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CASE REPORT

Case report of a mixed pulmonary large cell neuroendocrine carcinoma

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Abstract

A 57 year-old male patient was found to have a lesion in the middle lobe of his right lung using chest computed tomography (CT). Tumor cells were detected, and surgical excision was performed. The patient was diagnosed with mixed large cell neuroendocrine carcinoma, and underwent six cycles of a chemotherapy regimen comprising etoposide combined with cisplatin. Genetic testing revealed an EGFR mutation, which prompted oxitinib-targeted therapy. To date, no signs of recurrence or metastasis have been reported.

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Key words: pulmonary large cell neuroendocrine carcinoma; pulmonary adenocarcinoma; diagnosis; treatment

Case presentation

A 57 year-old male patient presenting in our hospital (the Sixth People's Hospital of Chengdu, China) in December 2020 was found to have a lesion (approximately 3.1 cm × 2.8 cm) in the middle lobe of his right lung using chest computed tomography (CT) (Fig. 1), with no cough, sputum, hemoptysis, or chest pain.

For further treatment, in January 2021, he was admitted to Sichuan Provincial Cancer Hospital, China, where enhanced CT of chest and abdomen revealed a soft tissue mass measuring 3.2 cm × 2.9 cm × 2.6 cm located in the middle lobe of the right lung, and suspected to be carcinoma. Metastases were not observed in lymph nodes or at distant sites. Enhanced magnetic resonance imaging of the head and bone scintigraphy revealed no signs of metastasis, while fibrobronchoscopic biopsy revealed the presence of tumor cells.

On January 19, 2021, radical resection of a right middle lobe carcinoma, including systematic lymph node dissection was performed to diagnose non-metastatic lung cancer and exclude surgical contraindications. Postoperative pathology revealed a macroscopic tumor size of 2.5 cm × 2.2 cm × 2 cm (Fig. 2). The tumor was hard and grey-white or grey-brown in color. Histological examination revealed a malignant tumor with some areas of adenoid structure, and a solid arrangement. Immunohistochemical analysis of the primary tumor showed CK7 (+), TTF-1 (–), NapsinA (–), Syn (few+), CgA (few+), P40 (–), ALK-V (–), ROS1 (–), BRAF V600E (–), and Ki67 (dense areas, 70%+). Combining histologic morphology and immunohistochemistry supported a diagnosis of mixed small cell carcinoma. Approximately 90% of this tissue was adenocarcinoma (mainly acinar type) and 10% was small cell neuroendocrine carcinoma. Histopathologic grading was scored as visceral pleura (+), bronchial margin (–), vascular margin (–), intravascular tumor plug (–), and airway spread (–). Lymph node

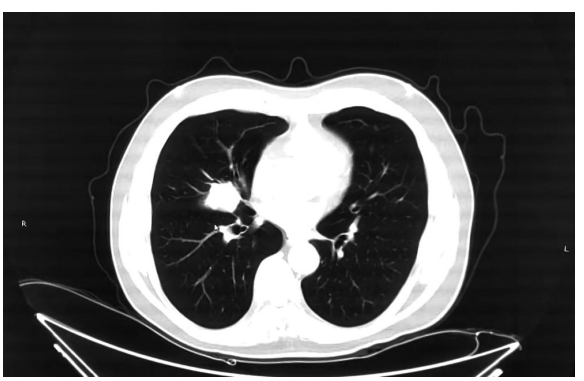

Fig. 1 Chest computed tomography shows that lesion is located in right lung middle lobe

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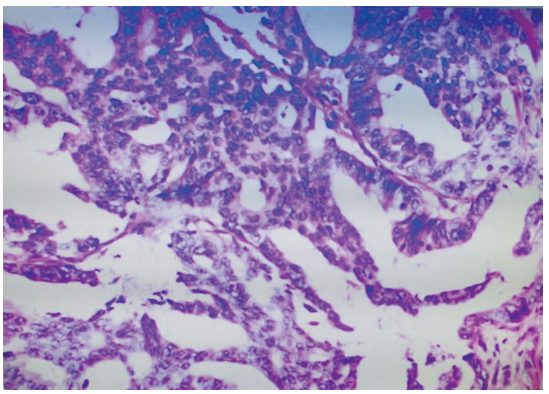

