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BRAIN METASTASIS IN EPITHELIAL OVARIAN CARCINOMA: REPORT OF TWO CASES

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ABSTRACT

Introduction: Brain, an otherwise common metastatic site in advanced carcinoma, rarely harbors metastatic lesion from primary epithelial ovarian carcinoma. Here, we reported two cases of brain metastasis in primary epithelial ovarian carcinoma.

Case A: A 46-year-old female, known case of stage IC papillary-adenocarcinoma-ovary diagnosed and treated 3-years ago, presented with right sided hemiparesis for 3-months duration. Patient was diagnosed having brain metastasis from ovary; and treated by surgery, WBRT (30 Gy/10 fractions) and chemotherapy with 3-different regimens successively. Patient was disease-free post 3rd-line chemotherapy and is currently on followed up.

Case B: Another 40-year-aged female, presented with progressive distension of abdomen, and diagnosed as metastatic ovarian adenocarcinoma. She received NACT with two different regimens followed by radical surgery; histopathology revealed serous cystadenocarcinoma. 6-months after surgery, patient presented with metastatic disease in brain. Patient was given WBRT (20 Gy/5 fractions) followed by 3rd-line chemotherapy Post chemotherapy follow-up scan revealed residual disease; but unfortunately, she defaulted our follow-up.

Conclusion: Selecting suitable therapy based on patient's condition & disease status is of utmost important in these rare patients and appropriate treatment can prolong survival in selective patients.

KEYWORDS :

INTRODUCTION

Brain is one of the most common metastatic site in majority of advanced stage cancer. New onset neurological symptoms in a known cancer patient, specially whose primary tumors is not eradicated completely, should always prompt the diagnosis of brain metastasis. However, brain metastasis in primary epithelial ovarian carcinoma is relatively rare and only an infinitesimal number of cases have been reported. Here, we described two cases of brain metastasis in primary epithelial ovarian carcinoma treated by combined modalities of treatment.

Case A

A 46-year-old female, gravida 5, para 5, presented to our OPD with right sided hemiparesis and slurring of speech for last 3-month duration. She was a known case of stage IC papillary adenocarcinoma ovary diagnosed 3-years ago and treated by radical surgery (total abdominal hysterectomy and bilateral salpingo-oopherectomy) followed by 6-cycles of adjuvant chemotherapy with 3-weekly paclitaxel and carboplatin regimen. The patient did not follow-up as directed with her treating oncologist as she was asymptomatic for 21-months post primary treatment.

On examination, patient had decreased power (4/5) in right upper and lower limb. Contrast enhanced magnetic resonance imaging (CEMRI) of brain revealed well defined lobulated thick-walled lesion (3.2 × 3.0 × 3.3 cm) in left frontal region with marked surrounding edema extending into left temporal and thalamo-ganglionic region. Patient was referred to Neurosurgery Department where left fronto-parietal craniotomy with gross tumor excision was done. Histopathology of surgical specimen revealed metastatic deposits from papillary adenocarcinoma of ovary; with immunohistochemistry (IHC) positivity of cytokeratin, EMA and CA-125; and negative for glial fibrillary acidic protein (GFAP) [Figure 1 (A, B & C)].

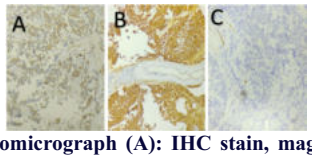

Figure 1: Photomicrograph (A): IHC stain, magnification ×20, neoplastic cells with widespread positivity for CA-125; (B) IHC stain, magnification ×20, neoplastic cells with positivity for EMA; and (C): IHC stain, magnification ×20, neoplastic cells negative for GFAP

Patient further received palliative whole brain radiation therapy (WBRT) 30 Gy in 10 fractions by Cobalt-60 teletherapy machine. Post RT, patient's general condition improved.

