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^{18}f-Fdg Pet/Ct Revealed of Rare Primary Lyphoepithelionma-Like Carcinoma of the Lung: A Case Report and Literature Review

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Abstract

We present a case of a 44-year-old woman was hospitalized for one year with intermittent coughing and expectoration. She has no history of smoking or previous medical conditions. DNA test positive for Epstein-Barr virus. Chest computed tomography (CT) showed a soft tissue mass in the left lower lobe of the lung and non-uniformity of image density. Part of the bronchus in the lower lobe of the left lung was compressed and occluded. On contrast-enhanced CT, the mass was inhomogeneously enhanced. Fluorine-18-fluorodeoxyglucose positron emission tomography/CT (^{18}F-FDG PET/CT) revealed the mass had significant uptake of FDG and maximum standard uptake value (SUVmax) was 10.7. The subsequent histopathologic examination confirmed the diagnosis of a primary lung lyphoepithelionma-like carcinoma (LELC). The patient was treated with chemotherapy.

Keywords: Lyphoepithelionma-like carcinoma ● Lung cancer ● ^{18}F-FDG PET/CT ● Case report

Introduction

Lymphoepithelioma-like carcinoma (LELC) is a rare type of cancer that usually occurs in the pharynx and foregut-derivative organs, including the salivary glands, thymus, stomach and liver [1]. Primary lung LELC is a rare subtype of non-small cell lung cancer, accounting for about 0.92% of other lung cancer types [2]. Lymphoepitheliomatoid carcinoma of the lung was first reported by Begin LR et al. in 1987[3].

Lung LELC is a large, centrally placeholder tumor with a smooth edge in imaging[4]. The diagnosis of lung LELC is mainly dependent on pathological and immunohistochemical results. Histologically, it is difficult to differentiate lung LELC from metastatic nasopharyngeal carcinoma. The diagnosis must be combined with the patient's history, endoscopy or magnetic resonance imaging (MRI) to evaluate whether the tumor is metastasized from nasopharyngeal tumor. Primary lung LELC can be diagnosed after exclusion of nasopharyngeal malignancy as a source. ^{18}F-FDG PET/CT examination has important application value in the diagnosis of pulmonary nodules or masses. Therefore, this study conducted a brief review of relevant literature.

Case report

A 44-year-old woman was hospitalized for one year with intermittent coughing and expectoration. She has no history of smoking or previous medical conditions. Laboratory tests for tumor markers showed the following results: neuron-specific enolase was 17.16ng/ml (0-16.3), non-small cell lung cancer associated antigen was 10.49ng/ml (0-3.3), squmaous cell carcinoma antigen was 1.74ng/ml (0-2.5), tumor specific growth factor 67.1U/L (0-68), carcino-embryonic antigen <0.5ng/ml (0-5). DNA test positive for Epstein-Barr (EB) virus. All the indicators related to mycobacterium tuberculosis were negative.

Chest CT showed a soft tissue mass with the size of 6.4cm×7.6cm×8.7cm in the left lower lobe of the lung and non-uniformity of image density. There were patchy and cable-like shadow around the mass. Part of the bronchus in the lower lobe of the left lung was compressed and occluded. On contrast-enhanced CT, the mass was inhomogeneously enhanced. The left pleura is thickened with a small effusion in the left pleural cavity. Therefore, this mass was considered a malignant neoplasm of the lung.

To further evaluate the nature of mass and the patient's whole-body condition, ^{18}F-FDG PET/CT examination was performed. On the maximum density projection(MIP) of the ^{18}F-FDG PET/CT, there was a mass of abnormal increased glucose metabolism on the left side of the chest. On cross-sectional view, the lesion had significant uptake of FDG and maximum standard uptake value (SUVmax) was 10.7. Bilateral hilar and mediastinal lymph nodes were not enlarged and FDG uptake was not abnormal. There was no abnormality in FDG uptake in the remaining tissues and organs of the body. Subsequently, the patient underwent puncture of the lesion. Microscopic pathology findings showed that the cancer cells were arranged in irregular nest-like structures, with elliptic nuclei, fine chromatin, interstitial fibrosis, coagulant necrosis and granulomatous nodules, and a large number of lymphocytes infiltration. The immunohistochemical results were as follows: CK(+), P63 (+), P40 (+), TTF-1 (-). Tissue *In situ* hybridization immunohistochemistry: EB virus (+). Based on biopsy and immunohistochemical results, the histological changes of this mass were consistent with lyphoepithelionma-like carcinoma (LELC).

