

BRAIN METASTASIS FROM OVARIAN CANCER : THREE CASES REPORT

METASTASE CEREBRALE DU CANCER OVARIEN : A PROPOS DE TROIS CAS

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Abstract

Brain metastasis is considered as a rare and late event in ovarian cancer. We present three cases of women with an ovarian cancer who developed brain metastasis. The first was a 67-year-old woman operated for an ovarian adenocarcinoma with postoperative chemotherapy. She underwent surgical removal of cerebellar metastatic carcinoma consistent with her ovarian primary with post-operative radiotherapy and chemotherapy. She had been followed without evidence of any recurrence. The second case was a 50-year-old woman followed for an ovarian adenocarcinoma with peritoneal carcinosis. She received courses of chemotherapy and got operated. She developed secondary left frontal lesion and bone marrow infiltration. She underwent palliative and decompressive radiotherapy with chemotherapy. The third was a 50-year-old woman, admitted for multiple brain metastasis from a right ovarian tumor. She underwent palliative radiotherapy and refused the treatment of the ovarian tumor.

Key-words: Ovarian carcinoma; Brain metastases; Multimodality treatment.

Résumé

Les métastases cérébrales sont considérées comme un événement rare et tardif du cancer ovarien. Nous présentons trois cas de femmes atteintes de cancer ovarien et développant des métastases cérébrales. Le premier cas est celui d'une femme de 67 ans opérée pour un adénocarcinome ovarien avec chimiothérapie postopératoire. Elle a eu une exérèse chirurgicale d'un carcinome cérébelleux métastatique de son primitif ovarien avec une radiochimiothérapie postopératoire. La 2^{ème} femme était de 50 ans suivie pour un adénocarcinome ovarien avec carcinose péritonéale. Elle a eu une chimiothérapie et a été opérée. Elle a développé une lésion secondaire frontale gauche avec infiltration de la moelle osseuse. Elle a eu une radiothérapie palliative et décompressive avec chimiothérapie. Le troisième cas était celui d'une femme de 50 ans, admise pour de multiples métastases cérébrales d'une tumeur ovarienne droite. Elle a eu une radiothérapie palliative et a refusé le traitement du primitif.

Mots - clés : Carcinome ovarien ; Métastase cérébrale ; Traitement multimodale.

ملخص

تعتبر نقائل الدماغ من الأحداث النادرة والمتأخرة في سرطان المبيض. نقدم ثلاث حالات لنساء مصابات بسرطان المبيض أصبن بنقائل دماغية. الحالة الأولى هي حالة امرأة تبلغ من العمر 67 عامًا أجريت عليها عملية جراحية لسرطان غدي في المبيض مع العلاج الكيميائي بعد الجراحة. خضعت لعملية استئصال جراحي لسرطان مخيخي منتشر و نابع عن مبيضها مع استخدام العلاج الإشعاعي الكيميائي بعد الجراحة. كانت المرأة الثانية تبلغ من العمر 50 عامًا متبوعة بسرطان غدي في المبيض مصحوب بسرطان الصفاق. خضعت للعلاج الكيميائي وخضعت لعملية جراحية. أصيبت بأفة ثانوية في الجبهة اليسرى مع تسلل نخاع العظم. كان لديها علاج إشعاعي ملطف و خافض للضغط مع العلاج الكيميائي. كانت الحالة الثالثة لامرأة تبلغ من العمر 50 عامًا تم قبولها لوجود نقائل دماغية متعددة من ورم في المبيض الأيمن. خضعت للعلاج الإشعاعي الملطف و رفضت العلاج البدائي.

الكلمات المفاتيح: سرطان المبيض ; ورم خبيث في الدماغ ; العلاج متعدد الوسائط.

INTRODUCTION

Brain metastasis, although a common and severe complication in lung and breast cancer [1], is considered as a rare and late event in ovarian cancer [2]. A variable incidence of 0.3–12 % has been reported in different studies as well as its association with poor prognosis [3]. Possibly, advances in neuroimaging have allowed careful follow-up of cancer patients, which together with longer survival from primary ovarian cancer, have led to more frequent and earlier detection of brain metastases [4]. The rarity and small number of patients affected, have prevented the establishment of a consensus for optimal therapy.

