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Case Report

Pulmonary Lymphoepithelioma-Like Carcinoma (PLELC) With a Completed Metabolic Response after Chemoradiotherapy: A Case Report and Review of the Literature

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Abstract

Pulmonary Lymphoepithelioma-Like Carcinoma (PLELC) is a rare subtype of lung cancer that typically appears in young non-smoker patients and mainly in the Asian population. At the time of diagnosis, symptoms are usually nonspecific. Histological examination is the gold standard for diagnosis. Compared with other lung cancer subtypes, PLELC appears to have a better prognosis. We report a locally advanced PLELC in a never smoker Asian female treated with chemo radiotherapy achieving a complete and maintained response. We also reviewed the available data on the treatment of these patients in the literature.

Keywords: Pulmonary Lymphoepithelioma-Like Carcinoma; Epstein - Barr virus; Chemotherapy; Radiotherapy

Introduction

Pulmonary Lymphoepithelioma-Like Carcinoma (PLELC) was first described in 1987 in a 40 year-old female, and it was associated with the Epstein - Barr virus (EBV) [1]. According to the 2015 WHO Classification of Lung Tumors, it is categorized as an infrequent epithelial tumor subtype, which accounts for less than 1% of all lung malignances [2]. PLELC is more common in the Asian population, young people with non-smoking history, without differences between genders [3]. Clinical manifestations are nonspecific. Histopathological examination is the gold standard for the diagnosis of PLELC. PLELC appears to have a better prognosis, with longer Overall Survival (OS) and Progression-Free Survival (PFS) compared to other subtypes of lung cancer

[4]. Predictive prognostic factors have been reported, although clinical evidence is not conclusive [5].

There are no clinical trials to establish the standard of care. Only retrospective studies have attempted to determine prognostic factors and which therapeutic strategy is better for these patients [5,6]. In early stages, surgery is recommended. Locally advanced and inoperable patients can be treated with Chemotherapy (ChT) and Radiotherapy (RT) [7]. Metastatic disease can also be treated with ChT regimens, although immunotherapy treatment is playing an increasingly important role [7–9].

Here, we present a patient with locally advanced PLELC treated with a combination of radiotherapy and chemotherapy.

Case Presentation

A 74-year-old never smoker Asian female presented in November 2021 with dyspnea and weight loss, and the chest Computed Tomography (CT) scan showed a mass in the left upper lobe of the lung and mediastinal lymph nodes. On physical examination, the patient presented good performance status and the examination of the nasopharynx was normal.

A Fiber Optic Bronchoscope (FOB) and an Endobronchial Ultrasound (EBUS) were performed but there was no evidence of malignancy in the samples. The study was completed by an 18FDG-PET-CT and it confirmed lung mass about 8 cm, and its Standardized Uptake Value (SUV) maximum was 16.4 (Figure 1A). In addition, left mediastinal and hilar lymph node involvement was described (Figure 1B). Lymph nodes at the left axillary level with affinity for 18FDG were also observed. Distant metastases were excluded. Pulmonary function tests were normal.

