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Gestational trophoblastic neoplasia with cardiac metastasis and multiple embolic manifestations: A rare case report

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ABSTRACT

Gestational trophoblastic neoplasia (GTN) is a highly treatable malignancy with cure rates of approximately 100% in low-risk and 90% in high-risk cases. This report details an 18-year-old primigravida diagnosed with high-risk GTN after preterm intrauterine death, presenting with significant vaginal bleeding and an elevated beta-human chorionic gonadotropin level exceeding 300,000 mIU/mL. Imaging revealed a large uterine mass with myometrial invasion and pulmonary metastasis. With a World Health Organization risk score of 8, the patient experienced severe embolic complications, including transient ischemic attacks and infarcts. Treatment involved multi-agent chemotherapy, anticoagulants, and antibiotics, which led to complete regression of the cardiac mass and remission after four cycles. This case highlights the challenges in the risk stratification and management of GTN with unusual metastatic sites, such as the heart. The independent high-risk factor of tumor age, highest in GTN following term pregnancy, may explain the propensity for unusual metastatic sites and poorer prognostic importance of timely diagnosis and treatment for optimal outcomes.

Key words: Gestational trophoblastic neoplasia; Cardiac metastasis; Embolic manifestations

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INTRODUCTION

Gestational trophoblastic neoplasia (GTN) is a spectrum of diseases with a high potential for lung and brain metastasis. Hence, chest radiography (CXR) is routinely included in the metastatic workup of GTN, and magnetic resonance imaging (MRI) of the brain with contrast is indicated whenever beta-human chorionic gonadotropin (hCG) values exceed 1,00,000 mIU/mL.[1,2] For those with high-risk disease with World Health Organization (WHO) risk scores >12, due to the risk of visceral hemorrhage, it is recommended to start with low-dose induction with electrophysiology (EP) (etoposide 100 mg/m^2/day intravenous and Cisplatin 20 mg/m^2/day on days 1 and 2, every 7 days) for the initial 1–3 cycles followed by multi-agent chemotherapy. However, much less guidance is available on the risk stratification, scoring, and management of GTN with metastasis to other visceral sites. Here, we report a rare case of successful treatment.

CASE REPORT

An 18-year-old primigravida with normal antenatal visits presented with reduced fetal movements for 4 days at 33 weeks of gestation. Examination and ultrasound could not demonstrate a fetal heartbeat, and a preterm intrauterine death (IUD) was delivered via lower segment cesarean section (LSCS).

Four months after LSCS, she presented with persistent vaginal bleeding and an elevated beta hCG level of

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>3,00,000 mIU/mL. Ultrasonography showed a large echogenic mass in the uterine cavity of size 5.4×7.2 cm with high vascularity. MRI confirmed a well-defined mass in the uterine cavity with junctional effacement, which was suggestive of myometrial invasion (Figure 1). Her thyroid-stimulating hormone level was suppressed, electrocardiogram showed sinus tachycardia, and she was administered beta-blockers for cardioprotection.

A staging workup was performed to diagnose the GTN. CXR showed four pulmonary metastases, each approximately 1 cm in size. MRI brain was normal. Her WHO score was 8, and she was initiated on multi-agent chemotherapy with EMA-CO.

Upon initiation of cycle 1 of EMA-CO, she suffered multiple embolic complications cascading one after the other, posterior circulation TIA on C1D8 and multifocal pure motor cortical infarcts involving the motor homunculus on the left side C1D13 (Figure 2).

A search for the origin of the emboli unravelled a 2.2×1.1 cm mass attached to the pulmonary veins on echocardiography. Anticoagulants and empirical antibiotics were initiated, and chemotherapy was continued. With ongoing chemotherapy, the size of the mass progressively decreased. On C2D14, she presented with right lower-limb vascular claudication, which was proven to be due to embolic etiology on computed tomography (CT) angiography.

CT angiography of the bilateral lower limbs showed no contrast opacification before bifurcation of the popliteal artery for a length of 1 cm; thin flow of contrast in the right anterior tibial artery, posterior tibial artery, and peroneal artery; complete occlusion noted distally; and ill-defined hypodensity in the middle pole of the right kidney with no contrast enhancement possibly an infarct (Figure 3).