The aim of this article is to describe clinical features, treatment and prognosis of three cases of brain metastases from ovarian cancer with a review of literature.

CASES REPORT

Case 1

A 67-year-old female operated one year ago for an ovarian adenocarcinoma, the treatment consisted of debulking (cytoreductive) surgery including total abdominal hysterectomy,

bilateral salpingo-oophorectomy, and omentectomy, followed by 6 cycles of adjuvant chemotherapy.

The patient went into remission for 06 weeks until she developed severe headaches, vomiting and vertigo requiring her admission to our department of neurosurgery. The neurological exam revealed static and kinetic cerebellar syndrome. The serum level of CA-125 was normal. The brain CT scan (Fig1) and MRI (Fig2) showed a solitary compressive left cerebellar mass with double component (cystic and nodular). This lesion demonstrated irregular intense nodular enhancement around the posterolateral portion of the mass with peripheral enhancement of the cyst.

The patient went through surgery and the mass was removed totally. Histopathological exam showed metastatic ovarian adenocarcinoma, consistent with the patient's known primary tumor (Fig3, 4). She underwent post-operative radiotherapy to the whole brain with 3 courses of chemotherapy. Metastatic work-up showed no evidence of abdominal recurrence. She remained apparently free of disease (Fig5) until she developed metastatic epidural dorsal spinal cord compression and underwent radiotherapy. She remained well and had been on observation for the past year without any recurrence.

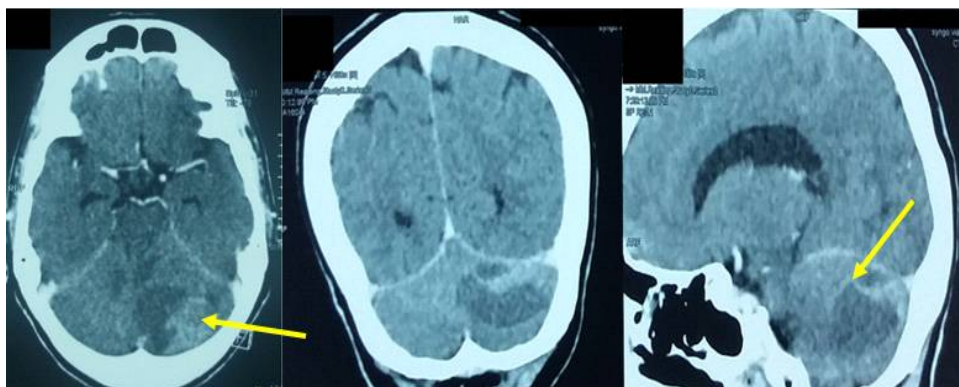


Figure 1: CT scan showing a double component left cerebellar mass with homogeneous and intense enhancement of nodular component and the margins (yellow arrows)

