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Case Report

A rare case of primary choriocarcinoma of lung metastasizing to brain

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Abstract

Primary choriocarcinoma of the lung (PCC) is a rare and aggressive malignancy with a poor prognosis. A 24-year-old female presented with headaches and seizures. Brain MRI revealed a metastatic lesion, and biopsy showed trophoblastic tumor cells. Elevated Beta-HCG levels suggested gestational trophoblastic disease, but imaging ruled out uterine involvement. Chest CT revealed a lung mass, and biopsy confirmed PCC. The diagnosis was established based on the absence of a uterine primary and lung involvement. Despite surgery and chemotherapy, prognosis remains poor. This case highlights the importance of considering PCC in patients with metastatic disease and high Beta-HCG levels, emphasizing the need for thorough evaluation for accurate diagnosis and timely treatment.

Keywords: Choriocarcinoma, Lung, Human β-hCG, Brain

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1. Introduction

Choriocarcinoma is a highly aggressive germ cell neoplasm composed of syncytiotrophoblasts, cytotrophoblasts, and variable intermediate trophoblasts and secreting beta-hCG. The prognosis of the disease depends on various factors. younger patient and antecedent molar pregnancies generally have a more favorable prognosis. A longer interval between the antecedent pregnancy and the diagnosis of choriocarcinoma, higher pre-treatment hCG levels, chemotherapy resistance, larger tumor size and brain or liver metastasis are associated with a worse prognosis.

The WHO scoring system assigns points based on these factors:

1. Low Risk: ≤ 6 points
2. High Risk: ≥ 7 points
3. Ultra-High Risk: > 12 points

Metastatic gestational choriocarcinoma of the lung with delayed presentation is a rare condition with only a handful of cases reported.[1] Primary pulmonary choriocarcinoma (PPC) is a rare tumor that generally affects young individuals.[2] The prognosis of this tumor is extremely poor, despite surgical and chemotherapeutic treatment.[3] We report a case of choriocarcinoma in a 24-year-old woman presented with headache and seizure.

2. Case Report

A 24-year-old female presented with complaints of occipital headache persisting for six months, along with episodes of generalized tonic-clonic seizures (GTCS). Brain MRI revealed internal capsular enhancement and a mass in the left parieto-occipital region, involving both cortical and subcortical areas. There was multiple hemorrhagic areas and no micro aneurysm. Given these findings, a brain biopsy was performed for further evaluation. Histopathological examination of the brain biopsy showed infiltrating pleomorphic tumor cells within the cerebral parenchyma, exhibiting extensive hemorrhage, necrosis, and the presence of cytotrophoblast and syncytiotrophoblasts. The findings were consistent with malignant neoplasm probably

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choriocarcinoma. Contrast-enhanced CT (CECT) of the abdomen and pelvis was unremarkable. However, CECT of the chest revealed a well-defined cystic lesion in the posterior segment of the right upper lung lobe. Further clinical history revealed that the patient had a history of first-trimester abortion, with no prior molar pregnancy. Laboratory investigations showed an elevated serum Beta-HCG level (>100,000 mIU/mL). A CT-guided fine-needle aspiration cytology (FNAC) of the lung mass was performed, revealing clusters of cohesive atypical epithelial cells with moderate cytoplasm, hyperchromatic nuclei, a few cells with high nuclear-to-cytoplasmic ratio, and marked necrosis. A lung biopsy was advised for confirmation.(**Figure 1**, **Figure 2**)

Histopathological examination of the lung biopsy (H&E stain) revealed solid sheets of atypical syncytiotrophoblasts, cytotrophoblasts, and intermediate trophoblasts with an infiltrative and destructive growth pattern, along with high mitotic activity, extensive necrosisng and haemorrhage. Based on these findings, a final diagnosis of primary choriocarcinoma of the lung with metastasis to the brain was established.