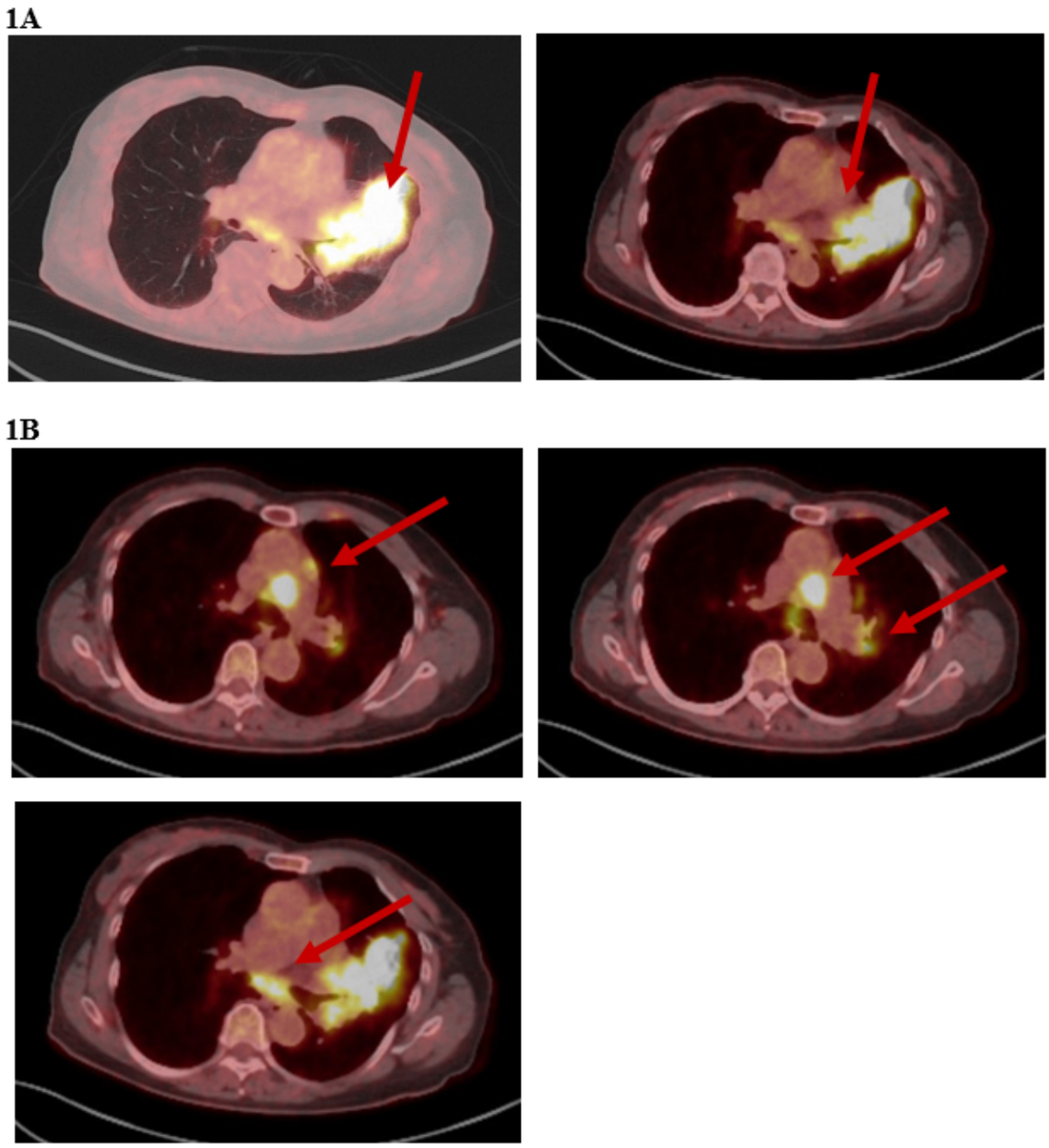

Figure 1: 18FDG-PET-CT images showing a bulky soft tissue mass in the left upper lobe (Figure 1A) and involvement of left mediastinal and hilar lymph node (Figure 1B).

To reach the diagnosis, a CT-guided Fine-Needle Aspiration (FNA) of the bulky lung mass was performed. The pathology report showed a tumor composed of oval spindle cells with intense cytologic atypia (Figure 2A). The Immunohistochemical (IHC) staining showed cytokeratins AE1/AE3 (+) (Figure 2B-2C), STAT-6 (+). The positive staining for STAT-6 was indicative of a solitary fibrous tumor; however, the intense positive staining for cytokeratin together with the negativity for CD34 did not allow the exclusion of an epithelial malignant tumor with sarcomatoid areas.