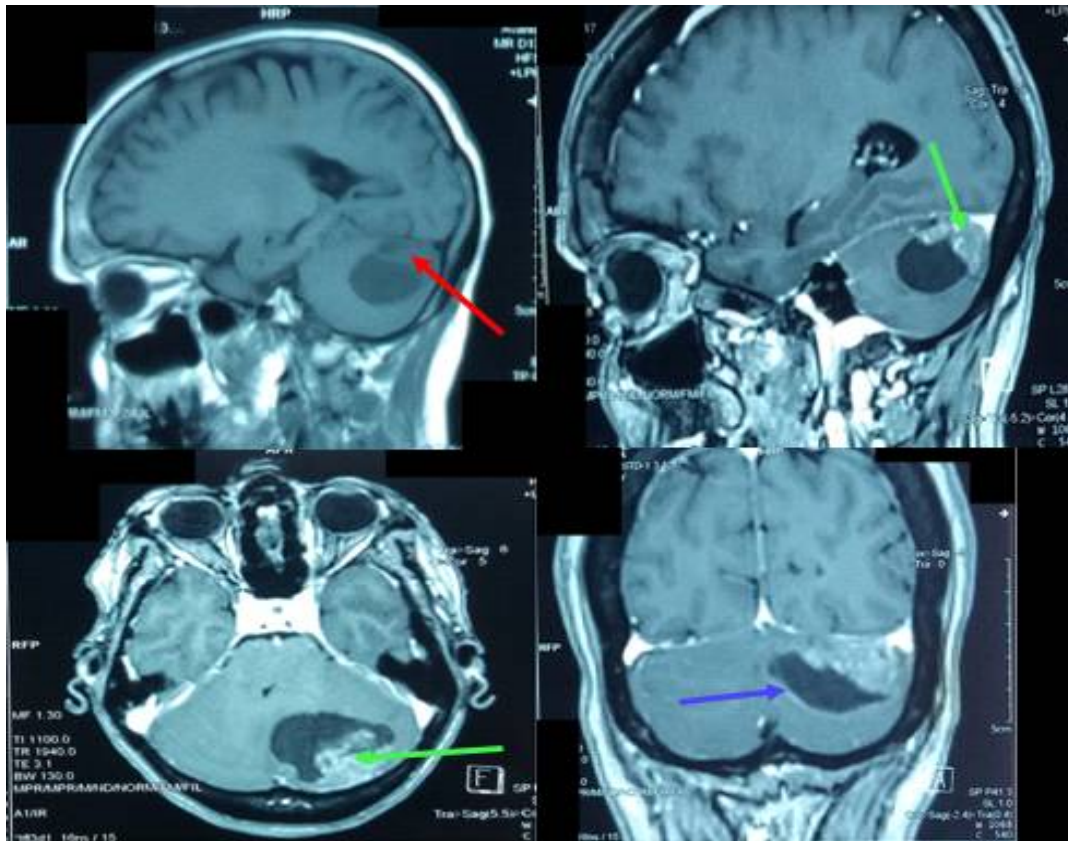


Figure 2: MRI sequences showing a solitary compressive left cerebellar mass with double component. The nodular mass is hypo intense on T1 (red arrow) with irregular enhancement (green arrow) and the cystic one show peripheral enhancement (blue arrow)

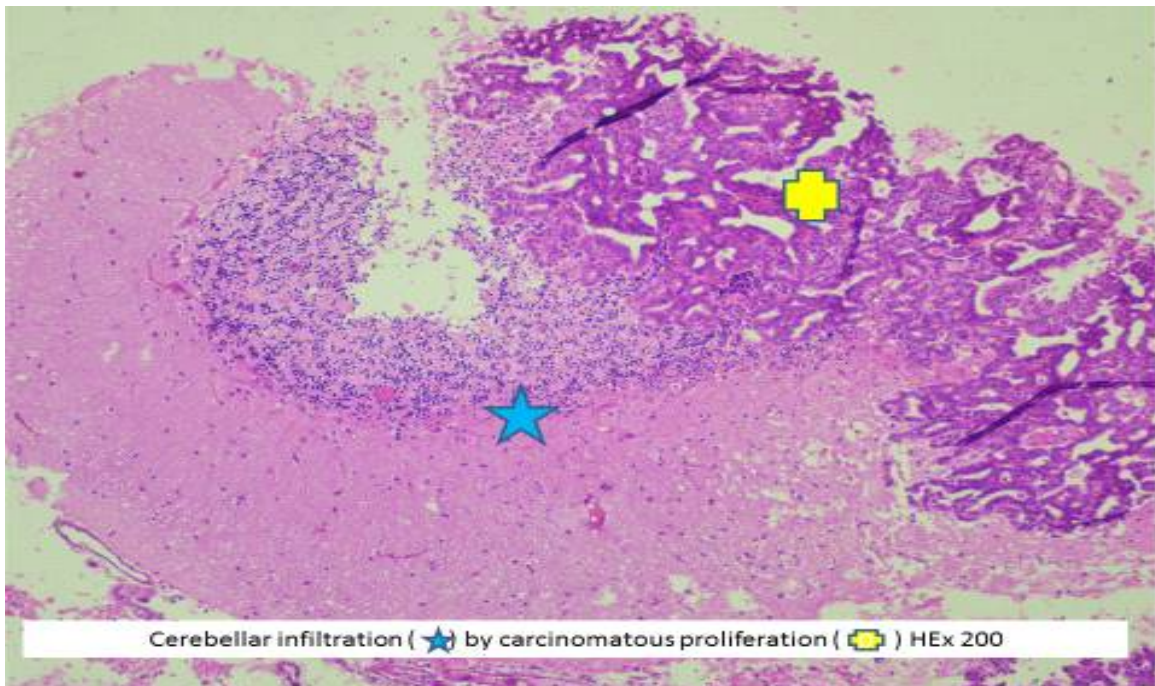


Figure 3 : Cerebellar infiltration (★) by carcinomatous proliferation (⊕) (HEx 200)

