Case Report

Camrelizumab combined with anlotinib for the treatment of small cell lung cancer: a case report and literature review

Yuqi Jiang[1]^, Lei Zhang[1], Fuyun Zhu[2], Hui Zhu[1], Xiaowen Cao[3], Yongchun Zhang[1]

[1]Department of Radiation Oncology, The Affiliated Hospital of Qingdao University, Qingdao, China; [2]Department of Oncology Hematology, Pingyi Hospital of traditional Chinese Medicine, Linyi, China; [3]Radiotherapy Technology Center, The Affiliated Hospital of Qingdao University, Qingdao, China

Correspondence to: Yongchun Zhang. Department of Radiation Oncology, The Affiliated Hospital of Qingdao University, 16 Jiangsu Road, Qingdao 266003, China. Email: zyc18661805058@163.com.

Abstract: Data in 2020 show that lung cancer is the second most common cancer with the highest morbidity and mortality in the world, among which small cell lung cancer (SCLC) accounts for about 15% of the total number of lung cancers, but the number of deaths accounts for 25% of lung cancers. SCLC is an aggressive malignancy disease with a high recurrence rate and poor prognosis. The survival rate of small cell lung cancer is lower than other types of lung cancer and the prognosis is very poor. At present, there is still a lack of effective therapeutic options for SCLC after the failure of second-line treatment. However, studies have shown that anti-vascular therapy and programmed death-1 (PD-1) inhibitors are effective in SCLC. In the present case, a combination therapy of camrelizumab, a PD-1 inhibitor, and anlotinib (an anti-angiogenic drug) was administered to treat a 58-year-old male patient with programmed cell death-Ligand 1 (PD-L1) negative metastatic SCLC accompanied by primary tongue cancer. A total of 28 cycles were used from March 2020 to November 2021. Until November 2021, the survival time of the patient is 31 months; he has survived for 19 months with no disease progression, and is currently classified as complete response (CR). Our study demonstrates that camrelizumab plus anlotinib may be a promising treatment option for patients with metastatic SCLC.

Keywords: Small cell lung cancer (SCLC); PD-1 inhibitors; anti-angiogenesis; case report

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Introduction

Small cell lung cancer (SCLC) is a type of lung cancer with poor prognosis, accounting for about 15% of the total incidence of lung cancer and 25% of lung cancer deaths (1,2). SCLC has low differentiation, rapid proliferation, high invasiveness, and neuroendocrine function; thus, when making a definite diagnosis, the proportion of contralateral lung or distant metastasis (extensive stage) is approximately two-thirds. Radiotherapy and chemotherapy are effective in the treatment of SCLC, but the remission period is short, the rate of recurrence and metastasis are high, and it is easily resistant to drugs. In previous studies, SCLC has shown a response rate of 60–80% to first-line treatment; however, only about 20% of patients with limited treatment duration were cured (3,4). About 80% of limited stage small cell lung cancer (LS-SCLC) patients and almost all patients with extensive stage small cell lung cancer (ES-SCLC) relapse within the first year of treatment (5). SCLC often occurs in older people and those accompanied by a variety of chronic basic diseases; the outcome of treatment is usually

^ ORCID: 0000-0003-0742-5469.

unsatisfactory and the curative effect is not good. After the disease progresses, patients with SCLC can only survive for a year or less (6). The median overall survival time (mOS) of patients with LS-SCLC and ES-SCLC is 15–20 months and 8–13 months, respectively (7), and the 5-year survival rates of LS-SCLC and ES-SCLC are 10–13% and 1–2%, respectively (7,8). Meanwhile, the mOS time of patients who receive second-line and further treatment is only 4–5 months (5).

In order to improve the survival status of patients with SCLC, the exploration of new treatment methods is crucial. Studies have shown that anti-angiogenic drugs and PD-1 inhibitors are effective in the treatment of SCLC. Camrelizumab is currently the cheapest PD-1 inhibitor approved for lung cancer in China after insurance reimbursement. Anlotinib is approved for the third or higher line treatment of small cell lung cancer in China. So we used camrelizumab combined with anlotinib to treat an elderly male patient with PD-L1 negative recurrent and metastatic SCLC and tongue cancer. This patient had multiple metastases after radical radiotherapy and chemotherapy, and the condition was completely relieved following treatment with this combination of drugs. At present, the disease control time has been more than 2 years. We found a case report of small cell lung cancer treated with camrelizumab and anlotinib (9). The patient in the before-mentioned case report received anlotinib 12 mg once daily, day 1–14, every 21 days, as we used anlotinib 10 mg. In addition, our patient had dual primary tongue cancer and lung cancer, with PD-L1 negative after testing. The two patients have achieved good therapeutic effects, which mutually verifies the effect of the combination of camrelizumab and anlotinib on small cell lung cancer and suggests the possible optimal dosage of anlotinib, and also shows good therapeutic effect on PD-L1 negative patients.

We present the following case report in accordance with the CARE reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-21-3860/rc).

Case presentation

A 58-year-old male patient was admitted to our hospital in March 2019 because of foreign body sensation in the pharynx, cough, and hemoptysis. Subsequent electronic laryngoscopy showed a cauliflower-like tumor on the right side of the root of the tongue. Magnetic resonance imaging (MRI) indicated a space-occupying lesion on the right side of the root of the tongue, with a high possibility of tumor, as well as a space-occupying lesion in the right cervical arterial sheath, with a high possibility of lymph node metastasis (*Figure 1*). Pathological biopsy of the root of the tongue revealed squamous cell carcinoma, highly differentiated (*Figure 2*). On April 1, 2019, chest Computed Tomography (CT) scan of the patient showed a 30.5 mm × 34.2 mm density shadow of soft tissue in the lower lobe of the right lung, not excluding tumor (*Figure 3*). Lung puncture biopsy of right lower lobe showed a poorly differentiated carcinoma. Immunohistochemistry (IHC) indicated cytokeratin (CK) (+), synaptophysin (Syn) (+), chromogranin A (CgA) (+), cluster of differentiation (CD) 56 (+), thyroid transcription factor-1 (TTF-1) (+), P40 (one of the subtypes of P63 protein) (–), Ki-67 (a nuclear protein encoded by the MKI-67 gene) (70%+) (*Figure 4*). Combined with morphology and IHC results, the patient was diagnosed with SCLC. On April 10, 2019, color Doppler showed that there were multiple enlarged lymph nodes in the II-V area of the right neck and multiple enlarged lymph nodes in the II-IV area of the left neck, but the patient refused lymph node biopsy. In view of the fact that most of the metastatic enlarged lymph nodes were located in areas II and III, and taking the imaging and clinical manifestations of the patients into consideration, the neck lymph nodes were most likely to have metastasized from the tongue cancer. The final diagnosis of the patient was right limited stage SCLC and squamous cell carcinoma of the tongue with enlarged cervical lymph nodes.

