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Clinical Features and Prognosis of Pulmonary Lymphoepithelioma-like Carcinoma: Summary of Eighty-five Cases

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Abstract

Pulmonary lymphoepithelioma-like carcinoma (PLELC) is a rare subtype of lung cancer. This retrospective analysis of 85 patients with PLELC was conducted to find the prognostic factors and to explore better treatment. PLELC had a better prognosis. Surgery was recommended mainly for the early stage and multimodality treatment for the advanced stage.

Background: Pulmonary lymphoepithelioma-like carcinoma (PLELC) is a rare subtype of lung cancer that is less reported and not well-understood. **Materials and Methods:** We investigated the clinical features of 85 patients with PLELC to determine the prognostic factors. **Results:** PLELC preferentially affected the young (71.8%) and nonsmokers (72.9%), without a significant difference in gender. Most (50.6%) patients were at the early stage with opportunity for operation, and patients at advanced stages mainly received multimodality treatment. The median follow-up duration was 17 months (range, 1-39 months) for the whole group, and the 3-year overall survival rate for patients in the early stage was 100%, whereas the 1-year and 2-year overall survival rate for patients in the advanced stage were 93% and 77%, respectively. The tumor stages ($P = .031$), distant lymph node metastasis ($P = .035$) and performance status ($P = .008$) were associated with progression-free survival in the univariate analysis, whereas performance status was an independent prognostic factor in the multivariate analysis ($P = .016$). The median progression-free survival in the paclitaxel plus platinum (12 months) group and gemcitabine plus platinum (10 months) group were significantly longer than that in the pemetrexed plus platinum (5 months) group ($P = .001$). **Conclusion:** PLELC had a better prognosis compared with other types of non–small-cell lung cancer and was sensitive to radiotherapy and chemotherapy. Gemcitabine plus platinum and paclitaxel plus platinum should be used as first-line treatment of PLELC, whereas the second-line treatment, if necessary, was always decided by the managing oncologist. The tumor stages and performance status were predictive in the prognosis of patients with PLELC.

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Keywords: Chemotherapy, Lung cancer, Lymphoepithelioma-like carcinoma, Prognosis, Progression-free survival

Introduction

Lymphoepithelioma-like carcinoma (LELC) is a rare cancer, most of which originates from the nasopharynx and few from foregut-derived organs including the salivary glands, stomach, lung, and thymus. Since 1987, Begin et al,[1] who first reported LELC, found that it was an epithelial carcinoma associated with Epstein-Barr virus (EBV) infection. For the past 30 years, more than 500 patients[2] with pulmonary lymphoepithelioma-like carcinoma (PLELC) were documented with specific ethnic and regional preference, especially patients from Asia, including Guangdong Province, Hong Kong, and Taiwan in China.[3-9] The World Health Organization Classification of lung tumor in 2004[10] classified PLELC into large-cell

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lung cancer, then it was removed from the group of large-cell lung cancer and classified as a subgroup of non–small-cell lung cancer (NSCLC) according to The World Health Organization Classification of lung tumors in 2015.[11] PLELC may have a better prognosis than other types of NSCLC, and most PLELC were detected at an early stage.[7,9]

PLELC tends to be misdiagnosed. In the current study, a retrospective analysis on 85 patients with PLELC was carried out in regard to clinical and pathologic characteristics to improve our understanding and to explore better treatment and prognostic factors.

Materials and Methods

Patients

We reviewed the profiles of patients who were diagnosed with PLELC from January 2013 to August 2017 at The First Affiliated Hospital of Guangzhou Medical University. Our research yielded a total of 105 cases. Patients with incomplete clinical evidence or those with nasopharyngeal carcinoma or malignant tumor in other organs were excluded. A total of 85 patients were included, and 20 were excluded.

The diagnostic methods of the 85 patients were as follows: 22 (25.9%) patients were diagnosed via percutaneous lung biopsy guided by computed tomography, 21 (24.7%) patients were diagnosed via bronchoscopy biopsy, 39 (45.9%) patients were diagnosed via surgical biopsy, and 3 (3.7%) patients were diagnosed via lymph node biopsy.

Methods

Information on age, gender, birth place, medical history, initial symptoms, serum tumor markers, radiologic features, pathologic characteristics, treatment, and survival rates, including the duration of progression-free survival (PFS), the duration of disease-free survival (DFS), and overall survival (OS), was collected. The duration of PFS_1 was defined as the period from the start of systematic therapy to the first disease progression or death, which was often used to evaluate the clinical efficacy for the advanced stages. Similarly, the duration of PFS_2 was defined as the period from the start of the second-line treatment to the second time of disease progression or death, and the median PFS duration was defined as the date of 50% of patients reaching disease progression. The duration of DFS was defined as the period from the initiation of systematic therapy to relapsed disease, which was often used to evaluate the clinical efficacy for postoperative patients. The OS duration was defined as the period from the time of diagnosis to the time of death for any cause or was censored at the time of last follow-up. We regarded PFS as the primary terminal indicator. Tumors over 3.5 cm in diameter according to radiographic reports were regard as larger tumor size.[12] Patients with an age over 60 years were defined as the elderly.[13] Pathologic staging was performed according to the Eighth Edition Lung Cancer Stage Classification.[14]

The follow-up duration was defined as the period from the date of diagnosis to the date of death for any cause or lost to follow-up. All 85 patients were followed up until November 2018 through telephone or clinical records. For patients who were lost to follow-up, the survival time was designated as the time of the last follow-up. SPSS16.0 was used for the statistical analysis. Survival functions were estimated by the Kaplan-Meier method and were compared using the log-rank test, whereas multivariate analysis was conducted with the Cox regression model. The differences between the two groups were compared by *t* test. The difference between the results from comparative tests was considered significant if the 2-sided *P* value was .05 or less.

