Anti-PD-1 Immunotherapy Combined With Antiangiogenic Therapy as Salvage Therapy in a Patient With Refractory Metastatic Peripheral Primitive Neuroectodermal Tumor: A Case Report and Literature Review

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Abstract

Background: Peripheral primitive neuroectodermal tumor (pPNET) is a relatively rare malignant neoplasm that usually occurs in children and young adults, associated with poor prognosis. However, standard treatment for refractory pPNET has not been determined.

Case presentation: A case of a 38-year-old woman with pPNET on the right shoulder and back, she had gained up to seven-and-a-half years survival undergoing these comprehensive treatment including surgery, radiotherapy, chemotherapy, antiangiogenic treatment. However, the tumor eventually progressed after receiving multiline treatment. With the patient's strong desire to receive immunotherapy, we finally adjusted the treatment plan to "anti-angiogenic tyrosine kinase inhibitor Lenvatinib combined with PD-1 inhibitor Toripalimab" for 2 cycles. Unfortunately, she developed grade 2-3 immune pneumonia after treatment.

Conclusions: To our knowledge, this is the first report of immunotherapy combined with antiangiogenic therapy in pPNET, which provides new ideas for the treatment of refractory pPNET.

Background

Primitive neuroectodermal tumor (PNET) is a very rare and highly malignant small round cell tumor with poor prognosis. The annual incidence of this disease is approximately 0.2/100,000-0.4/100,000, commonly occurs in children and young adults with a slight male predominance, and it possesses multidirectional differentiation potential^[1]. According to the tissue of origin, PNET can be divided into peripheral primitive neuroectodermal tumor (pPNET) and central PNET. Moreover, there are differences in immunohistochemical staining, genetic basis, predilection age, 5-year survival rate, metastasis routes and treatment regimens among them^[2]. Both pPNET and Ewing Sarcoma (ES), which originate as small round cells of fetal neuroectodermal cells, belong to Ewing sarcoma family. Due to the similarities in cytogenetics and histology, they are characterized by t(11;22)(q24;q12) translocation, which generates an abnormal fusion gene EWS-FLI1 with oncogenic properties. pPNET occurs mainly in the skeletal system and soft tissue, and also occurs in the heart, lung, reproductive organs, kidneys, pancreas and palate^[3]. This paper reports and analyzes the diagnosis and treatment of one patient with right shoulder and back pPNET over the past 6 years, providing valuable clinical experience for refractory pPNET.

Case Presentation

A 28-year-old female patient Xu, found a mass on the right shoulder and back with a size of about 9.0cm×9.0cm×4.5cm in 2014. The patient underwent mass resection on January 1, 2014 in The Second Affiliated Hospital of Xi'an Jiaotong University. The histopathological results showed a small round cell malignant tumor. The immunohistochemistry was positive for vimentin, and negative for CK, EMA, Desmin, myoglobin, myogenin, HMB 45, S-100, CD20 and CD3, the Ki67 index was 4%, suggesting primitive neuroectodermal tumor. There was an in situ recurrence of the tumor 5 years later, and the

enlarged resection was performed on January 18, 2016. During the operation, a mass of about 2.5×2.0×2.0cm in the deltoid muscle was observed with unclear boundary. The histopathological results (Fig. 1) revealed that the tumor lesions invade the surrounding rhabdomyous muscle tissue, no tumor tissue was observed at the upper, lower, left and right incised margins and the base.