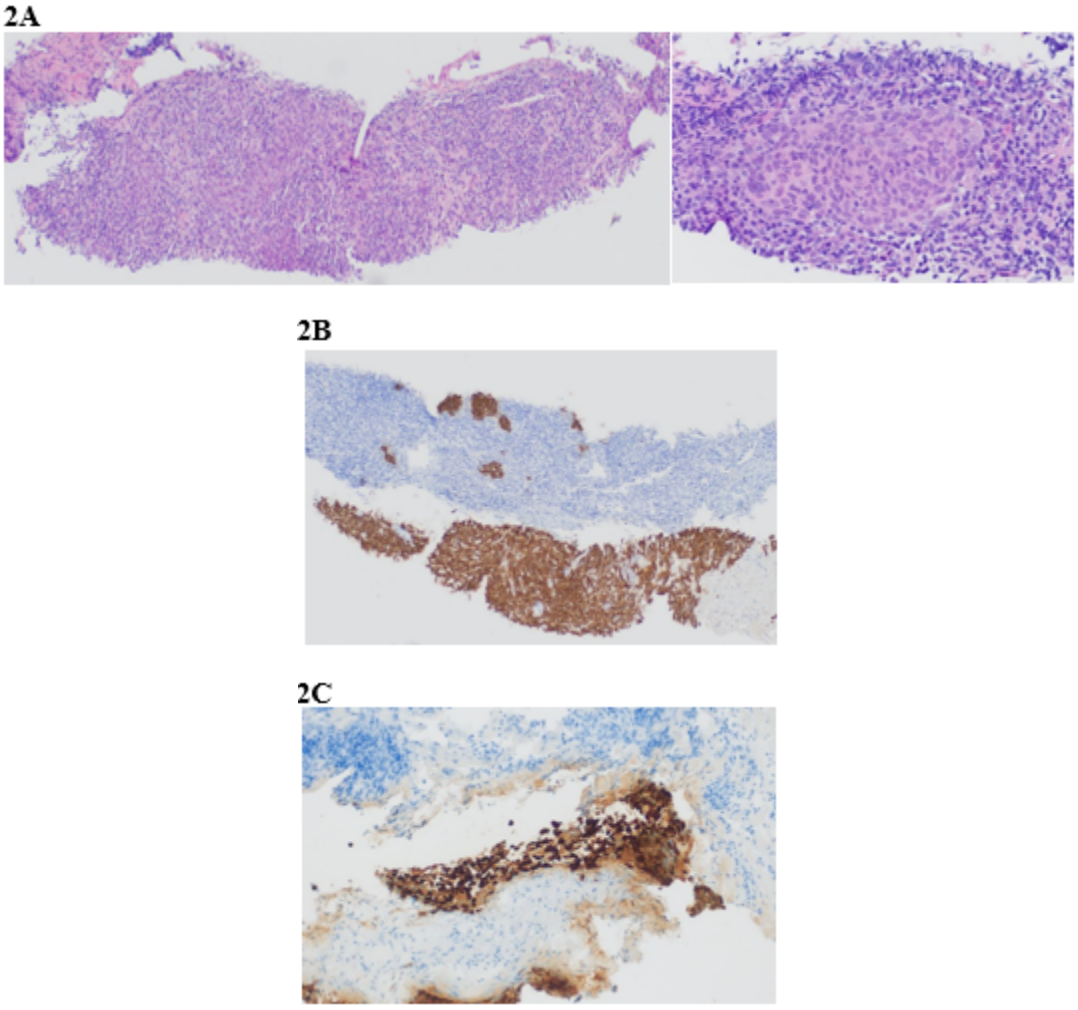

Figure 2: CT-guided core needle biopsy results. Hematoxylin and eosin stain. Proliferation of epithelial cells with abundant lymphoplasmacytic stroma. Large cells presenting large with ill-defined cytoplasm and very prominent nucleolus. There is a lymphoplasmacytic inflammatory infiltrate (Figure 2A). Immunohistochemical staining showed cytokeratins AE1/AE3 (+) (Figure 2B). In situ hybridization test. Positive result of the Epstein-Barr encoding region (EBER) (Figure 2C).