Results

Patient Characteristics

Among the 85 patients, 74 (87.1%) were from Guangdong Province and 11 (12.9%) from either Fujian or Hunan Province. Their age ranged from 26 to 79 years, and the median age was 54 years. In terms of their initial clinical manifestations, 42 (49.4%) had productive cough, 14 (16.5%) presented with hemoptysis, 9 (10.6%) had presented with other symptoms such as chest pain, chest tightness, shortness of breath, or cervical masses, and 20 (23.5%) were asymptomatic. The clinical characteristics are summarized in Table 1.

Table 1 Clinical Characteristics of All Patients

Group	No. Patients (%)
Gender	
Male	38 (44.7)
Female	47 (55.3)
Age, y	
< 60	61 (71.8)
≥ 60	24 (28.2)
Tumor size, cm	
< 3.5	27 (31.8)
≥ 3.5	58 (69.2)
Location	
Left	35 (41.2)
Right	47 (55.3)
Bronchi	3 (3.5)
Classification	
Peripheral	39 (45.9)
Central	46 (54.1)
Smoking	
Yes	23 (27.1)
No	62 (72.9)
Stage	
I	18 (21.2)
II	15 (17.6)
IIIa	9 (10.6)
IIIb/c	18 (21.2)
IV	25 (29.4)
Metastasis	
Regional lymph node	59 (69.4)
Distant lymph node	15 (17.6)
Bone	8 (9.4)
Liver	2 (2.4)

Table 2 Immunohistochemical Marker of All Patients

Immunohistochemical Marker	Total No. Patients	Positive, n (%)
CK	41	41 (100.0)
CK5/6	76	75 (98.7)
CK7	36	1 (2.7)
TTF-1	76	6 (7.9)
P63	85	85 (100.0)
EBER	85	85 (100.0)
EGFR	49	1 (2.0)

Abbreviations: EBERs = Epstein-Bar Virus-related RNAs; EGFR = epidermal growth factor receptor.

Serum Tumor Markers

We documented the serum tumor markers before treatment: 44 (68.8%) cases had elevated serum neuron-specific enolase (NSE), of whom only 5 (11.6%) cases had elevated more than 35 ng/mL[15]; 48 (75%) cases had elevated serum antigen of cytokeratin 19 fragment (CYFRA21-1), whereas all patients (100%) had normal levels of serum carcinoembryonic antigen (CEA); 20 (25.3%) patients had elevated levels of serum tumor-associated antigen 125 (CA-125), and 5 (6.3%) had elevated levels of serum tumor-associated antigen 153 (CA - 153). After 2 cycles of chemotherapy, we found that CA-125 ($t = 3.34$; $P = .003$) and CYFRA21-1 ($t = 2.09$; $P = .047$) had significantly declined, whereas NSE, CEA, and CA-153 had insignificantly declined ($P > .05$). Five (83.3%; n = 6) patients had baseline plasma EBV DNA $> 10^4$ copies/mL, and unfortunately, they were not monitored serially.

Radiographic Features

Tumors often presented as soft lesions, and the median diameter was 4.15 cm (range, 0.48-10.5 cm); 58 (69.2%) patients had larger tumor size, and the central lesions were significantly larger than the peripheral ones ($t = 3.85$; $P < .01$). There were 15 (30%) cases with tumors presenting as smooth boundary, 36 (42.9%) with shallow lobulation, 25 (29.8%) with spiculation, 9 (10.7%) with pleural indentation sign, and 5 (6%) with cavitation.

Pathologic Results

In most patients, the tumor cells were circular or oval with large nuclei (eosinophilic nuclei) and rich cytoplasm, clustered like syncytium and arranged in a solid nested bulk. The surrounding stroma was infiltrated by multiple lymphocytes and plasma cells, without apparent intercellular bridge and keratinization formation but with abundant fibrous tissue or collagen encompassed tumor cells. Owing to higher levels expression of CK, CK5/6, and P63 and lower levels expression of CK7, TTF-1, CgA, 5 patients were initially misdiagnosed as poorly differentiated squamous cell carcinoma. We accidently found that the tumor cells were surrounded by multiple lymphocytes and plasma cells with positive signals in situ hybridization of EBV-related RNAs (EBERs) through the pathology of secondary biopsy or operation; hence, we finally diagnosed them as PLELC. Immunohistochemical markers and epidermal growth factor receptor (EGFR) with paraffin section of lung tissue specimen are provided in Table 2.