On further follow up, CECT of abdomen and pelvis revealed ill-defined cystic lesion measuring 4.6 × 2.8 × 4.5 cm in left adnexa likely metastatic deposits [Figure 2 (A & B)] ; CA-125 was also found to be raised with a value of 100.8 U per milliliter. In view of recurrence, patient was re-challenged with 6-courses of chemotherapy with 3-weekly Paclitaxel and Carboplatin. Post chemotherapy, CECT of abdomen and pelvis revealed residual disease with CA-125 levels of 56.6 U/ML. Patient received second line chemotherapy with 4-weekly intravenous liposomal doxorubicin for 6-cycles. CECT of abdomen and pelvis, post 2nd line chemotherapy, demonstrated persistence of residual disease along left adnexa. She was given further 6-cycles chemotherapy with intravenous gemcitabine 1.4 gm (day 1,8 & 15 of a 28-day cycle).

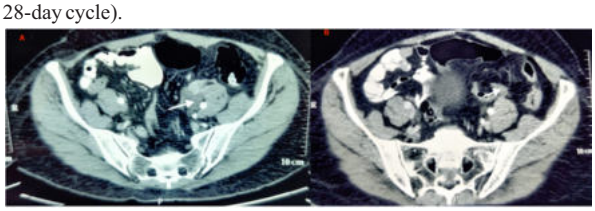

Figure 2: CECT Abdomen and pelvis (transverse section) showing Ill-defined lobulated lesion in left adnexa (A) along the left iliac vessels and (B) abutting the sigmoid colon and ilio-psoas muscle likely residual metastatic deposits.

Patient was disease-free post 3rd line chemotherapy with CA-125 levels having also within normal range (26.2 U/ML on last follow up). The patient is currently followed up in our outpatient clinic every 3 months; at the 14-month follow-up she remained asymptomatic.

Case B

Another 40-year-aged female, gravida 3, para 3, visited our OPD with complaining of painful, progressive distension of abdomen. CEMRI abdomen and pelvis revealed large (15.2 × 12.9 × 17.1 cm), solid cystic adnexal mass inseparable from both ovaries. Adnexal mass along with raised CA-125 level (832.9 U/ml) prompted the likely diagnosis of ovarian malignancy, and fine needle aspiration cytology confirmed as metastatic ovarian adenocarcinoma. As patient was inoperable, 6-cycles of neoadjuvant chemotherapy with 3-weekly paclitaxel and

carboplatin was given. Post chemotherapy CEMRI showed poor response in growth reduction and further 6-cycles of 2nd line chemotherapy with 4-weekly injection liposomal doxorubicin was given. Then patient underwent radical surgery (exploratory laparotomy with total abdominal hysterectomy and bilateral salpingo-oopherectomy and total omentectomy); histopathology of surgical specimen revealed low grade serous cystadenocarcinoma with omental & peritoneal deposits. Patient was advised for further 6-courses of adjuvant chemotherapy but patient denied and opted for 'drug-holiday'.

6-month after radical surgery, patient presented with complaining of headache, recurrent vomiting and dizziness. CECT brain revealed peripherally enhancing hypodense lesion (3.3 × 4.2 × 2.6 cm) in left cerebellum with perilesional edema indicating of brain metastasis. Neurosurgery opinion for metastatectomy was taken, but was not possible due to poor performance status. Patient was given palliative whole brain radiation 20 Gy in 5 fractions by Cobalt-60 teletherapy machine. Patient symptoms and general condition started to improved post radiation. Whole body PET CT scan [Figure 3 (A & B)] revealed disease both in brain (right cerebellum, 1.5. × 1.5 cm, SUVmax 8.1) and in primary site (left ovarian bed, 1.5 × 1.5 cm, SUVmax 3.2). Patient was given 6-courses of salvage chemotherapy with intravenous gemcitabine 1.4 gm day 1,8 & 15 of a 28-day cycle. Post chemotherapy follow-up scan revealed residual disease both in primary and metastatic sites. In view of good general condition, patient was offered further courses of chemotherapy, but unfortunately, she defaulted our follow-up.