To define the diagnosis, a CT-guided Core-Needle Biopsy (CNB) of the main pulmonary lesion was needed, which confirmed the diagnosis of a PLELC due to the cell morphology, the high lymphoid component and the positive result of the Epstein-Barr Encoding Region (EBER) in situ hybridization test (Figure 2C). A CNB of the left axillary adenopathy was also performed, which ruled out secondary involvement at that level.

Therefore, the final diagnosis was a PLELC in the left upper lobe of the lung with left mediastinal and hilar lymph node involvement (cT4N2M0, stage IIIB). The PD-L1 expression was 75%.

The clinical case was presented to the multidisciplinary thoracic tumor board, in which we decided to initiate treatment with sequential ChT and RT because the radiotherapeutic field was initially very extensive. The chemotherapy regimen prescribed was the combination of cisplatin 70mg/m2 on day 1 and gemcitabine 1gr/m2 on day 1 and 8 every 3 weeks. The patient received four cycles between February 2022 and May 2022 obtaining a partial metabolic and morphological response of the left pulmonary mass (Figure 3A) and of the mediastinal lymph nodes (Figure 3B) in the 18FDG-PET-CT according to RECIST 1.1. Due to the good response, the multidisciplinary thoracic tumor board decided to perform radical concomitant ChT and RT.