Treatment

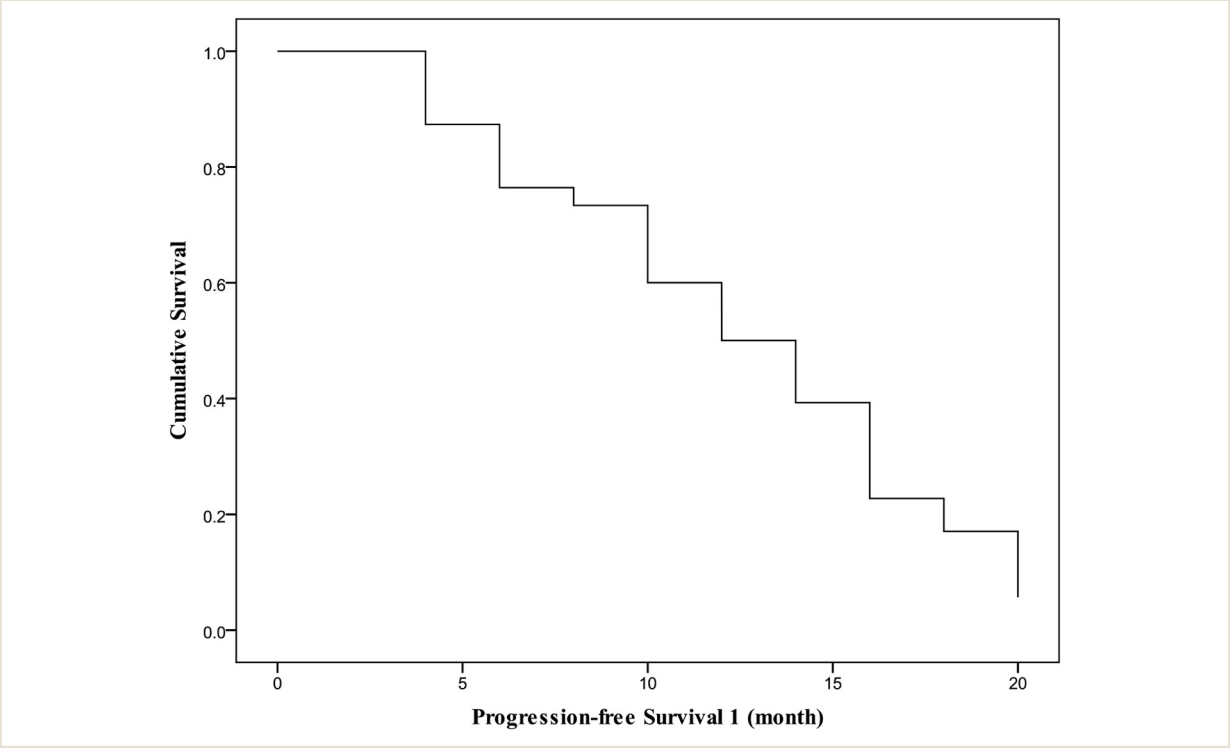
Forty-two patients were in the early stages, including 16 patients with radical resection and 26 postoperative patients with adjuvant or neoadjuvant chemotherapy. None of them received radiotherapy. In the advanced stages (IIIb/IV), 42 patients were treated with palliative chemotherapy as the first-line treatment, and one was treated with EGFR-tyrosine kinase inhibitor (EGFR-TKI) with quick disease progression in 30 days. In the 33 patients in advanced stages, there were 8, 9, and 16 cases treated with the platinum-based combination of pemetrexed (PP), paclitaxel (TP), and gemcitabine (GP), respectively. The other 9 cases, using unusual regimens or treating with palliative chemotherapy after palliative operation, could not be analyzed owing to the small number of cases. In the second-line treatment, 13 patients received palliative chemotherapy, including 4 with TP, 4 with GP, 3 with PP, 1 of whom received chemoradiotherapy, 2 patients who received palliative radiotherapy, 2 who received immunotherapy, 2 who received radiotherapy, 1 who was treated with bevacizumab, and the remaining 7 patients only received supportive treatment.

Survival Data and Prognostic Factors

A total of 85 patients were followed up until November 2018, with the follow-up duration ranging from 1 to 39 months; the median follow-up duration was 17 months. Seven (8.2%) patients were lost to follow-up, whereas 72 patients were still alive. In 42 patients in the early stage, only 4 had disease relapse in the mediastinal lymph nodes, lung, and bone metastasis, and relapsed in situ in 6, 12, 19, and 27 months, respectively. They were still alive and received palliative surgical treatment, chemotherapy, or chemoradiotherapy. The 3-year OS rate of patients in the early stage was 100%; the median DFS and OS was not reached. In the 43 patients at advanced stage, the 0.5-year and 1-year PFS_1 rate was 73% and 39%, respectively, and the median PFS_1 duration was 12 months (Figure 1). For the 19 patients who received second-line treatment, the 0.5-year and 1-year PFS_2 rate was 33% and 25%, respectively, and the median PFS_2 duration was 5.9 months (Figure 2). Six patients (2 at stage IIIb and 4 at stage IV) died (1 owing to acute myocardial infarction and 5 owing to tumor progression); the 1-year and 2-year OS rate of patients at advanced stage were 93% and 77%, respectively.

The associations among age, gender, tumor size and location, tumor stages, regional and distant lymph node metastasis, intrapulmonary metastasis, and pleural metastasis were analyzed (Table 3). Patients at earlier stage ($P = .031$), with better performance status (PS) ($P = .008$), and a lack of distant lymph node metastasis ($P = .035$) had significantly better prognosis (Figures 3-5), and PS ($P = .016$) was an independent factor for prognosis in the Cox regression model. The median PFS_1 was

Figure 1 Forty-three Patients with Pulmonary Lymphoepithelioma-like Carcinoma in the Advanced Stage. The 0.5-year and 1-year PFS_1 Rate Was 73% and 39% Respectively, and the Median PFS_1 Was 12 Months



Abbreviation: PFS_1 = progression-free survival$_1$ (the period from the start of systematic therapy to the first disease progression or death).

significantly different ($P = .001$) in patients using different regimens as first-line chemotherapy, including PP (5 months), TP (12 months), and GP (10 months) (Figure 6).

