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Case Report

An Unusual Case of Primary Pulmonary Choriocarcinoma with Brain Metastasis in a HIV Positive Patient

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ABSTRACT

Primary pulmonary choriocarcinoma (PPC) is a rare entity with propensity to rapid metastasis and associated poor outcomes. Pleural effusion has been rarely associated with PPC. We report a case of a 23 year old nulliparous female HIV positive who present with chest pains, dry cough and pleural effusions, with leukocytosis. Poor response to antibiotics prompted further evaluation which revealed PPC with fatal metastasis. Diagnosis of PPC was reached by raised levels of beta HCG, histology and immunohistochemistry. Combination chemotherapy with radiotherapy gave some hope; - however patient demised, mostly likely due to lung metastasis. This case left doctors wondering; - what if, the diagnosis was reached earlier.

Key words: Pulmonary, choriocarcinoma, pleural effusion, beta HCG, brain metastasis

INTRODUCTION

Primary non-gestational choriocarcinoma of the lung is an extremely uncommon condition. [1,2] It is a highly malignant intrapulmonary trophoblastic tumour most often affecting young adults. [3]

The lung site, presents majority of metastatic lesions including gestational choriocarcinoma accounting for prevalence of around 45% to 87%. [4] It is mandatory that all efforts are made in history taking, physical examinations, laboratory and radiology to exclude primary focus in the gonads, mediastinum, retroperitoneum, other midline structures and from many non-trophoblastic malignancies in the lung including conventional primary lung carcinomas which may produce or express ectopic placental hormones. [5]

We present a case of 23 year old HIV positive female patient who presented with both respiratory and neurological symptoms, with initial investigations unrevealing, in course of hospital stay metastatic lesions became rapidly evident and diagnosis of Primary pulmonary choriocarcinoma was made after thorough work up. The authors aim to add to the

literature importance of high index of suspicion for PPC especially in young adults, hence initiating diagnostic investigations and appropriate chemotherapy, as this has been shown to be lifesaving even in HIV positive patients with good CD4 counts.

CASE REPORT

A 23 year old nulliparous HIV positive female patient diagnosed in year 2008 not yet on antiretroviral treatment with CD4 count of 386 two(2) months ago presented to our referral hospital with history of dry cough for one week, which was associated with intermittent shortness of breath and right-sided pleuritic chest pains. She also reported generalized headache that had started four (4) days prior to her presentation. There was no history of fevers, excessive night sweats or significant weight loss. The headache was generalized, it was of dull-nature, not associated with neck pains, photophobia or vomiting. The headache was not relieved with Non-steroidal anti-inflammatory drugs bought over the counter. The patient denied recent miscarriages, she had seen her last menstruation three weeks prior to admission, she also denied periods of amenorrhoea and vaginal spotting and indeed urine pregnancy test done on her was negative.

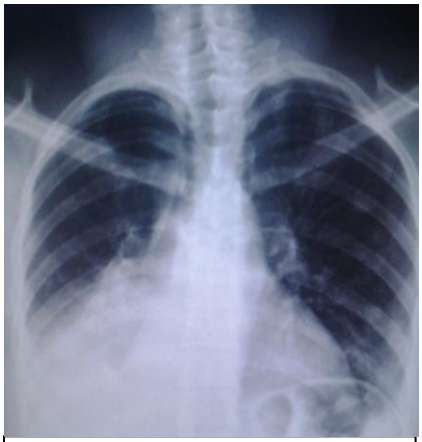

Figure 1: CXR done on admission

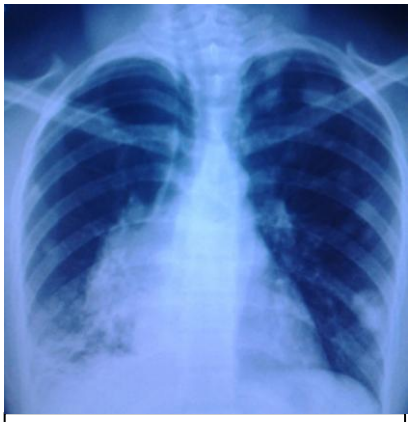

Figure 2: CXR after 7 days shows significant cannon ball lesions

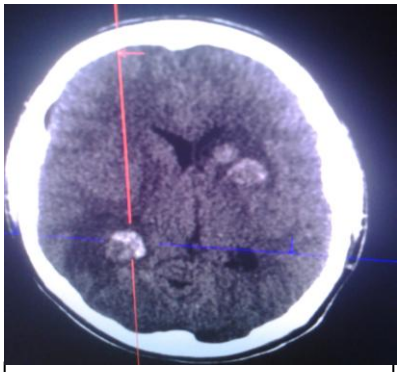

Figure 3: Non-contrasted CT brain: multiple hyperdense leions- hemorrhagic metastasis

