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ABOUT COVER

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CASE REPORT

Metastatic stomach lymphoepithelioma-like carcinoma and immune checkpoint inhibitor therapy: A case report

Guo-Feng Chen, Jun Wang, Yu Yan, Song Xu, Jian Chen

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Abstract

BACKGROUND

Pulmonary lymphoepithelioma-like carcinoma (PLELC) is a rare type of non-small-cell lung cancer. Stomach lymphoepithelioma-like carcinoma (LELC) metastasis secondary to PLELC has not been reported recently.

CASE SUMMARY

A 64-year-old female was admitted to our hospital for a regular gastroscopy examination with a 6-year history of surgical resection for left PLELC. Positron emission tomography/computed tomography suggested high accumulation of 18F-fludeoxyglucose in the gastric cardia region. Upper gastrointestinal endoscopy confirmed a large mass at the stomach fundus. Immunohistochemistry (IHC) of the biopsy suggested metastatic stomach LELC. Proximal gastrectomy showed that this 6.5 cm × 5.0 cm mass was located in the stomach fundus near the cardia. Histopathological examination showed a poorly differentiated carcinoma with prominent lymphoplasmacytic infiltration. IHC demonstrated that the tumor was positive for CK (AE1/AE3), p63, p40, p53, Ki-67 (70%), and EGFR (3+) and negative for CK7, CK20, Her2, and CD10. *In situ* hybridization analysis showed positive staining Epstein-Barr virus-encoded RNA. Tumor programmed cell death ligand 1 (PD-L1) expression score was 98%, and the combined positive score was

100, with no evidence of microsatellite instability. Thus, the patient was unequivocally diagnosed with metastatic stomach LELC secondary to pulmonary LELC. After discharge, this patient underwent PD-1 inhibitor treatment (toripalimab, 240 mg) every 3 wk for ten cycles, and she has had no tumor recurrence.

CONCLUSION
For gastric LELC metastasis, PD-1 inhibitor therapy could become a new therapeutic approach, though there is still no evidence from large data sets to support this.

Key Words: Stomach neoplasm; Pulmonary lymphoepithelioma-like carcinoma; Metastasis; Immune checkpoint inhibitor; Case report

Core Tip: Pulmonary lymphoepithelioma-like carcinoma (PLELC) is a rare type of non-small-cell lung cancer. Stomach lymphoepithelioma-like carcinoma (LELC) metastasis secondary to PLELC has not been reported recently. We present a 64-year-old female patient who was admitted to our hospital for a regular gastroscopy examination with a 6-year history of surgical resection for left PLELC. After proximal gastrectomy, histopathological examination showed a poorly differentiated carcinoma with prominent lymphoplasmacytic infiltration, suggesting stomach LELC metastasis. Tumor programmed cell death ligand 1 (PD-L1) expression showed a tumor proportion score of 98% and a combined positive score of 100. After discharge, this patient underwent PD-1 inhibitor treatment for ten cycles and has not experienced tumor recurrence. These findings suggest that for gastric LELC metastasis, PD-1 inhibitor therapy could become a potential therapeutic approach.

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INTRODUCTION

Pulmonary lymphoepithelioma-like carcinoma (PLELC) is a rare type of non-small cell lung cancer that tends to occur in young, nonsmoking, and Asian populations[1]. It has unique clinical and pathological features that are similar to those of undifferentiated nasopharyngeal carcinoma[2,3]. PLELC is characterized by Epstein-Barr virus (EBV) infection. According to whole-exome sequencing, targeted deep sequencing and single-nucleotide polymorphism arrays, the genetic lesions affect several critical pathways, including the NF-κB, JAK/STAT, and cell cycle pathways[4]. Along with conventional surgical resection, immunotherapy has become a focus of attention[5,6]. Although lymphoepithelioma-like carcinoma (LELC) metastasis has been reported, including subcutaneous[7], endotracheal[8], and lung door and mediastinal lymph nodes[9], stomach LELC secondary to PLELC has not been reported recently, nor have treatments for it.