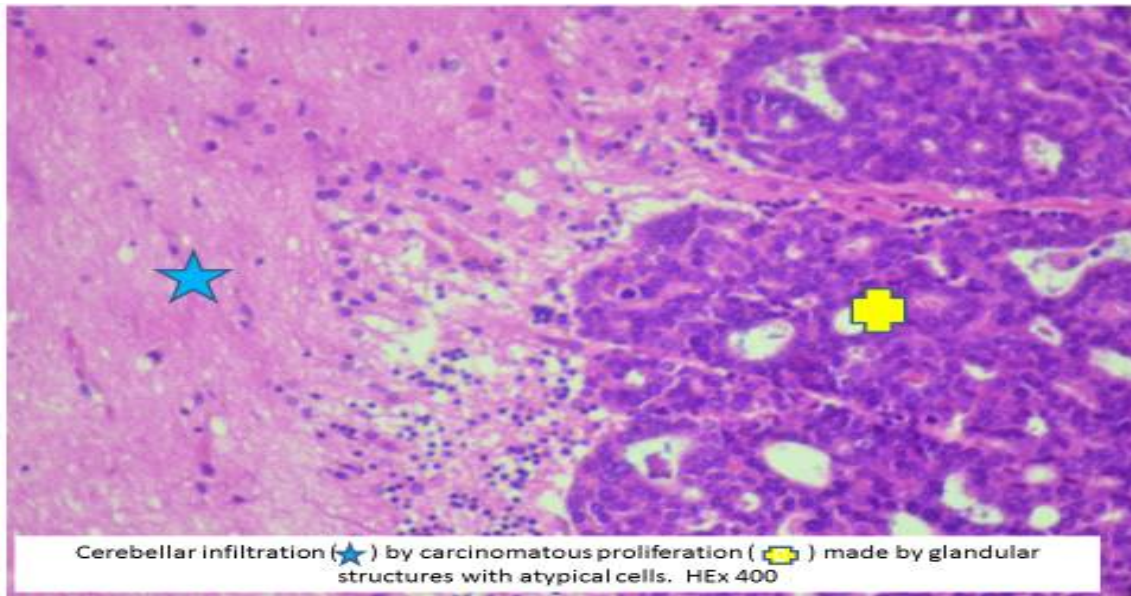


Figure 4 : Cerebellar infiltration (★) by carcinomatous proliferation (✚) made by glandular structures with atypical cells (He x 400)

