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Simultaneous Intratumoral Hemorrhage in Multiple Brain Metastases of Endometrioid Carcinoma: A Rare Presentation of A Rare Metastasis

Endometrioid Karsinomanın Çoklu Beyin Metastazında Eşzamanlı Tümöriçi Kanama: Nadir Bir Metastazın Nadir Bir Bulgusu

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ABSTRACT

Metastasis of endometrioid carcinomas to the brain is rare, usually solitary, and has a poor prognosis. Intratumoral bleeding is also a poor prognostic factor for metastatic brain tumors but rarely occurs in gynecological cancers. A female patient who was under chemotherapy for endometrioid carcinoma was admitted to the emergency department for recent deterioration and seizures. She had confusion and left hemiparesis, along with an elevated systolic blood pressure and platelet count of 45,000 /mL. An emergent computerized tomography and subsequent magnetic resonance imaging revealed multiple hemorrhagic metastatic lesions in both hemispheres and cerebellum. Brain metastasis of endometrioid carcinoma is rare and can present with intratumoral hemorrhage, which is associated with a poor prognosis and is more likely to occur in the setting of low platelet counts. This case highlights the importance of monitoring brain metastasis in patients with endometrioid carcinoma and considering the possibility of intratumoral hemorrhage.
Keywords: Endometrioid carcinoma; brain metastasis; hemorrhage; thrombocytopenia.

ÖZ

Endometrioid karsinomanın beyin metastazı nadir, genellikle tekil ve kötü prognozludur. Tümör içi kanama da metastatik beyin tümörleri için kötü prognoz faktörü olmakla birlikte jinekolojik kanserlerde nadiren gerçekleşir. Endometrioid karsinoma nedeniyle kemoterapi tedavisi devam etmekte olan bir kadın hasta, bilinçte kötüleşme ve nöbet nedeniyle acil servise getirildi. Konfüzyon ve sol hemiparezi mevcut idi. Sistolik kan basıncı yüksek, trombosit sayısı ise 45.000 /mL idi. Acil bilgisayarlı tomografi ve takiben çekilen manyetik rezonans görüntülemede her iki hemisferde ve serebellumda multipl hemorajik metastatik lezyon saptandı. Endometrioid karsinomanın beyin metastazı nadirdir ve tümör içine kanama ile prezente olabilir -ki kötü prognozla ilişkilidir ve daha çok düşük trombosit sayısı durumunda ortaya çıkabilir. Bu vaka endometrioid karsinomalı hastaların beyin metastazı açısından takip edilmesinin ve böyle durumlarda tümör içi kanama olasılığının göz önüne alınmasının önemini vurgulamaktadır.
Anahtar kelimeler: Endometrioid karsinoma; beyin metastazları; hemoraji; trombositopeni.

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INTRODUCTION

Endometrioid carcinomas are the most common type of endometrial cancer, but they may also arise from ovaries. Regardless of origin, they have similar, though not identical, properties and behavior (1). They usually spread locally and distant metastases are rare and mostly involve the lung, liver, and bone (2,3). The metastasis

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of endometrioid cancer to the brain is extremely rare and has an incidence of 0.3-1.16% in endometrial type and 0.49-11.54% in ovarian type (4,5). These metastases are associated with a poor prognosis and tend to occur as solitary lesions (6-9).

Since these tumors are rare, our knowledge of these metastases is limited (10,11). This case report aimed to present an unusual case that admitted with simultaneous hemorrhage in multiple metastatic lesions.

CASE REPORT

A 64-year-old female patient with right abdomen pain was diagnosed with a right adnexial mass. A tru-cut biopsy revealed a low-grade endometroid carcinoma, but its origin organ could not be determined histopathologically. Since concurrent metastatic thorax lesions were detected neither a surgical treatment nor an endometrial sampling was performed to determine its origin. She was put into a chemotherapy regimen of 9 cycles. Apart from occasional delays due to hematological disturbances, the treatment continued as planned.

