

Advanced large cell lung tumor with neuroendocrine differentiation in an HIV positive patient

Sir,

Human immunodeficiency virus (HIV) infection is well known to be associated with several cancers and respiratory complications. Lung cancer is one of the most common cancers in HIV-infected individuals. We report the case of a HIV-positive smoker male who was admitted with fever, cough and right-sided pleuritic chest pain. Imaging studies revealed the presence of right-sided pleural effusion with multiple pleural based nodules and right lower lobe mass. Histopathologic examination of the tissue showed large cell lung tumor with neuroendocrine differentiation (LCNEC). LCNEC is an extremely rare lung cancer with this being the only case reported in an HIV-positive patient.

A 49-year-old HIV-positive male smoker on antiretroviral therapy (tenofovir, emtricitabine and efavirenz) with good medication compliance presented with cough and progressively worsening right-sided pleuritic chest pain for 2 weeks. He also stated having loss of appetite and 23 kg weight loss over the last 2 months. He denied having any hemoptysis, abdominal or neurologic symptoms at presentation. There was no history of preexisting lung disease, diabetes, illicit drug abuse or lung infections. Fifteen days ago his CD4 cell count was 750/ μ l with an undetectable viral load.

Clinical examination showed stable vitals. Chest examination revealed decreased breath sounds on the right with decreased tactile vocal fremitus over the right middle and lower lung fields. Cardiovascular, abdominal, neurologic and skin examination failed to show any abnormality. Initial laboratory tests including complete blood counts and serum chemistries were within normal limits. Chest radiograph revealed a right-sided effusion without any mediastinal shift. Chest computed tomography (CT) scan confirmed the presence of a large

right-sided pleural effusion with multiple pleural based soft tissue densities and a right lower lobe mass [Figure 1].

Thoracocentesis showed an exudative hemorrhagic fluid with no malignant cells on cytologic examination. The patient underwent video-assisted thoracoscopic examination (VATS) with biopsy of the pleural-based soft tissue mass. Histopathologic examination of the tissue showed large cells with organoid growth pattern, high mitotic index and areas of necrosis [Figure 2]. The neuroendocrine phenotype was confirmed by the presence of positive staining for synaptophysin and chromogranin A.

Due to pleural involvement, the patient was diagnosed with a stage IV large cell lung cancer with neuroendocrine differentiation. The patient agreed for a trial of chemotherapy with carboplatin and etoposide. Initial work-up for metastatic spread of the disease failed to show any extra-thoracic involvement. Over the course of next 9 months, the patient's condition worsened with metastatic involvement of the liver and brain, ultimately leading to his death.

Lung cancer, the leading cause of cancer-related deaths in the general population is the third most common malignancy in HIV-infected individuals, preceded only by Kaposi's sarcoma and non-Hodgkin's lymphoma.^[1-3] The most common histologic variants of non-small cell

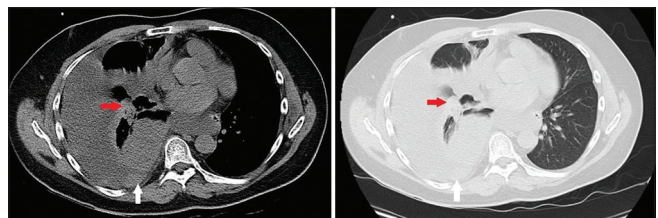


Figure 1: CT chest showing right-sided effusion with pleural-based soft tissue (white arrow) density and a right lower lobe mass (red arrow)

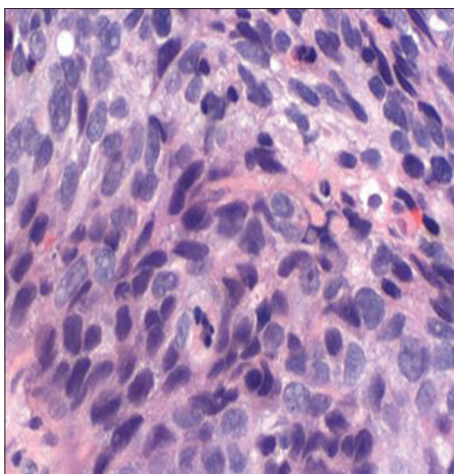


Figure 2: Histopathologic examination of pleural masses showing large cell tumor of lung origin

lung cancer seen in the patients infected with HIV are adenocarcinoma (31-50%), squamous cell carcinoma (19-36%) and large cell carcinoma (9-19%).^[4,5] Large cell lung tumors with neuroendocrine differentiation make up about 1.6-3.1% of all lung cancers in the general population.^[6] The association of LCNEC with HIV infection is even rarer. Extensive literature review failed to reveal any case report of LCNEC in an individual infected with HIV.

HIV infection is a well-known independent risk factor for lung cancer. The exact pathophysiology for increased incidence of lung cancer in the patients with HIV infection is unclear. HIV patients are diagnosed with lung cancer at earlier age (average age of diagnosis: 46 years) compared to HIV-negative patients who develop lung cancer.^[5,6] HIV-positive patients with lung cancer are also thought to have more advanced stages of lung cancer at the time of diagnosis with severe pulmonary symptoms. The diagnostic and treatment approach to lung cancer in HIV-infected patients is similar to those with lung cancer without co-infection with HIV.

In conclusion, HIV infection acts as an independent risk factor for lung cancer, with adenocarcinoma being the most common histopathologic variant and LCNEC being extremely rare. The diagnostic and treatment approach in the patients with lung cancer remains unaffected by

their HIV status. The only area of concern is the potential interaction between certain chemotherapeutic agents and antiretroviral medications. The worsened outcomes and poorer prognosis in the lung cancer patients with HIV infection as compared to those without HIV infection are attributed to the weakened immune system in the former.

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