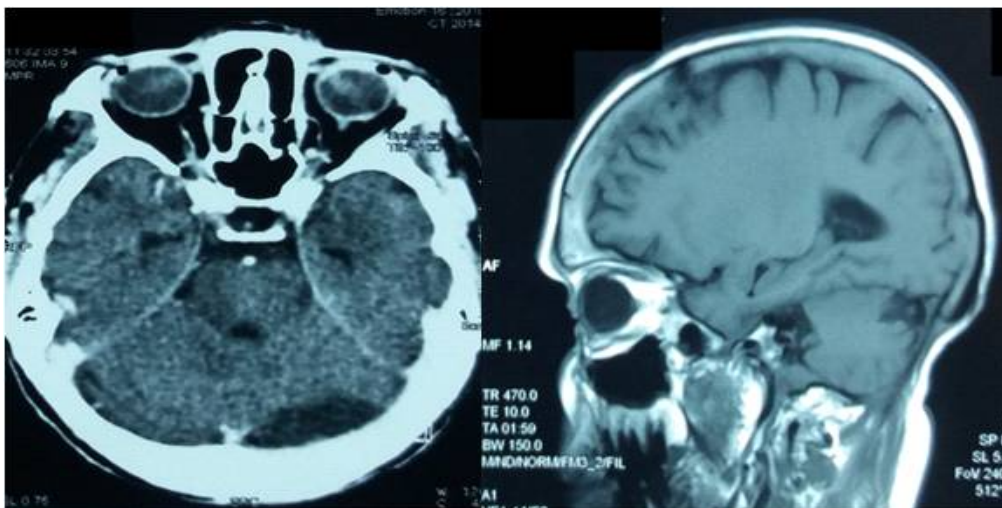


Figure 5: Post operative neuroimaging showing the regression of the cerebellar mass

Case 2

A 50-year-old woman followed, four years ago, for an ovarian adenocarcinoma with peritoneal carcinosis. She received three courses of chemotherapy then went through surgery. The surgery consisted of total abdominal hysterectomy, bilateral salpingo-oophorectomy, and omentectomy with lymph node removal. The histopathological exam showed an infiltrating serous adenocarcinoma of both ovaries. Then she received six courses of chemotherapy with complete remission over four years. She developed headaches with low back pain. The neurological exam was normal. The CA-125 level was not quantified. The cerebromedullary MRI showed

secondary left frontal lesion (fig 6) and bone marrow infiltration of T12, L1 and L2 (fig 7). The scan of the chest, abdomen and pelvis showed multiple cervico-thoraco-abdomino-pelvic lymph nodes. Stereotactic biopsy of the frontal lesion was performed and the histopathological exam concluded to cerebral adenocarcinoma related to the primary ovarian cancer. She underwent whole-brain palliative and decompressive radiotherapy with 3 courses of chemotherapy (Carboplatine). The patient showed clinical improvement during 4 months and then lost to follow-up.