From April to August 2019, the patient received head, neck, and chest radiotherapy with four cycles of simultaneous chemotherapy of EP regimen (etoposide 0.2 mg on day 1–3 + cisplatin 50 mg on day 1–2). During the treatment period, he experienced third-degree myelosuppression, and the symptoms were relieved after symptomatic supportive treatment. Subsequent head and neck MRI and chest CT revealed that the tumors had disappeared completely and the disease had reached complete remission (CR) (*Figures 1C*,*1D*,*3C*,*3D*). Thereafter, the patient was regularly re-examined in the hospital.

On December 9, 2019, MR plain scan and diffusion-weighted imaging (DWI) imaging showed multiple abnormal signals in the skull, which indicated the high possibility of metastatic tumor (*Figure 5*). The patient then received brain radiotherapy from December 2019 to January 2020. On February 26, 2020, a contrast-enhanced CT scan of the upper abdomen showed multiple low-density nodules and masses in the perirenal fat capsule, the right

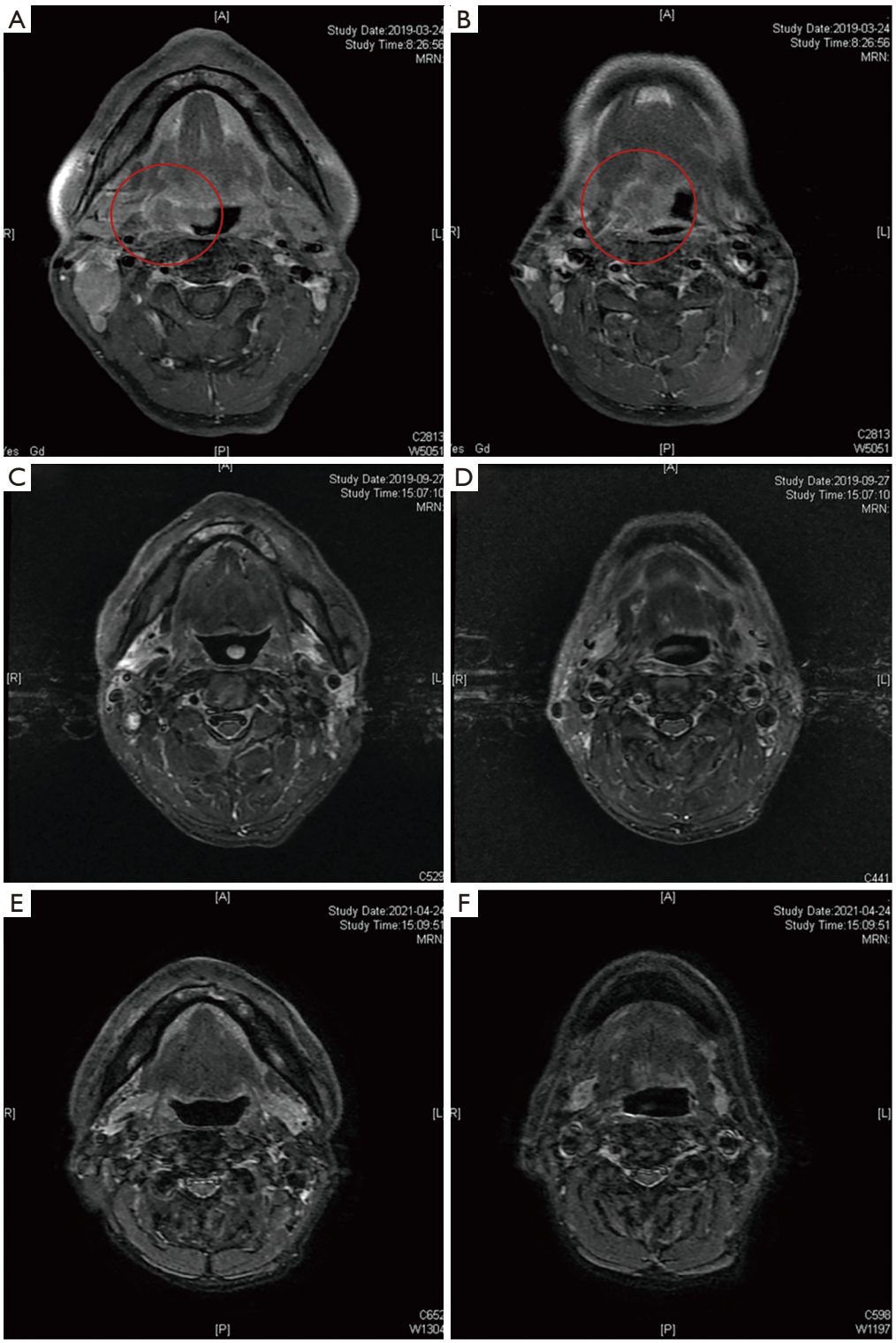

Figure 1 MRI of the head and neck. (A,B) Tumor masses in the right tongue base and right oropharynx on March 24, 2019. (C,D) The mass disappeared after radiotherapy in the head and neck on September 27, 2019. (E,F) Good disease control was observed in the latest examination of the patient on April 24, 2021. The red circle indicates the location of the tumor. MRI, magnetic resonance imaging.

