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Pulmonary lymphoepithelioma-like carcinoma: A complication of Epstein–Barr virus in a teenager

KEYWORDS
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Dear Editor:

Lymphoepithelioma-like Carcinoma is a rare Epstein–Barr virus (EBV)-associated epithelial malignancy with pronounced lymphocytic infiltration, which originates from the nasopharynx and a few from other foregut-derived organs (*i.e.* the salivary glands, stomach, lungs, and thymus).[1]

A 15-year-old Taiwanese boy presented with fever, cough, and weight loss for 3 weeks with tachypnea. X-ray showed a round opacity in the left lower lung with left bronchus narrowing (Fig. 1A). He was treated with broad spectrum antibiotics, but after four days he presented with new onset of a left-sided pleural effusion and persistent high fever. Computerized tomography showed irregularly-shaped subcarinal and pulmonary masses (Fig. 1B). Bronchoscopy revealed mucosal swelling of the left bronchus and narrowing of its lower branches. Positron emission tomography showed a pulmonary tumor with metastasis to the mediastinum, liver, and bones (Fig. 1C). Thoracoscopic biopsy revealed a pulmonary lymphoepithelioma-like carcinoma (PLELC) (Fig. 1D). Primary resection was not feasible because of extensive mediastinal, pulmonary and bronchial involvement as well as the presence of distant metastases. The Epstein–Barr virus-encoded small RNAs (EBER) *in situ* hybridization was diffusely positive (Fig. 1E) and plasma EBV DNA load was initially 355-fold elevated. No tumors were found in the head and neck CT scan and nasopharyngeal fiberoscopic examination. The levels of antigen of cytokeratin 19 fragment (CYFRA-21-1), serum neuron-specific enolase (NSE), tumor-associated antigen 125 (CA-125) were all elevated (7.70 ng/mL [<3.30], 30.32 ng/mL [<17.00], and 504.6 U/mL [<35.0], respectively). Serum tumor-associated antigen 153 (CA-153) and carcinoembryonic antigen (CEA) were within normal ranges (15.9 U/mL [<23.5] and 0.9 ng/mL [<5.0], respectively).

After chemotherapy containing paclitaxel and platinum, the clinical symptoms of fever and tachypnea and levels of EBV DNA and serum tumor markers improved. The EBV DNA decreased to 1.9-fold on day 69 but increased to 37-fold on day 93. The CA-125 decreased to normal range on day 69 and was not further evaluated; CYFRA-21-1 and NSE were not further evaluated after the initial evaluation at diagnosis. Follow-up chest X-ray on day 94 showed partial resolution of the mass effect (Supplemental Figure S1). The disease progressed 4 months after diagnosis and he subsequently died of refractory disease.

PLELC was first reported by Begin et al. in 1987 and is associated with EBV infection.[2] As a rare cancer, it is more commonly seen in East Asian populations, especially in regions with high prevalence of EBV infections: Southern China, Hong Kong and Taiwan. Our patient's age is younger compared to a study of 85 patients (range, 26–79 years; mean, 54 years).[3]

PLELC tends to be misdiagnosed. Metastatic nasopharyngeal carcinoma and non-Hodgkin's lymphoma are the two main differential diagnoses.[4] A comprehensive evaluation of the nasopharynx should be performed; immunohistochemical staining plays an important role in differentiating lymphoma from PLELC.[5] In the study by Qin