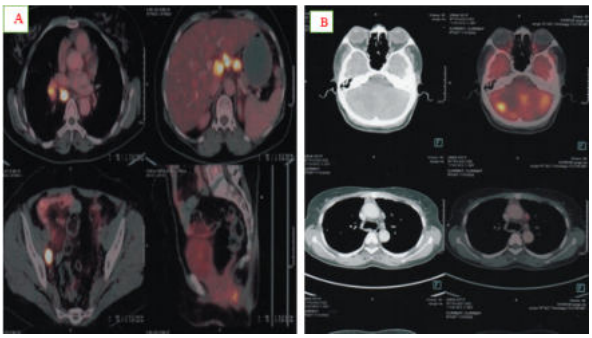

Figure 2: Whole body 18-FDG PET CT scan showing mass both in ovary and in brain for case (A) and (B)

DISCUSSION

Ovarian cancer is one of the leading causes of cancer related deaths in women. The majority of women with ovarian carcinoma have nonspecific abdominal and pelvic symptoms. Major half of ovarian carcinoma presented with metastatic disease, but it rarely extends outside the peritoneal cavity.[1] Central nervous system involvement or more precisely brain metastasis in ovarian carcinoma is very exceptional with an incidence of nearly 1%. [2] Brain metastases (BM) in ovarian carcinoma can present as initial symptoms, but mostly arise later in course of treatment. In a large retrospective review, only 5-cases of parenchymal brain metastasis were identified in 567-biopsy proven ovarian adenocarcinoma, accounting for an incidence of 0.9%.[3]

Among the differential diagnosis of brain metastases, one should keep in mind of second primary tumor in brain, abscess, cerebral infarction and hemorrhage; and obviously adverse effects of chemotherapy given for primary lesion.[4] Imaging can differentiate among these to some extent, biopsy is always confirmative.

Treatment for brain metastasis in these patients depends on several factors including primary treatment protocol, time of occurrence of brain metastasis, performance status of patient, modalities available and obviously patient's desire. Conservative management in terms of steroids, mannitol and anti-convulsants, if needed, should be started promptly without any hesitation.[5,6] Resectable metastatic lesion should be operated for curative as well as diagnostic benefit. However, in majority of cases surgery is not possible due to multiple lesions, poor general condition and involvement of critical structures. The next modality of treatment in such patients is radiation therapy (RT). Now-a-days, RT is must in brain metastasis patients irrespective of surgical status. Surgery combined with radiotherapy resulted in better outcomes compared with surgery or radiotherapy alone.[5,6,] Radiation therapy to brain can be given by different technique in different dose schedules. Although, application of SRS and SBRT are in increasing trends at present, still conventional whole brain radiation therapy (WBRT) is preferred in majority of centres.[7,8] Among different dose fractionation 30 Gy in 10 fractions, 37.5 Gy in 15 fractions and 20 Gy in 5 fractions are the well-practiced schedules.[9,10,11] WBRT in combination with surgery showed a more favourable median survival (23 months) than WBRT (5.33 months) or surgery (6.9 months) alone in brain metastasis patients.[12] Chemotherapy in such patients decided based on other sites of metastasis, burden of primary tumor, response to previous chemotherapy and available options. Anti-neoplastic drugs are chosen which have activity both in primary site (for ovarian adenocarcinoma) as well as in brain lesions. Platinum compounds (cisplatin and carboplatin) along with taxanes (paclitaxel), pegylated liposomal doxorubicin (PLD), topotecan, gemcitabine are the preferred drugs as they have good efficacy in ovarian adenocarcinoma and also cross blood-brain barrier (BBB) easily.[13]

Despite all modalities of treatment, brain metastasis patients have overall poor survival. Factors associated with bad prognosis are poor performance status, uncontrolled primary tumor, 4 or more brain metastases; and leptomeningeal disease, other sites of metastasis and response to primary chemotherapy.[14] Median survival of ovarian adenocarcinoma patients after developing brain metastasis was 8.2 months.[15]