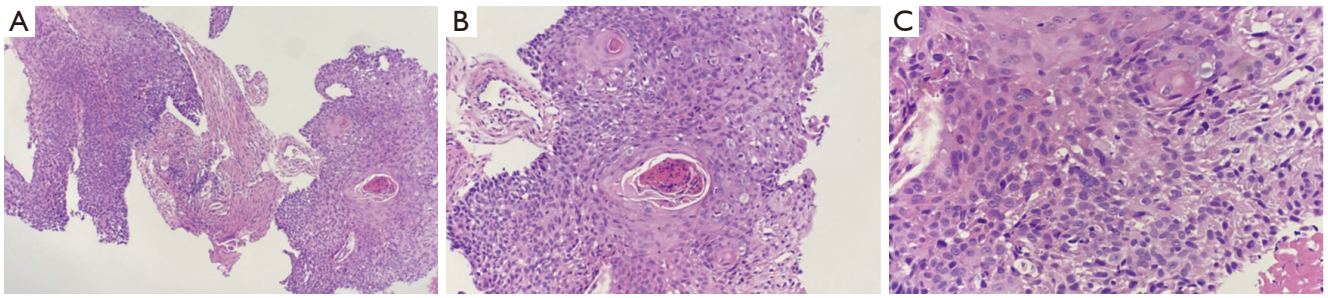

Figure 2 Histologic features of the tongue tumor: the proliferating epithelium had invaded the connective tissue, forming many interconnected nests of cells (nests of cancer); keratinization in the nest was similar to the epidermal process; and the formation of wheel lamellar bodies, called keratinization beads. (A) 10×10, H&E. (B) 10×20, H&E. (C) 10×40, H&E. H&E, hematoxylin and eosin.

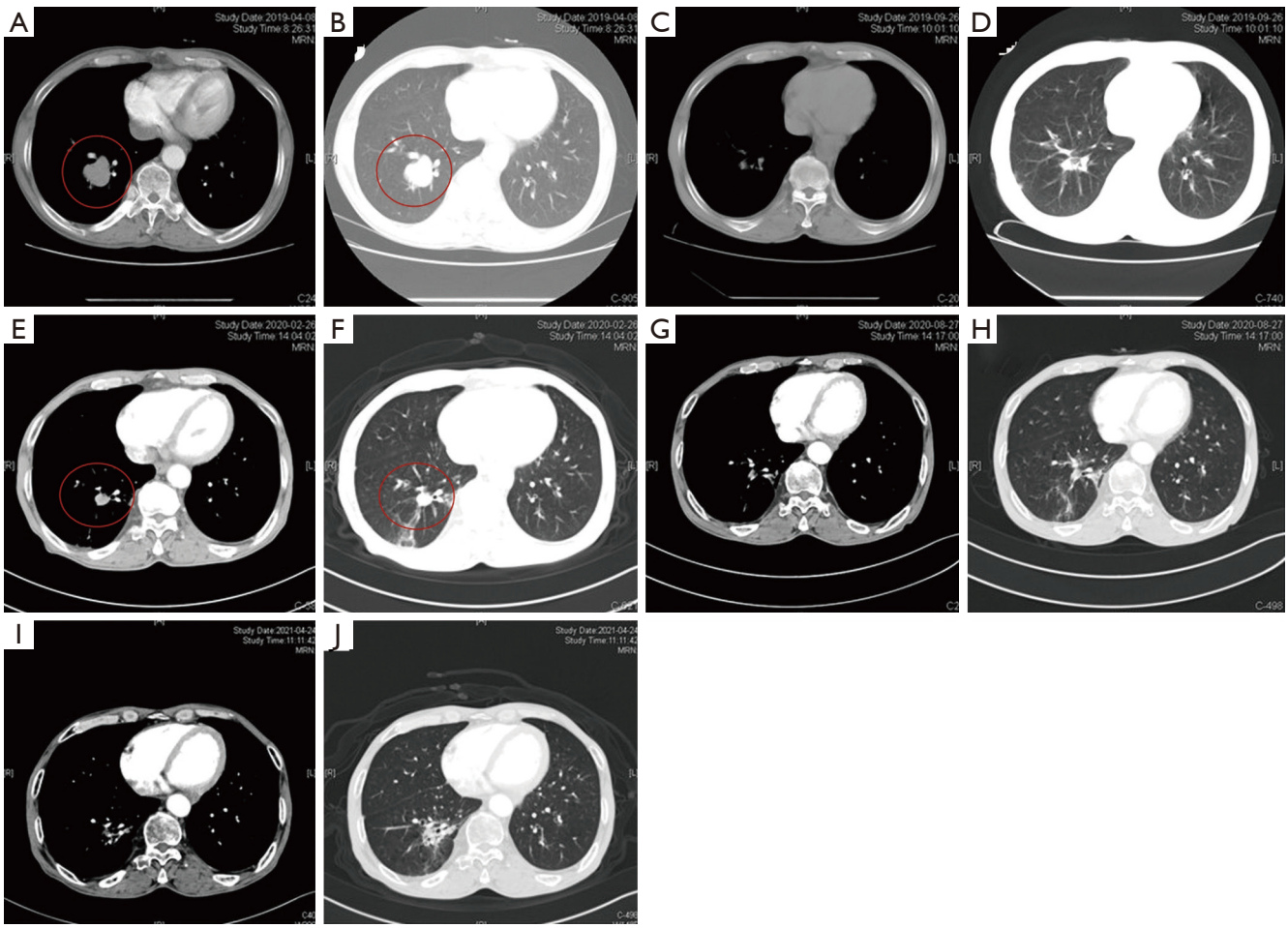

Figure 3 Chest computed tomography scan. (A,B) A massive soft tissue density shadow in the lower lobe of the right lung, which is about 30.5 mm × 34.2 mm, shallowly lobulated on April 8, 2019. (C,D) After radiotherapy and chemotherapy, the lung tumor disappeared on September 26, 2019. (E,F) SCLC recurrence on February 26, 2020. (G,H) After combination therapy with anlotinib and camrelizumab, the lung lesions disappeared on August 27, 2020. (I,J) No tumors were found on April 24, 2021. The red circle indicates the location of the tumor.