CASE PRESENTATION

Chief complaints

A 64-year-old female patient was admitted to our hospital for a regular gastroscopy examination.

History of present illness

There is no history of present illness.

History of past illness

The patient had a 6-year history of surgical resection for left PLELC. She underwent four cycles of gemcitabine plus cisplatin chemotherapy, four cycles of pemetrexed plus carboplatin chemotherapy, and 30 cycles of radiotherapy (Figure 1).

Personal and family history

The patient denied any chronic medical history, such as hypertension, diabetes, heart disease, or tobacco or alcohol (illicit drug) use.

Physical examination

On physical examination, the patient reported no obvious discomfort.

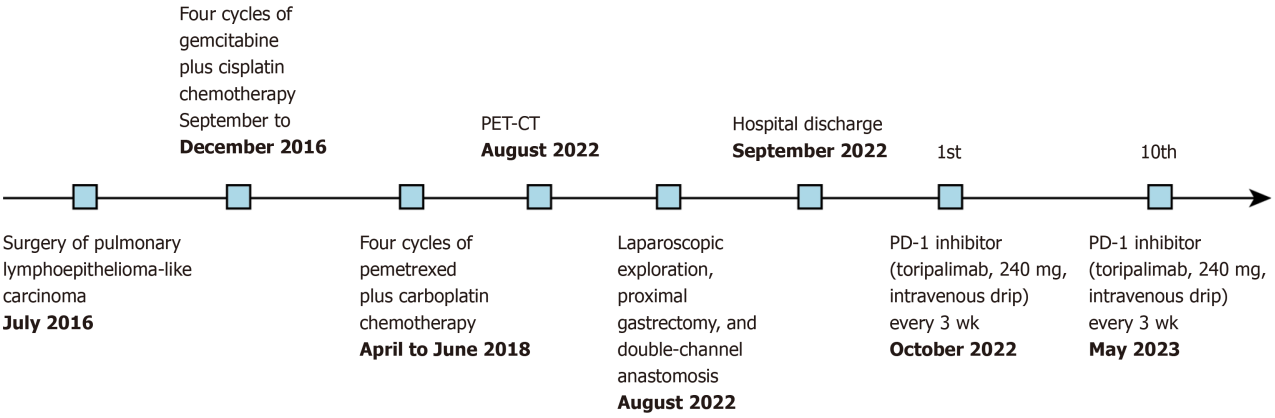

Figure 1 Timeline of history of past illnessthe, initial diagnosis, surgical intervention, postoperative adjuvant therapy, and follow-up period. PET-CT: Positron emission tomography/computed tomography; PD-1: programmed cell death 1.

Laboratory examinations

Laboratory findings included increased levels of tumor markers, such as carbohydrate antigen 125 (CA125) (36.9 U/mL; reference range, < 35 U/mL) and CA211 (5.9 ng/mL; reference range, < 5 ng/mL). A stool occult blood test was positive.

Imaging examinations

Gastroscopy revealed a space-occupying lesion in the cardia/fundus region of the stomach. A whole-abdominal contrast-enhanced computed tomography (CT) scan showed an irregular mass in the gastric cardia. Positron emission tomography/CT was also performed, which suggested high levels of 18F-fludeoxyglucose accumulation in the gastric cardia region (a maximum standardized uptake value of 20.03), indicating malignant tumors (Figure 2). Upper gastrointestinal endoscopy further confirmed a large mass of about 5 cm × 4 cm at the stomach fundus, and this submucosal bulge broke into the stomach cavity (Figure 3A). According to the immunohistochemistry (IHC) of the biopsy, the pathological diagnosis was a metastatic stomach lymphoepithelioma-like carcinoma.

FINAL DIAGNOSIS

Based on all the findings, the patient was diagnosed with metastatic LELC of the stomach.

