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Case Report

A Rare Gestational Trophoblastic Disease with Lung Metastases: A Case Report and Literature Review

Okello Malcom Mark[1,2]*, Musoke Sharrif[1], Alele David[1], Mawanda Anatoli[1,2,3,4], Omega Phillip[1,2,6], Boaz Mwesigwa[1,4,5], Tonny Okecha[2,3], Nassolo Sheila[7], Nakiyingi Lydia[7], Lukande Robert[2] and Kalungi Sam[1,2]

[1]*Department of Pathology, Mulago National Referral Hospital, Uganda*

[2]*Department of Pathology, Makerere University, Uganda*

[3]*Department of Pathology, Uganda Cancer Institute, Uganda*

[4]*Department of Pathology, King Ceasor University, Uganda*

[5]*Department of Biomedical Laboratory Technology and Molecular Biology, Makerere University, Uganda*

[6]*Department of Pathology, St. Mary's Hospital Lacor, Uganda*

[7]*Department of Internal Medicine, Makerere University, Uganda*

***Corresponding Author:** Okello Malcom Mark, Department of Pathology, Makerere University, Uganda.
Email: okellomalcom@gmail.com

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Abstract

We present a postmortem case report of a 42-year-old female, who passed away 3 days post-admission following severe respiratory distress. She was 4 months postpartum after an emergency cesarean section due to fetal distress and had a 3-week history of difficulty in breathing, associated with dyspnea, hemoptysis, pleuritic chest pain, orthopnea, palpitations, and dizziness. On examination, she presented with severe respiratory distress, pallor, tachycardia, and coarse bilateral crepitations on auscultation. A working diagnosis of gestational trophoblastic disease (GTD) with lung metastases complicated by Anemia was made. Differential diagnoses included pulmonary tuberculosis, pulmonary embolism, bacterial pneumonia, congestive heart failure, and antiphospholipid syndrome. Despite treatment with oxygen therapy and antibiotics, the patient deteriorated and was declared dead following unsuccessful cardiopulmonary resuscitation. Postmortem histopathological examination confirmed a diagnosis of placental site trophoblastic tumor (PSTT) with metastases to the lungs and liver. This case highlights the diagnostic challenge posed by GTD in resource limited setting such as Uganda, and clinicians must always have suspicion in such present with lung metastases and emphasizes the importance of early recognition and management.

Keywords: *Placental Site Trophoblastic Tumor; Postmortem Diagnosis; Lung Metastases; Gestational Trophoblastic Disease; Postpartum Complications*

Introduction

Gestational trophoblastic disease (GTD) encompasses a spectrum of disorders arising from abnormal trophoblastic tissue following pregnancy [1]. While most cases of GTD are benign, certain types, such as Placental Site Trophoblastic Tumor (PSTT), can present with malignant potential and metastasize to distant organs, including the lungs [2]. Lung metastases can be asymptomatic or may present with symptoms such as coughing up blood (hemoptysis), shortness of breath (dyspnea), chest pain, or increased pressure in the pulmonary

arteries, leading to pulmonary hypertension [3]. This case report discusses the clinical presentation, diagnostic challenges, and postmortem findings in a 42-year-old female who developed severe respiratory failure due to GTD with lung metastases.

Case Report

A 42-year-old female presented to the emergency unit of Mulago National Referral Hospital with a three-week history of progressively worsening shortness of breath, hemoptysis, and right-sided pleuritic chest pain. She was four months post delivery following an emergency cesarean section due to fetal distress. Additional symptoms included orthopnea, palpitations, dizziness, low-grade fever, drenching night sweats, and mild weight loss. She denied experiencing lower limb swelling, paroxysmal nocturnal dyspnea, or urinary symptoms. Her medical history revealed no known chronic illnesses, allergies, trauma, or prior blood transfusions. She was a para 6+1, with history of one abortion at two months of gestation. The other pregnancies resulted in spontaneous vertex deliveries without complications.

On examination, she was conscious but in severe respiratory distress, using accessory muscles to breathe. She was tachypneic (30 breaths/min), tachycardic (125 bpm), and hypotensive (102/48 mmHg). Respiratory examination revealed bilateral coarse crepitations across all lung fields. Cardiovascular, abdominal, and neurological examinations were unremarkable, except for a sub-umbilical midline incision scar from her recent cesarean section.