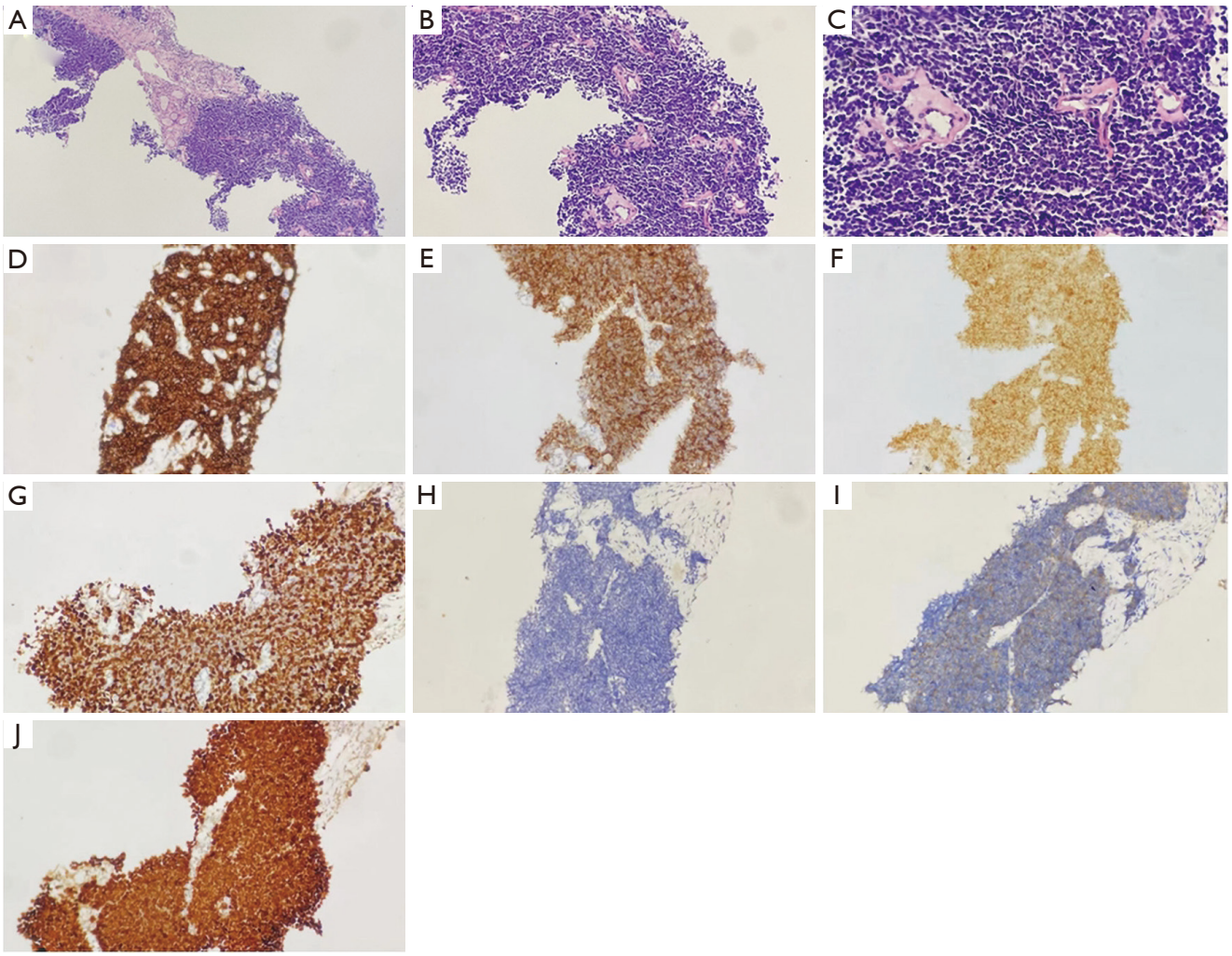

Figure 4 Lung puncture biopsy of right lower lobe. (A-C) H&E section showing that the cells were small, deformed by extrusion, and had an increased nucleus to plasma ratio. (D) IHC showing CD56 (+). (E) IHC showing CgA (+). (F) IHC showing CK (+). (G) IHC showing Ki-67: (70%+). (H) IHC showing P40 (–). (I) IHC showing Syn (+). (J) TTF-1 (+). (A) 10×10. (B) 10×20. (C)10×40. (D-J) 10×20. H&E, hematoxylin and eosin; IHC, immunohistochemistry.

adrenal area, and the mesenteric space below the tail of the pancreas, as well as enlarged retroperitoneal lymph nodes, which indicated a high possibility of metastasis (*Figure 6*). And CT showed SCLC has recurred in the lung.Perirenal biopsy demonstrated malignant tumor. IHC revealed that Ck-pan (pan Cytokeratin) (+), TTF-1 (+), Syn (+), CgA (+), CD56 (+), LCA (leukocyte common antigen) (–), p40 (–), Ki-67 (90%+), and PD-L1 were negative (*Figure 7*). Given the IHC results, the tumor was considered to conform to small cell carcinoma, and so we believed that it came from lung cancer and used second-line IP (irinotecan combined with cisplatin) systemic chemotherapy. However, IV myelosuppression occurred on the first day of chemotherapy, and we stopped the chemotherapy immediately. Subsequently, according to the patient and his family conditions, we switched the treatment regimen to camrelizumab (200 mg, every three weeks) combined with anlotinib (10 mg, once daily, day 1–14, every three weeks) on March 25, 2020 after obtained the informed consent from the patient. On August 27, 2020, follow-up contrast-enhanced abdominal CT showed that after 7 cycles of treatment with camrelizumab plus anlotinib, the multiple low-density nodules and masses in the mesenteric space had disappeared. No tumors were found in chest CT scan.

