Positive therapy outcome of lung squamous cell cancer: A case report

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Abstract. Lung cancer is a rapidly progressing disease with a poor prognosis. Lung squamous cell cancer (LSCC) accounts for 20-30% of lung cancer cases. Conventional chemotherapy and radiotherapy are the common options for LSCC. Nevertheless, the outcomes of these treatments are still unsatisfactory. The present report describes a rare case of LSCC with pericardial, cervical lymph node and extensive mediastinal lymph node metastases, who still survives today, in March 2022, more than 10 years after therapy and, therefore, this case study indicates a possible treatment regimen for patients with a similar condition. In conclusion, gemcitabine and cisplatin followed by radiotherapy were an effective treatment against pericardial and lymph node metastases from LSCC.

Introduction

Lung cancer is an aggressive cancer with a 5-year survival rate of 8% worldwide (1). Overall, 20-30% of lung cancer cases are lung squamous cell cancer (LSCC) and >60% of patients with LSCC are diagnosed with locally metastatic or advanced disease globally. Therefore, conventional chemotherapy, radiotherapy, immunotherapy and supportive treatment are the common options for patients with LSCC (2,3). To date, molecularly targeted therapies have not demonstrated an overall survival advantage for early-stage (stages I, II and IIIA) patients, for these patients, surgical resection is recommended (4). Although platinum-based adjuvant chemotherapy is recommended for stage II-IIIA disease, the recurrence rate is 30-70% (5). Most patients with stage III LSCC are candidates for non-surgical therapy, and concurrent chemoradiotherapy followed by immunotherapy is the current standard of therapy (4). Nevertheless, the outcomes of these treatments are still unsatisfactory (6).

The present report describes a rare case of a male patient diagnosed with LSCC with pericardial, cervical and extensive mediastinal lymph node metastases, who still survives today, in March 2022, >10 years after chemotherapy and radiotherapy. Therefore, this clinical case presents a promising therapeutic regimen for patients with a similar condition.

Case report

A 50-year-old man was admitted to the Pneumology Department in The Third Affiliated Hospital of Qiqihar Medical University, Qiqihar, P.R. China on May 16, 2011 after exhibiting cough with bloody sputum for 1 week. Other than the cough, he had no other symptoms such as chest pain, shortness of breath, fever, difficulty in breathing, fatigue, poor appetite or weight loss. The patient had a free medical history. He had a smoking history of 20 packs years (1 pack of cigarettes/day for 20 years), and had been a social drinker (1 bottle of beer/week) for ~20 years.

For physical examination, the patient's temperature was 36.5˚C, heart rate 71 bpm, respiratory rate 15 breaths/min, blood pressure 130/80 mmHg and oxygen saturation in room air 100%. A painless hard nodule (4x3 cm) was found in the right supraclavicular area, indicating abnormal enlarged lymph node, and coarse rales could be heard in the right pulmonary base indicating inflammation.

For laboratory examination, the serum tumor markers carcinoembryonic antigen and α-fetoprotein were 7.78 and 1.09 ng/ml, respectively. They were in the reference range (<20 and <5 ng/ml, respectively). *Mycobacterium tuberculosis* was not found in sputum culture.

For imaging examination, Computed tomography (CT) (Fig. 1A), revealed a flocculent mass (7x4 cm) with some empty bubbles (the largest being 2x1.5 cm) in the upper lobe of the right lung, indicating malignancy or inflammation. In addition, extensively enlarged lymph nodes were detected in the upper mediastinal regions (Fig. 2A), indicating metastases or inflammation, and pericardial thickening was also found.

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Ultrasonography revealed an abnormally blended and enlarged lymph node (4x3 cm) in the right cervical region, suggesting the possibility of metastases. Furthermore, head, abdominal and pelvic CT identified no abnormalities.