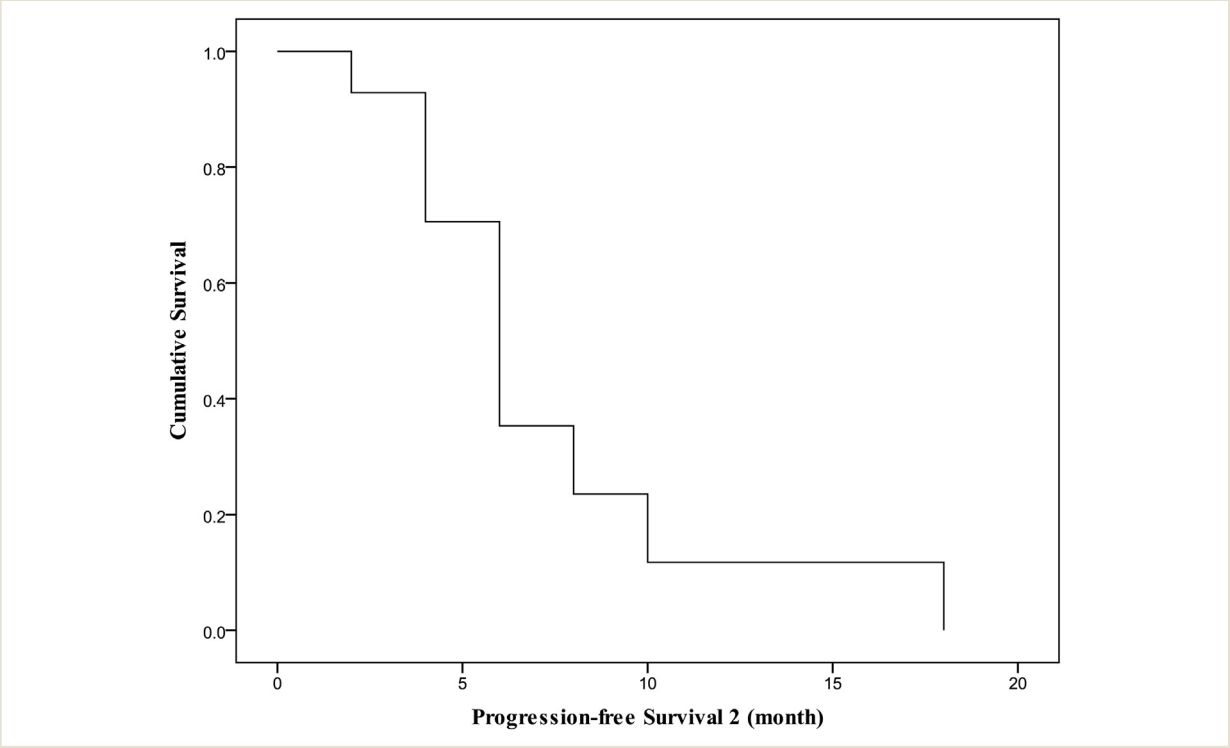
Discussion

PLELC, which has similar morphology with undifferentiated nasopharyngeal carcinoma, is a rare subtype of NSCLC and has often been identified in young nonsmokers who are, on average, 10 years younger than those with other types of NSCLC,[6] whereas Asian patients were 10 years younger than Caucasian patients in developed countries.[16] Some studies reported no differences between males and females,[3,7,17,18] whereas other studies showed a higher proportion of females.[4,6,19] In our study, most patients came from Guangdong Province, an area with a high prevalence of EBV infection, and the male:female ratio was 1:1.24, which was consistent with the study from Liang et al.[7,12] The median age of these patients was 54 years; 71.8% of them were aged 60 years or lower, and most (72.9%) were nonsmokers, which indicated that smoking might not be the main carcinogenic agent for PLELC. The clinical manifestations were similar to other types of lung cancer, including productive cough or sputum production with hemoptysis. Some of them were initially asymptomatic, which was consistent with reports by Chang et al.[4,7,12,17]

In the studies by Han et al,[9,20] most lesions presented as peripheral nodules with unclear boundaries and diameters of 3.5 cm or less, whereas Mo et al[21] reported that the lesions often presented as well-defined lobular boundaries with diameters larger than 3.5 cm adjacent to pleura. However, Ooi et al[22-24] found that the lesions often showed a well-defined lobulated border and tended to be located centrally in the right middle lobe and left lower lobe, with significantly larger sizes compared with peripheral tumors. In our study, tumors were often located centrally in the right lung with larger size compared with the peripheral tumors ($P < .01$), consistent with previous studies.[17,24] Therefore, it was proposed that PLELC was similar to other types of NSCLC but with larger tumor size ($\geq$3.5cm) and a central location. We suggested that physicians should be aware of excluding PLELC when a lesion with larger size was found in the areas with prevalence of EBV infection.

