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Role of Radiotherapy in Gestational Trophoblastic Neoplasia: A Case Report

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Abstract

Gestational trophoblastic neoplasia (GTN) is a placental tissues malignancy that is prone to massive bleeding. Multimodality treatment is often needed to treat GTN, such as surgery and radiotherapy. Radiotherapy has a palliative role in case of hemorrhage and/or intracranial metastases.

Radiotherapy is effective in controlling bleeding by destructing malignant blood vessels by inducing endothelial damage and increasing signal transduction pathway leading to apoptosis and increasing adhesion of thrombocytes to vascular endothelia resulting fibrosis. No dose and fractionation schemes are proven more effective than others, but longer fractions scheme (>5 fractions) and BED10 > 39 Gy show no additional benefit in hemostatic control or in reduction of re-bleeding rate.

Brain metastatic lesions are prone to bleeding that might need craniotomy for blood evacuation or brain decompression. WBRT can be given concurrently with chemotherapy in brain metastatic GTN cases. Higher WBRT total dose (>22 Gy) is associated with higher 5-year local control rates.

Keywords: gestational trophoblastic neoplasia, radiotherapy, hemostatic radiation, whole brain radiotherapy

Introduction

Gestational trophoblastic neoplasia (GTN) is a malignancy that arise from placental tissues and prone to massive bleeding that could lead to hemorrhagic shock or even death. Although the main treatment of GTN is chemotherapy, multimodality treatment is often needed, such as surgery and radiotherapy.[1]

This study aims to emphasize the role of radiotherapy in GTN cases. In this study, the mechanisms of hemostatic radiotherapy to control bleeding as well as the association of different fractions schemes and BED_{10} in resolving bleeding or in reduction of re-bleeding rate will be evaluated. The effect of aiding WBRT in the treatment of brain metastases GTN and how the total dose affects local control are also reviewed.

Case Report

A 24-year-old woman presenting with vaginal bleeding and a vaginal mass (Image 1a). Patient had a history of delivering a 2,200-gram stillbirth baby 5 months before. Ultrasound 2 weeks before delivery showed gestational age of 33 weeks. After delivery, patient experienced heavy bleeding and underwent curettage 1 day after delivery. The bleeding remained though with a much smaller volume.

Serum β hCG level was found significantly increased with 297,330.8 mIU/mL and serum hemoglobin (Hb) was 8.9 g/dL. After transfusion, Hb remained low (6.7 g/dL). Abdominal ultrasound showed an enlarged uterus with a hypo-hyperechoic mass invading uterus with positive hypervascularization with uterine size of

9.0 x 12.8 x 11.9 cm. Thorax Xray shows multiple nodular opacity and infiltrates in bilateral lung. The patient was then diagnosed with stage III GTN and classified as high-risk GTN with prognostic score 9.

Patient then underwent total hysterectomy, bilateral salpingectomy, hypogastric artery ligation and vaginal mass biopsy. Histological findings were choriocarcinoma with a lymph and vascular invasion. Vaginal mass biopsy also showed similar tumor characteristics.

Patient treated with EMA/CO regimen chemotherapy 1 week after surgery. 3 days after starting chemotherapy, patient complained massive vaginal bleeding from the vaginal mass that was not controlled with medications and compression bandages. Vital sign remained within normal limit with serum Hb 4.4 g/dL. Hemostatic radiotherapy was then indicated with 2-dimensional (2D) technique from 2 beams (Anterior-Posterior and Posterior-Anterior) with dose 15 Gy in 3 fractions with 10-MV photon.

After 3 fractions, patient no longer complained any bleeding and the vaginal mass also appeared smaller with the size of 2.5 x 3 x 2 cm (Image 1b). Serum β hCG afer 1 cycle of EMA/CO decrease significantly to 306.75 mIU/mL. After 6 cycles of chemotherapy, vaginal mass was no longer can be seen or palpated. Serum hCG was 7.79 mIU/mL.