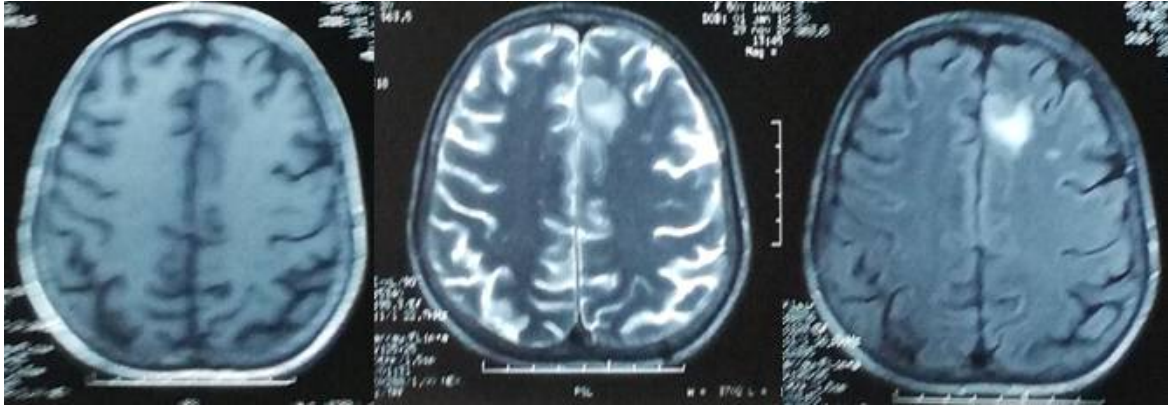


Figure 6 : MRI sequences showing the left frontal lesion

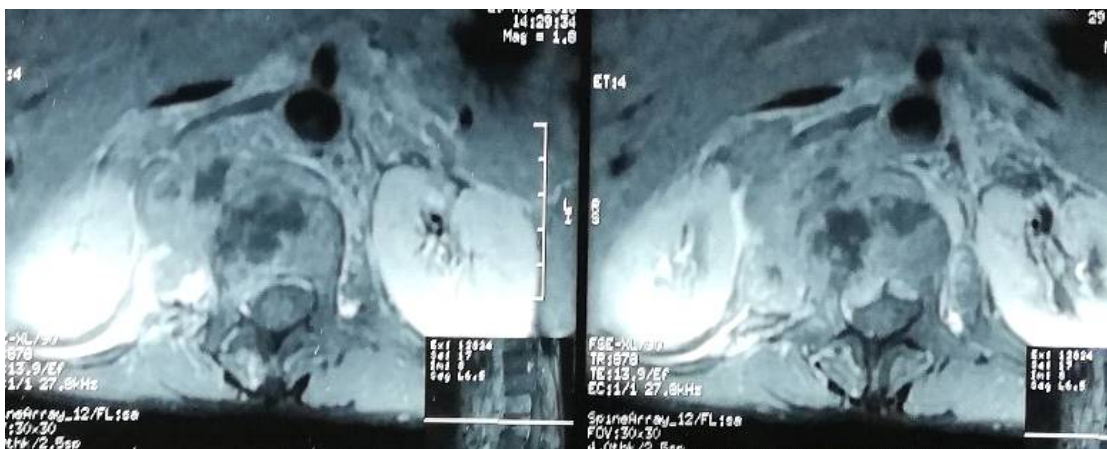


Figure 7: Medullary MRI showing the bone marrow infiltration of T12, L1 and L2

Case 3

A 50-year-old woman, who has consulted for progressive headache without other symptom. The neurological exam was normal. The CA-125 level was not quantified. The CT scan showed multiple brain metastasis over and under tentorial. The scan of the chest, abdomen and pelvis showed a right ovarian tumor. She underwent whole-brain palliative radiotherapy (30 Gy) with partial improvement and she refused the treatment of the ovarian tumor (surgery and chemotherapy). Three months after radiotherapy she was free of symptoms but still refuses any other treatment

DISCUSSION

Brain metastases from cancers of the female genital tract, apart from choriocarcinoma, are uncommon. They are generally found in association with extensively disseminated systemic disease. The hematogenous dissemination of tumor cells to the lungs and secondary to the brain via the pulmonary vasculature, is the principal mechanism of the

spread from the genital tract to the brain [5]. Ovarian cancer has the highest incidence of brain metastasis compared to other gynecological cancers [6]. The reported incidence ranges widely from less than 1–12 % [3]. However, it is possible that the real incidence of brain metastasis from ovarian cancer is higher because most reports are from clinical studies and very few postmortem studies have been performed, especially with the advances in neuroimaging.

Symptoms of brain metastases can be focal or generalized. Headache is the most common symptom, and it is present in 40%–50% of cases. Headache was present in all our cases. Multiple metastases or metastases located in the posterior fossa, are the most associated with headache. It can be associated with visual disturbances, confusion, vomiting, and syncopal episodes. The location of the lesions highly influences the clinical manifestations of brain metastases. Hemiparesis is the most common sign, followed by altered mental

status. For our patients, neurological exam was normal in 2 cases, and a cerebellar syndrome was found in one case. All the patients presenting with coma died within 2 days to 2 weeks of diagnosis. The cerebral hemisphere was the most common site of metastasis, followed by the cerebellum. The falx cerebri and spinal cord were rare sites of metastasis. In our cases, the lesions were infra-tentorial, supra-tentorial and spinal.

In order of decreasing frequency, cerebral metastases included the parietal lobe, the frontal lobe, and the temporal lobe [7]. However, Pakneshan S et al [3] found cerebellum to be the most common site of intracranial metastasis for ovarian cancer. This may be due to the rich blood supply of the cerebellum.

Brain imaging in ovarian cancer metastasis shows various radiological appearances including calcification, intratumoral hemorrhage, numerous metastatic lesions, and leptomeningeal involvement [4]. The incidence of detecting solitary lesions is not frequent among patients with brain metastases from ovarian cancer [8]. Multiple metastatic lesions were found in all our cases.