One and a half months after the 7th chemotherapy cycle, which was six months after the initial diagnosis, she had progressive deterioration for 3 days. After rapid worsening accompanied by 2 episodes of generalized tonic-clonic convulsions, she was admitted to the hospital by her relatives. Her Glasgow Coma Scale score was 10/15 (E3M5V2) and she had left hemiparesis. An emergent computed tomography (CT) scan revealed multiple foci of hyperdense lesions suggestive of metastatic hemorrhage (Figure 1). Magnetic resonance imaging (MRI) revealed multiple contrast-enhancing mass lesions in the left temporooccipital, right temporoparietal, right frontal, and right frontoparietal area, of which the right temporoparietal one was the largest with 46 mm diameter. The lesions compressed the right lateral and 3rd ventricles and caused a midline shift of 12 mm towards the left (Figure 2). Her platelet (PLT) count was 45000 /mL.

The first-degree relatives of the patient were informed about the poor prognosis regardless of surgical treatment and offered decompressive craniectomy for palliative purposes but they rejected it. In-depth history from relatives revealed that she was having an argument prior to deterioration and systolic blood pressure measured at the emergency department was higher than her baseline values. Conservative medical management was initiated in the intensive care unit, but the patient eventually deceased. Written informed consent for this study was obtained from a first-degree relative of the patient since the patient was not able to cooperate.

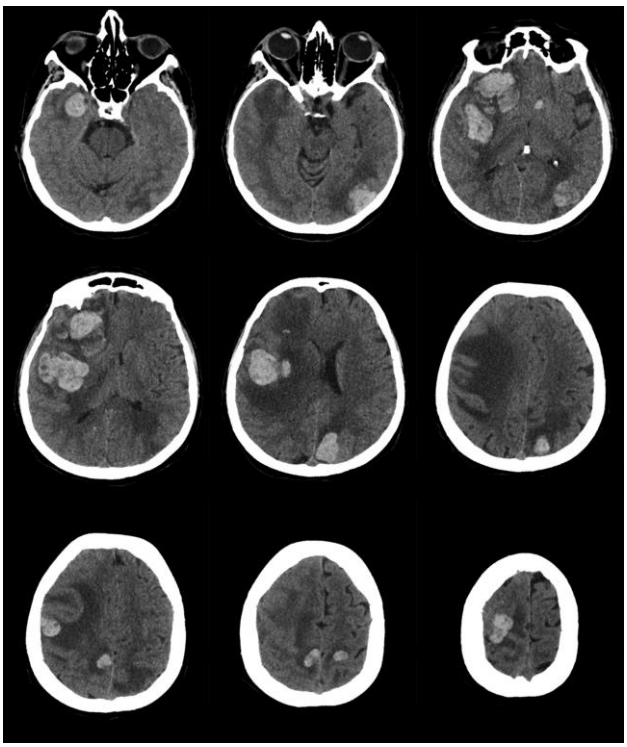

Figure 1. Axial CT scan shows significant hemorrhage and swelling in the frontal, temporal, and parietal lobes of the right hemisphere, with the largest lesion measuring 4x4.5 cm located in the parietal lobe. Additionally, smaller lesions with similar characteristics are observed in the left hemisphere, specifically in the parietal and occipital lobes as well as the left caudate nucleus. The edema causes partial effacement of the right lateral ventricle and a midline shift to the right by 12 mm.

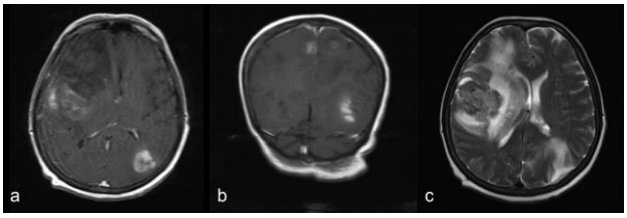

Figure 2. MRI images of the metastatic lesions are seen in **(a)** contrast-enhanced T1-weighted axial, and **(b)** coronal sequences. The extent of edema and midline shift is best visualized in **(c)** T2-weighted axial sequence.