For biopsy, tissue specimens were fixed in 10% formalin at 20˚C for 12 h, sectioned at a thickness of 5 μm, stained with hematoxylin for 10 min and eosin for 20 sec at 20˚C, and observed by light microscopy. Bronchoscopy confirmed bronchitis in the upper lobe of the right lung. Subsequent biopsy of the right cervical lymph node confirmed a poorly differentiated invasive squamous cell carcinoma, which may have metastasized from the lung (Fig. 3). Unfortunately, the patient refused further immunohistochemical examination because of economic concerns.

The pulmonary lesion was not improved after 2 weeks of treatment of piperacillin sodium and tazobactam sodium and aztreonam (approved by chest CT; Figs. 1B and 2B). After taking into consideration the patient's condition, the cervical lymphatic metastases were confirmed, and the patient was transferred to the Department of Medical Oncology in the same hospital. Combined therapy of docetaxel and carboplatin was started on June 16, 2011. Nevertheless, after two courses of chemotherapy, the pulmonary lesion and extensively enlarged lymph nodes were not improved (Figs. 1C and 2C). In addition, pericardial effusion was observed (Fig. 4A). Between July 27 and December 9, 2011, the patient was subjected to four courses of gemcitabine and cisplatin as a second-line regimen. Furthermore, radiotherapy of 60 Gy (2 Gy/day x 30 days) was administered on December 1, 2011. The side effects of these treatments were mild leukopenia, mild anemia, mild thrombocytopenia, mild hepatic function impairment, mild radiation esophagitis, poor sleep quality, decreased appetite and intermittent constipation.

The final diagnosis of the presented case was LSCC with pericardial, cervical lymph node and extensive mediastinal lymph node metastases. The effectiveness of treatment was evaluated by imaging examination (Figs. 1D-J, 2D-J and 4B and C), which was supported by a gradually diminished pulmonary lesion, lymph node enlargement and pericardial effusion.

Changes of the lesion over time by chest CT scan of the lung: Before any treatment (2011-5-16, 8x5 cm); after anti-inflammatory treatment (2011-6-3, 8x5 cm); during therapy of docetaxel + carboplatin (2011-7-9, 8x4.5 cm); during therapy of gemcitabine + cisplatin (2011-9-19, 6x3.5 cm); during therapy of gemcitabine + cisplatin (2011-11-30, 4x1.5 cm); after therapy of gemcitabine + cisplatin + radiation (2012-10-8, 3.5x1 cm); review (2014-4-11, disappeared); review (2016-8-18, 2018-7-3 and 2020-2-10, no relapse).

Changes of the enlarged lymph nodes over time by chest CT scan of the mediastinum: Before any treatment (2011-5-16, extensively enlarged lymph nodes); after anti-inflammatory treatment (2011-6-3, extensively enlarged lymph nodes); during therapy of docetaxel + carboplatin (2011-7-9, extensively enlarged lymph nodes); during therapy of gemcitabine + cisplatin (2011-9-19, some enlarged lymph nodes); during therapy of gemcitabine + cisplatin (2011-11-30, few enlarged lymph nodes); after therapy of gemcitabine + cisplatin + radiation (2012-10-8, no enlarged lymph nodes); review (2014-4-11, 2016-8-18, 2018-7-3 and 2020-2-10, no enlarged lymph nodes).

Changes of the pericardial effusion over time by echocardiography: Moderate pericardial effusion after therapy of docetaxel and carboplatin (2011-7-20); little pericardial effusion during therapy of gemcitabine + cisplatin + radiation (2011-12-7); no pericardial effusion after therapy of gemcitabine + cisplatin + radiation (2012-2-1).

