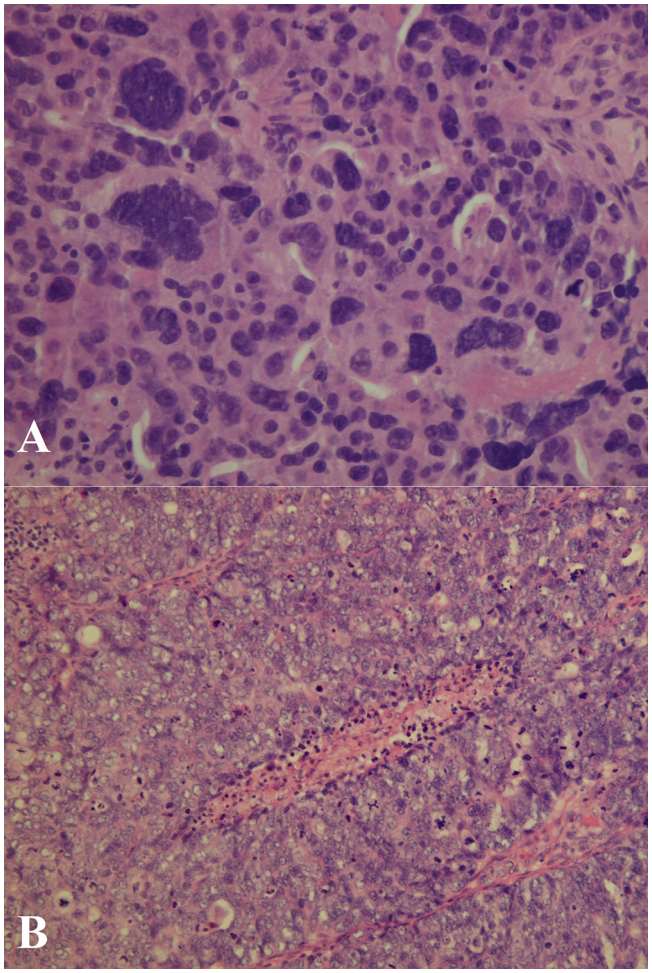

Fig. 3. Neoplastic elements with large and markedly pleomorphic nuclei, with numerous atypical mitoses (E&E) (40×) (A); Solid papillary neoplasm with extensive necrotic areas (E&E) (20×) (B).

discharged on the sixth post-operative day. Then, the patient was addressed to a radiotherapist and an oncologist to undergo a possible adjuvant therapy.

She is followed-up every four months and so far, a further brain MRI showed no evidence of disease progression or recurrence. 13 months after last surgical procedure, she has a stable disease and shows no signs of clinical deterioration (Fig. 7).

3. Discussion

Brain metastases occasionally present themselves as cystic lesions, and the exact pathogenesis of cyst formation has not yet been clarified [15]. Some authors state that the exudative fluid, usually seen as edema surrounding the metastatic tumor, tends to collect inside the tumor and expand as a cystic mass [16]. Cumings [17] hypothesized that cyst formation is due to tumor degeneration followed by transudation of fluid from peritumoral blood vessels. Moreover, Gardner et al. [18] suggested that the cystic components in brain tumors are interstitial fluid without its normal drainage route, due to the lack of lymphatics in the surrounding pathological brain. Large cysts cause neurologic deficits due to their mass effect. Single, large cystic brain tumors have been traditionally treated with surgery [3]. The cystic characteristic is usually seen in patients affected by brain metastasis from lung cancer, but it also may occur in other metastatic tumors like breast, kidney, pancreas, and melanoma [19].

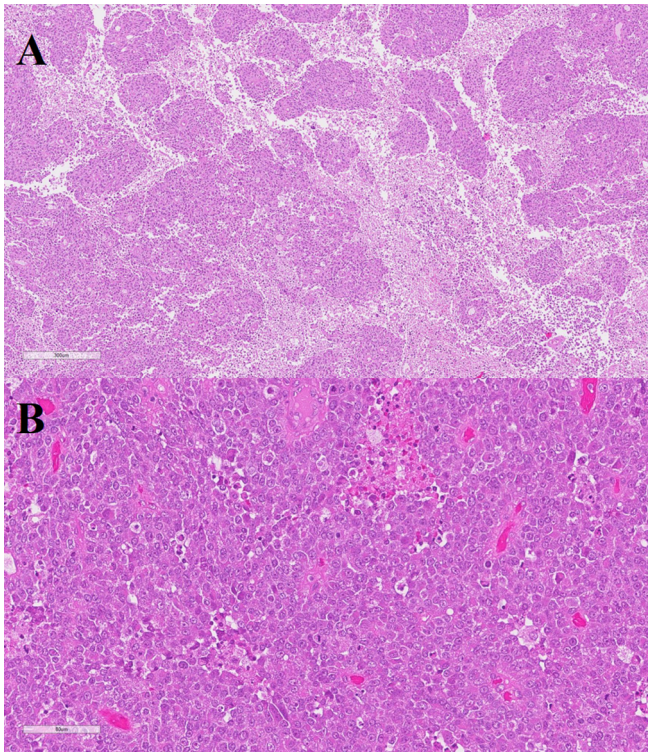

Fig. 4. High grade solid neoplasia with necrosis and papillary features (10×) (A); Neoplastic cells with abundant eosinophilic cytoplasm, high mitotic rate and atypical mitotic figures (E&E) (B).