DISCUSSION

The most frequently seen gynecological malignancies are endometrial and ovarian cancers (12). 70-80% of endometrial carcinomas and 10% of ovarian carcinomas are endometrioid carcinoma. They evolve from similar precursor cells and though they are not identical (as a result of different microenvironments), they have similar clinicopathological features (1).

Though brain metastasis is rare in endometrial and even rarer in ovarian endometrioid cancers, it is associated with poor prognosis (8). This may be due to the fact that most patients with brain metastasis are already in the advanced stages of the disease (10). Since this type of metastasis is rare, there is currently no standard treatment algorithm for brain metastasis, but treatment options include whole-brain radiotherapy, surgical resection, stereotactic radiotherapy, chemotherapy, and molecular targeting (9).

Since brain metastasis is rare, brain imaging is not typically included in routine follow-up. This type of metastasis is rarely diagnosed incidentally and patients often present with neurological symptoms depending on the location of the lesions (4,11). In our case, the patient had no neurological symptoms until intratumoral hemorrhage occurred.

Overall and gross intratumoral hemorrhage incidence in central nervous system tumors is 14.6% and 5.4% respectively. And these hemorrhages generally present in acute-on-chronic settings, rather than acute collapse (13). In a recent study, the incidence of intratumoral hemorrhage in metastatic brain tumors was 12.3% (14). Such hemorrhage is associated with poor prognosis in metastatic brain tumors and is more common in certain types of cancer such as melanoma, choriocarcinoma, thyroid carcinoma, hepatocellular carcinoma, and renal cell carcinoma (15,16). Hemorrhagic brain metastasis of endometrioid carcinoma, on the other hand, is rarely reported in the literature (17,18).

The exact mechanism behind intratumoral hemorrhage is not well understood, however, it is thought to be caused by a combination of factors such as endothelial proliferation with obliteration, vessel compression or distraction due to rapid tumor growth, and the abnormal characteristics of tumor vessels such as thin walls, poor development, and dilation, which contribute to the fragile structure of these vessels (13,19). Tumor invasion and necrosis can also lead to bleeding (20). Anticoagulation therapy is a known risk factor for intratumoral hemorrhage, while chronic hypertension is not (13,21). Additionally, Kondziolka et al. (13) reported thrombocytopenia (PLT <50000 /mL) in 4 out of 49 cases of macroscopic intratumoral hemorrhage. Although spontaneous hemorrhage is not typically expected unless the PLT count falls below 10000 /mL, the brittle nature of tumor vessels may predispose them to bleeding at a PLT count above 10000 /mL. In the case discussed, the bleeding was not restricted to a single lesion but occurred simultaneously in multiple lesions suggesting a global cause. It is possible that a temporary hypertensive period led to an increase in intracranial pressure, causing the rupture of fragile tumor vessels, and the bleeding was aggravated by improper hemostasis due to low PLT count. To the best of our knowledge, this case is among rare examples of hemorrhagic brain metastasis of endometrioid adenocarcinoma. Moreover, while previous cases had solitary lesions, this case had multiple metastatic lesions that bleed simultaneously.

CONCLUSION

Brain metastasis of endometrioid carcinoma is rare but should not be overlooked. Routine brain imaging should be considered to diagnose the disease at an early stage before multiple metastases occur. It is also important to note that the abnormal vasculature of metastatic brain tumors can make them prone to bleeding in thrombocytopenia, even at levels that would not typically result in spontaneous bleeding in healthy individuals.

Informed Consent: Written informed consent was obtained from a first-degree relative of the patient (since the patient was not able to cooperate) for publication and images.