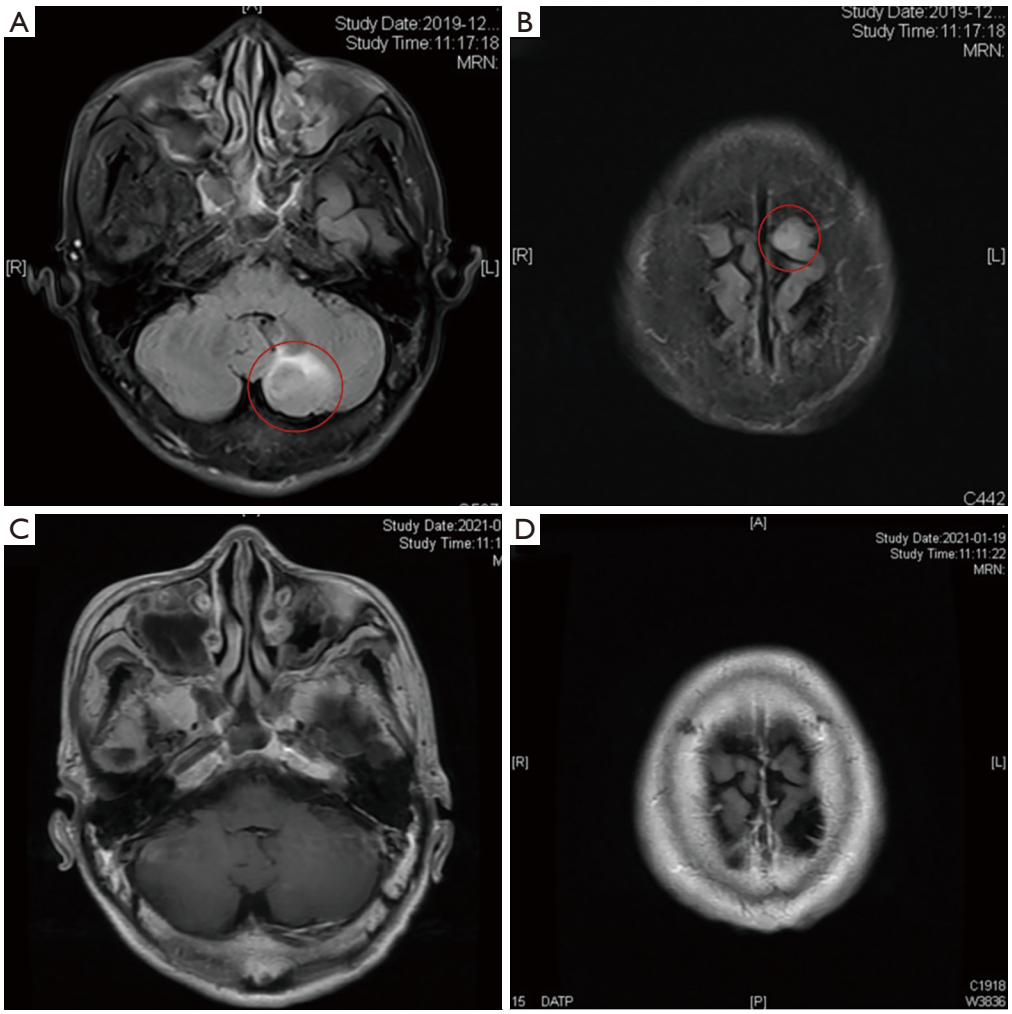

Figure 5 Brain metastases before and after treatment. (A,B) The patient had abnormal lumps in his brain on December 9, 2019. (C,D) After radiation to the head, the brain metastases disappeared completely on January 19, 2020. The red circle indicates the location of the tumor.

This patient was reviewed approximately once every 6 months after his condition became stable. His last re-examination was conducted on April 24, 2021 and the patient achieved CR (*Figures 1E,1F,3I,3G,6I-6L*). Until November 2021, the survival time of the patient is 31 months. From the time of recurrence, the patient has survived for 23 months. From the time of two drugs used, he has survived for 19 months.

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

SCLC is a high-grade neuroendocrine cancer, accounting for about 15% of all lung cancers. Approximately two-thirds of patients have distant metastasis at the time of their first diagnosis. The most common metastatic sites include the lung, brain, liver, adrenal gland, and bone. The treatment of very early patients includes surgery and adjuvant platinum combined chemotherapy.

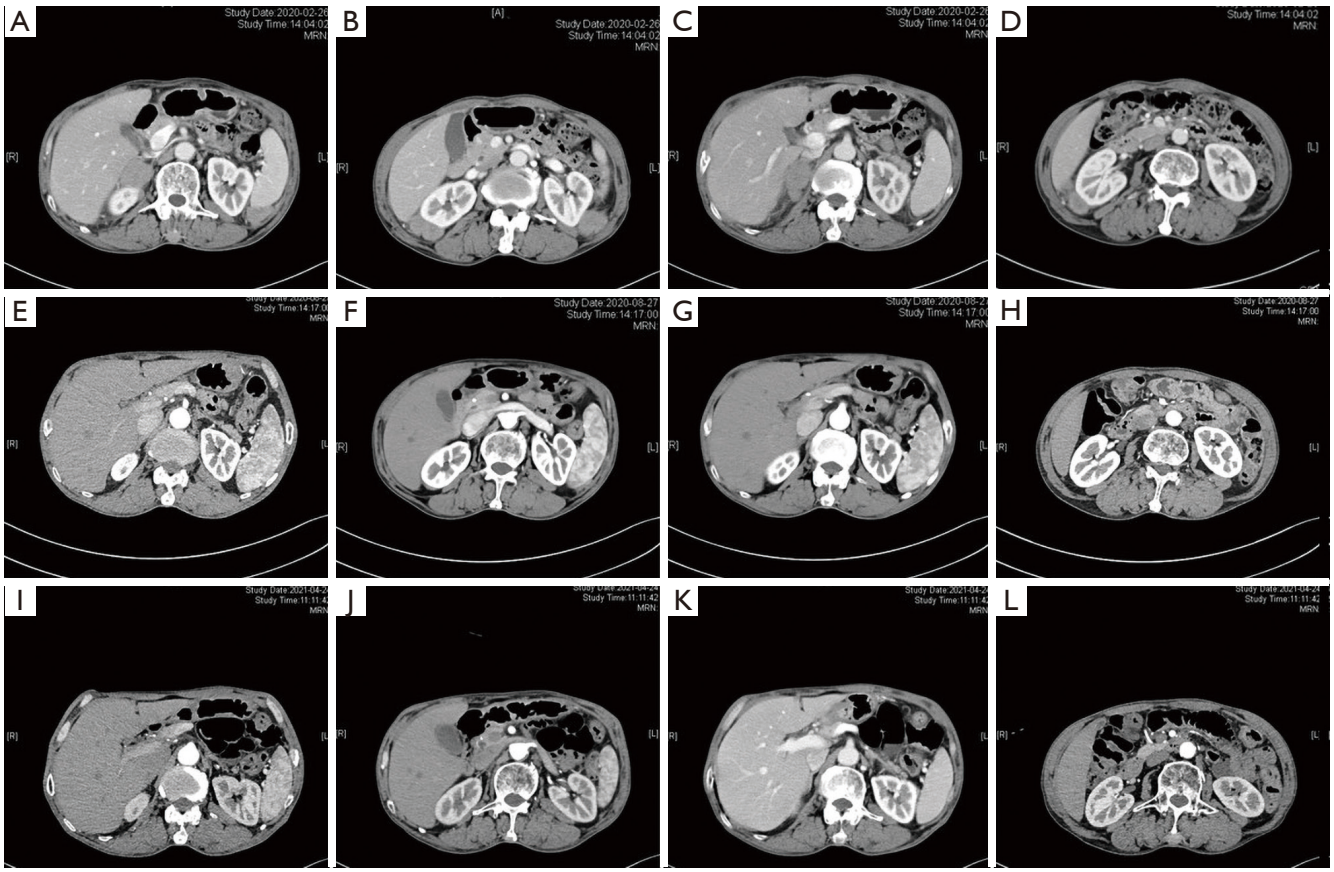

Figure 6 Abdominal metastatic tumor. (A-D) Multiple low-density nodules and masses were observed in the perirenal adipose sac, right adrenal area, and mesenteric space below the tail of the pancreas on February 26, 2020. (E-H) After treatment with anlotinib and camrelizumab, multiple low-density nodules and masses in the mesenteric space below the tail of the pancreas disappeared on August 27, 2020. (I-L) In the latest health check, the disease had not progressed at all and was well controlled (April 24, 2021).