Initial investigations included a complete blood count, which showed moderate microcytic hypochromic anemia (hemoglobin 7.2 g/dL) and leukocytosis (24.11 x 10^3/µL) with neutrophil predominance (88.5%). A chest X-ray revealed multiple large, round opacities consistent with cannonball metastases. Based on these findings, a working diagnosis of gestational trophoblastic disease (GTD) with lung metastases was made. Differential diagnoses included pulmonary embolism, tuberculosis, bacterial pneumonia, and heart failure.

Due to resource constraints, advanced imaging studies such as chest and abdominal computed tomography (CT) and computed tomography pulmonary angiography (CTPA) were not performed. The patient started on intravenous dexamethasone (16 mg/day), paracetamol (1g every 8 hours), oral morphine (5 mg every 4 hours), and oxygen therapy targeting saturations above 92%. On the second day, intravenous antibiotics (piperacillin/tazobactam 4.5g every 8 hours and metronidazole 500 mg every 8 hours) and intravenous fluids (2.5 liters of normal saline over 24 hours) were added. Despite these interventions, her condition rapidly deteriorated, and she succumbed to cardiopulmonary arrest on the third day.

The gross examination of the uterus during autopsy showed a hemorrhagic necrotic friable tumor mass in the uterine cavity with invasion into the myometrium as shown in figure 1 and 2. Examination of the lungs during autopsy revealed multiple hemorrhagic and necrotic tumor nodules as shown in figure 3 consistent with metastatic lesions. Histopathological analysis of the lung tissue showed atypical, bizarre epithelioid cells with a mixed population of clear and eosinophilic cytoplasm, indicative of metastatic trophoblastic disease as shown in figure 4. A similar tumor nodule was identified beneath the liver capsule. Histologic examination of the uterus revealed infiltration of the myometrium by atypical hyperchromatic intermediate trophoblasts without chorionic villi shown in figure 5, consistent with a diagnosis of placental site trophoblastic tumor (PSTT). Immunohistochemistry demonstrated a high Ki-67 proliferation index (70%) (Figure 9), with negative p63 (Figure 6), inhibin (Figure 7), and TTF-1 (Figure 8), confirming the diagnosis of PSTT.