Changes of the blood routine over time: Before any treatment (2011-5-17, all items were in the reference range); after anti-inflammatory treatment (2011-6-4, all items were in the reference range); during therapy of docetaxel + carboplatin (2011-7-7, all items were in the reference range); during therapy of gemcitabine + cisplatin [2011-8-8; WBC $3.9x10^9$/l (reference range, 4.0-10.0$x10^9$/l); PLT $109x10^9$/l (reference range, 120-380$x10^9$/l)]; during therapy of gemcitabine + cisplatin [2011-8-16; WBC $3.6x10^9$/l; RBC $3.59x10^{12}$/l (reference range, 3.80-5.30$x10^{12}$/l); HGB 106 g/l (reference range, 110-170 g/l)]; during therapy of gemcitabine + cisplatin (2011-10-13; RBC $3.26x10^{12}$/l); after therapy of gemcitabine + cisplatin + radiation (2012-1-8; RBC $3.16x10^{12}$/l); review (2012-11-19, 2013-9-28, 2014-4-14, 2015-7-7, 2017-5-28, 2019-9-10 and 2020-5-5, all items were in the reference range).

Changes of the blood biochemistry over time: Before any treatment (2011-5-17, all items were in the reference range); after anti-inflammatory treatment (2011-6-4, all items were in the reference range); during therapy of docetaxel + carboplatin (2011-7-7, all items were in the reference range); during therapy of gemcitabine + cisplatin [2011-10-8; γ-glutamyl transpeptidase (GGT) 59 U/l (reference range: 0-50 U/l)]; during therapy of gemcitabine + cisplatin (2011-10-31; GGT 58 U/l); after therapy of gemcitabine + cisplatin + radiation (2012-1-8, all items were in the reference range); review (2012-11-19, 2013-9-28, 2014-4-14, 2015-7-7, 2017-5-28, 2019-9-10 and 2020-5-5, all items were in the reference range).

The tumor biomarkers, carcinoembryonic antigen, α-fetoprotein, neuron-specific enolase, glycoantigen-199 and squamous epithelial cell carcinoma antigen were in the reference range (on 2020-5-5).

The changes of blood routine and biochemistry demonstrated that the patient had gradually recovered from leukopenia, anemia and thrombocytopenia. The patient still survives healthily today, in March 2022, more than 10 years after diagnosis.

Discussion

This patient had a flocculent mass with some empty bubbles in the upper lobe of the right lung; extensively enlarged lymph nodes in the upper mediastinal regions with pericardial thickening; and an abnormally blended and enlarged lymph node in the right cervical region; all of which confirmed a poorly differentiated invasive squamous cell carcinoma with histological features similar to lung cancer. These findings suggested a primary lung cancer with multiple metastases.

The patient had no primary heart disease or pericardial effusion. After two courses of chemotherapy (docetaxel + carboplatin), the pulmonary lesion and enlarged lymph nodes were not improved, and pericardial effusion was observed. All the drugs (including docetaxel + carboplatin) had been administrated to him have no side effect of causing pericardial effusion. Furthermore, pericardial effusion is the most

