Primary pulmonary lymphoepithelioma-like carcinoma combined with situs inversus totalis

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To the Editor: According to World Health Organization (WHO) histologic classification of lung tumors, primary pulmonary lymphoepithelioma-like carcinoma (LELC), belonging to the other and unclassified carcinoma, is considered as a rare subtype of variants of lung cancer. The first case of pulmonary LELC was reported in 1987. Many studies showed a close relationship between Epstein-Barr virus (EBV) infection and pulmonary LELC. Then, it has been found that the incidence in the Asian population was significantly higher than that in the Western population. Situs inversus totalis (SIT) is a rare autosomal recessive condition in which the organs in the chest and abdomen are positioned in a mirror image from their normal location to the other side of the body. Some investigations demonstrated that the incidence of SIT is approximately 1/5000 to 1/10,000 in live births. Here, we report a rare case of primary pulmonary LELC combined with SIT.

A 58-year-old non-smoking Chinese woman presented to Zhujiang Hospital in September 2015 with intermittent fatigue and mild shortness of breath for 1 month. She was evaluated with a chest computed tomography (CT) scan, which revealed a 16 mm × 14 mm nodule close to pleura with a well-defined margin in the superior segment of the right lower lobe [Figure 1A and 1B]. No distant metastatic lesions or enlarged lymph nodes were observed. Then, CT scan also identified that all organs inside the thoracic and abdomen are inversely positioned [Figure 1C and 1D]. SIT was diagnosed by these findings. Otherwise, head and neck magnetic resonance imaging (MRI) scan were performed and no lesion was observed [Figure 1E and 1F]. And emission computed tomography (ECT) was also obtained and no bony metastasis was found.

Percutaneous transthoracic needle biopsy (PTNB) was used for the pathological diagnosis of the nodule. Microscopically, individual tumor or well-defined nests of tumor cells, large polygonal undifferentiated epithelial cells with oval and pleomorphic nuclei, were surrounded by abundant lymphocytes and plasmacytes in the stroma [Figure 2A and 2B]. The neoplastic cells showed positive for cytokeratin (CK) [Figure 2C], CK/H, P63, epidermal growth factor receptor (EGFR), P53, Ki-67, and negative for cytokeratin 7 (CK7), thyroid transcription factor-1 (TTF-1), synaptophysin (SYN), CD56, anaplastic lymphoma kinase-D5F3 (ALK-D5F3). Meanwhile, EBV-encoded RNA (EBER) by in situ hybridization was positive for neoplastic cells as well [Figure 2D]. Based on these histological findings, the nodule was diagnosed as primary pulmonary LELC.

According to CT and MRI findings, the pathological stage was T1N0M0. After successful surgical treatment without adjuvant radiotherapy or chemotherapy, no recurrence and complication were observed at follow-up of more than 2 years.

SIT, a rare condition of abnormal visceral rotation, denoting complete inversion of thoracic and abdominal viscera. Since the technical challenges that orientation is more complicated and requires more surgery wise in surgical processes, SIT continues to be interesting and noteworthy in the surgical realm.
LELC is a rare malignant tumor. It was reported that nasopharynx is the most common site. According to the reports, LELC can also occur in the extra-nasopharyngeal organs, such as lacrimal gland, lung, skin, and bladder. It is estimated that pulmonary LELC accounts for only 0.9% of all primary lung cancers. Some studies found that pulmonary LELC is more common in Asians than in Westerners. Furthermore, the mean age of pulmonary LELC was reported to be 10 years younger. It is believed that the prognosis of pulmonary LELC is better. Therefore, the incidence of primary pulmonary LELC with SIT is extremely rare.

Several studies figured out a close relationship between EBV infection and pulmonary LELC. Normally, for further distinguishing pulmonary LELC from other types of lung cancer, EBV infection evidence should be collected. In our case, in situ hybridization with EBER positive was observed in some malignant cells (Figure 2D).

Pathologically, pulmonary LELC was close to undifferentiated nasopharyngeal carcinoma (NPC). The characteristics of the histological findings in primary pulmonary LELC represents the large polygonal tumor cells with amphophilic cytoplasmic and indistinct cell boundaries,
individual tumor or well-defined nests of tumor cells surrounding with abundant lymphocytes and plasma-cytes.\textsuperscript{[2]} Massive lymphocytes infiltration in tumor may suggest the enhanced or robust immunological response, indirectly indicating a better prognosis.\textsuperscript{[2]} In our case, both typical tumor cells and extensive lymphocytes and plasmacytes infiltration were observed [Figure 2A and 2B]. Additionally, pulmonary LELC needed to be differentiated from non-Hodgkin lymphoma and metastatic nasopharyngeal carcinoma. And nasopharyngeal carcinoma was excluded by head and neck MRI scan in our case [Figure 1E and 1F].

In radiography, it was reported that no specific image was observed by CT scan, which was similar to bronchogenic carcinomas.\textsuperscript{[1]} Some reports demonstrated that well-defined and smooth borders with variable dimensions, vascular encasement and peribronchovascular nodal spread were more common in pulmonary LELC.\textsuperscript{[3]} In our case, the CT scan showed a nodule close to pleura with a well-defined margin without vascular encasement [Figure 1A and 1B], and no metastatic lesion was found, suggesting an early stage of disease (T1N0M0).

Surgery is the major curative treatment of pulmonary LELC in early stage.\textsuperscript{[1,3]} Chemotherapy and radiotherapy could be used or combined in an advanced stage.\textsuperscript{[1,3]} However, no standard chemotherapy was recommended for the treatment of pulmonary LELC due to its rarity. Based on the disease stage of this case, video-assisted
Thoracoscopic lobectomy was performed, without additional chemotherapy and radiotherapy. And no recurrence and complication were observed at follow-up of more than 2 years.

Some reports also demonstrated that SIT can combine with different kinds of tumors from the common types, such as gastric cancer and colorectal cancer, to the rare types, including solid pseudopapillary tumor of the pancreas (SPTP) and pulmonary LELC in this report. However, the relationship between SIT and malignant tumors is still unknown, which needs further investigation.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Conflicts of interest

None.

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