TREATMENT

Based on the above diagnosis, we performed laparoscopic exploration, proximal gastrectomy, and double-channel anastomosis between the esophagus, residual stomach, and jejunum. Surgical resection of the tumor revealed a large mass located in the stomach fundus near the cardia, presenting as a type of ulcer infiltrate with a size of 6.0 cm × 5.0 cm (Figure 3B). Pathology after surgery showed a poorly differentiated carcinoma of the gastric fundus of 6.5 cm × 5.0 cm. Only one perigastric LN showed positive metastasis (1/24). Histopathological examination by hematoxylin and eosin staining of the stomach tumor sections showed a poorly differentiated carcinoma with prominent lymphoplasmacytic infiltration (Figure 4A). IHC analysis demonstrated that the tumor was positive for CK (AE1/AE3), p63, p40, p53, Ki-67 (70%), and EGFR (3+) and negative for CK7, CK20, Her2, Muc-5AC, Muc-6, Muc-2, and CD10. *In situ* hybridization showed positive staining for EBV -encoded RNA (Figure 4B). Moreover, the ICH results of the positive LN were consistent with those of the stomach lesions. When we analyzed tumor programmed cell death ligand 1 (PD-L1) expression, we found a tumor proportion score of 98% and a combined positive score of 100, with no evidence of microsatellite instability. The pathological findings were consistent with those reported for pulmonary LELC. Thus, the patient was unequivocally diagnosed with stomach LELC metastatic secondary to pulmonary LELC. After 16 d of routine treatment following gastrectomy, the patient was discharged.

OUTCOME AND FOLLOW-UP

The patient underwent immune checkpoint inhibitor (ICI) treatment with a PD-1 inhibitor (toripalimab, 240 mg, intravenous drip) every 3 wk after discharge (September 6, 2022). On outpatient follow-up, the patient stayed on schedule for ten cycles of PD-1 inhibitor treatment. So far, no adverse events and no tumor recurrence have occurred.