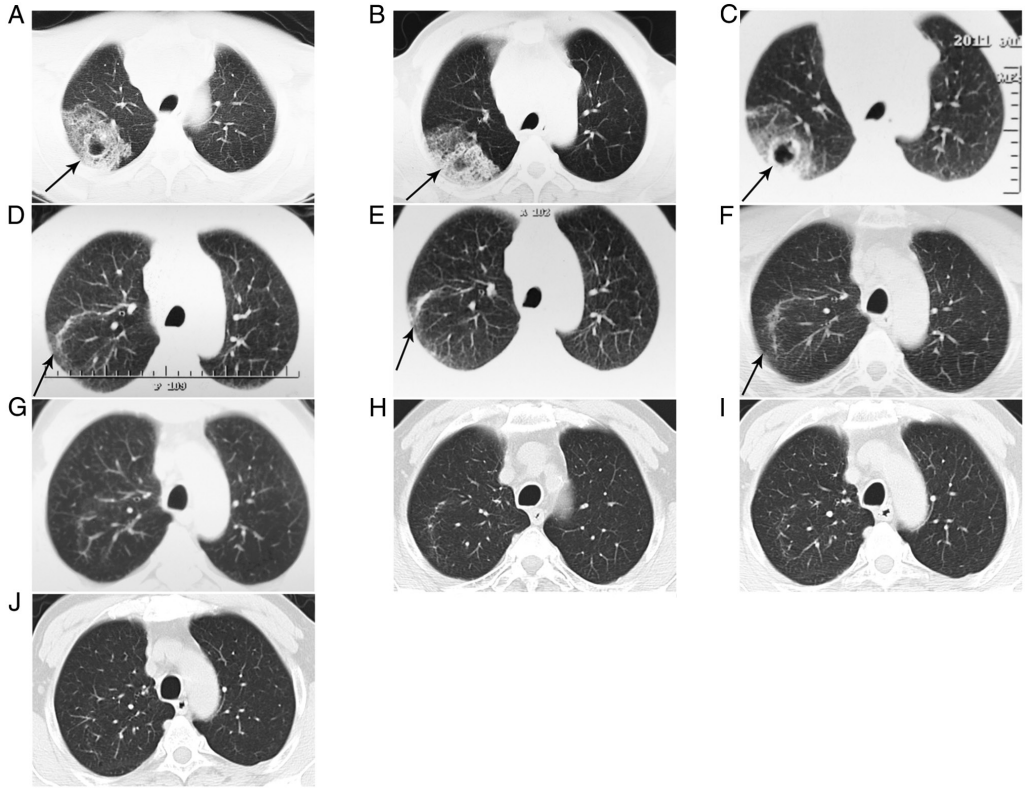

Figure 1. Changes of the lesion over time by chest computed tomography scan of the lung. (A) Before any treatment (2011-5-16). (B) After anti-inflammatory treatment (2011-6-3). (C) During therapy of docetaxel + carboplatin (2011-7-9). (D) During therapy of gemcitabine + cisplatin (2011-9-19). (E) During therapy of gemcitabine + cisplatin (2011-11-30). (F) After therapy of gemcitabine + cisplatin + radiation (2012-10-8). (G) Review (2014-4-11). (H) Review (2016-8-18). (I) Review (2018-7-3). (J) Review (2020-2-10). Arrows indicate the lesion.