Monitoring of the serum tumor markers may have implications for the diagnosis, treatment, and disease surveillance of lung cancer. NSE is a marker highly expressed in neuroendocrine carcinoma. NSE > 35 ng/mL is an indicator of small-cell lung cancer, and elevated CEA and CA125 can be found in adenocarcinoma, whereas CYFRA21-1 may be increased in squamous cell carcinoma.[15] However, the association between serum tumor markers and PLELC is unclear. Xia et al[25] reported that CA-125 was elevated in 77.8% (7/9) of the patients with PLELC; hence, elevated CA-125 might be one of the indicators of PLELC. Liang et al[7] reported that the level of serum NSE and CYFRA21-1 may be correlated with the disease activity and recommended regular follow-up during the treatment. In our study, NSE was elevated in most of patients but it remained less than 35 ng/L, which indicated that PLELC had part of neuroendocrine function as

Figure 2 Nineteen Patients with Pulmonary Lymphoepithelioma-like Carcinoma in the Advanced Stage. The 0.5-year and 1-year PFS_2 Rate Was 33% and 25% Respectively, and the Median PFS_2 Was 5.9 Months



Abbreviation: PFS_2 = progression-free survival$_2$ (the period from the start of the second-line treatment to the second time of disease progression or death).

compared with small-cell lung cancer. Fiala et al[26] have reported that 10% to 20% of patients with NSCLC have elevated NSE, and they were characterized by rapid lymph node metastasis and sensitivity to radiotherapy, which suggested that it may be associated with the better response to chemoradiotherapy in PLELC. Seventy-five percent of patients had higher CYFRA21-1 levels, and they declined significantly after effective treatment, which may suggest that PLELC might be a subtype of squamous cell lung cancer, and this could be used as evaluation of the therapeutic effect. Of our patients, 25.3% showed elevation of CA-125, which differed from the findings reported by Xia et al,[25] but it was also related to effective treatment. Therefore, our study recommended that CA-125 and CYFRA21-1 could be used to monitor the disease activity and response to the treatment of PLELC. A possible role of the free circulating EBV DNA in nasopharyngeal carcinoma in regard to prognostication, prediction of recurrence, and the response to therapy has been suggested, and similarly, several studies had reported that plasma EBV DNA concentration could be a useful molecular marker for monitoring and prediction of recurrence and overall survival in patients with PLELC, and high EBV DNA concentration was associated with shorter OS and DFS in the initial detection.[27] In our group, 5 of 6 patients had elevated plasma EBV DNA. Plasma EBV DNA could be a good tumor marker for PLELC, and we need to pay attention in the future.

The diagnosis of PLELC mainly depends on pathology. Some researchers[6,12] have pointed out that PLELC is characterized by higher expression of CK, CK5/6, and P63 and minor expression of CK7, TTF-1, and CgA. Liang et al[7] considered that PLELC was derived from epithelial tissue instead of neuroendocrine or glandular epithelium. In our study, patients had similar manifestations as the study reported by Liang et al[7]; notably, they lacked intercellular bridge and keratinization formation, which differed from squamous cell carcinoma. In our study, there were 5 patients misdiagnosed as lowly differentiated squamous cell carcinoma and then diagnosed as PLELC by a repetitive biopsy for infiltration with multiple lymphocytes and plasma cells in stroma with positive signals in situ hybridization of EBERs, which was similar to the finding of a case report.[18] Therefore, we speculated that the classification of PLELC might need to be changed. Meanwhile, when lowly differentiated squamous carcinoma was diagnosed in EBV endemic areas, especially in patients whose tumor cells lacked intercellular bridges and keratinization formation with stroma infiltration of multiple lymphocytes and plasma cells, PLELC should be considered, and a multisite biopsy should be done to exclude the possibility of PLELC if necessary.

Most patients with PLELC were diagnosed at an early and resectable stage, and radical resection was the primary treatment to achieve a cure.[3,6,16,28] Hence, surgery was recommended for patients with early stage disease, and neo-adjuvant or adjuvant chemotherapy ($P < .05$) for the postoperative patients at stage IIIa could obtain a better prognosis,[7] whereas chemotherapy and (or) radiotherapy were the primary treatment for patients at an advanced stage, and platinum-based combination with third-generation chemotherapeutic drugs were recommended

Table 3 Clinical Characteristics of 43 Patients at Advanced Stages and Analysis of Prognostic Factors for Progression-free Survival