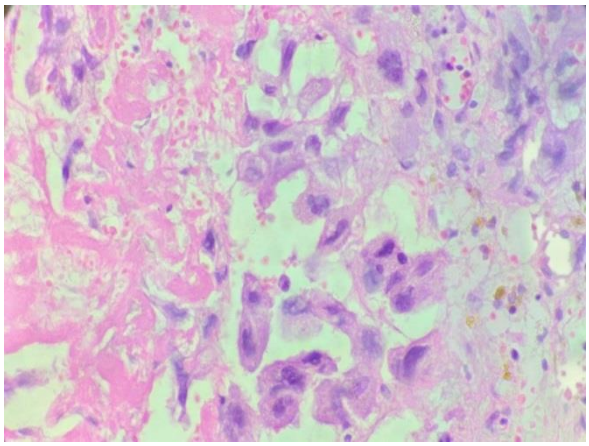

Figure 1: Infiltrating large and pleomorphic tumor cells into the brain parenchyma with extensive hemorrhage necrosis and syncytiotrophoblasts (H&E stain 40X) - Metastatic choriocarcinoma of brain

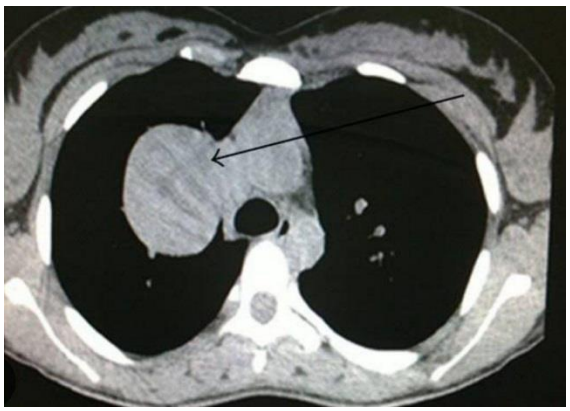

Figure 2: CECT chest – large solid cystic lesion in posterior segment of right upper lobe

3. Discussion

Choriocarcinoma is a rare malignant germ cell tumor of trophoblastic origin composed of trimorphic trophoblasts, including multinucleated syncytiotrophoblasts, mononuclear cytotrophoblasts, and intermediate trophoblasts. The syncytiotrophoblasts are responsible for the production of β-hCG. The pathogenesis of primary choriocarcinoma of the lung remains elusive. Three hypotheses have been proposed for the development of primary pulmonary choriocarcinoma.[1,6]

What makes our case unique is the substantial delay in the onset of the choriocarcinoma. In this case, the choriocarcinoma of the lung represented metastases that arose from unknown trophoblastic disease from a pregnancy. We believe the delay was a result of spontaneous regression of the choriocarcinoma after metastasis. This unique phenomenon has been cited in literature as the "burned out" hypothesis, which reflects the unique and specific feature of choriocarcinoma. That is, it is known to metastasize and become dormant before a primary lesion is detected.[3,8,9]

In the present case, the patient presented with occipital headaches and generalized tonic-clonic seizures, prompting an MRI brain, which revealed an enhancing mass in the left parieto-occipital region and internal capsule. A brain biopsy showed pleomorphic tumor cells with extensive necrosis and hemorrhage, including syncytiotrophoblasts, leading to a diagnosis of metastatic carcinoma, likely of trophoblastic origin. Given the markedly elevated Beta-HCG levels, an initial suspicion of gestational trophoblastic disease was considered. However, whole-body imaging ruled out uterine or ovarian involvement. CECT of the chest revealed a cystic lesion in the right upper lobe. FNAC and lung biopsy confirmed primary pulmonary choriocarcinoma (PCC).

The absence of a uterine primary and localized lung involvement established PCC as the origin, with brain metastasis as the presenting feature. Chemotherapy was given and patient responded to it. After one year follow up with PET, new lesion was not evident and size of the primary tumor has decreased.