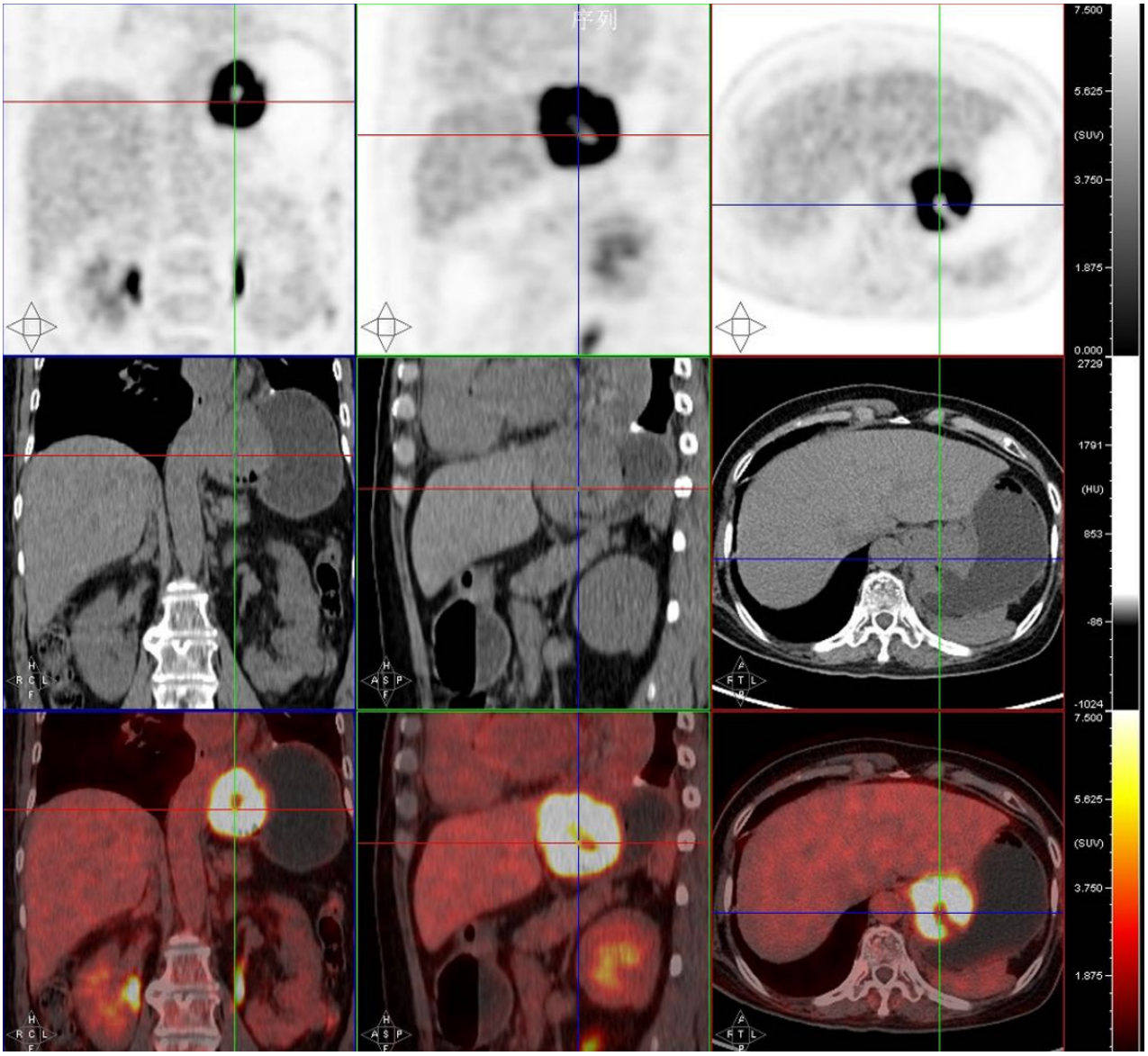

Figure 2 Positron emission tomography/computed tomography showing high accumulation of ^{18}F-fludeoxyglucose in the gastric cardia region. A maximum standardized uptake value of 20.03.

DISCUSSION

Pulmonary LELC is a rare type of non-small-cell lung cancer. Cases of pulmonary or metastatic LELC have been reported recently, but to our knowledge, this is the first report of stomach LELC metastasis secondary to a pulmonary tumor.

The most common approach for treating LELC is multimodal therapy. The expression of PD-1/PD-L1 may be related to the prognosis of LELC[10]. Growing evidence shows that ICIs are effective against pulmonary LELC[5]. One study reviewed 36 patients with PLELC treated with PD-1/PD-L1 inhibitors[6]. The objective response rate of all 36 patients was 57.6%, and the patients with higher PD-L1 expression were more likely to have a tumor response. In another study in which patients received multiple treatments that were ineffective, including surgery, chemotherapy and radiotherapy, ICIs proved to be a feasible option[11]. The efficacy of ICI therapy in patients with metastatic stomach LELC is unknown.

In one metastasis study[9], the patient was diagnosed with PLELC as well as metastasis to the mediastinal lymph nodes and liver. After five cycles of nivolumab, the tumor and the lesions in the liver became smaller. The values of CYFRA21-1 and NSE dramatically decreased. Another study found advanced thymic LELC with bone marrow metastases[12]. This patient responded well to toripalimab after 10 months of therapy. Based on the above evidence, we gave our patient a PD-1 inhibitor (toripalimab, 240 mg, intravenous drip) every 3 wk after discharge for ten cycles, with no radiographical evidence of tumor recurrence.