Tumor-bed adjuvant radiotherapy was performed postoperatively from February 16 to March 22, 2016, CTV-TB: DT6250cGy/ 25F/36D. PET/CT examination suggested bone metastasis of the left 4th and 6th ribs, right 6th rib and 10th thoracic vertebra when patient developed chest and back pain (Xijing Hospital, November 8, 2016). Therefore, the evaluation results suggested disease progression, and 9 cycles of systemic chemotherapy with CAV/IE regimen were performed. According to the RESIST1.1 standard for solid tumors, the efficacy during chemotherapy was evaluated as stable disease (SD). After chemotherapy, oral apatinib maintenance therapy was given for more than 1 year. When assessment of disease progression on August 2018, 2 cycles of "amlotinib with 12mg/d, d1-14, Q3W" targeted therapy were given, after which the patient discontinued the drug on her own. Re-progression of disease was assessed on October 2018, local palliative radiotherapy was performed on multiple bone metastases successively, and good local disease control could be achieved after radiotherapy. Subsequently, three cycles of chemotherapy with "albumin paclitaxel plus gemcitabine" regimen were performed on April, June and July 2019. NGS gene tests of blood taken during chemotherapy revealed mutations in the ANKRD11 gene, with a mutation frequency of 0.6%, and RPS6KB2 gene, with a mutation frequency of 0.5%. On September 2019, Chest CT examination indicated multiple pulmonary metastasis in both lungs, and targeted therapy of "amlotinib with 12mg/d, d1-14, Q3W" was given for 2 cycles. Chest CT examination on January 2020 indicated increased metastasis in the lung, and 3 cycles of chemotherapy with "docetaxel plus gemcitabine" regimen were given in January, March, and April 2020, and the efficacy evaluation after treatment was PD. From May to November 2020, the treatment plan was adjusted to "Cabozantinib" targeted therapy, and the therapeutic effect during this period was evaluated as SD. In December 2020, due to progressive abdominal pain of the patient, imaging examination suggested that the tumor had invaded the diaphragm and metastasized to the spleen and retroperitoneal para-vascular lymph nodes, and the treatment plan was adjusted to targeted therapy of "Lenvatinib".

Throughout the whole treatment progress, the patient gradually developed multiple bone metastases, successively underwent the third thoracic vertebra exploration decompression bone graft fusion and internal fixation plus the ninth thoracic vertebra bone cement implantation, and palliative analgesic radiotherapy for bone metastases in the left 6th and 8th dorsal ribs, left iliac crest, left frontal bone, the thoracic 1st, 2nd and 8th vertebral bodies, and surgical area of thoracic 3rd vertebral body. All of the above bone metastases could be well controlled after radiotherapy. However, owing to multiple radiotherapy sites adjacent to the chest, the patient gradually developed imaging manifestations of radiation pneumonia, and pulmonary function examination indicated severe mixed ventilation dysfunction.

Under the strong willingness of patient to accept immunotherapy, we finally adjusted the treatment plan to "anti-angiogenic tyrosine kinase inhibitor Lenvatinib combined with PD-1 inhibitor Toripalimab" for 2

cycles on February 2021 after evaluating the absence of obvious immunotherapy contraindications. On March 10th 2021, stereotactic body radiotherapy (SBRT) with doses of 25 Gy/5f for retroperitoneal metastases was performed as a result of intolerant lumbar and back pain in patient, and was shown to be effective in pain relief. But the patient began to experience symptoms such as cough, sputum, chest tightness, and dyspnea, which gradually worsened. On March 24th 2021, grade 3 immune pneumonia (checkpoint inhibitors pneumonitis, CIP) combined with bacterial infection was diagnosed, and immunotherapy was permanently discontinued (Fig. 2A.B.C). An intravenous infusion of methylprednisolone 60 mg/d was given every 12h for anti-inflammatory treatment, along with antibiotics. Three days later, the dose of methylprednisolone was reduced to 40 mg/d. After 2 weeks of adequate doses of steroids and antibiotics, the patient's symptoms improved significantly, with methylprednisolone reduced to 10 mg per day. One month later, chest CT scan showed that intrapulmonary infiltration further deteriorated than before (Fig. 2D). The patient is still receiving the best supportive care.