An essential factor in determining surgical strategy is the size and the location of the brain tumor [3]. Schoeggl et al. [20] reported that brain lesions with a maximum diameter < 17 mm had a better outcome after radiosurgery. Sneed et al. [21] noted that tumor volume was very strongly related to patient survival. Petrovich et al. [22] proved that tumor volume influences survival rate by showing that the local tumor control rate one year post-treatment was 90% in tumors < 3 mL and 78% in larger lesions (11 months for lesions < 1 mL and 6 months for lesions with volume > 9 mL).

It is exceedingly rare for ovarian cancer to spread to the brain, however, if it does occur, the most common epithelial ovarian carcinoma associated with this is of serous histotype [23–25].

In the literature it hast been reported that large cystic brain metastases from breast cancer are associated with poor outcome [26], but to the best of our knowledge there are no reports of ovarian cystic brain metastases of very large/"giant" size, and there is no correlation between this finding and prognosis. This paper aims to highlight these aspects to improve treatment. In the patient presented, due to the huge dimensions, the lesion was treated with craniotomy and microsurgical resection.

If the future follow-ups will confirm the poor prognosis for patients affected by large cystic ovarian brain metastases, minimally invasive treatment like stereotactic aspiration or radiosurgery could be suggested, as reported [3].

In our experience, at last follow-up (13 months), the patient did not present oncological progression; this is a good clinical result, as reported in the literature, which documents a median survival after brain metastasis surgery of 18 months [26–29]. Thus, we suggest treating large ovarian cystic brain metastases with radical surgical removal, also using modern techniques and tools like neuronavigation with fiber tracking reconstruction, IONM, intraoperative computed tomography (iCT), contrast-enhanced ultrasound (CEUS) and awake surgery (if tolerated by the patients), to improve safety and effectiveness.

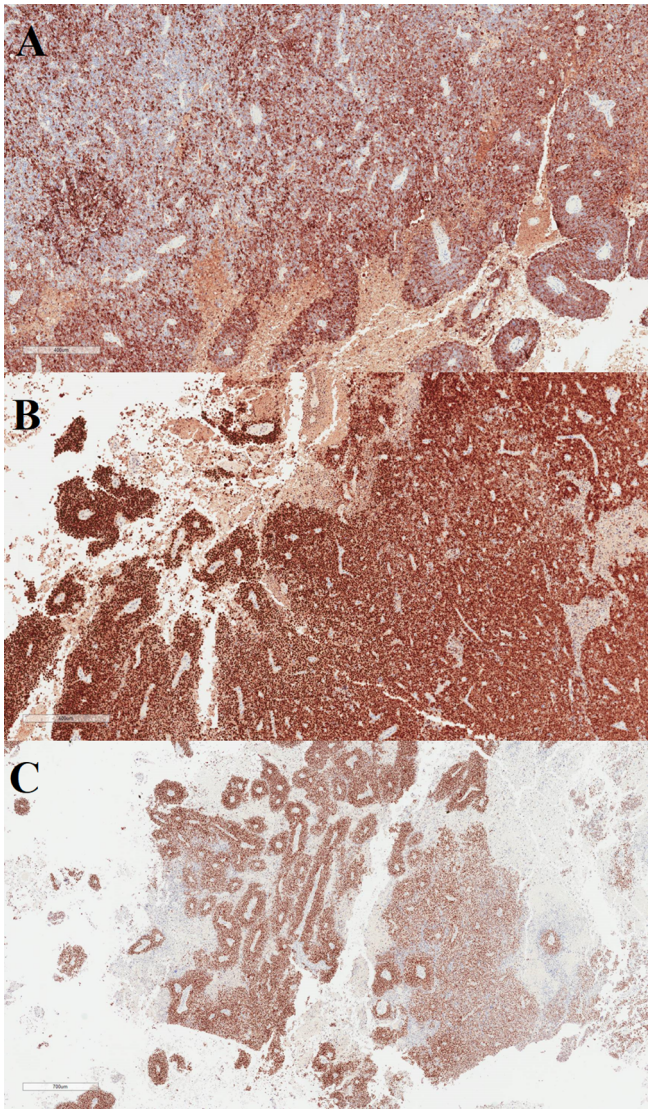

Fig. 5. Diffuse positivity for CKAE1/AE3 showing epithelial differentiation (A); diffuse positivity for PAX8 showing origin from female genital tract (B); diffuse positivity for WT1 showing serous histotype (C).

