Case Report

Adverse skin reactions induced by sintilimab in advanced lung squamous carcinoma: a case report and review of the literature

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Background: Sintilimab is an immune checkpoint inhibitor (ICI). It can induce immune-related Adverse Events (irAEs). Severe adverse skin reactions are rare, but the mortality rate is high. We report the first case of successful treatment of adverse skin reactions using traditional Chinese medicine (TCM).

Case Description: Here we present the case of a 67-year-old male with advanced lung squamous carcinoma. After 8 cycles of chemotherapy, the patient's disease progressed and the treatment regimen was adjusted to sintilimab combined with albumin paclitaxel and cisplatin. Thirty-two days after this cycle, the patient reported a sporadic rash with pruritus on the face, front chest, and both upper limbs. The area of rash was 40%, and the adverse reaction was grade 3. The level of interleukin-related indicators was above normal. The patient's skin symptoms disappeared after treatment with hormones, TCM, and other drugs. The patient's adverse skin reaction was due to an immune-related toxicity caused by sintilimab, so treatment with sintilimab was suspended. The albumin-paclitaxel plus cisplatin regimen was continued to treat lung cancer.

Conclusions: Although rare, case of fatal adverse reaction caused by sintilimab have been reported. We recommend early monitoring and recognition of symptoms. During management, high-dose hormones combined TCM may be helpful.

Keywords: Sintilimab; adverse skin reactions; immune checkpoint inhibitors (ICIs); traditional Chinese medicine (TCM); case report

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Introduction

In recent years, the discovery of immune checkpoint inhibitors (ICIs) has had landmark significance in the treatment of cancer. ICIs activate the immune response of tumors and restore the body's autoimmune function, and thus, achieve anti-tumor effects. Sintilimab was launched in China in June 2021. Sintilimab combined with chemotherapy is the first-line treatment for advanced squamous non-small cell lung cancer (NSCLC). Sintilimab is a human immunoglobulin G4 monoclonal antibody that binds to the programmed death 1 (PD-1) receptor, blocks its interaction with programmed death-ligand 1 (PD-L1) and PD-L2, and blocks the immunosuppressive response mediated by the PD-1 pathway, including the anti-tumor immune response.

Immune-related adverse skin reactions to sintilimab are usually mild and are often self-limited, and severe adverse skin reactions are rare. It has been reported that the incidence rates of sintilimab alone and sintilimab combination therapy are <3% and <5%, respectively, but the mortality rate is high. The incidence rate of fatal immune-related adverse skin reactions is 0.3–1.3% (1). The common clinical symptoms of immune-related adverse skin reactions include non-specific maculopapular rash, Stevens-Johnson syndrome, drug hypersensitivity syndrome, pruritus, vitiligo skin lesions, psoriasis, alopecia, bullous pemphigoid, and acquired hemangioma.

This article reports the case of an elderly patient with advanced lung squamous carcinoma, who was treated with the PD-1 inhibitor sintilimab at our hospital and experienced skin immune-related adverse reactions. This case shows that given their widespread use, it is important to consider ICIs in the differential diagnosis of immune-related adverse skin reactions. This is the first case of successful treatment of adverse skin reactions using traditional Chinese medicine (TCM). During management, TCM may be helpful. We present the following case in accordance with the CARE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-5925/rc).

Case presentation

A 67-year-old, unmarried, male was admitted to the Department of Traditional Chinese Medicine Oncology of The First Affiliated Hospital of Hebei North University on March 8, 2022 due to cough and expectoration for 2 years and 7 months. He was undergoing radiotherapy for lung cancer at the time. Some 10 years earlier, the patient had undergone surgery for appendicitis. He had had a smoking habit of 40 cigarettes a day for 50 years, but had quit smoking 2 years ago. He had no alcohol addiction. His father died of emphysema at 73 years old, and his mother died of myocardial infarction at 63 years old. He had no familial history of cancer, hypertension, or other genetic problems. He had no history of drug or food allergies.

In August 2020, the patient presented to The First Affiliated Hospital of Hebei North University with cough and expectoration for 1 year without obvious inducement. From July 2020, the patient's sputum was bloody, dark red in color, and the blood volume was 3–5 mouthfuls per day. There were no symptoms of fever, night sweats, chest pain, or chest fullness.

On August 31, 2020, the patient underwent a computed tomography (CT) examination, and the results showed a space-occupying lesion of the left lung and obstructive pneumonia. An electronic bronchoscopy showed lung cancer in the left upper lobe of the lung. The pathological findings were squamous cell carcinoma. On September 10, 2020, a whole-body bone scan of the patient showed an abnormality in the left acetabulum, the nature of which was not determined. As the bilateral shoulder joint and bilateral knee joint were abnormal, the possibility of bone degeneration was considered. On September 17, 2020, the patient underwent a craniocerebral enhanced magnetic resonance imaging examination but no tumor lesions were found.