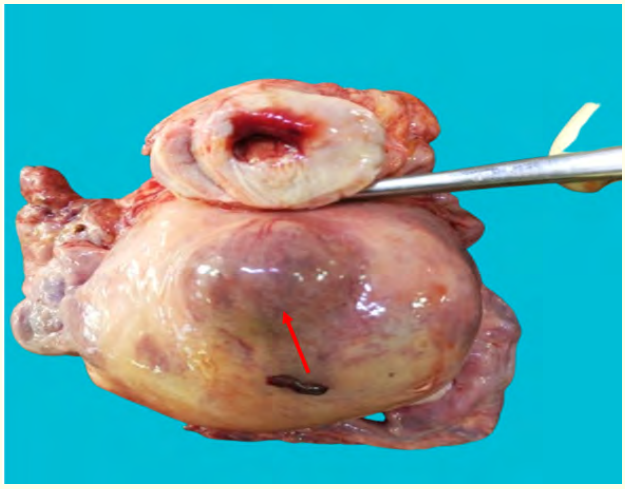

Figure 1: *Gross appearance of uterus at autopsy.*

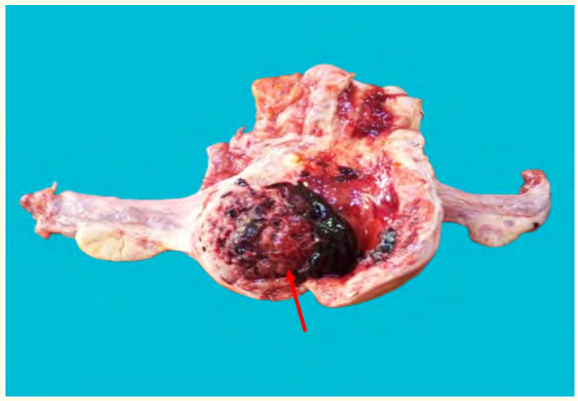

Figure 2: *Tumor bulging through the myometrium but no perforation.*

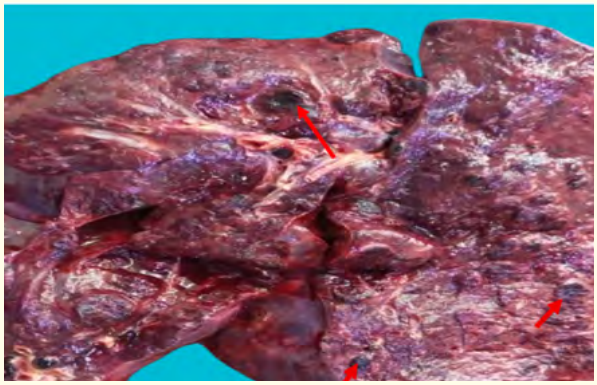

Figure 3: *Tumor nodules on the cut surfaces of the lung (red arrows).*

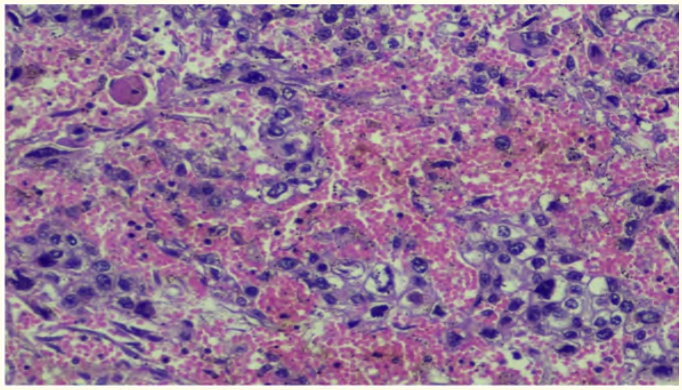

Figure 4: *Photomicrograph of the lungs (H&E X400).*

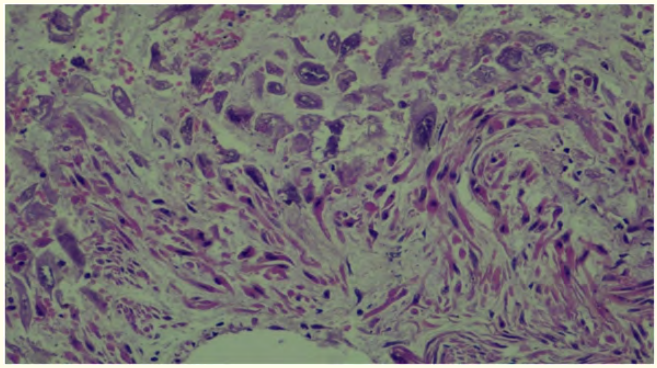

Figure 5: *Photomicrograph of the uterus (H&E X400).*

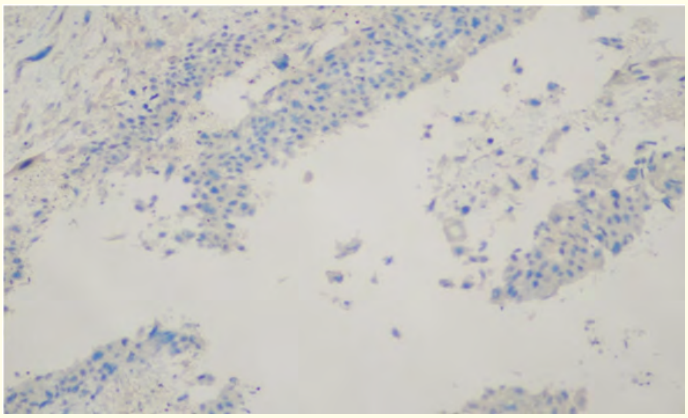

Figure 6: *p63 Immunostaining of lung tumor (IHC P63 X200).*

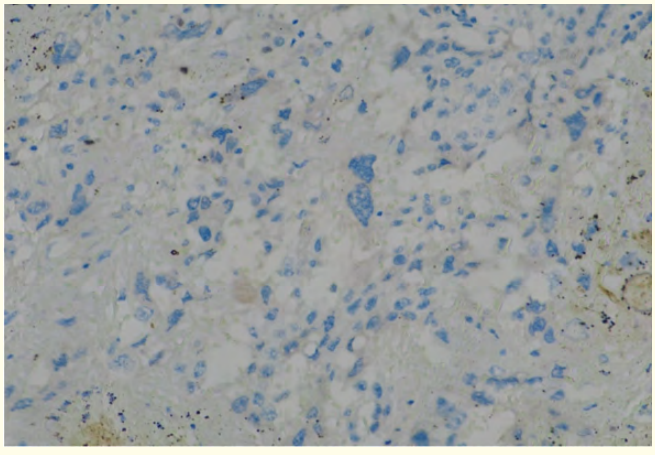

Figure 7: *Immunostaining of uterine tumor (IHC Inhibin X200).*

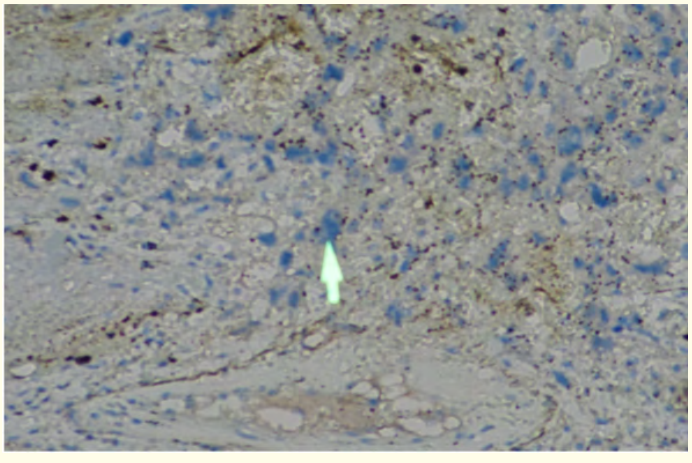

Figure 8: *TTF 1 Immunostaining of lung (IHC TTF 1 X200).*

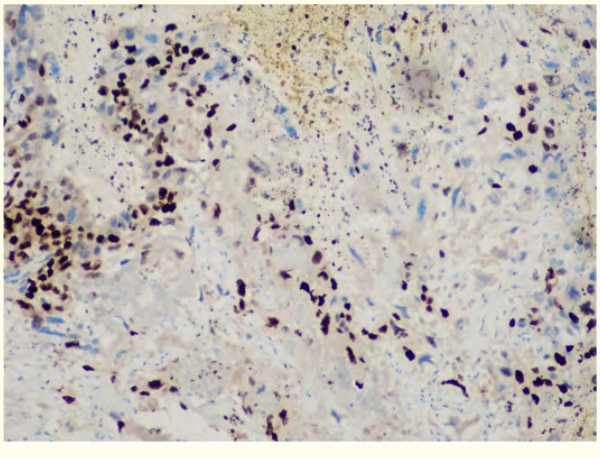

Figure 9: *kI-67 Immunostaining of uterine high proliferation of about 70% (IHC Ki-67 X200).*

Discussion

Gestational Trophoblastic Disease (GTD) refers to a group of rare pregnancy-related disorders characterized by the abnormal proliferation of trophoblastic tissue, which forms part of the placenta [1]. It includes the pre-malignant partial and complete hydatidiform moles, as well as the malignant forms such as invasive moles, choriocarcinoma, placental-site trophoblastic tumor, and epithelioid trophoblastic tumor [2].