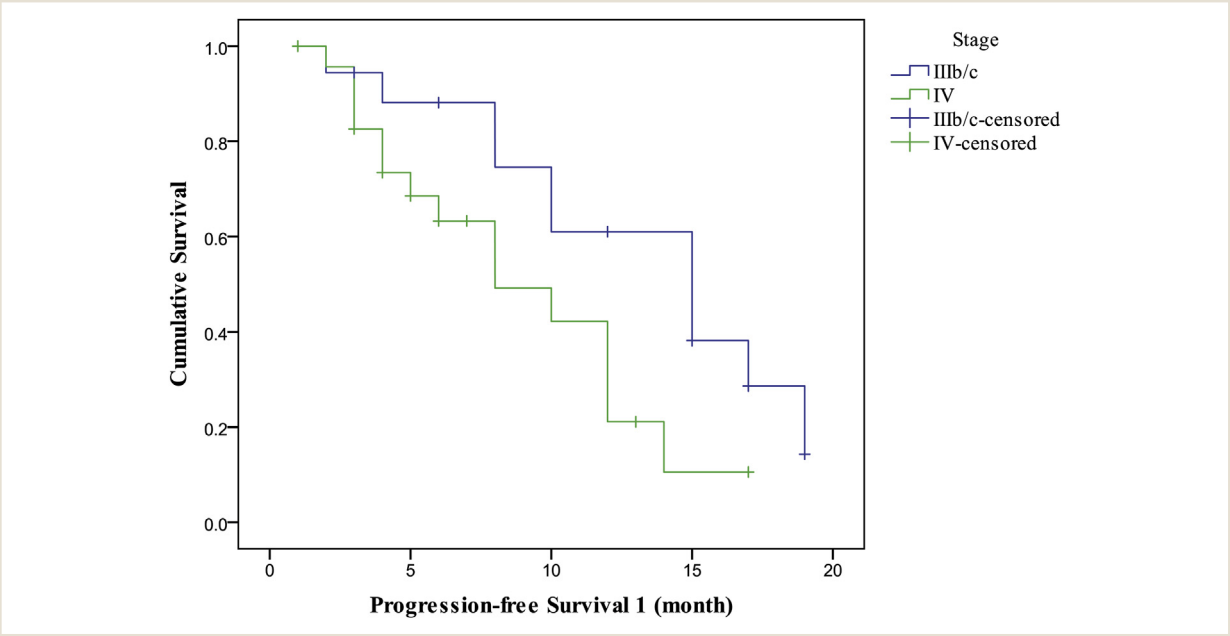
Group	No. Patients (%)	Progression-free Survival$_1$	
		Univariate Analysis: *P*	Multivariate Analysis: *P*
Gender			
Male	25 (58.1)	.563	*
Female	18 (41.9)		
Age, y			
< 60	31 (72.1)	.903	*
≥ 60	12 (27.9)		
Tumor size, cm			
≤ 3.5	5 (11.6)	.888	*
> 3.5	38 (88.4)		
Classification			
Peripheral	16 (37.2)	.887	*
Central	27 (62.8)		
Smoking			
Yes	7 (16.7)	.101	*
No	36 (83.7)		
Distant lymph node			
Yes	13 (30.2)	.035	.387
No	30 (69.8)		
Stage			
IIIb/c	17 (39.5)	.031	.226
IV	26 (60.5)		
Performance status			
≤ 1	30 (69.8)	.008	.016
≥ 2	13 (30.2)		
First-line treatment regimen			
PP	12 (27.9)	*	*
TP	11 (25.6)		
GP	17 (39.5)		
INP	1 (2.3)		
AP	1 (2.3)		
EGFR-TKI	1 (2.3)		

Abbreviations: AP = doxorubicin plus platinum; EGFR-TKI = epidermal growth factor receptor-tyrosine kinase inhibitor; GP = gemcitabine plus platinum; INP = vincristine plus doxorubicin plus platinum; PP = pemetrexed plus platinum; TP = paclitaxel plus platinum.
*Analysis could not be done.

as first-line treatment.[5,28] Some studies reported that[4,7] PLELC was sensitive to PP, GP, TP, and 5-fluorouraeil plus a platinum-based regimen. There were 33 patients with advanced PLELC who were treated with PP, TP, and GP for palliative chemotherapy. The TP and GP group achieved a significantly longer PFS than the PP group ($P = .001$), and we proposed that PLELC had a similar pathology to squamous cell lung cancer, whereas pemetrexed achieved a better response to non-squamous NSCLC.[29] We recommended that GP or TP should be adopted as first-line chemotherapy for PLELC. In addition, EGFR-TKIs had clinical significance for lung cancer management.[30] However, few reports had been conducted to demonstrate the EGFR mutation rates and the response to EGFR-TKIs. Liang et al[7] reported 39 cases with all-negative EGFR mutation, and Chang et al reported[31-33] that the mutation rates were 1.8% to 17.4%. In our group, there was only 1 patient with EGFR mutation, who had been treated with EGFR-TKI for only 1 month with quick disease progression, which indicated that the mutation rate of EGFR in PLELC was lower and might not be the primary oncogene for this disease. Therefore, PLELC could hardly benefit from targeted therapy. Moreover, the second-line treatment if necessary was always decided by managing oncologist. In our group, most patients received multimodality treatment, including immunotherapy, which was a new but potential treatment, and programmed cell death-ligand may be potential therapeutic targets for PLELC.[34]

PLELC had a better prognosis than other types of NSCLC.[7,9,16,17] Lin et al reported[6] that the 3-year recurrence-free survival rate was 73% for 39 patients who underwent surgery. Tay et al reported 28 patients with PLELC, and the 2-year OS rates for stage I/II, stage III, and stage IV disease were 100%, 85.7%, and 61.5%, respectively, whereas the 5-year OS rates was 100%,