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REFERENCES

1. McConechy MK, Ding J, Senz J, Yang W, Melnyk N, Tone AA, et al. Ovarian and endometrial endometrioid carcinomas have distinct CTNNB1 and PTEN mutation profiles. Mod Pathol. 2014;27(1):128-34.
2. Piura E, Piura B. Brain metastases from endometrial carcinoma. ISRN Oncol. 2012;2012:581749.
3. Bhambhvani HP, Zhou O, Cattle C, Taiwo R, Diver E, Hayden Gephart M. Brain metastases from endometrial cancer: clinical characteristics, outcomes, and review of the literature. World Neurosurg. 2021;147:e32-9.
4. Moroney MR, Wheeler LJ, Corr BR. Clinical presentation of brain metastases from endometrial carcinoma: A case series. Gynecol Oncol Rep. 2019;28:79-83.
5. Pakneshan S, Safarpour D, Tavassoli F, Jabbari B. Brain metastasis from ovarian cancer: a systematic review. J Neurooncol. 2014;119(1):1-6.
6. Gardner AB, Charo LM, Mann AK, Kapp DS, Eskander RN, Chan JK. Ovarian, uterine, and cervical cancer patients with distant metastases at diagnosis: most common locations and outcomes. Clin Exp Metastasis. 2020;37(1):107-13.
7. Zhang Y, Grant MS, Stepp WH, Clark LH. Clinical characteristics of CNS metastases from primary gynecologic cancers. Gynecol Oncol Rep. 2019;30:100518.
8. Karpathiou G, Camy F, Chauleur C, Dridi M, Dal Col P, Peoc'h M. Brain metastases from gynecologic malignancies. Medicina (Kaunas). 2022;58(4):548.
9. Wang Q, Zhang F, Gao H, Xu Y. Successful treatment of a patient with brain metastases from endometrial cancer using Niraparib: a case report. Ann Palliat Med. 2021;10(1):818-27.
10. Gien LT, Kwon JS, D'Souza DP, Radwan JS, Hammond JA, Sugimoto AK, et al. Brain metastases from endometrial carcinoma: a retrospective study. Gynecol Oncol. 2004;93(2):524-8.
11. Uccella S, Morris JM, Multinu F, Cliby WA, Podratz KC, Gostout BS, et al. Primary brain metastases of endometrial cancer: A report of 18 cases and review of the literature. Gynecol Oncol. 2016;142(1):70-5.
12. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA Cancer J Clin. 2020;70(1):7-30.
13. Kondziolka D, Bernstein M, Resch L, Tator CH, Fleming JFR, Vanderlinden RG, et al. Significance of hemorrhage into brain tumors: Clinicopathological study. J Neurosurg. 1987;67(6):852-7.
14. Ulu E, Ozturk B, Atalay K, Okumus IB, Erdem D, Gul MK, et al. Diffusion-weighted imaging of brain metastasis: correlation of MRI parameters with histologic type. Turk Neurosurg. 2022;32(1):58-68.

15. Hamed M, Schäfer N, Bode C, Borger V, Potthoff AL, Eichhorn L, et al. Preoperative metastatic brain tumor-associated intracerebral hemorrhage is associated with dismal prognosis. Front Oncol. 2021;11:699860.
16. Burth S, Ohmann M, Kronsteiner D, Kieser M, Löw S, Riedemann L, et al. Prophylactic anticoagulation in patients with glioblastoma or brain metastases and atrial fibrillation: an increased risk for intracranial hemorrhage? J Neurooncol. 2021;152(3):483-90.
17. Lieschke GJ, Tress B, Chambers D. Endometrial adenocarcinoma presenting as pituitary apoplexy. Aust N Z J Med. 1990;20(1):81-4.
18. Vijayakumar V, Rajasundaram S, Prasad PVU, Vimalathithan NS, Saravanan S, Venkatesan R. Brain oligometastasis from synchronous uterine malignancies. Indian J Surg Oncol. 2020;11(Suppl 1):87-9.
19. Guyon J, Chapouly C, Andrique L, Bikfalvi A, Daubon T. The normal and brain tumor vasculature: morphological and functional characteristics and therapeutic targeting. Front Physiol. 2021;12:622615.
20. Hottinger AF, DeAngelis LM. Etiology of tumor-related intracranial hemorrhage. In: Carhuapoma JR, Mayer SA, Hanley DF, editors. Intracerebral Hemorrhage. New York, USA: Cambridge University Press; 2009. p.31-40.
21. Ostrowski RP, He Z, Pucko EB, Matyja E. Hemorrhage in brain tumor - An unresolved issue. Brain Hemorrhages. 2022;3(2):98-102.