Successful Treatment with Carboplatin and Pemetrexed for Multiple Lymph Node Metastases of Lymphoepithelioma-like Carcinoma from an Unknown Primary Site

Yuichiro Yasuda¹, Kazunori Tobino¹,², Yuki Ko¹, Mina Asaji¹, Yoshikazu Yamaji¹, Kosuke Tsuruno¹, Hiroyuki Miyajima¹, Yosuke Mukasa¹ and Noriyuki Ebi¹

Abstract

We herein report the case of an 80-year-old Japanese man with multiple lymph node metastases of lymphoepithelioma-like carcinoma (LELC) from an unknown primary site. The patient was admitted to our hospital due to hoarseness and left supraclavicular lymphadenopathy. Contrast-enhanced whole-body computed tomography revealed mediastinal, left supraclavicular, and left axillary lymphadenopathy. A left supraclavicular lymph node biopsy was performed and the specimen was consequently diagnosed as exhibiting LELC. The patient’s Eastern Cooperative Oncology Group performance status was 0, therefore he was started on chemotherapy with carboplatin and pemetrexed. His lymph nodes responded well to four cycles of chemotherapy without any intolerable adverse effect.

Key words: lymphoepithelioma-like carcinoma, cancer of unknown origin, carboplatin, pemetrexed

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Introduction

Lymphoepithelioma-like carcinoma (LELC) is a malignancy with morphologic features similar to those of undifferentiated nasopharyngeal carcinoma (NPC) that occur outside the nasopharynx (1). It has been reported that LELC develops in organs such as the salivary glands, uterine cervix, thymus, lung, skin, stomach, and breast; however, there are no reports of LELC with an unknown primary site. Moreover, there is no standard chemotherapy for LELC due to the rarity of the disease. We herein report a rare case of multiple lymph node metastases of LELC from an unknown primary site successfully treated with carboplatin (CBDCA) and pemetrexed (PEM). To our knowledge, this is the first case report of LELC treated using this regimen in the English literature.

Case Report

An 80-year-old Japanese man presented to our hospital with a two-week history of hoarseness and left supraclavicular lymphadenopathy.

The patient, an ex-smoker and non-drinker, had a history of diabetes mellitus. His Eastern Cooperative Oncology Group (ECOG) performance status (PS) was 0. He did not have a history of tuberculosis or exposure to asbestos. His vital signs were within the normal limits, although a physical examination revealed left supraclavicular lymphadenopathy. An elastic, hard, immovable, and non-tender lymph node was detected, and a chest X-ray showed tracheal deviation to the right side (Fig. 1). A contrast-enhanced whole-body computed tomography (CT) disclosed mediastinal, left supraclavicular and left axillary lymphadenopathy (Fig. 2A-C), and a 18 F-fluorodeoxyglucose positron-emission tomography (FDG-PET) image showed abnormally...
strong accumulation of FDG in these lymph nodes (Fig. 2D-F). Furthermore, laboratory tests demonstrated increased levels of C-reactive protein (3.31 mg/dL), tumor markers [carcinoembryonic antigen (6.4 ng/mL), soluble cytokeratin-19 fragments (5.3 ng/mL), pro-gastrin-releasing peptide (138 pg/mL)] and soluble interleukin-2 receptor (803 U/mL); however, no elevation of angiotensin-converting enzyme was noted. Laboratory tests also showed positive results for Epstein-Barr virus (EBV) viral-capsid antigen (VCA) IgG (8.6, normal, <0.5), negative results for EBV VCA IgM and EBV Epstein-Barr nuclear antigen (EBNA) IgG, and revealed increased EBV-DNA copies (5.1×10^7). Esophagogastroduodenoscopy disclosed only early-stage esophageal cancer. In order to obtain biopsy specimens of the mediastinal lymph nodes, endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) was performed. However, the pathological findings did not indicate the correct diagnosis due to the small biopsy specimens. Therefore, a left supraclavicular lymph node biopsy was performed under general anesthesia. The atypical cells showed indistinct cell borders with prominent nucleoli and were found to be arranged in nests with marked lymphocyte infiltration under high magnification (hematoxylin and eosin staining). An immunohistochemical study showed focal positive staining for AE1/AE3 and negative staining for leukocyte common antigen (LCA) (Fig. 3A-C). In addition, an association with EBV was observed on Epstein-Barr virus-encoded small RNA (EBER) in situ hybridization (Fig. 3D). Therefore, the lymph node biopsy specimen was diagnosed as exhibiting LELC based on these findings. Subsequently, gadolinium-enhanced magnetic resonance imaging (MRI) and biopsies of the nasopharynx using nasopharyngeal fiberscopy were performed, which showed no malignant findings. Due to the advanced stage of the disease and presence of left axillary lymph node metastasis, chemotherapy was started. The chemotherapy regimen included CBDCA administered AUC 5 on Day 1 and PEM 500 mg/m^2 on Day 1 of a 28-day cycle. Grade 4 neutropenia, Grade 3 thrombocytopenia, and a Grade 1 canker sore were observed during the treatment, and contrast-enhanced whole-body CT performed after four cycles of chemotherapy showed a reduction in the mediastinal lymph nodes and left axillary lymph nodes (Fig. 4), with a partial response according to the Response Evaluation Criteria in Solid Tumors (version 1.1).
Figure 3. Hematoxylin and Eosin staining of the biopsy specimen. Under high magnification, the atypical cells showed indistinct cell borders with prominent nucleoli and were found to be arranged in nests with marked lymphocyte infiltration (A). Immunohistochemical staining was positive for AE1/AE3 (B) and negative for LCA (C). The tumor cells were focally positive for EBER on in situ hybridization (D).