In cycle three, the cardiac mass regressed completely. She recovered without any deficits, and her beta-hCG level continued to fall and normalize with four cycles

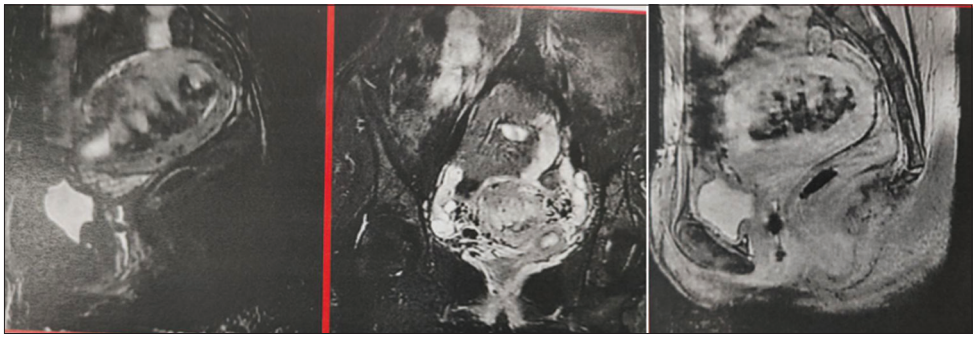

Figure 1: Magnetic resonance imaging of the pelvis showing uterine mass with junctional zone effacement

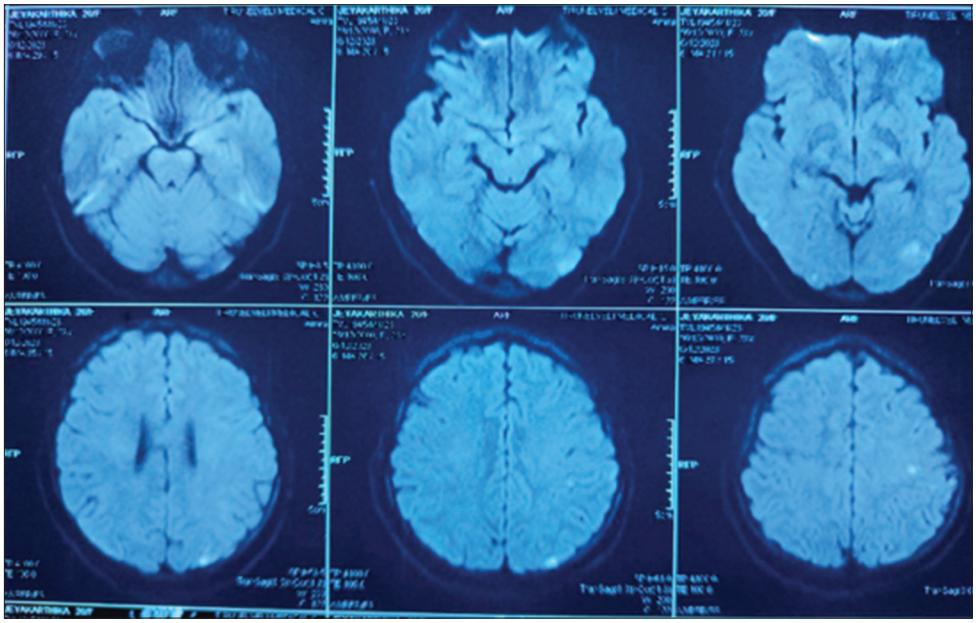

Figure 2: Magnetic resonance imaging of the brain showing multifocal cortical infarcts suggestive of embolic aetiology