The standard treatment for LS-SCLC is etoposide + carboplatin/cisplatin chemotherapy combined with chest radiotherapy and brain prophylactic radiotherapy. Clinical trials have reported that the mOS is 25–30 months, and the 5-year survival rate is 30–35% (10). Systemic chemotherapy is the main treatment for extensive SCLC. For recurrent and metastatic SCLC, cisplatin/carboplatin-based systemic chemotherapy is still the mainstay treatment, and local radiotherapy is used for the residual lesions of primary or metastatic lesions. However, the overall efficiency is low and the control time is short.

Zhao *et al.* analyzed the efficacy of irinotecan (CPT-11), topotecan (TPT), paclitaxel (PTX), and docetaxel (DTX) in 116 patients with relapse or progression after first-line chemotherapy. Among the different chemotherapy groups, the disease control rate (DCR) of PTX was the highest (78.57%), and the objective remission rate (ORR) of CPT-11 was the highest (22.22%). The median progression-free survival time (PFS) of CPT-11, TPT, PTX, and DTX was 91, 74.5, 81, and 50 days, and the mOS was 595, 154, 168.5, and 184 days, respectively (11). In another phase III study, the ORR of topotecan in patients with SCLC treated with topotecan was 16.9%, the median PFS was 3.5 months, and the mOS was 7.8 months (12). The median PFS of patients treated with carboplatin and etoposide was significantly longer than that of patients treated with topotecan alone [4.7 months, 90% confidence interval (CI):3.9–5.5; 2.7 months, 90% CI: 2.3–3.2] (13).

In order to resolve the low cure rate, high recurrence rate, and short OS time of SCLC treatment, exploring new treatments has become a particular research focus. Immunotherapy and anti-vascular therapy have shown

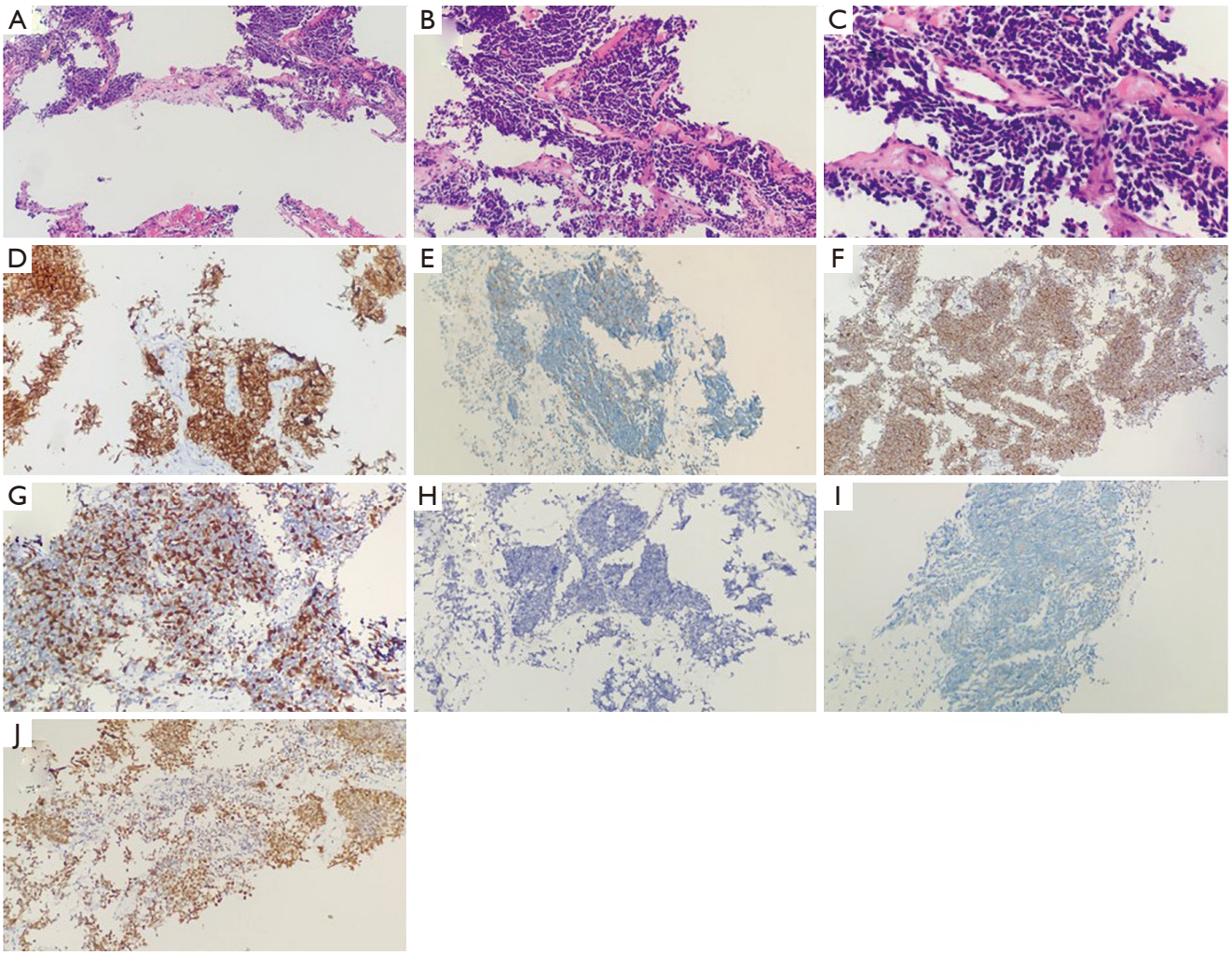

Figure 7 Perirenal biopsy. (A-C) H&E section. (D) IHC showing CD56 (+). (E) IHC showing CgA (+). (F) IHC showing CK (+). (G) IHC showing Ki-67(90%+). (H) IHC showing PD-L1: (–). (I) IHC showing Syn (+). (J) IHC showing TTF-1 (+). (A) 10×10. (B) 10×20. (C) 10×40. (D-J) 10×20. H&E, hematoxylin and eosin; IHC, immunohistochemistry.

excellent therapeutic effects in the treatment of non-small cell lung cancer (NSCLC), and some clinical research and exploration have been carried out in SCLC.