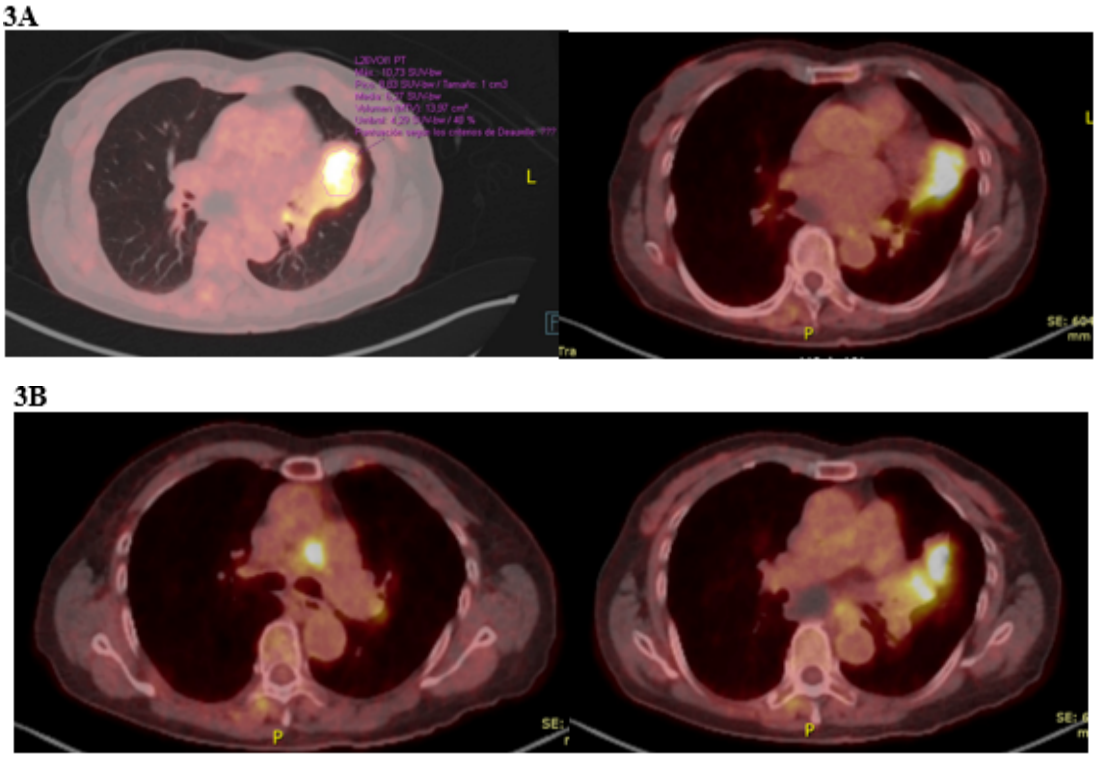

Figure 3: 18FDG-PET-CT images after 4 cycles of cisplatin and gemcitabine. The images showed a partial metabolic and morphological response of the left pulmonary mass (Figure 3A) and of the mediastinal lymph nodes (Figure 3B) (according to RECIST 1.1).

Regarding RT treatment, 66 Gy were administered at a fractionation of 2 Gy/day in daily fractions. The treatment volumes were: PTV1 (planning tumor volume) that included the left lung lesion and PTV2 that included the ipsilateral hilar-mediastinal adenopathies. It was administered by VMAT (volumetric arc radiotherapy) technique and 6MV energy in linear accelerator (Figure 4). The prescription indications were met in both PTVs, as well as the constraints in organs at risk. Daily verification was performed by Image-Guided RT (IGRT). Concomitantly, the patient received 7 weekly cycles of cisplatin 20 mg/m2 between June 2022 and July 2022.

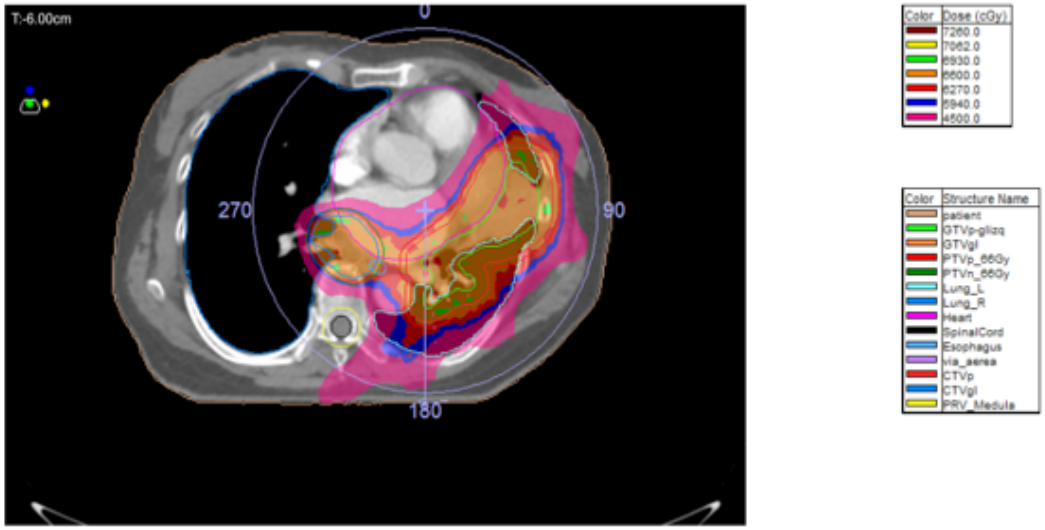

Figure 4: Radiation treatment planning. Prescription: total dose 66 Gy for both PTV volumes. Technique VMAT. Isodose 66 Gy, 62, 70 Gy (95%) and 69, 30 Gy (105%).

In October 2022, the 18FDG-PET-CT showed a new nodule of 18 mm in the right upper lobe of the lung and a complete metabolic response of the primary tumor and mediastinal lymph nodes. The patient underwent a CT-guided FNA that was insufficient for diagnosis. The clinical case was resubmitted to the multidisciplinary thoracic tumor board which decided to administer Stereotactic Body Radiation Therapy (SBRT) to the pulmonary nodule despite the lack of pathological confirmation due to the high SUV (14.16).