In our cases, the first patient was in recursive partitioning analysis (RPA) class I, while the second patient was initially in RPA class III. According to literature, RPA class III has a poor median survival (2.3 months) compared to class I (7.1 months).[16] However, post WBRT, the general condition and symptoms both dramatically improved in the 2nd patient and thus also the chance of survival. This show the weight of WBRT to increase survival in brain metastasis patients. Our reports also demonstrate the importance of surgical excision of metastatic brain lesion as done in first patient. Removal of brain metastasis by surgery followed by adjuvant WBRT along with systemic chemotherapy to control primary disease helped to eradicated the disease burden completely in first patient. In the second case, despite installation of similar regimen systemic chemotherapy and near-same cumulative dose WBRT as in first case, inoperability of brain lesions does not suppress the disease burden both from metastatic and primary site.

CONCLUSION

A few survived patients of brain metastasis undergoing WBRT experienced radiation-induced dementia. Still the standard of care is WBRT in patients with numerous brain metastasis irrespective of primary site, whereas surgery and SRS are reserved for particular cases. Brain metastasis in ovarian carcinoma in comparatively rare and obviously worsen the prognosis in patients. Radiation therapy combined with systemic chemotherapy is the preferred approach described in literature. Selecting suitable therapy based on patient's condition & disease status is of utmost important and appropriate treatment can prolong survival in selective patients.

REFERENCES

1. Matulonis, U. A., Sood, A. K., Fallowfield, L., Howitt, B. E., Sehouli, J., & Karlan, B. Y. (2016). Ovarian cancer. Nature reviews. Disease primers, 2, 16061. https://doi.org/ 10.1038/nrdp.2016.61
2. Pectasides, D., Aravantinos, G., Fountzilas, G., Kalofonos, C., Efstathiou, E., Karina, M., ... & Dimopoulos, M. A. (2005). Brain metastases from epithelial ovarian cancer. The Hellenic Cooperative Oncology Group (HeCOG) experience and review of the literature. Anticancer research, 25(5), 3553-3558.
3. Mayer, R. J., Berkowitz, R. S., & Griffiths, C. T. (1978). Central nervous system involvement by ovarian carcinoma: a complication of prolonged survivial with metastatic disease. Cancer, 41(2), 776–783. https://doi.org/10.1002/1097-0142 (197802) 41:2<776::aid-cncr2820410253>3.0.co;2-e
4. Jin, J., Zhou, X., Liang, X., Huang, R., Chu, Z., Jiang, J., & Zhan, Q. (2011). A study of patients with brain metastases as the initial manifestation of their systemic cancer in a Chinese population. Journal of neuro-oncology, 103(3), 649–655. https://doi.org/ 10.1007/s11060-010-0440-1
5. Suh JH, Kotecha R, Ahluwalia MS, Vogelbaum MA. Metastatic cancer to the brain. In: DeVita VT Jr, Lawrence TS, Rosenberg SA, eds. DeVita, Hellman, and Rosenberg's Cancer: Principles & Practice of Oncology. 11th ed. Philadelphia: Wolters Kluwer, 2019, pp. 3394-414
6. Chhabra A, Mishra M, Patchell RA, Regine W, Kwok Y. Palliation of Brain and Spinal Cord Metastasis. In: Halperin EC, Wazer DE, Perez CA, Brady LW, editors. Perez and Brady's principles and practice of radiation oncology. 7th ed. Philadelphia: Wolter Kluwer; 2019, pp. 2134-47.
7. Achrol, A. S., Rennert, R. C., Anders, C., Soffietti, R., Ahluwalia, M. S., Nayak, L., Peters, S., Arvold, N. D., Harsh, G. R., Steeg, P. S., & Chang, S. D. (2019). Brain metastases. Nature reviews. Disease primers, 5(1), 5. https://doi.org/10.1038/s41572-018-0055-y