In order to exclude the lung lesion from nasopharyngeal carcinoma metastasis, the patient underwent nasopharyngeal MRI examination and found no abnormality. In addition, the otolaryngologist examined the nasopharynx by fiberscopy and did not find any abnormalities. We also re-read the ^{18}F-FDG PET/CT images to suggest normal glucose metabolism in nasopharyngeal tissue. Ultimately, the patient was diagnosed with primary lung lymphoepithelioma-like carcinoma, the TNM stage was considered as T4N0M0 IIIA. Due to the large size of the lesion, the patient and his family refused surgical treatment and requested conservative treatment. Therefore, the patient received systemic chemotherapy. The patient's lung CT reexamination indicated that the lesion was significantly smaller than before after 2 months treatment, indicating that the therapy was effective (Figure 1).

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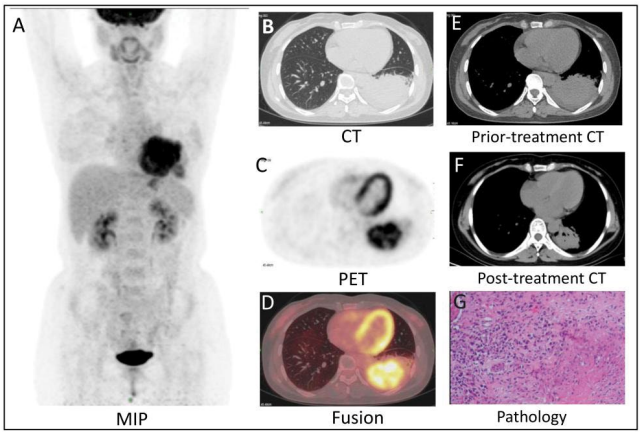

Figure 1. (A). On the MIP of the ^{18}F-FDG PET/CT show a mass of abnormal increased glucose metabolism on the left side of the chest. **(B,C,D).** On cross-sectional view, the lesion with the size of 6.4cm×7.6cm×8.7cm had significant uptake of FDG and maximum standard uptake value was 10.7. **(E,F).** Pathpathology and Immunohistochemistry were considered as lung lymphoma-like carcinoma (G: HE, 20× magnification). After chemical treatment, CT indicated a significant reduction of the lung lesions.

Table 1. Review of the literature on the imaging characteristics of primary lung lymphoepithelioma-Like carcinoma detected by ^{18}F-FDG PET/CT.

Patient	First Author(Year)	Country	Gender/ Age(year)	Diagnosis	Size	SUVmax	EB virus	Location of primary cancer	Therapy	Follow-up time	Treatment effect
1	(2022)#	China	Female /44	PPLELC	6.4×7.6 × 8.7cm	10.7	+	inferior lobe of left lung	Chemotherapy	2 months	Effective
2	Fırıncıoğluları,A (2020)	Turkey	Male /51	PPLELC	Diameter 3.0cm	7.5	+	Inferior lobe of left lung	Surgery and Chemotherapy	NG	No recurrence
3	Aktas, GE(2017)	Turkey	Meal /69	PPLELC	Diameter 2.42cm	16.2	-	Hilum of right lung	Right upper lobe segmentectomy	3 years	No recurrence
4	Hiu Yan Chan (2015)	Hong Kong, China	Female/54	PPLELC	7.9 × 6.2 cm	7.6	+	Apicoposterior segment of left upper lobe	Left pneumonectomy	NG	NG
5			Female /60	PPLELC	NG	14.1	NG	Right lower lung	NG	NG	NG
6			Male /66	Postoperative recurrence of PPLELC	2.8 × 2.2 cm	9.1	NG	Adjacent to the surgical resection margin	Surgery and Chemotherapy	3 mouths	Effective
7			Female /65	Mediastinum, right hilar and intraperitoneal lymph node metastasis	4.5 × 3.5 cm	12.5	NG	Right middle lobe lung	Radiotherapy and Chemistry therapy	3 years	Disease recurrence
8	Chan, JKI (2017)	Macau, China	Female /59	PPLELC and lung adenocarcinoma	4.0 × 3.1 × 2.0cm	12.3	+	upper lobe of left lung	Surgery	NG	No recurrence
9	Dong, A(2015)	China	Male /83	PPLELC	NG	34.5	NG	upper lobe of right lung	Video-assisted thoracoscopic lobectomy	NG	NG
10	Yener, NA(2012)	Turkey	Male /62	PPLELC	Diameter 2.0cm	NG	+	Right lung mun	Pneumonectomy	4 months	No recurrence
11	Shen, DH(2012)	Taiwan,China	Female /75	PPLELC	Diameter 2.6 cm	5.0	NG	Right lung	Video-assisted thoracoscopic surgery	NG	NG

Our study reported cases.