A few cases has been reported in the literature. Munakomi S reported similar case in a young female with multiple hemorrhagic metastasis to brain from choriocarcinoma of lung.[8] Tiantian Zhou BS reported metastasis to brain and lung in a 24-year-old female but the primary origin was vagina.[10] Metastasis, necrosis and hemorrhage are common presentation because the malignant trophoblastic cells has tendency to invade the vessels and form micro aneurysm. Choriocarcinoma affects all sexes and arises in gonadal and non-gonadal sites, particularly in the mediastinum, retroperitoneum, and pineal gland. Rare cases with site of origin in the bladder, prostate, Para testicular adnexa, vulva, placenta, pelvis, uterus, kidney, nasal sinuses, and other sites have also been reported.[4,9]

WHO prognostic scoring system (includes age, antecedent pregnancy, interval between diagnosis and index pregnancy, hCG levels, largest tumor size, location and number of metastases, chemoresistance).[14]

1. Low risk: ≤ 6
2. High risk: ≥ 7
3. Ultra high risk: > 12

FIGO anatomic staging includes:

1. I: confined to uterine corpus
2. II: extending to adnexa and vagina
3. III: extending to lung
4. IV: other metastatic sites

The older age, arising from nonmolar pregnancy, long interval between index pregnancy and diagnosis, markedly elevated hCG, large tumor burden, metastasis to brain and liver, chemoresistance has poorer outcomes. Various ancillary technique can be used to confirm the diagnosis.[11] Positive for AE1/AE3, HCG, GATA3 and Glypican 3. Syncytiotrophoblast cells are positive for Inhibin, HPL and CK7. Mononucleated trophoblast are positive for SALL4, Beta catenin and P63. It should be differentiated from invasive hydatidiform mole, other germ cell tumor like embryonal carcinoma, squamous cell carcinoma arising in teratoma and non choriocarcinomatous trophoblastic tumor. In the present case immunohistochemistry was done only for Ki67 and cytokeratin-AE1/AE3. Ki67 was 80-90% and cytokeratin was positive.

Genetic testing can also be done for better understanding of disease. A germline mutation in the TP53 gene, a tumor suppressor gene, has been linked to an increased risk of developing gestational choriocarcinoma. Short tandem repeat (STR) analysis is used to differentiate gestational choriocarcinoma from non-gestational choriocarcinoma[12] when origin of tumor is unknown. This will help the clinician in planning treatment protocol as prognosis and chemotherapy may vary in both the cases. Genetic counseling plays a significant role in understanding the inheritance patterns and risk factors associated with choriocarcinoma. This counseling helps individuals understand their personal and family history, identify potential risks, and make informed decisions about their reproductive health and potential cancer management options.[13]

Primary extragenital choriocarcinoma most often arises in the retroperitoneum, in the mediastinum, or intracranially. Although metastasis to the lung is not infrequent, PCC originating in the lung is extremely rare. The rarity of the occurrence of PCC and the small size of tumor samples makes it challenging to diagnose either by cytology or bronchoscopy biopsy alone. The prognosis of extragonadal choriocarcinoma is usually poor, with various symptoms seriously affecting quality of life. Resection followed by adjuvant chemotherapy appears to represent the best treatment for PCC of the lung.[5,8]

4. Conclusion

Primary choriocarcinoma of the lung (PCC) is a rare, aggressive malignancy with a poor prognosis. This case presented with neurological symptoms due to brain metastasis, leading to an extensive diagnostic workup. Elevated Beta-HCG levels initially suggested gestational trophoblastic disease, but imaging ruled out uterine involvement. A lung mass was identified, and histopathology confirmed PCC. Most choriocarcinomas originate from the uterus, but this case is rare as the patient's uterus was normal, and the primary origin was the lung. Notably, the diagnosis was first made based on brain metastasis, with the lung primary identified subsequently. Early recognition is crucial, as PCC responds poorly to treatment despite surgery and chemotherapy.[7] This case highlights the importance of taking a complete patient history and considering PCC in patients with metastatic disease and high Beta-HCG levels. In cases with brain lesions, a thorough primary workup should be conducted to ensure accurate diagnosis and timely management.

5. Source of Funding

None.

6. Conflict of Interest

The authors declare no conflicts of interest.

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