Discussion

The prognosis of pPNET depends on various factors such as patient age, tumor site, tumor volume, metastatic disease, and treatment regimen, in which the choice of treatment regimen plays a vital role^[1]. To date, there are no standard guidelines for management of pPNETs because of the paucity of cases arising in various body sites. Generally, patients with localized disease can have a 5-year survival of 50–60%, while patients with relapse and metastasis have a 5-year survival less than 20%^[8, 9]. The main treatment methods of pPNET include surgical resection, radiotherapy, and chemotherapy. Surgical resection acts as the cardinal treatment method of pPNET. Radical surgical resection of the tumor can remove the occupation effect, reduce local recurrence and eliminate drug-resistant tumor cells, thus providing the basis for improvement in effectiveness of postoperative radiotherapy and chemotherapy. The function of extensive, complete or nearly complete surgical resection has been considered to be critical to local tumor control and prolonged survival^[1, 4]. Small round cell tumors such as Ewing's sarcoma family usually respond well to radiation^[5]. Therefore, radiotherapy plays an important role in the treatment of PNET. Radiotherapy is used as an important local treatment, especially when the tumor is very large and located in a functional organ or complex anatomical location. Postoperative radiotherapy has been implied to reduce local recurrence and provide prolonged survival^[6]. It cannot be ignored that chemotherapy is an indispensable systemic therapy for patients with pPNET. Due to the similarity between pPNET and ES, the chemotherapy regimen for pPNET was mainly inferred from the treatment regimen for Ewing's sarcoma. Alternate vincristine-doxorubicin-cyclophosphamide (VDC) with isophoramide-etoposide (IE) is currently the standard chemotherapy regimen recommended in North America for patients with localized Ewing's sarcoma family tumors^[7]. A large retrospective study suggested that main parameters leading to better overall survival included more complete surgical resection, with more than 10 cycles of chemotherapy and VDC/IE regimen^[1]. Several combinations of agents have shown encouraging results in retrospective or phase II studies. Topotecan plus cyclophosphamide and temozolomide plus irinotecan are most commonly used. Other regimens include gemcitabine combined with docetaxel and high-dose of ifosfamide, but the survival results of these

regimens are not satisfactory ^[10]. Therefore, new treatment strategies are urgently needed to improve the prognosis of these patients.

Anti-angiogenic tyrosine kinase inhibitors have been widely used in the treatment of advanced bone and soft tissue sarcoma (STS), bringing new breakthroughs in efficacy and prognosis of patients. Cabozantinib, a tyrosine kinase inhibitor targeting vascular endothelial growth factor receptor-2(VEGFR-2) and c-MET, that are overexpressed and whose activity is negatively associated with outcomes for patients with osteosarcoma or Ewing sarcoma^[11]. Cabozantinib has been shown to inhibit the growth and viability of Ewing sarcoma cell lines in vitro ^[12]. CABONE was designed as a multicentre, single-arm, two-stage, phase 2 trial to investigate the efficacy and safety of cabozantinib in patients with advanced Ewing sarcoma^[13]. It enrolled heavily pretreated patients with Ewing sarcoma (n = 45), patients were treated with cabozantinib 60 mg once daily (adults) or 40mg/m² once daily (adolescents). For the efficacy evaluable patients with Ewing sarcoma (n = 39), overall response rate (ORR) was 26% (n = 10) by 6 months, median progression free survival (PFS) was 4.4 months (95% CI 3.7–5.6), and median overall survival(OS) was 10.2 months (95% CI 8.5– 18.5). It has been initially shown that Cabozantinib has certain efficacy in patients with recurrent ES, with tolerable adverse reaction. Due to the similarity between pPNET and ES, patients with pPNET is expected to benefit from anti-angiogenic therapy for survival improvement. Ayako et al have reported a five-months PFS with Pazopanib (a multi-target anti-angiogenic tyrosine kinase inhibitor) in a patient with recurrence of primary pulmonary PNET ^[14], which further confirming the above views. With the successful application of immunotherapy in multiple solid tumors, new approach for advanced STS immunotherapy are being explored based on the understanding of the underlying cellular and molecular mechanisms of dynamic interactions between tumor stroma, tumor cells and immune infiltration in sarcoma tissue. Compared to other solid tumors, STS possess a low frequency of somatic cell mutations, and are generally considered as "cold tumors" that are insensitive to immunotherapy. SARC028 is the first multicentre, open-label, phase 2 study to evaluate the effectiveness of immune checkpoint blockade(ICL) in patients with advanced STS^[15]. Results from the SARC028 trial showed that Pembrolizumab in advanced STS had a median PFS of 4.2 months, an ORR of 18%, and a PFS rate of 32% at 6 months.. The efficacy of Pembrolizumab correlated with the STS subtype. In specific sarcoma tissue types, such as undifferentiated polymorphic sarcoma and alveolar soft tissue sarcoma, Pembrolizumab showed better immune efficacy. However, Pembrolizumab showed no significant benefit in 13 patients with ES, possibly due to the highly immunosuppressive tumor microenvironment. Only one patient with ES had a partial response, indicating that a small number of patients with ES could benefit from immunotherapy. In this kind of rapidly growing aggressive malignancy, more effective ICI combination treatment strategies are clearly needed to achieve better clinical disease control. However, it has been reported that the response rate of anti-PD-1 antibody combined with anti-CTLA-4 antibody in the treatment of advanced sarcoma is less than 20%^[16].