8. Barbour, A. B., Jacobs, C. D., Williamson, H., Floyd, S. R., Suneja, G., Torok, J. A., & Kirkpatrick, J. P. (2020). Radiation therapy practice patterns for brain metastases in the United States in the stereotactic radiosurgery era. Advances in radiation oncology, 5(1), 43-52.
9. Nieder, C., Berberich, W., & Schnabel, K. (1997). Tumor-related prognostic factors for remission of brain metastases after radiotherapy. International journal of radiation oncology, biology, physics, 39(1), 25–30. https://doi.org/10.1016/s0360-3016 (97) 00 154-5
10. Andrews, D. W., Scott, C. B., Sperduto, P. W., Flanders, A. E., Gaspar, L. E., Schell, M. C., Werner-Wasik, M., Demas, W., Ryu, J., Bahary, J. P., Souhami, L., Rotman, M., Mehta, M. P., & Curran, W. J., Jr (2004). Whole brain radiation therapy with or without stereotactic radiosurgery boost for patients with one to three brain metastases: phase III results of the RTOG 9508 randomised trial. Lancet (London, England), 363(9422), 1665–1672. https://doi.org/10.1016/S0140-6736(04)16250-8
11. Rades, D., Bohlen, G., Lohynska, R., Veninga, T., Stalpers, L. J., Schild, S. E., & Dunst, J. (2007). Whole-brain radiotherapy with 20 Gy in 5 fractions for brain metastases in patients with cancer of unknown primary (CUP). Strahlentherapie und Onkologie : Organ der Deutschen Rontgengesellschaft ... [et al], 183(11), 631–636. https://doi.org/ 10.1007/s00066-007-1763-5
12. Cohen, Z. R., Suki, D., Weinberg, J. S., Marmor, E., Lang, F. F., Gershenson, D. M., & Sawaya, R. (2004). Brain metastases in patients with ovarian carcinoma: prognostic factors and outcome. Journal of neuro-oncology, 66(3), 313–325. https://doi.org/ 10. 1023/b:neon.0000014516.04943.38
13. Wilson, M. K., Pujade-Lauraine, E., Aoki, D., Mirza, M. R., Lorusso, D., Oza, A. M., du Bois, A., Vergote, I., Reuss, A., Bacon, M., Friedlander, M., Gallardo-Rincon, D., Joly, F., Chang, S. J., Ferrero, A. M., Edmondson, R. J., Wimberger, P., Maenpaa, J., Gaffney, D., Zang, R., … participants of the Fifth Ovarian Cancer Consensus Conference (2017). Fifth Ovarian Cancer Consensus Conference of the Gynecologic Cancer InterGroup: recurrent disease. Annals of oncology : official journal of the European Society for Medical Oncology, 28(4), 727–732. https://doi.org/10.1093/annonc/mdw663
14. Wohl, A., Kimchi, G., Korach, J., Perri, T., Zach, L., Zibly, Z., Harel, R., Nissim, U., Spiegelmann, R., Nass, D., & Cohen, Z. R. (2019). Brain Metastases from Ovarian Carcinoma: An Evaluation of Prognostic Factors and Treatment. Neurology India, 67 (6), 1431–1436. https://doi.org/10.4103/0028-3886.273627
15. Pakneshan, S., Safarpour, D., Tavassoli, F., & Jabbari, B. (2014). Brain metastasis from ovarian cancer: a systematic review. Journal of neuro-oncology, 119(1), 1–6. https://doi.org/10.1007/s11060-014-1447-9
16. Gaspar, L., Scott, C., Rotman, M., Asbell, S., Phillips, T., Wasserman, T., McKenna, W. G., & Byhardt, R. (1997). Recursive partitioning analysis (RPA) of prognostic factors in three Radiation Therapy Oncology Group (RTOG) brain metastases trials. International journal of radiation oncology, biology, physics, 37(4), 745–751. https:// doi. org/ 10.101 6/s0360-3016(96)00619-0