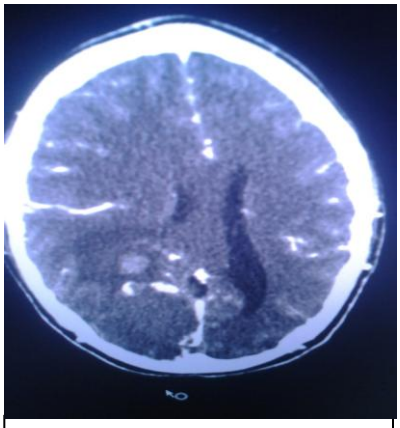

Figure 4: contrast CT brain. Hemorrhagic metastasis with midline shift

Physical examination revealed a healthy female with no stigmata of advanced HIV infection. Her vital signs were grossly normal with pulse rate (PR) 86bpm, Respiratory rate (RR) 20bpm, Blood pressure (BP) 106/61mmHg. She was not in any distress and respiratory examination was significant for stony dullness and reduced vocal resonance in the right base, the rest of respiratory examination was normal. Neurological examination did not reveal any cranial nerve deficits, pupils were equally reactive to light and accommodation, there was no neck stiffness, and Kerning's and Brudyzinsky signs were negative. The rest of systemic examinations including cardiovascular, abdominal and musculoskeletal systems were intact. At admission an Emergency head CT-Scan was done to rule out space occupying lesion and found to be normal, this was followed a Lumbar puncture to rule out meningitis. The cerebrospinal fluid findings were essentially normal; there was no growth after 72 hours. Chest x-ray done at admission was positive for right-sided basal pleural effusion (figure1).Laboratory investigations done at admissions revealed Full blood picture with White blood cell (WBC)=15.20/mm^3 (4-10), Absolute Neutrophil=10.8/mm^3(2-7), Absolute lymphocyte=1.2mm^3(1-3), Haemoglobin(Hb)=12.6g/dl(12-15), platelet =304/l(150-400).Liver functions and renal functions tests were within normal range except for a slightly low albumin of 34.1g/l(35-55). Other tests done included CD4which turned out to be 396 cells/ul (>350) and urine microscopy which was essentially normal. Blood and urine culture yielded no growth. Induced sputum for acid fast bacilli (AFB) and gene expert were negative. Diagnostic Thoracocentesis was unsuccessful. Based on patients' history, physical examination, laboratory investigations and radiology, a provisional diagnosis of pneumonia with parapneumonic effusion was made. She was put on a course of antibiotics at admission for community acquired pneumonia including Intravenous (iv) Cefotaxime 1gm 8hourly and Tablets Doxycycline 100mg 12 hourly as per National Guidelines.

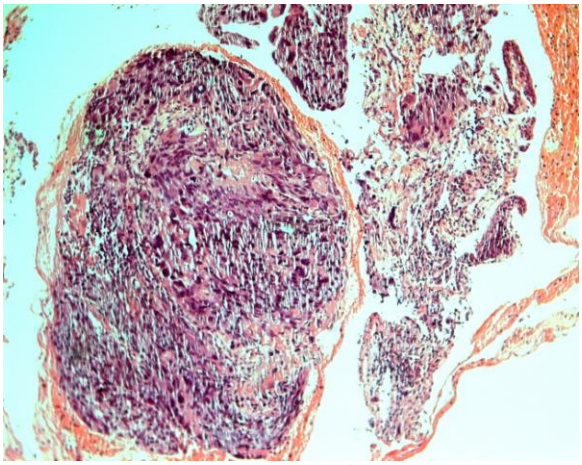

Figure 5: Tissue infiltration with nests of large malignant cells characterized by large hyperchromatic nuclei with abundant vacuolated cytoplasm in a hyaline matrix (H&E, 10X).

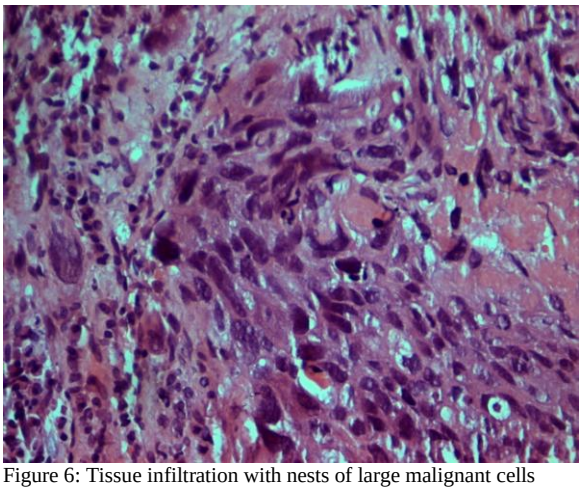

Figure 6: Tissue infiltration with nests of large malignant cells characterized by large hyperchromatic nuclei with abundant vacuolated cytoplasm in a hyaline matrix (H&E, 40X).