Fig. 2 Postoperative pathology shows that tumor cells (HE ×40)

metastasis was present in the second and fourth group lymph nodes (1/2), seventh group lymph nodes (2/5), a tenth group lymph node (1/1), and a bronchial root lymph node (1/1). The pathological stages were pT2N2M0 and IIIA. Genetic testing revealed an EGFR exon 21 mutation (L858R). Paraffinized tissue sent to the West China Hospital (Chengdu, China) for pathological consultation diagnosed as mixed large cell neuroendocrine carcinoma, with the adenocarcinoma component accounting for 90% of the mass. Large cell neuroendocrine carcinoma accounted for approximately 10% of the mass. Metastatic carcinoma was found in all lymph node sections. Immunophenotypic results suggested adenocarcinoma component metastasis.

After excluding chemotherapy contraindications, six cycles of etoposide combined with cisplatin chemotherapy (etoposide 160 mg ivgtt d1–3 + cisplatin 40 mg ivgtt d1–3) were administered from March 2021 to August 2021. Grade III myelosuppression occurred during chemotherapy and was enhanced by leukocyte promotion therapy. CT reexamination after completing chemotherapy showed no signs of tumor recurrence or metastasis.

In September 2021, the patient began taking oxitinib (Astrazeneca, trade name Terissa) 80 mg po qd. Skin rashes appeared on his face after one month of oxitinib administration. This condition improved upon symptomatic treatment without serious adverse reactions.

To date, the patient has had no signs of tumor recurrence or metastasis.

Discussion

Pulmonary large-cell neuroendocrine carcinoma (PLCNEC) is a rare type of non-small cell lung carcinoma characterized by high malignancy and poor prognosis, accounting for approximately 3% [1, 2] of lung carcinomas. Most patients are already in an advanced stage at time of initial diagnosis. Due to lack of large cohort clinical studies, the current treatment remains controversial [3, 4].

Surgical resection is the main treatment for PLCNEC and achieves improved prognosis in early-stage patients [5, 6]. Postoperative adjuvant chemotherapy can reduce the recurrence rate in patients with stage II disease or above [7]. Some studies have found that the efficacy of platinum-containing chemotherapy regimens is better than that of platinum-free chemotherapy. Thus, the etoposide-platinum regimen currently seems to be the better choice [8, 9]. Most scholars currently recommend etoposide combined with a platinum regimen as the first-line chemotherapy for patients with PLCNEC. The therapeutic efficacy of radiotherapy for patients with PLCNEC is unclear. However, it may prolong the overall survival of patients who were unsuitable for surgery, had postoperative residual lesions, or were in an advanced stage [10, 11]. PLCNEC patients with EGFR mutation have shown good responses to EGFR-tyrosine kinase inhibitors [12, 13]. Since gene mutations are extremely rare in patients with PLCNEC, their clinical value requires further study. Some studies have found that the expression of programmed cell death-ligand 1 can be detected in patients with PLCNEC, suggesting that immunotherapy may be effective [14, 15].

Mixed pulmonary large cell neuroendocrine carcinoma with high malignancy had a worse prognosis than PLCNEC in our study, and was characterized by large cell neuroendocrine carcinoma in some regions and adenocarcinoma in other regions. Its treatment is still in an exploratory stage. The patient in our case study was a middle-aged male diagnosed with pulmonary large cell neuroendocrine carcinoma with adenocarcinoma stage III. He was actively treated with surgical resection and etoposide combined with a platinum chemotherapy regimen. Genetic testing revealed an EGFR mutation which prompted oxitinib-targeted therapy. The patient is still under close follow-up, with no signs of tumor recurrence or metastasis; therefore, the efficacy and safety of this regimen remains to be clarified in follow up studies.

Conclusion

In conclusion, a standard treatment regimen has not yet been determined for mixed pulmonary large cell neuroendocrine carcinoma because of its rarity and complex pathological manifestations. We expect that more therapeutic methods will be examined, leading to improved prognosis for future patients.

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Conflicts of interest

The authors indicated no potential conflicts of interest.

Author contributions

All authors contributed to data acquisition, data interpretation, and reviewed and approved the final version of this manuscript.

Data availability statement

Not applicable.

Ethical approval

Not applicable.

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