It is well known that the up-regulation of pro-angiogenic factors (including VEGF) in the tumor microenvironment and tumor angiogenesis play important roles in maintaining the immunosuppressive tumor microenvironment^[17]. Anti-angiogenic therapy can change the immunosuppressive tumor

microenvironment by normalizing tumor blood vessels and inhibiting immunosuppressive cells, thus enhancing the effect of immunotherapy [18]. Immuno-checkpoint inhibitors combined with antiangiogenic therapy have achieved encouraging survival outcomes in partial clinical trials of STS. A single-center, single-arm, phase II clinical trial of vascular endothelial growth factor inhibitor axitinib combined with pembrolizumab in 33 patients with advanced or metastatic STS showed that the 6-month progression-free survival rate (PFSR) of patients was 46.9%, and the median OS was 18.7 months [19]. Another single-arm phase Ib/II clinical trial aimed to explore the effectiveness and safety of nivolumab plus sunitinib in patient with advanced or metastatic STS. After a median follow-up of 17month,the median PFS was 5.6 months, pFSR was 48% (95% CI,41%-55%) at 6 months and median OS was 24 months^[20]. In comparison, sunitinib monotherapy in a phase II study of 50 patients with advanced STs showed a PFSR of 22% at 6 months and mPFS of 1.8 months [21] and Pembrolizumab for advanced soft tissue sarcomas with mPFS of 4.2 months and PFS at 6 months of 32%[15]. Thus, Patients with advanced sarcomas may benefit more from immunocheckpoint inhibitors combined with antiangiogenic therapy.

With the patient's strong desire to receive immunotherapy, we finally provided the treatment regimen of VEGF inhibitor Lenvatinib combined with PD-1 inhibitor Toripalimab. After 2 cycles of treatment, the patient's back pain became more severe, and SBRT with dose of 25 Gy/5f was given for the retroperitoneal metastasis and the pain was gradually relieved. The synergistic mechanism between radiotherapy and immunotherapy may be that radiotherapy enhances the efficacy of anti-tumor immunotherapy by inducing increased antigen expression, promoting tumor antigen processing and presentation, recruitment of immune cells, and activation of CD8 + T cells [22–23]. However, the imaging examination of this patient indicated larger and more numerous of tumor lesions in short term after treatment, and gradually developed grade 3 checkpoint inhibitor pneumonitis(CIP)after radiotherapy. Retrospective analysis indicated that the occurrence of CIP was associated with basic pulmonary disease, baseline impaired pulmonary function, and multiline therapy [24]. Results of a meta-analysis showed that combination immunotherapy (such as dual immunotherapy, immunotherapy combined with chemotherapy, radiotherapy or targeted therapy) can increase the risk of immune pneumonia [25]. However, the patient in this case developed grade 3 CIP after radiotherapy. The possible mechanism involved that the occurrence of CIP was related to the "radiation-induced recall response" [26], that is, the local inflammatory reaction after the application of certain drugs in patients who had previously received radiotherapy. In addition, high dose radiotherapy can also directly kill tumor cells, increase the release of antigen, enhance the sensitivity of local immune response, and then affect the occurrence of CIP. Considering the patient's previous radiation pneumonia, poor pulmonary function and multiline therapy, we should pay more attention to the safety of combination therapy.

Conclusions

Based on the above analysis, this patient had achieved seven-and-a-half years survival after previous comprehensive treatment, including surgery, radiotherapy, chemotherapy and anti-angiogenesis targeted

therapy, which was far beyond the data reported before, suggesting that multidisciplinary comprehensive treatment can benefit the survival of this patient. After taking immunotherapy combined with anti-angiogenesis therapy, the patient's disease was uncontrolled, and grade 3 CIP appeared, illustrating that the patient's tolerance and safety should be fully evaluated when the combination therapy is adopted in advanced disease.