A meta-analysis conducted by Lin *et al.* showed that angiogenesis inhibitors plus chemotherapy (ACT group) had significant advantages in objective response rate [relative risk (RR) =1.34; 95% CI: 1.19–1.51; P<0.00001] and extended PFS [hazard ratio (HR) =0.86; 95% CI: 0.73–1.01; P=0.07] compared with the chemotherapy alone group (CT group), but there was no significant improvement in the overall survival rate (HR =1.05; 95% CI: 0.94–1.17; P=0.36) (14).

Anlotinib is a new type of multi-target small molecular polytyrosine kinase inhibitor, which can effectively inhibit vascular endothelial growth factor receptor, fibroblast growth factor receptor, platelet-derived growth factor receptor α, β, and c-kit (15). Liang *et al.* studied SCLC after first-line maintenance therapy with anlotinib. The median PFS and OS of the anlotinib group were 5.2 (95% CI: 3.8–6.6) months and 9.6 (95% CI: 6.3–12.9) months, which were better than 3.5 (95% CI: 3.1–4.0) months and 7.3 (95% CI: 6.1–8.4) months in the control group, and the difference was statistically significant (P<0.05) (16). Lin *et al.* studied the clinical efficacy and adverse reactions of anlotinib in the treatment of ES-SCLC. The ORR was 16.7%, the DCR was 73.3%, the PFS was 4.2 months, and the OS was 8.6 months (17). In a randomized, double-blind, phase

II clinical trial ALTER 1202, the median PFS of patients with third-line or more SCLC in the anlotinib group was 4.1 months, compared with 0.7 months in the placebo group (HR =0.19, P<0.0001). Also, the DCRs were 71.6% and 13.2% (P<0.0001), while the ORRs were 4.9% and 2.6% (P=1.00) in the two groups, respectively. The median OS in anlotinib and placebo groups were 7.3 months (95% CI: 6.1–10.3) and 4.9 months (95% CI: 2.7–6.0), respectively, reducing the risk of death by 47% (HR =0.53; 95% CI: 0.34–0.81; P=0.0029) (18).

Immunotherapy has also been explored in the treatment of SCLC around the world. The cytotoxic T lymphocyte-associated protein 4 (CTLA-4) and programmed death-1 (PD-1) inhibitors are the most widely studied immune checkpoint pathways. Treatment with antibodies against CTLA-4 can restore the immune response by increasing the accumulation, survival rate of memory T cells, and the depletion of regulatory cells (Tregs) (19). Blocking PD-1 or PD-L1 with monoclonal antibody (MAb) can activate cytotoxic T lymphocytes and cell-mediated immune response to tumor cells or pathogens, and reverse the Treg-mediated inhibitory effect (20,21).

In a randomized, double-blind phase III study (CA184-156), the efficacy and safety of the CTLA-4 antibody, ipilimumab, or placebo plus etoposide and platinum were evaluated in newly diagnosed ES-SCLC patients. There was no difference in the mOS (primary end point) between patients receiving chemotherapy plus ipilimumab and those receiving chemotherapy plus placebo: 11.0 and 10.9 months, respectively (HR =0.94; 95% CI: 0.81–1.09; P=0.3775). Furthermore, no difference was observed in the efficacy of PFS or tumor response, and the incidence of side effects and discontinuation of chemotherapy plus ipilimumab were higher compared to the chemotherapy plus placebo group (18% *vs.* 2%) (22). In the CHECKMATE331 phase III trial, patients with recurrent SCLC received the PD-1 inhibitor, nivolumab, and standard chemotherapy. In the global cohort, there was no significant improvement in OS compared with chemotherapy. The mOS was 7.5 months and 8.4 months, respectively (HR =0.86; 95% CI: 0.72–1.04; P=0.11). Nivolumab did not improve the survival rate of patients with recurrent NSCLC. However, the mOS of the two groups in the Chinese cohort was 11.5 months and 7.0 months, respectively (HR =0.70; 95% CI: 0.42–1.17). The results showed that nivolumab reduced the risk of death in Chinese patients by 30% (23). In the CheckMate032 study, 109 patients received third-line or later PD-1 inhibitor nivolumab monotherapy. The median follow-up time was 28.3 months, the ORR was 11.9% (95% CI: 6.5–19.5), and the duration of overall response (DOR) was 17.9 months (95% CI: 3.0–42.1). After 6 months, 17.2% of the patients had no progress, and the 12- and 18-month OS rates were 28.3% and 20.0%, respectively. For patients who were effective with nivolumab treatment, most of them could obtain long-lasting DOR. On the whole, the nivolumab treatment was well tolerated (24).

The CASPIAN phase III clinical trial found that the OS of patients with SCLC treated with the PD-L1 inhibitor, durvalumab, combined with chemotherapy versus chemotherapy alone were 13.0 and 10.3 months, respectively (HR =0.73, P=0.0047), which is a 27% reduction in the risk of death. The 12-month OS rates were 53.7% and 39.8%, respectively, signifying an increase of 13.9%. The ORRs were 67.9% and 57.6%, respectively, which is an increase of 10.3%. The combined chemotherapy with durvalumab was included in the first-line treatment of extensive small cell lung cancer. Based on the IMpower133 study of the global phase I-III clinical trial, the PD-L1 inhibitor, atezolizumab, plus EP group had a significantly prolonged the OS in the first-line treatment of SCLC compared with the placebo plus EP group. The mOS of the two groups were 12.3 and 10.3 months (HR =0.70; 95% CI: 0.54–0.91; P=0.0069), and the 2-month OS rates were 51.7% and 38.2%, respectively. The combination chemotherapy of atezolizumab was also included in the first-line treatment. In a meta-analysis, Facchinetti *et al.* found that adding PD-1/PD-L1 inhibitors to chemotherapy could significantly improve the OS (HR =0.76; 95% CI: 0.68–0.85; P<0.00001), PFS (HR =0.75; 95% CI=0.68–0.84; P<0.00001), and ORR (OR =1.28; 95% CI: 1.04–1.57; P=0.02) (25).