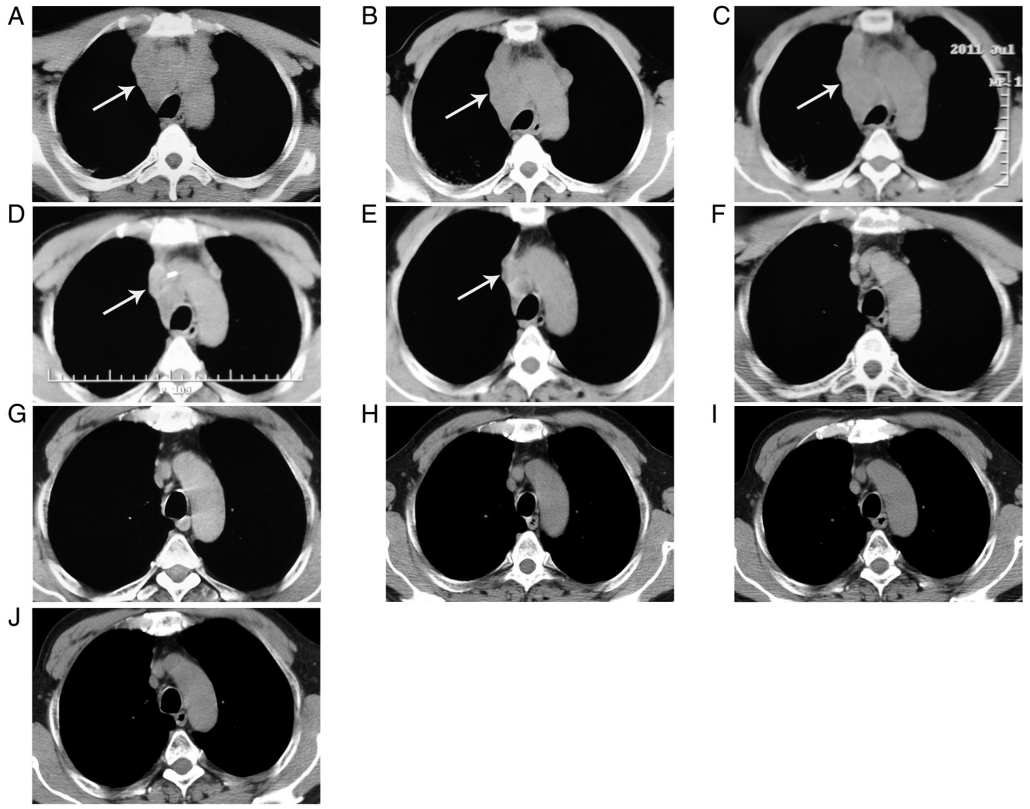

Figure 2. Changes of the enlarged lymph nodes over time by chest computed tomography scan of the mediastinum. (A) Before any treatment (2011-5-16). (B) After anti-inflammatory treatment (2011-6-3). (C) During therapy of docetaxel + carboplatin (2011-7-9). (D) During therapy of gemcitabine + cisplatin (2011-9-19). (E) During therapy of gemcitabine + cisplatin (2011-11-30). (F) After therapy of gemcitabine + cisplatin + radiation (2012-10-8). (G) Review (2014-4-11). (H) Review (2016-8-18). (I) Review (2018-7-3). (J) Review (2020-2-10). Arrows indicate enlarged lymph nodes.

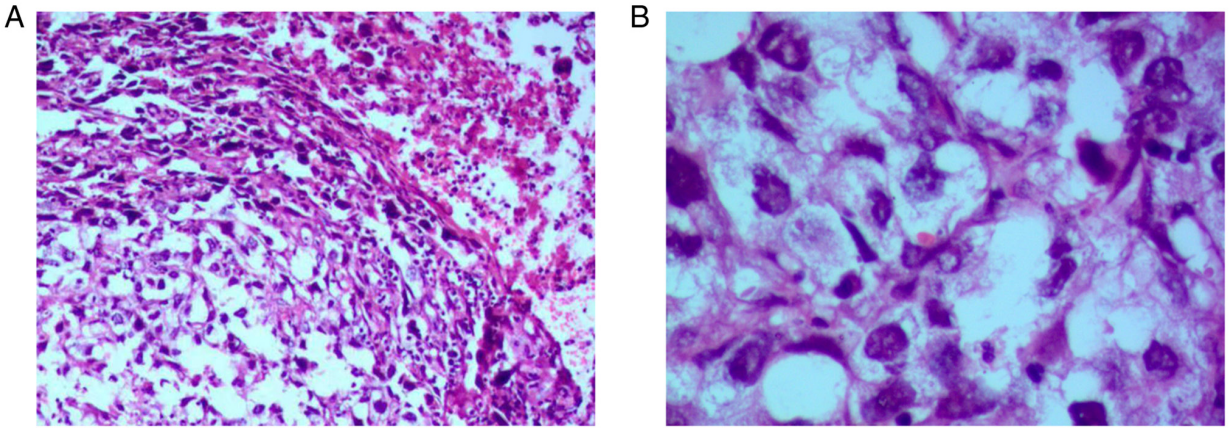

Figure 3. Tissue specimens of cervical lymph node obtained at biopsy confirm a poorly differentiated invasive squamous cell carcinoma. (A) H & E staining, (magnification, x100). (B) H & E staining (magnification, x400). H & E, Hematoxylin and eosin.