Abbreviations

pPNET

peripheral primitive neuroectodermal tumor;ES:Ewing Sarcoma;SD:stable disease;CT:Computed tomography;STS:soft tissue sarcoma;PFS:progression free survival;OS:overall survival;CR:Complete remission;PFSR:progression-free survival rate;ICI:immune checkpoint blockade;VEGF:vascular endothelial growth factor receptor; VDC:vinCRlstone-doxorubicin-cyclophosphamide;IE:isophoramide-etoposide;CIP:checkpoint inhibitor pneumonitis

Declarations

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Written informed consent was obtained from the patient for publication of this case report.

Authors' contributions

Qiaoyun Chen and Ronghui Jin reviewed the relevant literature and participated in the drafting of the manuscript. Gaili An participated in the revision of the manuscript. Qiaoyun Chen,Ronghui Jin,Qifan Wu and Xu Li participated in the information collection. Gaili An is corresponding authors. All authors read and approved the revised manuscript.

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Availability of data and materials

Not applicable.

Ethics approval and consent to participate

Not applicable as this is a case report, not a clinical study.

Consent for publication

Written informed consent for the publication of patient clinical details and clinical images was obtained from the patient.

Competing interests

The authors declared there were no competing interests.

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References

[1] Liu Y, Yuan Y, Zhang F, et al. Outcome of multidisciplinary treatment of peripheral primitive neuroectodermal tumor[J]. Scientific Reports, 2020,20(10):15656.

[2] Woeste M R, Bhutiani N, Hong Y K, et al. Primitive neuroectodermal tumor incidence, treatment patterns, and outcome: An analysis of the National Cancer Database[J]. Journal of Surgical Oncology, 2020,122(6):1145-1151.

[3] Gao L, Zhu Y, Shi X, et al. Peripheral primitive neuroectodermal tumors: A retrospective analysis of 89 cases and literature review[J]. Oncology Letters, 2019,18(6):6885-6890.

[4] Demir A, Gunluoglu M Z, Dagoglu N, et al. Surgical Treatment and Prognosis of Primitive Neuroectodermal Tumors of the Thorax[J]. Journal of Thoracic Oncology, 2009,4(2):185-192.

[5] Becker R G, Gregianin L J, Galia C R, et al. What is the impact of local control in Ewing sarcoma: analysis of the first Brazilian collaborative study group – EWING1[J]. BMC Cancer, 2017,17(1):420.

[6] Shunsuke I, Yoichi I, Masahiro N, et al. Primary epidural extra-osseous ewing sarcoma/peripheral primitive neuroectodermal tumor of the cervical spine curatively treated by surgery and adjuvant chemoradiotherapy: A case report and review of the literature[J]. Interdisciplinary Neurosurgery, 2020,23.

[7] Gaspar N, Hawkins D S, Dirksen U, et al. Ewing Sarcoma: Current Management and Future Approaches Through Collaboration[J]. Journal of Clinical Oncology, 2016,33(27):3036-3046.

[8] Scurr, M. How to Treat the Ewing's Family of Sarcomas in Adult Patients[J]. Oncologist, 2006,11(1):65-72.

[9] Galindo C R, Spunt S L, Pappo A S. Treatment of Ewing sarcoma family of tumors: current status and outlook for the future.[J]. Pediatric Blood & Cancer, 2010,40(5):276.

[10] Ben Kridis W, Toumi N, Chaari H, et al. A Review of Ewing Sarcoma Treatment: Is it Still a Subject of Debate?[J]. Reviews on Recent Clinical Trials, 2017,12(1):19-23.