The clinical presentation of GTD varies depending on the specific type, but common symptoms include abnormal vaginal bleeding, a uterus larger than expected for gestational age, and sometimes hyperemesis, hyperthyroidism, and high hCG levels [3]. Patients with invasive or metastatic disease may experience symptoms such as hemoptysis, dyspnea, neurological deficits, or abdominal pain resulting from metastatic spread [4].

The global incidence of GTD varies, with hydatidiform mole occurring in approximately 0.57 to 2 per 1,000 pregnancies, while the more severe choriocarcinoma is rarer, affecting between 1 in 40,000 and 9.2 in 40,000 pregnancies [2,5]. The incidence of GTD differs globally, with higher rates observed in parts of Asia, the Middle East, and Africa [2].

Risk factors for gestational trophoblastic disease (GTD) include maternal age extremes (< 20 years or > 40 years), a prior history of GTD (increasing recurrence risk by 1 - 2%), ethnic and geographic predisposition (higher incidence in Southeast Asia, the Philippines, and parts of Latin America), genetic abnormalities such as androgenetic origins in complete moles and diandric triploidy in partial moles, reproductive history including prior miscarriage, infertility, or high parity, nutritional deficiencies (e.g. folic acid, protein, and carotene), and the use of assisted reproductive technology (ART), which may slightly increase the risk of abnormal trophoblastic growth [6-9].