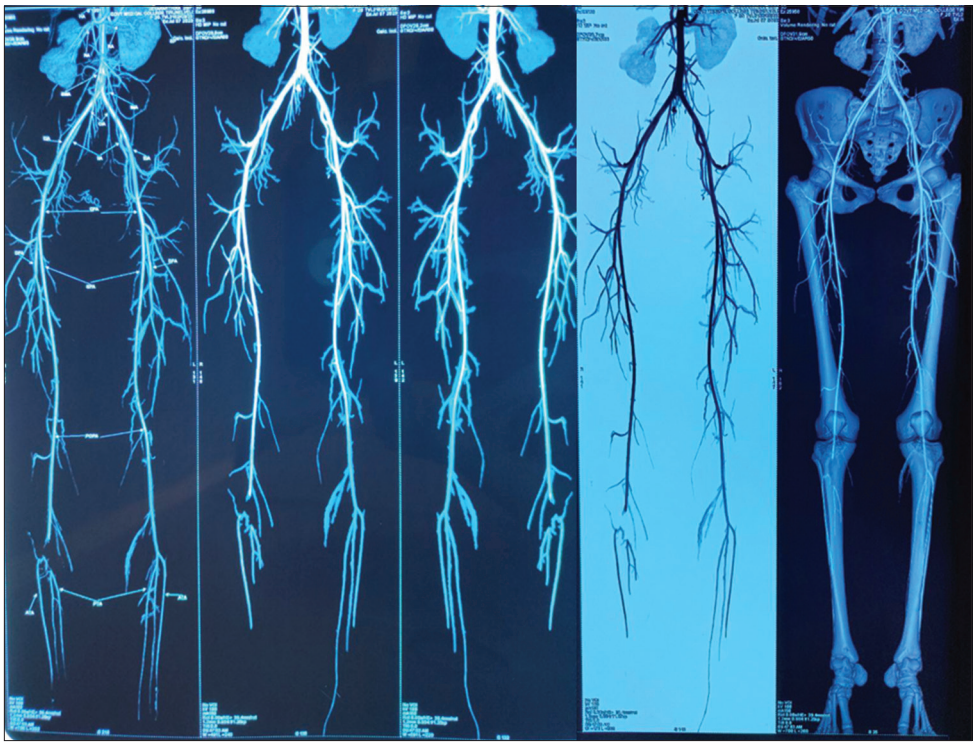

Figure 3: Embolic aetiology by computed tomography angiography

of EMA-CO (Table 1). Three consolidation cycles were administered. She is currently disease-free and is regularly followed up.

DISCUSSION

This case report raises many concerns encountered in the everyday clinical management of GTN, such as how to score GTN when antecedent pregnancy is unknown or falls in between, how to score with visceral metastasis other than those mentioned in the scoring, and how to deal with cardiac metastasis and embolic complications. The WHO risk stratification scores were 0 for antecedent molar pregnancy, 1 for abortion, and 2 for GTN following-term pregnancy. However, the scoring strategy for preterm IUDs that have crossed the period of viability and hence could not be labeled as abortion and in situations where the antecedent pregnancy could not be ascertained beyond doubt is unclear.

Bagshawe et al., a pioneer in GTDs in 1976, developed a framework based on the WHO risk scoring. In his original work, on a case series of 317 patients of Charing Cross Hospital, he concluded that in situations where naked eye changes of hydatiform mole or histopathological confirmation of molar changes could not be documented, or the antecedent pregnancy could not be confirmed, or in a few occasions where the patients had no antecedent pregnancy, to be labeled as "non-molar abortion" for risk

Table 1: Trends of beta hCG

	BETA hCG in IU/mL
Pre C1	>3,00,000
Pre C2	3628
Pre C3	60.41
Pre C4	12.05
Pre C5	3.89
Pre C6	2.92
Pre C7	1.12

stratification.[3] This scenario of an unknown antecedent pregnancy decreases the accuracy of another parameter in risk scoring of the GTN interval from the antecedent pregnancy. There is a significant underestimation of the interval from the antecedent pregnancy in these scenarios, and it is significantly high when the antecedent pregnancy is a term delivery.[3]

Visceral metastasis

GTNs frequently metastasize to the lungs, liver, spleen, genitourinary tract, and brain, based on which a modified WHO scoring system has been formulated. However, few occasional case reports of unusual sites of metastasis have been documented in the literature. GTN with cardiac metastasis has been documented only a handful of times in the literature. Table 2 shows the list of previously reported cases.[5-13]

This collection of cases of GTN with cardiac metastasis puts forth many propositions that are to be addressed: (1)

Table 2: List of other reported cases of gestational trophoblastic neoplasia with cardiac metastasis