The last control of the patient was in December 2023 and the 18FDG-PET-CT showed reduction of the nodule of the right upper lobe of the lung and maintained complete metabolic response for the rest of the disease. Clinically, the patient is asymptomatic.

Discussion

PLELC commonly appears in young people compared to other lung cancer subtypes. In addition, epidemiological characteristics might differ in western countries with a median age of 65 years and a little higher prevalence in males [10]. Our patient developed the disease at an older age than most of the Asian females described in the literature.

The gold standard for the diagnosis of the PLELC is the histopathological examination and it is not distinguishable from Nasopharyngeal Carcinoma (NPC). Microscopically, this tumor is formed by undifferentiated carcinoma cells with a variable nuclei and imprecise cytoplasmic borders forming syncytial sheets and nests. It shows a stroma infiltrated by lymphoplasmacytic and other inflammatory cells. PLELC is associated to EBV, positive in almost all patients [1]. In contrast to other subtypes of lung cancer, EGFR mutations, ALK gene rearrangement and ROS1 aberrations are rarely found in the PLELC [11]. In this reported patient the inconclusive immunohistochemistry results for other lung tumors subtypes and the cancer cells morphology after the first FNA made the initial diagnosis uncertain. However, after the CNB, the positive result of EBV, the abundant lymphoid infiltrate and the undifferentiated cancer cells were essential to reach the final diagnosis.

Different studies have suggested that early stage, high PD-L1 expression, ki-67 index, metabolic tumor volume or LDH levels could be predictive prognostic factors in patients with PLELC [5]. Regarding PD-L1 expression, recent research has reported that the expression of PD-L1 in patients with PLELC is frequently high [11], which resembles our patient. Due to this fact, immunotherapy is being used in these patients with encouraging results [8], even in the neoadjuvant setting [9].

PLELC is described as a radiosensitive and chemosensitive type of tumor. Locally advanced and inoperable patients can be treated with a RT and ChT. Recommended RT doses range 50-70 Gy, so 66Gy in 33 daily fractions were administered to our patient [7]. Regarding ChT treatment, the patient received four cycles of induction ChT with cisplatin and gemcitabine, and consecutively 7 weekly cycles of cisplatin concomitant with RT. Platinum-based doublet is reported as the best ChT scheme for patients with PLELC, although it is uncertain which chaperon

is the best for the platinum doublet [7]. For the selection of the presented ChT regimen, the results in patients with NPC were also considered [12]. A recent meta-analysis showed that those patients who underwent RT treatment had better outcomes, which might be related to the similarities between PLELC and NPC [3], although this results are controversial when compared with other individual studies [4].

A recent study analyzed the results of three options of treatment for PLELC: definitive chemoradiotherapy, radical surgery plus adjuvant chemoradiotherapy, and radical surgery plus adjuvant ChT [7]. With a median follow-up time of 47.4 months, the 3-year PFS and 3-year OS rates were 66.0% and 92.4%, respectively, for all patients. Multivariate analysis revealed no significant difference in PFS between both arms (p=0.354), but two options obtained significantly longer PFS than radical surgery plus adjuvant ChT (p<0.001; p=0.039). Regarding OS, no significant differences were observed among the three options, although the first two options tended to improve survival compared to the last group [7]. They concluded that patients with stage III-N2 of PLELC present with a good prognosis and RT plays a pivotal role among different treatment options.

In conclusion, we reported an Asian patient with EBV-positive primary PLELC in the left upper lobe of the lung with left mediastinal and hilar lymph node involvement. Our patient received four cycles of induction ChT with cisplatin and gemcitabine, and consecutively a total dose of 66Gy and 7 weekly cycles of cisplatin. This treatment is an excellent option for locally advanced and inoperable patients with promising results.

Conflict of Interest: The authors report no conflicts of interest in this work.

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