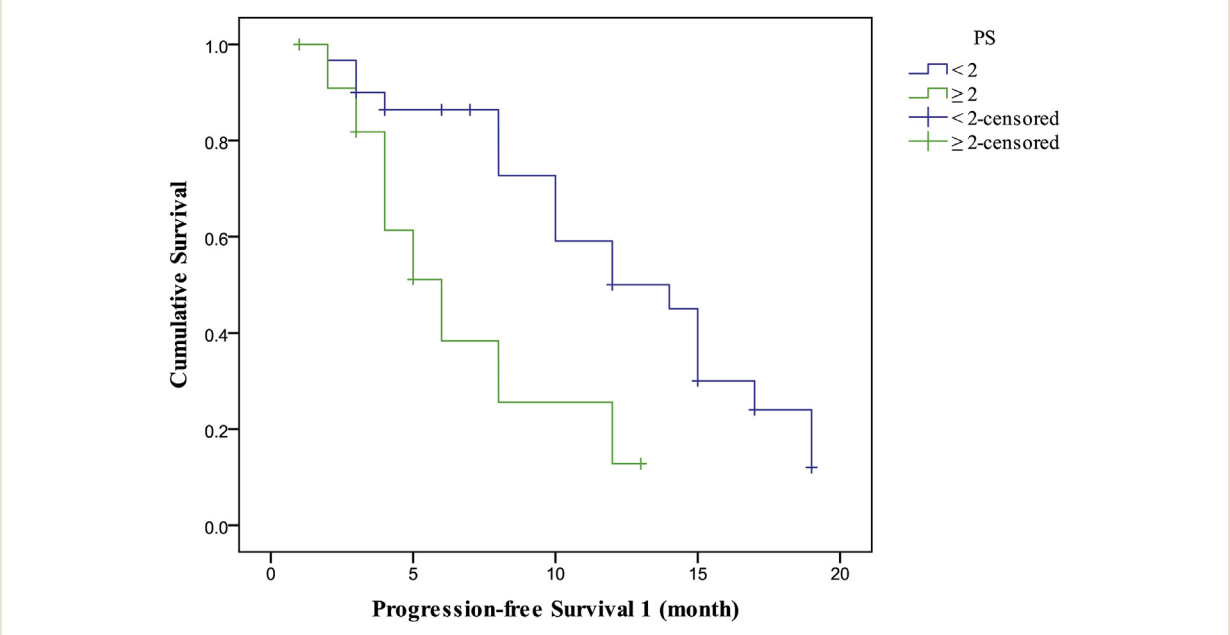
Figure 3 Forty-three Patients with Pulmonary Lymphoepithelioma-like Carcinoma. PFS_1 Was Associated with tumor Stage ($P = .031$)



Abbreviation: PFS_1 = progression-free survival$_1$ (the period from the start of systematic therapy to the first disease progression or death).

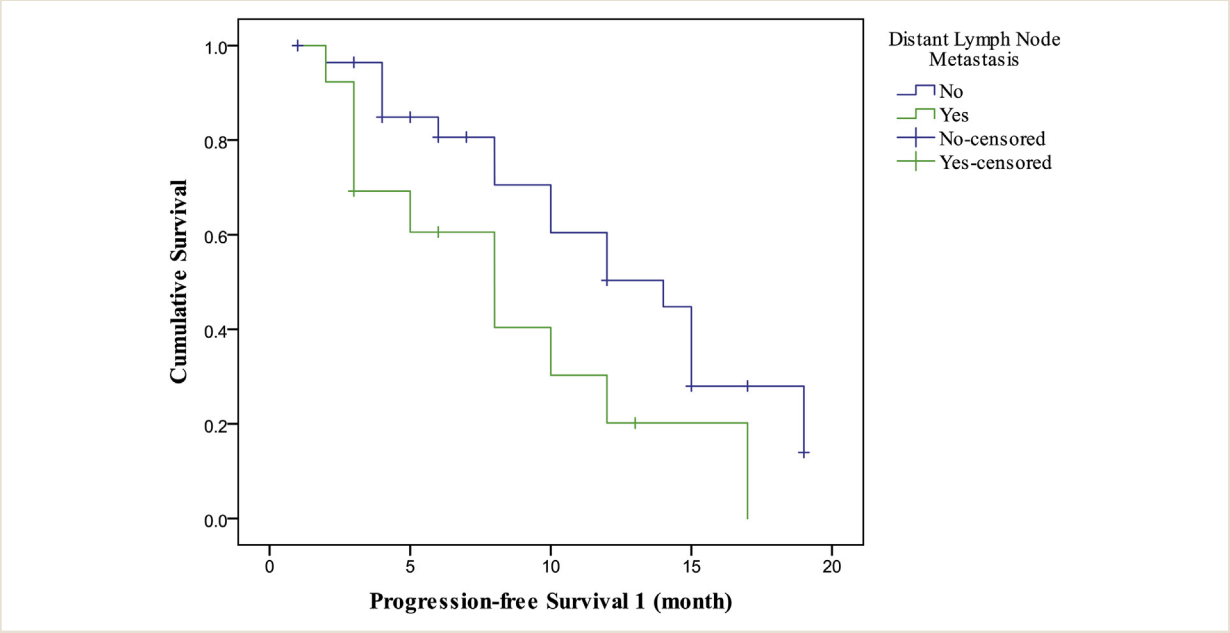
85.7%, and 9.6%, respectively.[35] In our study, a similar prognosis was displayed. The 3-year OS rate of patients at early stage was 100%; the 1-year and 2-year OS rate of patients at advanced stage were 93% and 77%. The median PFS_1 and PFS_2 was 12 and 5.9 months for patients at advanced stages, and the 0.5-year and 1-year PFS_1 and PFS_2 rate was 73% and 33%, 39% and 25%, respectively. In the univariate analysis, tumor stages, distant lymph node metastasis, and PS were significantly correlated with the prognosis

Figure 4 Forty-three Patients with Pulmonary Lymphoepithelioma-like Carcinoma. PFS_1 Was Associated with Patient's PS ($P = .008$)



Abbreviations: PFS_1 = progression-free survival$_1$ (the period from the start of systematic therapy to the first disease progression or death); PS = performance status.