- [11] Schoffski P, Blay J Y, Ray-Coquard I. Cabozantinib as an emerging treatment for sarcoma[J]. *Curr Opin Oncol*, 2020,32(4):321-331.
- [12] Fleuren E D, Roeffen M H, Leenders W P, et al. Expression and clinical relevance of MET and ALK in Ewing sarcomas[J]. *Int J Cancer*, 2013,133(2):427-436.
- [13] Italiano A, Mir O, Mathoulin-Pelissier S, et al. Cabozantinib in patients with advanced Ewing sarcoma or osteosarcoma (CABONE): a multicentre, single-arm, phase 2 trial[J]. *Lancet Oncol*, 2020,21(3):446-455.
- [14] Ayako, Takigami, Hideaki, et al. Pazopanib Confers a Progression-free Survival in a Patient with Ewing's Sarcoma/Primitive Neuroectodermal Tumor of the Lung.[J]. *Internal medicine (Tokyo, Japan)*, 2019,58(9):1335-1339.
- [15] Tawbi H A, Burgess M, Bolejack V, et al. Pembrolizumab in advanced soft-tissue sarcoma and bone sarcoma (SARC028): a multicentre, two-cohort, single-arm, open-label, phase 2 trial[J]. *Lancet Oncology*, 2017,18(11):1493-1501.
- [16] D'Angelo S P, Mahoney M R, Van Tine B A. Nivolumab with or without ipilimumab treatment for metastatic sarcoma (Alliance A091401): two open-label, non-comparative, randomised, phase 2 trials[J]. *Lancet Oncology*, 2018,19(3):416-426.
- [17] Motz G T, Coukos G. The parallel lives of angiogenesis and immunosuppression: cancer and other tales[J]. *Nature Reviews Immunology*, 2011,11(10):702-711.
- [18] Yang J, Jing Y, Liu B. Targeting VEGF/VEGFR to Modulate Antitumor Immunity[J]. *Frontiers in Immunology*, 2018,9:978.
- [19] F B, F M, Tks B, et al. Axitinib plus pembrolizumab in patients with advanced sarcomas including alveolar soft-part sarcoma: a single-centre, single-arm, phase 2 trial[J]. *The Lancet Oncology*, 2019,20(6):837-848.
- [20] Martin-Broto J, Hindi N, Grignani G, et al. Nivolumab and sunitinib combination in advanced soft tissue sarcomas: a multicenter, single-arm, phase Ib/II trial[J]. *Journal for ImmunoTherapy of Cancer*, 2020,8(2):11515.
- [21] George S, Merriam P, Maki R G. Multicenter Phase II Trial of Sunitinib in the Treatment of Nongastrointestinal Stromal Tumor Sarcomas[J]. *Journal of Clinical Oncology*, 2009,27(19):3154-3160.
- [22] Goedegebuure R, Klerk L, Bass A J, et al. Combining Radiotherapy With Anti-angiogenic Therapy and Immunotherapy; A Therapeutic Triad for Cancer?[J]. *Frontiers in Immunology*, 2019,9:3107.
- [23] Crocenzi T, Cottam B, Newell P, et al. A hypofractionated radiation regimen avoids the lymphopenia associated with neoadjuvant chemoradiation therapy of borderline resectable and locally

advanced pancreatic adenocarcinoma[J]. Journal for Immunotherapy of Cancer, 2016,4:45.

[24] Ma K, Lu Y, Jiang S, et al. The Relative Risk and Incidence of Immune Checkpoint Inhibitors Related Pneumonitis in Patients With Advanced Cancer: A Meta-Analysis[J]. Frontiers in Pharmacology, 2018,9:1430.

[25] Su Q, Zhu E C, Wu J B, et al. Risk of Pneumonitis and Pneumonia Associated With Immune Checkpoint Inhibitors for Solid Tumors: A Systematic Review and Meta-Analysis[J]. Frontiers in Immunology, 2019,10:108-123.

[26] Tilda, Passat, Yann, et al. [Physiopathological mechanisms of immune-related adverse events induced by anti-CTLA-4, anti-PD-1 and anti-PD-L1 antibodies in cancer treatment].[J]. Bulletin Du Cancer, 2018,105(11):1033-1041.

Figures

Figure 1

Postoperative pathological results showed as (Right shoulder and back) small round cell malignant tumor, combined with medical history and immunohistochemistry, suggesting the possibility of primal nerve ectodermal tumor. Immunohistochemistry results showed positive for CD99, Vimentin, Syn, and negative for CD56,CgA,NSE,WT-1,HMB-45,LCA,CK,desmin,actin,CK5/6,S-100,P63, CK8/18 and Calponin, with Ki-67 index of approximately 30%. PAS-staining was positive in partial cells.

Figure 2

Computed tomography (axial section) of the thorax (A:Lung imaging baseline before immunotherapy and anti-angiogenic therapy, B: Lung imaging after 1 cycle of treatment, C: Lung imaging after 2 cycle of treatment, D:Lung imaging after methylprednisolone of treatment).