Author	Age	Last gestation	GTD history	Localisation in heart	Surgical treatment	Medical treatment	Outcome
Kishore *et al.*[4]	27	NA	NA	LA - septum	Excision of LA tumor	Adriamycin+Mtx	Expired
Wen xu *et al.*[5]	33	Term	NA	LA – Left lower & middle PV	Biopsy from scalp	EMA – CO x 6; EMA – EP x 2	Expired
Mac Lowry *et al.*[6]	28	Term	+ (molar pregnancy – 5 years ago)	LA	Craniotomy	Mtx	Expired
Seigle *et al.*[7]	28	Term	NA	LV	NA	NA	Expired
Perroni *et al.*[8]	22	Term	NA	RV	Excision of RV mass	EMA – CO x 12+IT Mtx	Remission
Bohlmann *et al.*[9]	41	Term	NA	LA – Right inferior PV	LA mass excision	EMA – CO x 9	Remission
Bozaci *et al.*[10]	53	Abortion	NA	RV	-	EMA – CO x 2; EMA – EP x 5	Remission
Vasiljevic *et al.*[11]	26	Term	Choriocarcinoma	Ischemic heart disease	NA	Mtx & act - D	Expired
Akaike *et al.*[12]	28	Mole	+	LV	NA	Mtx, act D, VBL	Expired
Yahua Li *et al.*[13]	36	Term	NA	LA - PV	Biopsy of chest tumor	NA	NA
Present case	18	Non molar abortion	NA	LA - PV	NA	EMA – CO x 7	Remission at 5 months

most of these cases have occurred after term pregnancy or after non-molar abortion, (2) the immediate antecedent pregnancy being a mole is not observed in any of these cases, (3) most of these cases harbored cardiac secondaries in the left atrium, and (4) the excellent cure with multi-agent chemotherapy-EMA-CO and EMA-EP.

The independent high-risk factor, tumor age, as described by Kim et al., explains the unusual metastatic sites and, hence, the poorer prognosis of GTNs following term pregnancy. In his study, he described four independent worst prognostic factors: (1) tumor age >12 months, (2) the number of metastatic sites, (3) metastatic sites other than the lung and vagina, and (4) previously failed chemotherapy, of which tumor age had the highest risk.[14] Bagshawe et al., also described the significance of the age of the tumor (time from antecedent pregnancy to initiation of chemotherapy) as those tumors with the lowest tumor age have survival rates near 100%, and those tumors with the highest tumor age have fatality rates nearing 100%.[15] Tumor age is highest for term pregnancy; lowest for molar gestation. Hence, they are associated with unusual metastatic sites and poor prognosis with term gestation.

Cardiac metastasis of the GTN is often localized to the LA. It is hypothesized to be due to the high propensity of these tumors to reach the lung four and their subsequent spread through the pulmonary veins (non-pulsatile, continuous, low-gradient flow) to reach the LA. With chemotherapy, the tumor tissue from the LA embolizes into the systemic circulation, leading to ischemic events. Ischemic symptoms resolve at a much faster pace than expected for a general thrombotic event. The early resolution of these ischemic symptoms might be explained by the non-viability of the embolized tumor and the continuing multi-agent chemotherapy.

Multi-agent chemotherapy for GTN with EMA-CO is highly effective, as shown by Newlands et al., with an overall survival rate of around 85%, a conversion rate of around 80%, and a very low relapse rate of 5.4% following EMA-CO.[16] Salvage rates remained high in such patients with the addition of a platinum agent to the regimen. Kishore et al. also proposed that the poorer prognosis associated with cardiac metastasis might be because of accelerated tumor spread due to surgical manipulation.[4] The use of chemotherapy alone warrants better survival in these cases, and hence, in reproductive-age women who present with cardiac mass, it might be better to consider the possibility of GTN metastasis in the differential diagnosis and to consider analyzing beta hCG to aid in the timely diagnosis of GTN, a potentially curable malignancy, without causing much morbidity.

CONCLUSION

GTN is one of the oldest known malignancies that has undergone rapid changes in survival outcomes, from being universally fatal to being 95% curable. However, there are challenges to overcome in achieving a cure rate of 100%. Hence, more detailed knowledge of the intricate aspects of this disease may aid in achieving it, along with the preservation of reproductive potential.

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