Discussion

Radiotherapy has a palliative role in case of hemorrhage and/or intracranial metastases.

Hemostatic radiotherapy

Both primary and metastatic GTN tumor are hyper vascular and prone to massive bleeding. Bleeding is treated initially with medications and compression dressings. Laparotomy, hysterectomy, vessel ligation or embolization can be indicated in case of uncontrolled bleeding.

Hemostatic radiation provides less preparation than other operative measures. Radiation can destruct malignant blood vessels by inducing endothelial damage and increasing signal transduction pathway leading to apoptosis.[2] Radiation causes increased adhesion of thrombocytes to vascular endothelia resulting fibrosis. Radiation might cause damage on vessels intima causing capillary necrosis and formation of thrombus that blocks lumen and lead to hemostasis.[3]

Radiation therapy can control bleeding within 24 – 48 hours after first radiation dose.[4] Patient should also be in a hemodynamically stable condition to be transported to radiotherapy department and should maintain stable during the positioning, immobilization, and treatment process.

Radiation is given local to the bleeding tumor usually with simpler techniques (mostly in 2D or 3D technique) considering this treatment is given in an emergency setting. Dose and fractionation scheme for hemostatic radiation is widely varied, commonly in a single fraction of 8 – 10 Gy, shorter fractions scheme (3 – 5 fractions with 4 – 8 Gy/fraction), or with longer fractions scheme (30 – 45 Gy in 10 – 15 fractions). No dose and fractionation scheme are proven more effective than others.[5]

Longer fractions scheme (>5 fractions) and $BED_{10} > 39$ Gy show no additional benefit in hemostatic control or in reduction of re-bleeding rate.[6] Longer fractions scheme is also associated with higher interruption frequencies and longer hospital stay.

Intracranial Palliation Radiotherapy

Brain metastasis is associated with poorer outcomes

Figure 1. Vaginal mass appeared smaller afer systemic chemotherapy and radiotherapy. a) Vaginal mass before therapy with the size of 5 x 6 x 4 cm b)Vaginal mass afrer 3 fractions of radiotherapy.

than lung or vaginal metastasis. Survival rate of patients who have brain metastasis before treatment is 75%, much higher than the survival of patients with new brain metastasis recurrence after therapy (38%) and patients with brain metastasis that develop while on treatment (0%).[7]

Multimodality treatment is usually needed in GTN brain metastasis cases since the lesions are prone to bleeding that might need craniotomy for blood evacuation or brain decompression.[8] Intrathecal methotrexate 12.5 mg or higher IV methotrexate dose (1g/m^2) may be given concurrently with whole brain radiation therapy (WBRT).[7] WBRT has both tumoricidal effect and hemostatic effect for potential bleeding lesions.

The recommended dose for WBRT is 20 – 40 Gy in 10 – 20 fractions given concurrently with chemotherapy, with consideration of booster at certain lesions in selected cases.[7] WBRT total dose is associated with local control as patients treated with <22 Gy have a lower 5-year local control rates (24%) compared to patients treated with total dose 22 – 36 Gy with 91% 5-year local control rates.[7]

The result of combination radiotherapy and chemotherapy on treating GTN brain metastasis remains controversial. One study shows that systemic chemotherapy combined with WBRT lead to lower survival rate (75%) compared to systemic chemotherapy combined with intrathecal methotrexate (71.5 – 85%).[9] On the contrary, another study shows that only 24% patients treated with systemic chemotherapy alone survived whereas 50% of 18 patients treated with combination of systemic chemotherapy and WBRT survived.[8]

Conclusion

Radiotherapy has a palliative role in case of hemorrhage and/or intracranial metastases. Although no dose and fractionation schemes are deemed more effective than others, longer fractionation scheme is associated with higher interruption frequencies and longer hospital stay with no additional benefit in controlling bleeding and reducing re-bleeding rate.

WBRT can be given concurrently with chemotherapy in brain metastatic GTN cases. Higher total dose is associated with higher 5-year local control rates.

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