For this case, two questions are worth considering. First, what is the pathway through which lung cancer metastasizes to the stomach? Although gastric metastasis from lung cancer is rare, it can spread to the gastrointestinal tract through hematogenous and lymphatic routes[13]. Based on the findings in the positive LN, which was consistent with those in the stomach lesions, we believe that this patient's gastric metastasis was through the lymphatic pathway. Second, do we have better treatment options, such as PD-1 inhibitor treatment, before surgery? Because of the growing evidence about PD-1

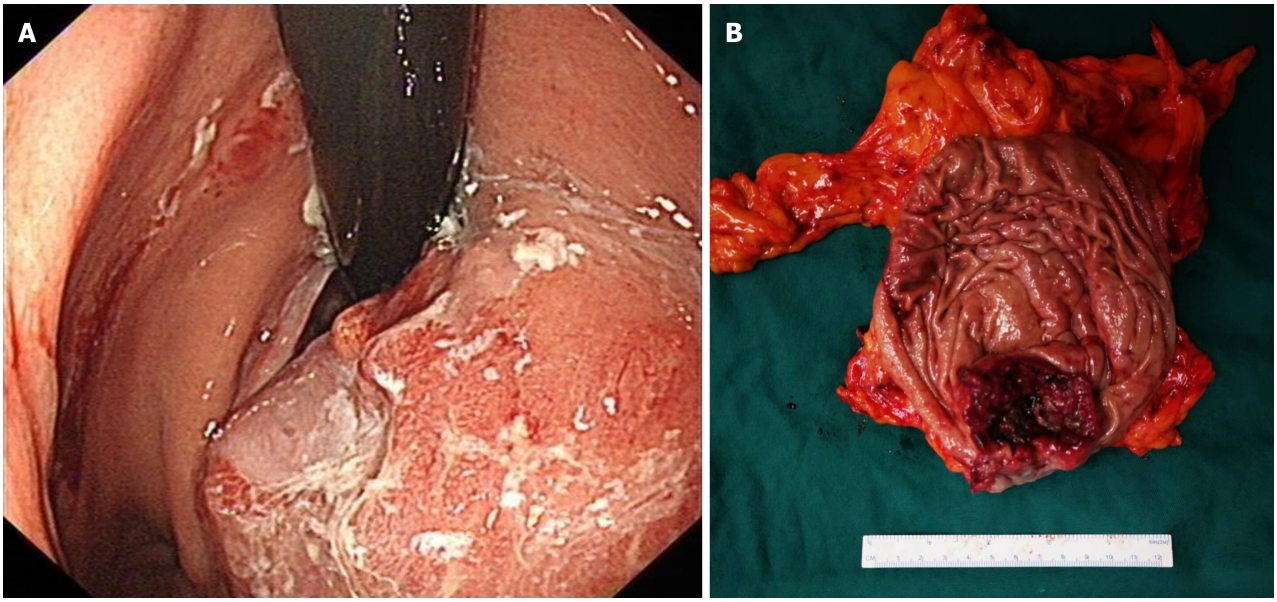

Figure 3 Upper endoscopy and surgical resection. A: The presence of a large mass of about 5 cm × 4 cm at the stomach fundus was confirmed by upper endoscopy; B: Surgical resection of the tumor revealed a large mass located in the stomach fundus near the cardia, showing a type of ulcer infiltrate measuring 6 cm × 5 cm.