Brain metastases are a major harmful event in the natural history of most malignancies. There is no consensus for the treatment of brain metastasis from ovarian cancer due to its rarity and the limited number of cases reported until now. Overall, the survival rate is better for solitary lesions and for patients who underwent surgical resections. Therapeutic options are abstention for patients with progressive widespread metastatic disease; rapid treatment to correct life-threatening complications of metastases, including obstructing hydrocephalus and increased intracranial pressure; and various other treatment strategies, like corticosteroids, whole-brain radiotherapy (WBRT), surgery, radiosurgery, chemotherapy, and recently stereotactic radiosurgery (SRS) and gamma-knife radiosurgery (GKRS) [7]. The features that guide the therapeutic approach are the number and location of the metastases, the presence or absence of extracranial disease, previous treatment, performance status, and neurosurgery possibilities. The treatment purpose is to relieve neurologic symptoms. However, isolated solitary brain metastases and multiple metastases are not treated in the same way. In fact, craniotomy with resection of metastases followed by WBRT is indicated for patients with isolated solitary brain metastases. For patients with multiple central nervous system metastases or inaccessible lesions, the treatment is often palliative. Thus, these patients receive WBRT

with or without chemotherapy [9]. Thus, in case 1, the patient underwent surgery followed by WBRT associated with chemotherapy. In case 2, the patient underwent palliative radiochemotherapy after histological confirmation. WBRT applied individually has the potential to decrease neurological symptoms and prolong median survival up to 3-6 months [2]. In their literature review, Piura and Piura reported that brain metastases therapy with combination of surgery, WBRT and chemotherapy, or combination of surgery and WBRT or SRS (stereotactic radiosurgery)/GKRS (gamma-knife radiosurgery) yielded to better survival results (median survival of 20, 17, and 18 months, respectively) than therapy of brain metastases with surgery alone, WBRT alone, chemotherapy alone, WBRT and chemotherapy, and no treatment (median survival of 6.7, 4.5, 7.5, 9.1, and 1.4 months, respectively). Thus, apparently, multimodal therapy including surgical resection of the brain metastases followed by WBRT (\pm chemotherapy) or with SRS/GKRS is associated with the best survival [10]. In the review by Pakneshan et al., longer survival was described by combination surgery, radiation and chemotherapy compared to whole brain radiation alone (20.5 months versus 9.1 months; $p = 0.04$) [3]. Surgical resection highly improved the survival compared to other methods of treatment [11]. Chemotherapy is an important part of standard treatment for ovarian cancer and even extracranial recurrence. Its role in the treatment of brain metastases remains somewhat controversial concerning the management of ovarian carcinoma [9]. In fact, it is admitted that the blood-brain barrier (BBB) limits delivery of large-in-size hydrophilic drugs to the brain, determining which agents and doses will be used [12]. Also, some researchers think that improvement in the efficacy of chemotherapy delays recurrence in the abdominal and pelvic cavity, but that the BBB blocks water-soluble cisplatin and lowers the concentration in the central nervous system, increasing the incidence of brain metastasis [13]. Recently, SRS (for instance linear accelerator- or gamma-knife-based) became another promising therapy option in brain metastases from ovarian cancer. SRS is mostly indicated for patients with no more than 3 cerebral lesions, which are treated with one single high-dose radiation fraction [14]. Because of that, brain relapse in ovarian cancer is generally a palliative situation, quality of life should be one of the main purposes that has to be considered in the decision on the optimal therapy

strategy [9]. Therefore, Treatment using radiation and surgery with or without chemotherapy for brain metastases from ovarian cancer can improve survival especially for those patients with no other distant disease. The possibility of using SRS is a very promising option that should be further investigated in future trials and integrated into a multimodal approach [15].

CONCLUSION

Brain metastasis is a rare and fatal outcome of ovarian cancer. It is associated with a very poor survival. Brain imaging studies are suggested to be a part of the follow-up routine of patients after primary treatment of ovarian carcinoma. Besides, immediate search of brain metastasis should be done in front of the emergence of one or more neurological symptoms and signs in patient with ovarian using brain imaging studies. A better outcome might be obtained using multimodality therapy. A small number of patients were included in the reported studies, that's why multicenter clinical trials are needed for further investigation to critically evaluate the clear benefit of these treatment options in selected patients.

Stereotactic radiosurgery might be a promising strategy for the future, with its capability to remove inaccessible lesions with an efficiency equivalent to surgical resection. Future studies should focus on the integration of stereotactic radiosurgery into the multimodal approach, to obtain optimal surgical tumor removal even in patients with multiple lesions prior to any application of chemotherapy.

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