Figure 4. CT images showed a reduction in the multiple sites of lymphadenopathy after four cycles of chemotherapy.

Discussion

Bégin et al. first reported LELC in 1987 and observed a relationship between LELC and EBV (2). EBV is strongly associated with LELC of the lung, although this association is observed only in specific ethnic and geographic groups, including Chinese, Japanese, Taiwanese, and Eskimos (3). The presence of EBV in LELC has also been demonstrated using polymerase chain reaction for EBV-DNA, in situ hybridization for EBV-DNA and RNA and immunohistochemistry for EBV-associated proteins (4, 5). However, it has been reported that there is no association between EBV and LELC in Western populations and that EBV is not a requisite for the etiology or pathogenesis of LELC (6). In the present case, the tumor cells were focally positive for EBER on in situ hybridization. Pathologically, LELC is indistinguishable from undifferentiated NPC; therefore, performing an endoscopic biopsy and MRI of the nasopharynx is essential in order to exclude the possibility of metastasis of NPC (7). In the present case, we also excluded the possibility of NPC based on MRI and biopsies of the nasopharynx. For advanced or metastatic stages of LELC, the benefit of chemotherapy remains poorly understood due to the rare occurrence of the lesion. Liang et al. retrospectively reviewed 52 patients with pulmonary LELC. In that report, 17 patients received chemotherapy, including paclitaxel (PTX) / docetaxel (DOC) + cisplatin (CDDP) / CBDCA, CDDP + PEM, gemcitabine (GEM) + CDDP, PTX/DOC + CDDP + 5-FU, and GEM + vinorelbine (VNR). The disease control rate (combined complete response, partial response, and stable disease) was over 77.8% (8). In the current case, the patient was elderly (80 years), however, his ECOG PS was 0 and he had no severe comorbidity. Therefore, CBDCA-based
doublet chemotherapy was thought to be feasible for him. Moreover, he wanted to avoid any possible adverse effect, such as peripheral neuropathy, that may hinder his work as a documentary writer. Consequently, we chose CBDCA+PEM therapy for the patient. As for adverse events, Grade 4 neutropenia, Grade 3 thrombocytopenia, and a Grade 1 canker sore were noted; however, the patient completed all four cycles of chemotherapy. To our knowledge, this is the first case report of LELC treated with this regimen in the English literature.

In conclusion, combination chemotherapy with CBDCA and PEM is thought to have a favorable treatment effect and tolerability in patients with LELC and may be a therapeutic regimen for chemotherapy, especially for elderly patients.

The authors state that they have no Conflict of Interest (COI).

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References