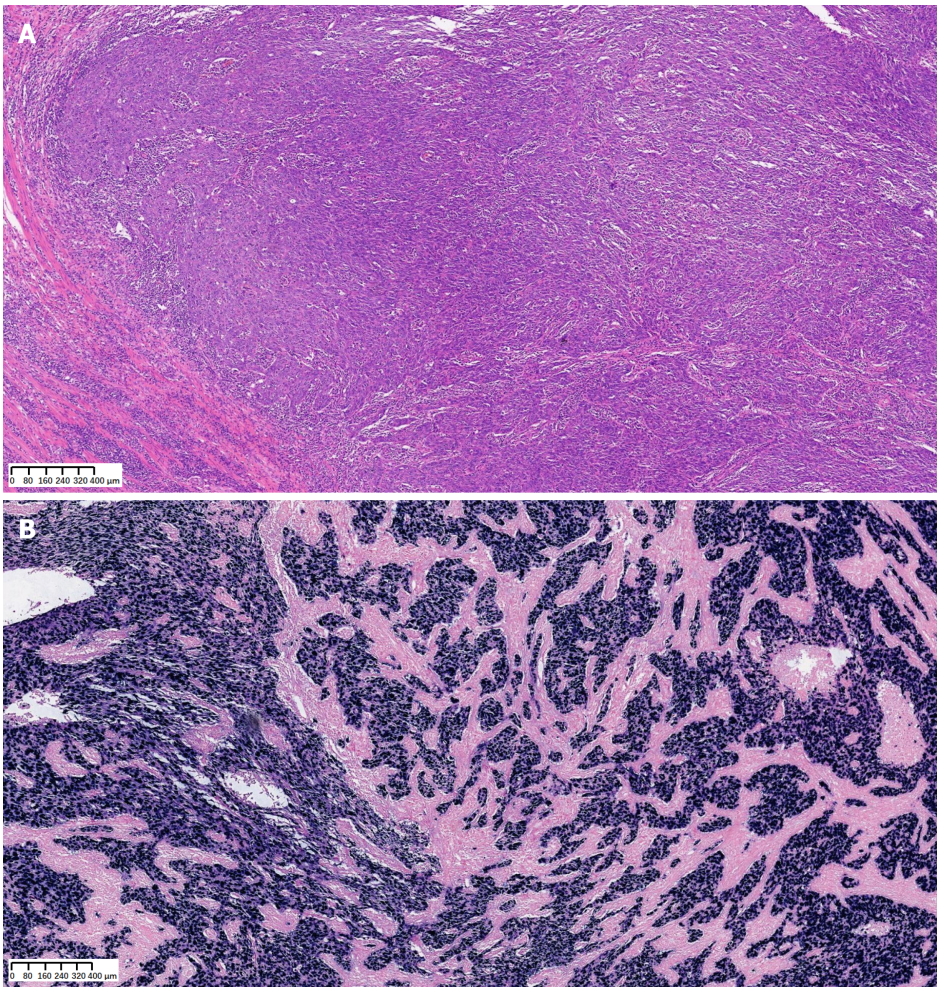

Figure 4 Hematoxylin and eosin staining and *in situ* hybridization. A: Histopathological examination of a stomach tumor section by hematoxylin and eosin staining, showing poorly differentiated carcinoma with prominent lymphoplasmacytic infiltration; B: *In situ* hybridization analysis showing positive staining for Epstein-Barr virus-encoded RNA.

inhibitors in pulmonary or metastatic LELC, we may prioritize PD-1 inhibitors in later-stage cases, especially for patients who cannot undergo surgical resection.

In conclusion, the present case presents a rare type of stomach tumor secondary to pulmonary LELC. This case demonstrates the necessity of IHC for differential diagnosis. ICIs such as PD-1 inhibitors may play an important role in the treatment of metastatic LELC.

CONCLUSION

The case suggested that for metastatic gastric LELC, PD-1 inhibitor therapy can become a potential therapeutic approach. However, there is still a lack of evidence from large data and large samples to support this.

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FOOTNOTES

Author contributions: Chen GF and Wang J contributed equally to this work; Chen GF and Wang J wrote draft of the manuscript and participated in the patient's treatment; Xu S performed the gastroscopy and provided the images; Yan Y, as a pathologist, performed the histological findings; Chen J supervised the study, developed the concept and edited the paper; and all authors have approved the final version of the manuscript.

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REFERENCES

1 **Sathirareuangchai S**, Hirata K. Pulmonary Lymphoepithelioma-like Carcinoma. *Arch Pathol Lab Med* 2019; **143**: 1027-1030 [PMID: 30672338 DOI: 10.5858/arpa.2018-0149-RS]

2 **Chen B**, Zhang Y, Dai S, Zhou P, Luo W, Wang Z, Chen X, Cheng P, Zheng G, Ren J, Yang X, Li W. Molecular characteristics of primary pulmonary lymphoepithelioma-like carcinoma based on integrated genomic analyses. *Signal Transduct Target Ther* 2021; **6**: 6 [PMID: 33414372 DOI: 10.1038/s41392-020-00382-6]