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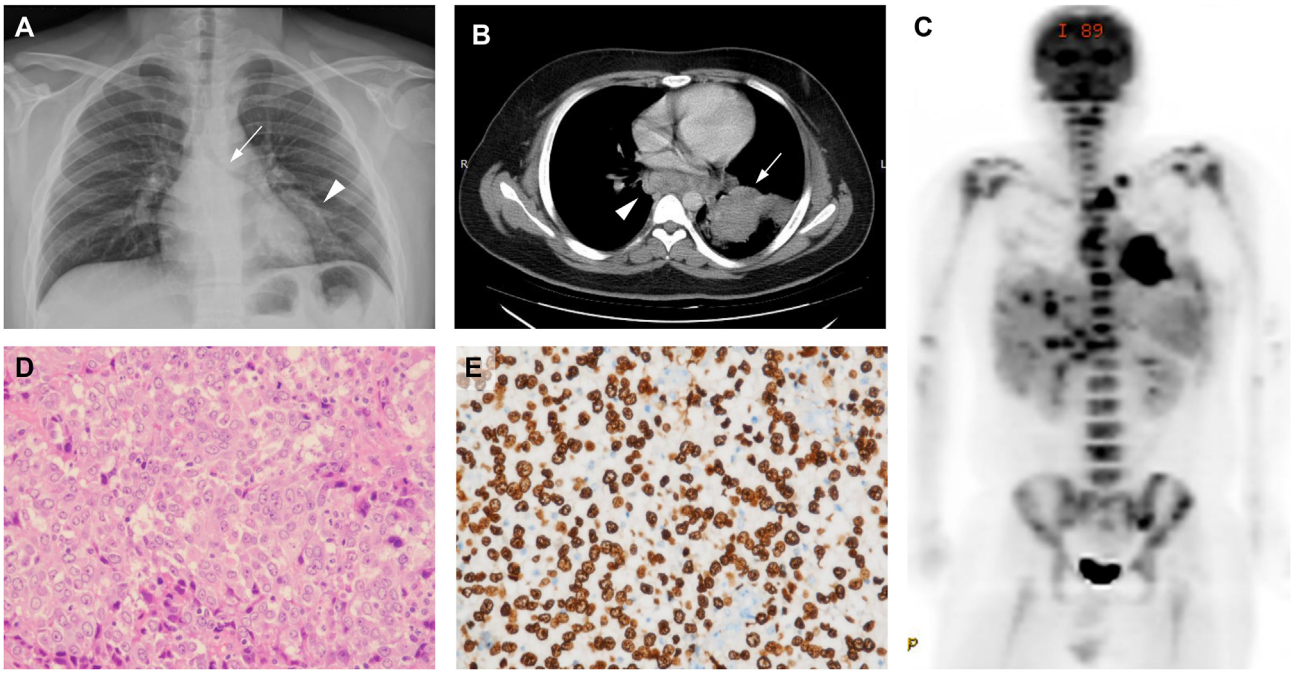

Figure 1. Imaging and histopathological findings of the teenage boy with PLELC. **(A)** Chest X-ray showed a round opacity in the left lower lung (arrowhead) with left bronchus narrowing (arrow). **(B)** Computerized tomography showed irregular-shaped subcarinal (arrowhead) and pulmonary (arrow) masses. **(C)** Positron emission tomography showed a pulmonary tumor with metastases to the mediastinum, liver, and bones. **(D)** Histopathology revealed a malignant tumor composed of anaplastic or poorly differentiated cells arranged in infiltrative pattern in the inflammatory-rich and fibrotic stroma, with tumor cells of prominent nucleoli, eosinophilic to clear cytoplasm and marked nuclear pleomorphism (hematoxylin and eosin stain, 400 ×). **(E)** The Epstein—Barr virus-encoded small RNAs (EBER) *in situ* hybridization was diffusely positive (EBER, 400 ×).

et al., 75%, 68.8%, 25.3%, 6.3% and 0% patients had elevated serum antigen of CYFRA21-1, NSE, CA125, CA153 and CEA, respectively.[3] Our patient had elevated CYFRA21-1, NSE, and CA125, which declined after chemotherapy.

If the tumor can be removed, radical resection is the primary treatment. Neo-adjuvant and/or postoperative adjuvant chemotherapy for patients with stage IIIa disease may result in a better outcome. Chemotherapy and/or radiotherapy are the primary modalities of treatment for patients with advanced disease. Plactitaxel or gemicitabine plus platinum have been recommended as first-line palliative treatment of PLELC.[3]

In conclusion, PLELC is a rare type of EBV-related cancer that should be included in the differential diagnoses of pulmonary masses in adolescents and young adults of East Asian descent, especially in EBV-endemic areas.

Declaration of competing interest

Non declared.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jmii.2023.02.006.

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