Pathogenesis of gestational trophoblastic disease (GTD) involves abnormal fertilization leading to uncontrolled trophoblastic proliferation, with complete moles arising from androgenetic duplication of paternal chromosomes (46,XX or 46,XY) and partial moles resulting from dispermic fertilization, producing a triploid karyotype (69,XXX; 69,XXY) [7]. Malignant transformation, such as choriocarcinoma, originates from highly mitotic trophoblastic cells, often following molar pregnancies, miscarriages, or term deliveries [10].

The diagnosis of gestational trophoblastic disease (GTD) typically involves a combination of clinical evaluation, laboratory tests, and imaging studies. Serum human chorionic gonadotropin (hCG) measurement is a key diagnostic marker, with elevated levels found in most cases of GTD [11]. Pelvic ultrasound provides critical information, often revealing characteristic features such as the “snowstorm” appearance in complete moles [2]. Histopathological examination confirms the diagnosis by identifying trophoblastic proliferation and distinct morphological patterns [12]. Additional imaging, including chest X-rays or CT scans, is used to detect metastatic spread [13].

In this case report, the diagnosis was based on the patient’s clinical presentation of abnormal Per vaginal bleeding after pregnancy, dyspnea, hemoptysis, and the identification of “cannonball” metastases on chest X-ray-findings strongly suggestive of metastatic GTD. Serum hCG levels were only moderately elevated, consistent with the lower hCG levels typically observed in PSTT. Consistent with Ngan., *et al*. [2], this case also demonstrated moderate hCG levels, differentiating it from choriocarcinoma, where hCG levels are typically much higher.

Histopathological examination revealed atypical intermediate trophoblasts infiltrating the myometrium, leading to a definitive diagnosis of placental site trophoblastic tumor (PSTT). To further support the diagnosis, immunohistochemical analyses were performed using P63, Inhibin, TTF-1, and Ki-67 = 70% which confirmed the malignant trophoblastic origin of the tumors and highlighted the aggressive and metastatic nature of PSTT. Histologically, this case is consistent with the findings of Alexander., *et al*. [14], who describe

PSTT as comprising mononuclear intermediate trophoblasts with extensive tissue invasion. Additionally, Zeng., *et al.* [15] emphasize the utility of Ki-67 and P63 markers in confirming trophoblastic differentiation and predicting aggressive behaviour.

The treatment of GTD depends on the type and extent of the disease. For low-risk GTD, single-agent chemotherapy, such as methotrexate or actinomycin D, is typically effective [7]. High-risk cases often require multi-agent chemotherapy, including EMA/CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine) [16]. Surgical intervention, such as hysterectomy, may be necessary for localized disease resistant to chemotherapy or to manage complications [2]. This management approach aligns with the findings of Porter., *et al*. [17], who advocate for aggressive chemotherapy in metastatic PSTT. Furthermore, a review by Joyce CM., *et al.* [18] emphasizes the importance of individualized treatment strategies based on tumor biology and patient factors. In this case, the patient unfortunately did not receive chemotherapy.

Conclusion

This case underscores the diagnostic complexity and aggressive nature of metastatic GTD, particularly PSTT. An integrated approach combining clinical, radiological, and pathological data is essential to differentiate GTD from other postpartum conditions. Increased awareness, especially by clinicians in resource limited community, and timely intervention are crucial in reducing the morbidity and mortality associated with rare GTD subtypes. The tumor is potentially curable at an early stage. Late diagnosis is often fatal as seen in this case. Uganda being a resource limited sub-Saharan country, appropriate direction of medical resource is important to save life. Uniquely this occurred after cesarean section delivery.

Ethical Considerations

In accordance with local and national regulations, this case report was exempt from formal ethical approval.

Conflict of Interest Statement

The authors declare that there are no conflicts of interest related to this study.

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Data Availability Statement

All data generated or analyzed during this study are included in this article. Additional information is available from the corresponding author upon reasonable request.

Author Contributions

O.M.M: Conceptualization, data curation, writing – original draft, writing - review and editing. M.S: Initial pathological diagnosis. A.D: Reviewed postmortem report. M.A: Review and editing. B.M: Literature view and drafting the final manuscript. T.O: Review and editing. N.S: Review and editing. N.L: Review and editing. L.R: Review and editing. K.S: Project administration, supervision, review and editing.

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