3 **Fan Y**, Li C, Qin J, Lu H. Primary pulmonary lymphoepithelioma-like carcinoma. *Med Oncol* 2020; **37**: 20 [PMID: 32146584 DOI: 10.1007/s12032-020-1344-3]

4 **Hong S**, Liu D, Luo S, Fang W, Zhan J, Fu S, Zhang Y, Wu X, Zhou H, Chen X, Chen G, Zhang Z, Zheng Q, Li X, Chen J, Liu X, Lei M, Ye C, Wang J, Yang H, Xu X, Zhu S, Yang Y, Zhao Y, Zhou N, Zhao H, Huang Y, Zhang L, Wu K. The genomic landscape of Epstein-Barr virus-associated pulmonary lymphoepithelioma-like carcinoma. *Nat Commun* 2019; **10**: 3108 [PMID: 31311932 DOI: 10.1038/s41467-019-10902-w]

5 **Archwamety A**, Ruangchira-Urai R, Akewanlop C, Korphaisarn K. Primary pulmonary lymphoepithelioma-like carcinoma treated with immunotherapy: A case report and literature review. *Thorac Cancer* 2022; **13**: 2539-2541 [PMID: 35830974 DOI: 10.1111/1759-7714.14580]

6 **Zhou N**, Tang H, Yu S, Lin Y, Wang Y. Anti-PD-1 antibodies, a novel treatment option for advanced chemoresistant pulmonary lymphoepithelioma carcinoma. *Front Immunol* 2022; **13**: 1001414 [PMID: 36561745 DOI: 10.3389/fimmu.2022.1001414]

7 **Shima T**, Taniguchi K, Kobayashi Y, Kakimoto S, Fujio N, Uchiyama K. Clinical silence of pulmonary lymphoepithelioma-like carcinoma with subcutaneous metastasis: a case report. *World J Surg Oncol* 2019; **17**: 128 [PMID: 31340830 DOI: 10.1186/s12957-019-1671-z]

8 **Mlika M**, Hamdi B, Marghli A, El Mezni F. About a lymphoepithelioma-like carcinoma of the lung with an endotracheal localization. *Tunis Med* 2018; **96**: 451-453 [PMID: 30430492]

9 **Qiu ZX**, Zhou P, Wang K. Primary Pulmonary Lymphoepithelioma-Like Carcinoma Response Favorably To Nivolumab: A Case Report. *Onco Targets Ther* 2019; **12**: 8595-8600 [PMID: 31802895 DOI: 10.2147/OTT.S219512]

10 **Sha Z**, Wei Y, Gao T, Luo Y, Chen J, Li T, Hu L, Niu X, Lin Z, Lv W, Pei X. Clinical observation of pulmonary lymphoepithelioma-like carcinoma. *J Thorac Dis* 2021; **13**: 5683-5690 [PMID: 34795918 DOI: 10.21037/jtd-21-1369]

11 **Wu Z**, Xian X, Wang K, Cheng D, Li W, Chen B. Immune Checkpoint Blockade Therapy May Be a Feasible Option for Primary Pulmonary Lymphoepithelioma-like Carcinoma. *Front Oncol* 2021; **11**: 626566 [PMID: 33981599 DOI: 10.3389/fonc.2021.626566]

12 **Li YJ**, Li YW, Cui GH, Li SH, Deng YW, Lu D. Advanced thymic lymphoepithelioma-like carcinoma with bone marrow metastases treated by immunotherapy combined with antiangiogenesis therapy: a case report. *Anticancer Drugs* 2022; **33**: 686-690 [PMID: 35324515 DOI: 10.1097/CAD.0000000000001293]

13 **Tang D**, Lv J, Liu Z, Zhan S, Gao Y. Gastric Metastasis of Primary Lung Cancer: Case Report and Systematic Review With Pooled Analysis. *Front Oncol* 2022; **12**: 922016 [PMID: 35875072 DOI: 10.3389/fonc.2022.922016]

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