Camrelizumab is a PD-1 inhibitor that was invented in China. Researchers conducted a randomized, open, multicenter phase 3 trial (CAMEL) in patients with non-squamous NSCLC. Treatment with camrelizumab plus carboplatin and pemetrexed improved the PFS compared with chemotherapy alone. Their median OS is 11.3 months (95% CI: 9.6–15.4) versus 8.3 months (95% CI: 6.0–9.7), HR =0.60 (95% CI: 0.45–0.79) (26). However, there are few experiments on the treatment of SCLC, and thus, there is no specific data. However, based on the above research, camrelizumab is a promising prospect in the treatment of SCLC.

In recent years, increasing attention has turned to combination therapy, and numerous projects have explored the efficacy of different drug combinations. Among them, PD-1 inhibitors combined with antiangiogenic drugs

showed good performance. The combination of PD-1 and PD-L1 will transform the initial CD4+T cells into Tregs and inhibit the response of T cells by promoting the induction and maintenance of Tregs. Therefore, PD-1/PD-L1 blockers can reverse treg-mediated inhibition of effector T cells *in vitro* (21). Abnormalities in the tumor microenvironment (TME) can negatively affect the efficacy of PD-1/PD-L1 blockade by reduce the long-term stable efficacy. In TME, angiogenesis driven by vascular endothelial growth factor (VEGF) is a key driver of tumor-associated immunosuppression (27). Abnormal blood vessels mediate immune escape, which reduces the efficacy of immunotherapy by impeding delivery of drugs, oxygen, and effector T cells. Abnormal tumor blood vessels tend to cause hypoxia and acidosis in TME, leading to inhibition of anti-tumor immunity through various mechanisms (28,29). Therefore, tumor angiogenesis and the suppression of immune function will promote each other, thus when anti-angiogenesis drugs and PD-L1 are combined, the combination can effectively stimulate the immune response of the body, demonstrate a synergistic anti-tumor effect, which provides a theoretical basis for the combination of anti-angiogenesis drugs and immune checkpoint inhibitors against tumor.

Meder *et al.* found that the combination of vascular endothelial growth factor (VEGF) inhibitors and anti-PD-L1 targeting therapy can improve the therapeutic effect in an autologous mouse model of SCLC. In SCLC mouse models, when combined with VEGF inhibitors, PD-L1 inhibitors significantly improved median PFS and OS compared with anti-PD-L1 monotherapy (PFS: 3 *vs.* 2 weeks; P=0.0166, OS: 6 *vs.* 4 weeks; P=0.0231), and it is noteworthy that the OS of SCLC mice treated with combined anti-VEGF/anti-PD-L1 was superior to mice treated with standard combined chemotherapy regimen (median OS was 5 weeks and 6 weeks, respectively, P=0.1312).VEGF promotes the expression of the inhibitory receptor, T cell immunoglobulin domain and mucin domain-3 (TIM-3), on the T cell surface, which leads to the resistance of SCLC to PD-1 therapy. Therefore, the addition of anti-PD-1 targeting therapy to anti-VEGF may be a potential therapeutic strategy for SCLC (30).

The PASSION study conducted by Jie Wang's team included 47 SCLC patients with extensive platinum resistance who were treated with the anti-angiogenic drug, anlotinib (375 mg intravenously per day) and PD-1 inhibitor camrelizumab (375 mg intravenously every two weeks). Of the 47 patients, 16 achieved objective remission. The ORR was 34%, the DCR in all patients was 68.1%, the median PFS was 3.6 months, the median OS was 8.4 months, and the 6- and 12-month OS rates were 63.3% and 36.3%, respectively. Regardless of the patient's previous sensitivity to chemotherapy (recurrence after ≥90 days) or resistance (recurrence within <90 days), the ORR was good (37.5% *vs.* 32.3%), the median PFS was 3.6 *vs.* 2.7 months, and the median OS was 9.6 *vs.* 8 months, respectively. The incidence of treatment-related grade 3 and above adverse events was 72.9%, and the overall adverse reactions could be managed (31).

The PFS of recurrent SCLC patients treated with anlotinib combined with PD-1 inhibitors as second-line therapy was significantly longer than that of patients treated with PD-1 inhibitors alone (n=14; 5.0 *vs.* 3.0 months; P=0.005). Compared with chemotherapy alone (n=41) or PD-1 inhibitors (n=62), the combination of anlotinib and PD-1 blockade was an independent predictor of PFS prolongation (P<0.001) (32).

The medical diagnoses of our patient were primary malignant squamous cell carcinoma of the tongue and pulmonary SCLC. He was treated with radiotherapy of tongue, neck, and chest successively, simultaneously combined with the EP regimen. After first-line treatment, both conditions were well controlled and the curative effect was evaluated as CR. However, brain metastasis occurred 4 months after first-line treatment and brain radiotherapy was performed. Extensive metastasis of the abdominal cavity occurred 1 month after brain radiotherapy. Second-line irinotecan combined with cisplatin chemotherapy regimen was then used; however, the patient developed IV-degree myelosuppression and failed to complete the first cycle of chemotherapy. After communicating with the patient and his family, he was treated with anlotinib combined with camrelizumab. He achieved PR after one course of treatment. At the time of writing, a total of 28 cycles of camrelizumab plus anlotinib were used. Until November 2021, the survival time of the patient is 31 months. From the time of recurrence, the patient has survived for 23 months. From the time of two drugs used, he has survived for 19 months and finally achieved CR.

SCLC has a high degree of malignancy, easy recurrence and metastasis, and short survival time. Although breakthroughs have been made in first-line therapy in recent years, the treatment of recurrent small-cell lung cancer is still an unsolved problem. Through continuous exploration,

it has been proved that ROVA-T targeted therapy, PARP inhibitors, AKTl inhibitors, vascular targeted therapy and immunotherapy have good therapeutic effects on SCLC, indicating a new treatment direction for SCLC. However, how to accurately combine these treatment methods to formulate the most reasonable strategy is still unclear and need to be addressed.

Utilizing anti-vascular and immunotherapy shows a certain curative effect, and is expected to improve the therapeutic effect and prolong the survival time of patients. The treatment applied in this case showed a good effect, which provides a further research direction for the treatment of SCLC. But the drugs are more expensive and not included in the guidelines, the relatively small sample size of patients enrolled in clinical studies and rare clinical application. As this study was a single case review, further studies are required to validate our findings.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-21-3860/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-21-3860/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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