After seven (7) days of antibiotics, in view of worsening respiratory symptoms, a control chest x-ray was performed (figure2); it showed multiple roundish lesions (cannon balls) which suggested a possibility of metastatic pulmonary carcinoma. A thorough physical examination (including breast, thyroid and pelvis) were re-

performed to establish source of the primary malignancy, they were all normal. Gynaecological review including cervical curettage also did not elicit any lesions suggestive of intrauterine primary malignancy. Computerized tomography of abdomen and pelvis were found to be normal. Blood for tumour markers revealed: - alpha-feto protein (AFP) =0.92pg/l, (0-20), Cancer antigen 125(CA 125) = 77.1U/ml (1-35), Carcinoembryonic antigen (CEA) =5.28µmol/l (1.4-5.6), beta human chorionic gonadotropin (beta HCG=65325.48mIU/ml (0-10).

At this point, a definitive diagnosis of pulmonary choriocarcinoma was considered and patient booked for urgent bronchoscopy. Gross findings of bronchoscopy were of multiple fragile masses easily bleeding, histology and immunohistochemistry confirmed a diagnosis of choriocarcinoma.

The patient was referred to oncology department, this time with worsening headache. Computerized tomography (CT)-Brain to rule out brain metastasis was performed and it revealed multiple hemorrhagic brain metastases (figure 3 and 4). The patient was adjudged to have high risk pulmonary choriocarcinoma with brain metastasis(prognostic score index of 9 due to brain metastases, pretreatment HCGlevel and number of metastatic sites identified) and started on whole brain radiotherapy and combination chemotherapy consisting of Etoposide, Methotrexate, Dactinomycin.

After two weeks of treatment patient made a gradual improvement with less headache and chest pains, control beta HCG was 54728.57m IU/ml (0-10); however, she developed severe acute respiratory failure and demised despite resuscitation efforts. Autopsy was denied by her parents.

PATHOLOGICAL FINDINGS:

Gross

Bronchoscopy revealed a greyish fragile masses on the right bronchus that were easily bleeding to touch, particles ranging from 0.5cm by 1cm were sent for histology

Microscopy

The section contained small fragments of bronchial tissue infiltration with nests of large malignant cells characterised by large hyperchromatic nuclei with abundant vacuolated cytoplasm in a hyaline matrix (figure 5 and 6). Differential diagnosis included poorly differentiated squamous cell carcinoma, Metastatic Gestational trophoblastic Disease, neuroendocrine Carcinoma. Immunohistochemistry and special stains report was positive for beta HCG, and negative for both mucin and p63. Thyroid – transcription factor-1(TFT-1) was not performed.

DISCUSSION

This case highlights a young female who had acute presentation of dry cough and chest pains with leukocytosis which was initially treated as parapneumonic effusion with efforts to rule out Tuberculosis. The patient also had headache, at time of presentation, of which both Brain CT-Scan and Lumbar puncture were normal.

The most common symptoms in patients with Primary Pulmonary Choriocarcinoma (PPC) in order of frequency are chest pain and hemoptysis. [6] Pleural effusion may also be a rare associated feature in PPC. [2]

The patient reported in this case report did not present with hormonal problems such as amenorrhea, vaginal spotting or genital bleeding which is a common feature of most beta HCG producing tumors. [6] This is mostly likely because of rapid progression of the disease giving no time for noticeable hormonal problems. [7]

All the efforts were made to exclude possibility of either a primary lung tumour or tumours from elsewhere producing beta HCG. They included radiographic investigations and extensive gynaecological review. Immunohistochemistry performed ruled out the possibility of either primary adenocarcinoma of breast, lung, kidney, bladder, liver and cholangiocarcinoma as mucin was negative. [8] On the other hand;- primary tumour of squamous epithelial origin and poorly differentiated carcinomas were ruled out by negative p63. [9] Positive beta HCG in immunohistochemistry was the evidence of a tumour of choriocarcinoma type, and a response to treatment by decreasing levels of beta-HCG that was seen after starting chemotherapy shows that indeed the tumour in the lung was primarily a choriocarcinoma. [10]

The presented patient was HIV positive with CD4 of 396cells/µl.HIV seropositivity has been found to be a poor prognostic factor in Choriocarcinoma. [11-13] Other studies have shown HIV positive patients with CD4 above 200cells/µl once initiated on standard chemotherapy fare as good as HIV negative patients, and rapid intervention is usually life-saving. [10,14-15]

We find this case to be unusual, whereby a patient presented with pleural effusion, leukocytosis and headache at the same time, indicating possibility of brain metastasis at the time of presentation; however this was missed by both chest x-ray and Brain CT-Scan. A high index of suspicion for choriocarcinoma would have led to performing beta HCG and initiating appropriate therapy before more fatal metastasis became evident.

CONCLUSION

Primary pulmonary choriocarcinoma is a rare disease entity which is more common in young adults; it tends to metastasize rapidly to other sites with poor outcomes. Despite the fact that HIV positivity is considered to be a poor prognostic marker for choriocarcinoma, patients with good CD4 fare well, hence young patients with pulmonary manifestations including pleural effusion should always be thoroughly investigated to rule out choriocarcinoma, as this will lead to prompt diagnosis, early chemotherapy and better outcomes.

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