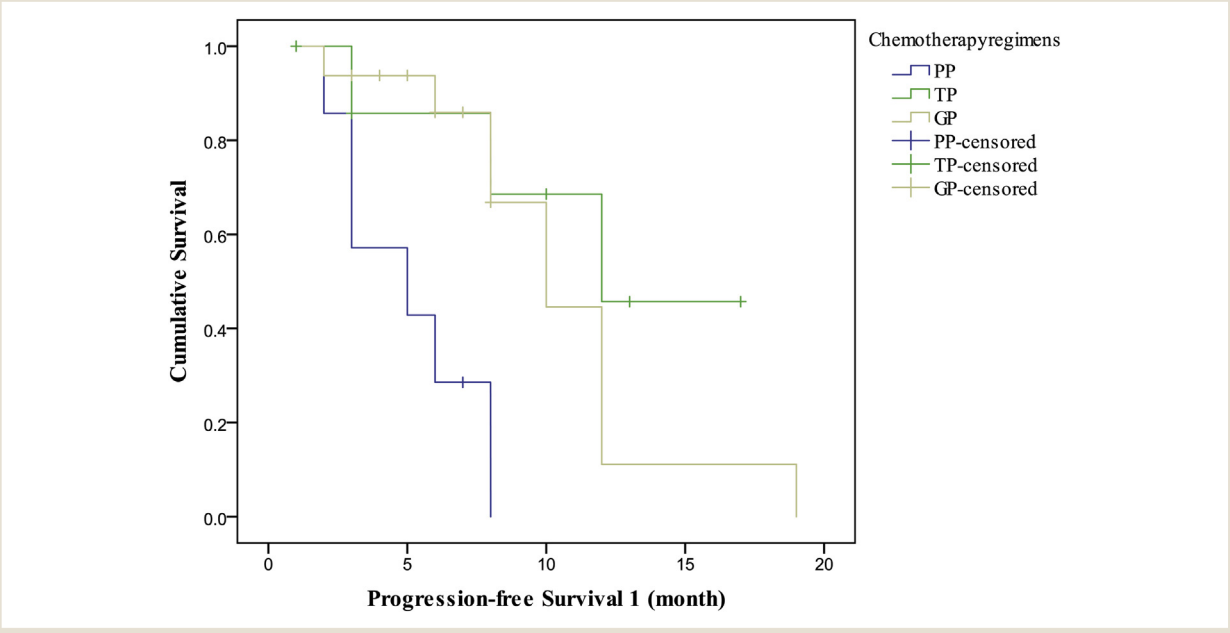
Figure 5 Forty-three Patients with Pulmonary Lymphoepithelioma-like Carcinoma. PFS_1 Was Associated with Patient's Distant Lymph Node Metastasis ($P = .035$)



Abbreviation: PFS_1 = progression-free survival$_1$ (the period from the start of systematic therapy to the first disease progression or death).

of patients at advanced stages, and in multivariate analysis, PS was also the independent risk factor of prognosis, whereas age, gender, smoking status, tumor size and location, regional lymph node metastasis, lung metastasis, and pleural metastasis of patients was not correlated with the prognosis, which agreed with the findings by Lin et al.[5,7]

Figure 6 Thirty-three Patients with Pulmonary Lymphoepithelioma-like Carcinoma. PFS_1 Was Associated with the First-line chemotherapy Regime ($P = .001$)



Abbreviations: GP = gemcitabine plus platinum; PFS_1 = progression-free survival$_1$ (the period from the start of systematic therapy to the first disease progression or death); PP =pemetrexed plus platinum; TP = paclitaxel plus platinum.

There are limitations in our study. First, this study was retrospective, and partial clinical data were incomplete. Secondly, PLELC is a rare subtype of lung cancer, and the number of cases in this study was limited. A prolonged follow-up and a larger number of patients are essential in future studies.

Conclusion

PLELC is prevalent in Southeast Asian, young nonsmokers. There are no obvious preferences in gender. PLELC is mostly manifested as a central mass with a large size, and is closely related to EBV infection. In terms of treatment, surgery is recommended mainly for early stage patients, and multimodality therapy is recommended for advanced stage patients; we suggest that GP and TP are used as first-line chemotherapy, whereas the second-line treatment, if necessary, be decided by the managing oncologist. Furthermore, targeted therapy might not provide definite benefit to patients with PLELC. Tumor stages, distant lymph node metastasis, and PS are correlated with the prognosis of PLELC.

Clinical Practice Points

- PLELC is a rare subtype of lung cancer and has a better prognosis compared with other types of NSCLC.
- Because of similar characteristics, more attention should be paid to exclude PLELC before making a diagnosis of poorly differentiated squamous cell carcinoma. Meanwhile, a biopsy could be performed at different sites or repetitively if necessary.
- PLELC has a better response to GP and TP than PP; thus, GP and TP are preferentially recommended as the first-line chemotherapy regimens for PLELC.

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Disclosure

The authors have stated that they have no conflicts of interest.

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