PPLELC=Primary Lung Lymphoepithelioma-Like Carcinoma,**NG**=not given, **SUVmax**=Maximum Standard uptake value, **EB**=Epstein2Barr.

Discussion

Lymphoepithelioma-like carcinoma, originally seen in the nasopharynx, refers to undifferentiated carcinoma dominated by lymphocyte infiltration [2]. A primary lung cancer that mimicking undifferentiated Nasopharyngeal carcinoma (NPC) known as lymphoma epithelial tumor-like carcinoma was first reported in 1987 by Begin LR et al.[3] in 1987 first reported a primary lung cancer similar to undifferentiated nasopharyngeal carcinoma called lymphoma epithelial tumor-like carcinoma. Some studies believe that the average age of the disease is younger than that of other types of lung cancer, and there is no significant gender difference, and the incidence of non-smokers is higher [4]. Almost all of the Chinese patients (>90%) had EB virus-positive tumors [4]. The clinical symptoms of lung LELC are non-specific, and cough, sputum and chest pain are common [5-7]. The first clinical symptoms of the patient we reported were cough and expectoration, without any symptoms of infectious diseases.

Lung LELC is no significant specificity on imaging and tends to be confused with other lung malignancies [4]. According to previous literature, the maximum diameter of lung LELC varies from 1.5 to 8cm. Most of the

tumors were isolated, mostly in the right lung. In this case, the lesion was located in the lower lobe of the left lung with a maximum diameter of 8.7cm. The diagnosis of lung LELC is mainly dependent on pathological and immunohistochemical results. Histologically, the typical lung LELC consists of undifferentiated carcinoma cells with ill-defined cytoplasmic borders arranged in syncytial sheets and nests [2]. The tumour cell nuclei are round, oval or elongated with mildly irregular nuclear outline, vesicular chromatin and distinct nucleoli [8]. However, it is difficult to differentiate lung LELC from metastatic nasopharyngeal carcinoma. The diagnosis must be combined with the patient's history, endoscopy or MRI to evaluate whether the tumor is metastasized from nasopharyngeal tumor. Primary lung LELC can be diagnosed after exclusion of nasopharyngeal malignancy as a source [2].

^{18}F-FDG PET/CT examination has important application value in the diagnosis of pulmonary nodules or masses. However, the incidence of lung LELC is low and ^{18}F-FDG PET/CT has been used to evaluate the disease in fewer cases. Therefore, this study conducted a brief review of relevant literature. We performed electronic literature searches of the PubMed, Embase and Cochrane Library databases for English-language articles from the earliest available date of indexing through 25 June 2021. The following key words were used for the selection of studies: FDG, PET, LELC, lung, pulmonary. All English case reports of FDG PET/CT for lung LELC were included in the analysis. Nine case reports were retrieved. Two cases reported by Japanese authors [9, 10] were excluded because the original texts were not available. Finally, only seven articles [5-7, 11-14] met the criteria, including four from China [11-14] and three from Turkey [5-7]. Five patients tested positive for Epstein-Barr virus (Table 1).

The FDG uptake was significant in lung LELC lesions on ^{18}F-FDG PET/CT imaging [5, 13]. According to the published literature, its SUVmax ranges from 5.0 to 34.5. In our study, ^{18}F-FDG PET/CT was performed to further evaluate the benign and malignant of lesions and pre-treatment stages after the discovery of lung mass. The lesion of the left lower lobe abnormally uptake glucose metabolism and SUVmax was 10.7 on PET imaging. Lung LELC is highly sensitive to ^{18}F-FDG, and PET/CT is helpful to perfect palliative strategy and improve prognosis.

Most reported patients are in the early stages of resectable disease, and surgical resection for therapeutic purposes is the preferred method [15]. The patient was treated with chemotherapy after clear diagnosis. After two months later, the lesion was significantly reduced, indicating that the treatment was obviously effective. At present, there is no consensus on chemotherapy programs in advanced patients.

In conclusion, under the exclusion of nasopharyngeal malignancy, the possibility of primary lung lymphoepithelioma-like carcinoma is considered for isolated pulmonary nodules or masses with high metabolism on ^{18}F-FDG PET/CT and tested positive for EB virus.

Conflict of Interest

The authors declare that they have no conflicts interests.

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