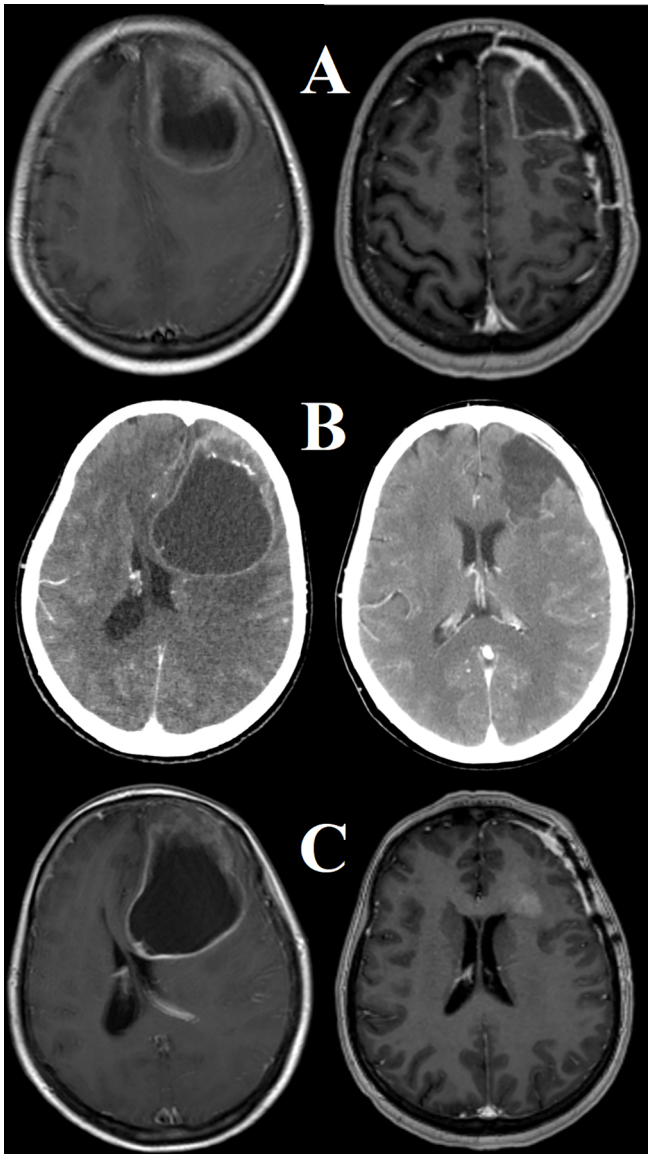

Fig. 7. Pre- and post-operative follow-up imaging comparison showing no oncological recurrence: preoperative and one-month post-operative T1-weighted brain MRI after Gd administration showed satisfying brain decompression and peripheral reactive enhancement (A); preoperative and 4-months postoperative post-contrast brain CT scan showed no contrast enhancement nor tumor recurrence (B); preoperative and 12-months post-operative T1-weighted brain MRI after Gd administration showed minimal reactive left frontal contrast enhancement (C).

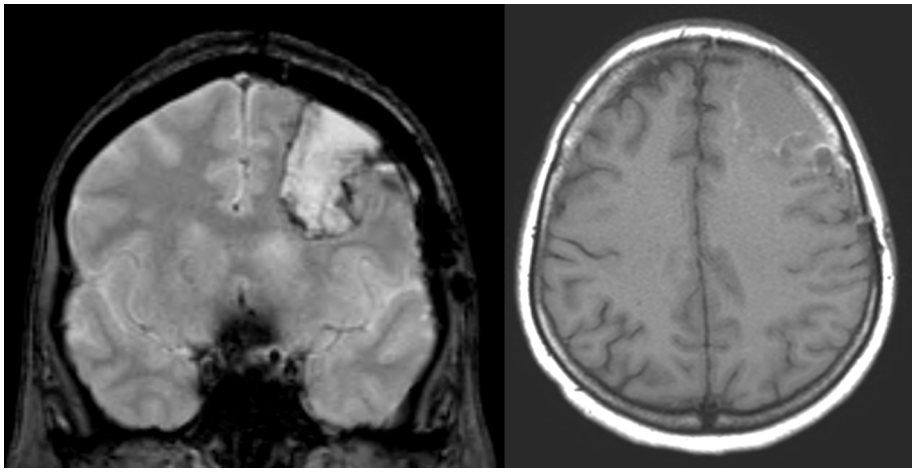

Fig. 6. Post-operative imaging – brain MRI performed on day 2, showing satisfying tumor removal: coronal post-operative gradient-echo sequences showing minimal peripheral hypointense signal, relative to common post-operative blood component hold by hemostatic agents used during surgery (left); axial postoperative T1-weighted sequences showing postoperative washing fluid and minimal hyperintense signal due to hemostatics (right).

4. Conclusions

Although patients affected by brain metastases are managed by a multidisciplinary oncologic group, the presence of a large cystic metastasis with symptoms of intracranial hypertension needs a radical and safe surgical removal. This report suggests that ovarian cystic brain metastases may present an acceptable clinical outcome and could be tackled with good results with more extensive treatments.

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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