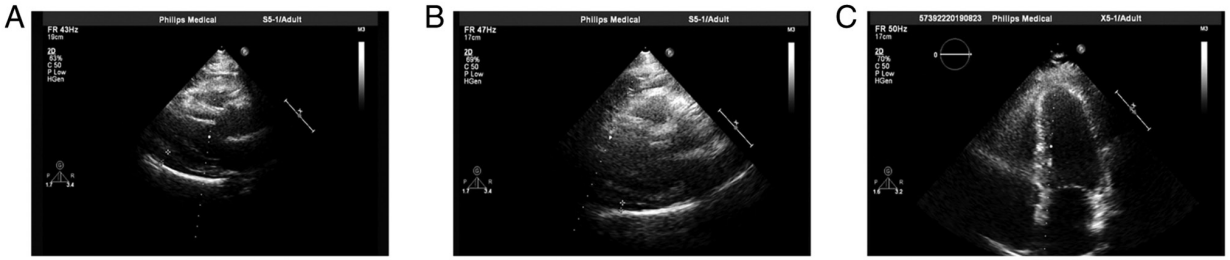

Figure 4. Changes of the pericardial effusion over time by echocardiography. (A) Moderate pericardial effusion after therapy of docetaxel and carboplatin (2011-7-20). (B) Little pericardial effusion during therapy of gemcitabine + cisplatin + radiation (2011-12-7). (C) No pericardial effusion after therapy of gemcitabine + cisplatin + radiation (2012-2-1).

common clinical manifestation of pericardial metastatic disease. Therefore, it was concluded that pericardial effusion was due to pericardial metastasis from lung cancer.

At present, cisplatin is the preferred regimen used concurrently with radiotherapy for locally advanced non-small-cell lung cancer (NSCLC) (7). For patients with LSCC and distant metastasis, the National Comprehensive Cancer Network guidelines recommend cisplatin and gemcitabine as the first-line regimen (8). In the present case, the patient had been treated with docetaxel and carboplatin as first-line chemotherapy for two courses. However, lesions were not improved and pericardial effusion emerged. Therefore, a new regimen of gemcitabine and cisplatin combined with radiotherapy was administered. After the second-line treatment, a complete response of the pulmonary lesion and cervical and mediastinal lymph node enlargement and pericardial effusion were confirmed using chest CT, cervical ultrasound imaging and echocardiography. Some researchers have reported promising clinical outcomes of gemcitabine, cisplatin and radiotherapy. Ma *et al* (9) reported that patients with squamous cell lung cancer treated with gemcitabine and cisplatin as an adjuvant therapy achieve improved outcomes. Yang *et al* (10) reported that gemcitabine with cisplatin was an effective induction therapy before surgery for patients with NSCLC. Zwitter *et al* (11) reported that gemcitabine, cisplatin and radiotherapy achieved improved disease control compared with traditional regimens for advanced NSCLC. These studies echoed the present report. Furthermore, Das *et al* (12) reported that a trial of docetaxel + carboplatin + radiotherapy results in promising outcomes in stage III patients with NSCLC. Nevertheless, docetaxel + carboplatin as a first-line treatment option was not effective in the present case.

The present patient survives healthily >10 years after diagnosis, which is much longer compared with the median overall survival of 21.8 months reported by Driesen *et al* (13) after induction with gemcitabine and cisplatin followed by concurrent chemoradiotherapy for patients with unresectable locally advanced NSCLC. The present study considered that the reasonable treatment plan, a free medical history and a positive psychological state contributed greatly to the patient's survival. Although it is only a rare case, it may offer a promising therapeutic regimen to patients with a similar condition.

In conclusion, administration of gemcitabine + cisplatin + radiotherapy (performed after chemotherapy) was considered to be an effective regimen against pericardial, cervical lymph node and extensive mediastinal lymph nodes metastases from squamous cell lung carcinoma. This case may offer a promising therapeutic regimen to patients with a similar condition.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

YL is the patient's physician, reviewed the literature, and contributed to acquisition, analysis and interpretation of data and manuscript drafting. JY contributed to manuscript drafting and acquisition of data. XJS and SNL analyzed and interpreted the imaging findings. SL reviewed the literature, and contributed to conception and design of the study, analysis and interpretation of data, and drafted, reviewed and edited the manuscript. SL and YL confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

The patient signed informed written consent about treatment interventions, his data collection and submission for publication.

Competing interests

The authors declare that they have no competing interests.

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