

# Rhinitis may be a clinical symptom of primary pulmonary lymphoepithelioma-like carcinoma, an incidental finding during the COVID-19 pandemic

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*To the Editor:* Primary pulmonary lymphoepithelioma-like carcinoma (PPLELC) is considered to be a rare type of lung cancer and is caused by long-term Epstein–Barr virus infection with clinical symptoms similar to most lung cancers. During the COVID-19 pandemic, we treated a seemingly asymptomatic patient with PPLELC comorbidity who was admitted to the hospital for an acute attack of chronic rhinitis. The chest computed tomography (CT) scans showed an abnormal mass in the patient's lung. Based on this clinical case, we propose that there is a positive correlation between chronic Epstein–Barr virus-related rhinitis and PPLELC. In addition, we recommend that patients with rhinitis who are infected by the Epstein–Barr virus receive continuous antiviral therapy with regular monitoring of the viral concentration and CT scans.

A 48-year-old non-smoking female patient, from Hunan Province (China), visited her local hospital for fear of being infected with COVID-19 as she experienced symptoms of sneezing and runny nose. The patient had a previous history of chronic rhinitis for at least 2 years. In most cases, symptoms of chronic rhinitis were mild and only presented nasal cavity secretions. Severe rhinitis is usually manifested as runny nose, nasal congestion, and difficult respiration. If these symptoms are not treated, it generally ameliorates or disappears after 5–7 days of initial symptoms. Based on measures to control the COVID-19 pandemic, all patients are required to undergo a throat swab test and chest CT scan. In addition, this patient also underwent viral detection of nasal secretions and serum as the patient showed flu-like symptoms. The Epstein–Barr virus was detected in her nasal secretions and serum. However, her chest CT scans revealed a mass in the left upper lung, which was determined to be a malignant tumor. The 2-[(18)F] fluoro-2-deoxy-D-glucose (FDG)-positron emission to-

mography (<sup>18</sup>F-FDG PET/CT) showed a mass in the left lung lingula lobe, with a maximum area of 34 mm × 32 mm, high expression of the <sup>18</sup>F-FDG imaging agent, and the maximum value of standardized uptake value (SUV<sub>max</sub>) of 23.9 kBq/mL [Supplementary Digital Content, Figure 1A, <http://links.lww.com/CM9/A570>, indicated by the arrow 1]. The imaging agent distribution in the <sup>18</sup>F-FDG PET/CT scan of the nose was abnormal with a maximum value of Standardized Uptake Value of 6.6 kBq/mL [Supplementary Digital Content, Figure 1A, <http://links.lww.com/CM9/A570>, indicated by arrow 3], which suggests a possible long-term chronic infection caused by viruses or bacteria. According to the 8th edition staging of the Union for International Cancer Control (UICC), the lung cancer of the preoperative clinical staging of T2aN1M0.

The patient was subsequently admitted to the General Hospital of Central Theater Command of the People's Liberation Army for lung resection. On May 15, 2020, the patient underwent left video-assisted thoracoscopic surgery (VATS) pneumonectomy, as the intraoperative evaluation showed that the tumor had spread to both the upper and lower lobes. Postoperative pathological results indicated the presence of PPLELC in the left lung tumor [Supplementary Digital Content, Figure 1B, <http://links.lww.com/CM9/A570>] and confirmed metastatic carcinoma in the lymph nodes of group 11, but not in groups 5, 7, 9, and 10. Immunohistochemical analysis found panCK (+), CK5/6 (+), P40 (+), P63 (+), TTF-1 (–), CK7 (–), CD56 (–), Ki-67 (+30%), EBER (+), and PD-L1 (+80%). Postoperative genetic testing of the resected specimen for 20 common gene targets (BGI-Shenzhen [Headquarters]: Shenzhen, 518083, China) revealed no mutated genes as *EGFR* (Exon 18/19/20/21/T790), *FGFR2*, *FGFR3*, *ROS1*, *RET*, *PIK3CA* (Exon 10/12,

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coding exon 9/20), *ALK*, *KRAS* (Codon 12/13/61/146), *NRAS* (Codon 12/13/61), *KIT* (Exon 9/11), *BRCA1*, *BRCA2*, and *ERBB2* (Exon 20/copy number amplification).

PPELCL accounts for only 0.25% to 0.9% of all rare non-small cell lung cancers (NSCLC) in China,<sup>[1]</sup> and only a few cases have been reported in the literature. Most studies about PPELCL have found the Epstein–Barr virus in the serum of patients. The pathological diagnosis of PPELCL needs to meet the following two conditions: first, undifferentiated epithelial cells accompanied with a large number of lymphocyte infiltration observed on pathological sections; second, the Epstein–Barr virus detected in tumor tissues.<sup>[1–3]</sup> However, the pathologic features of PPELCL are very similar to those of nasopharyngeal carcinoma.<sup>[1,3]</sup> An untreated Epstein–Barr viral infection is the most significant risk factor for nasopharyngeal carcinoma.<sup>[4]</sup> Moreover, it has been previously demonstrated that the Epstein–Barr virus might utilize the NF- $\kappa$ B pathways, leading to a range of epithelial carcinomas including PPELCL and nasopharyngeal carcinoma.<sup>[4]</sup> This suggested that PPELCL and nasopharyngeal carcinoma have certain similarities, and that the Epstein–Barr virus may play a key role in both of them. PPELCL generally presented with clinical features common to other types of lung cancer, such as cough, hemoptysis, chest pain, chest tightness, and so on.<sup>[1,2]</sup> This patient was a case of PPELCL with rhinitis as the first symptom. With a history of chronic rhinitis for many years, and her rhinitis confirmed as having been caused by the Epstein–Barr virus, a potential association is inferred between rhinitis and PPELCL. On the other hand, this case happened to be discovered because of the necessity for chest CT scans of all patients seeking medical attention during the COVID-19 epidemic. It suggests that we should strengthen the management of potential lung cancer patients,<sup>[5]</sup> for example, remind patients who are at high risk for lung cancer to have a chest CT scan. If so, this patient's tumor would have been detected when at a much smaller volume and the patient's left lung lingula lobe would not have suffered from such great damage.

In conclusion, patients with Epstein–Barr virus-related rhinitis should continue to be followed, because Epstein–Barr virus that has not been completely eliminated may cause PPELCL in the future. Lung cancer patients with Epstein–Barr virus-related rhinitis should be differentially diagnosed with PPELCL and metastasis of nasopharyngeal carcinoma.

### Declaration of patient consent

Written informed consent for the publication of all clinical details and images was obtained from the patient.

### Conflicts of interest

None.

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