On September 12 and October 15, 2020, the patient received 2 cycles of cisplatin (130 mg, D2–4) plus gemcitabine (1.8 g, D1 and D8). On November 28, 2020, the patient underwent a chest CT examination, and the results showed that there was no significant change in the left lung mass compared to the results of the CT examination in September 2020. The doctor was of the opinion that the patient was unresponsive to chemotherapy, so the patient's treatment regimen was adjusted to albumin paclitaxel (200 mg, D1) plus cisplatin (130 mg, D2–4). On January 7, 2021, the patient underwent CT examination, and the results showed that the lesion was smaller than before, and the treatment was effective. The evaluation effect was partial response (PR). The patient continued to receive 5 cycles of albumin paclitaxel plus cisplatin for lung

Highlight box

Key findings

- A 67-year-old male patient developed an immune checkpoint inhibitor (ICI)-related skin toxicity after a single administration of sintilimab.

What is known and what is new?

- The patient's skin symptoms disappeared after treatment with hormones, traditional Chinese medicine (TCM), and other drugs.
- In the early stage, ICI-mediated adverse reactions do not usually have typical symptoms, and thus are difficult to identify and easy to ignore.

What is the implication, and what should change now?

- The early identification and correct treatment of immune-related adverse events (irAEs) play an important role in maximizing the anti-tumor effect of immune therapy and improving patient outcomes.

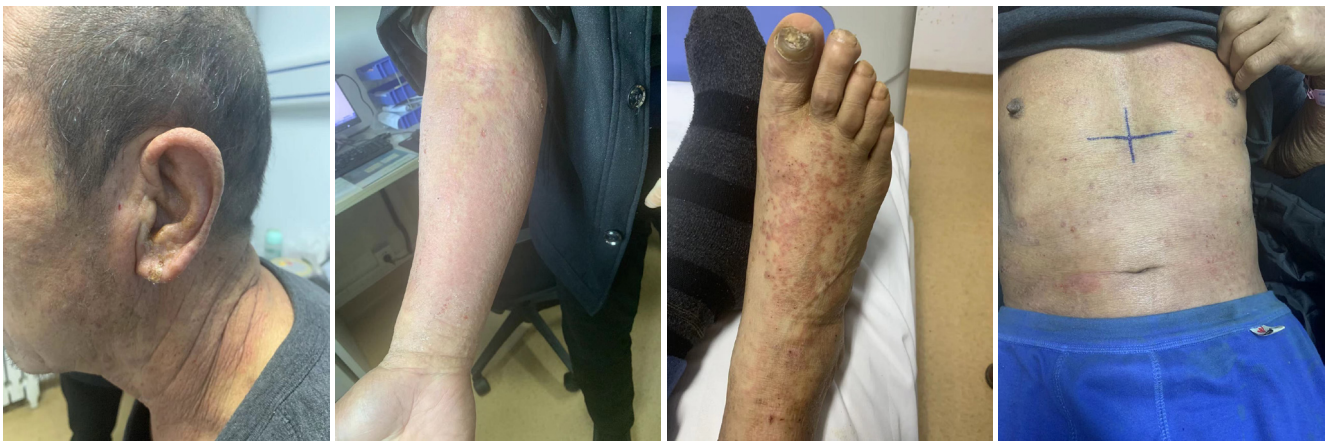

Figure 1 Symptoms of rash all over the patient's body before treatment.

cancer.

On December 3, 2021, the patient's CT examination results showed that the lesion was more advanced than before and was evaluated as progressive disease (PD). The patient's regimen was adjusted to sintilimab (200 mg) combined with albumin paclitaxel and cisplatin. On February 23, 2022, the patient was hospitalized for further treatment. The patient reported sporadic rash with pruritus on the face, front chest and both upper limbs from January 5, 2022. The patient had not paid attention to these symptoms, and the symptoms were not relieved after the application of halometasone ointment.

On February 24, 2022, a dermatology consultation was requested for the patient. The patient's body was scattered with red papules, scratches and scabs. The dermatological diagnosis was eczema dermatitis, which may have been caused by medication. The recommended treatment options were thalidomide (1 tablet twice daily), avastine capsules (1 tablet 3 times daily), and halometasone cream (twice daily, applied to the skin). During this treatment, the patient underwent an imaging examination, which showed a reduction in the soft tissue shadow of the left lung hilum, new small lymph nodes in the bilateral axillae, and bilateral axillary lymph nodes enlargement (2.3 cm × 0.6 cm on the left side and 1.5 cm × 0.8 cm on the right side). The doctor was of the opinion that the patient had axillary lymph node metastasis, and the efficacy was evaluated as stable disease (SD). The radiotherapy department was asked to consult, and the treatment plan provided by the doctor was chest radiotherapy with planning target volume (PTV) 60 Gy/30 fractions. The patient started radiotherapy on March 6, 2022, and immunotherapy was suspended. The use of pantoprazole injection, fat emulsion, and amino acid injection was also suspended.

The patient was admitted to the Department of Traditional Chinese Medicine Oncology on March 8, 2022. The physical examination results showed that the patient had a height of 172 cm, a weight of 75 kg, a body surface area of 1.87 m^2, an interleukin (IL)-1β level of 54.9 pg/mL (0–12.4 pg/mL), an IL-2 level of 34.2 pg/mL (≤7.5), an IL-5 level of 9.7 pg/mL (≤3.1 pg/mL), an IL-6 level of 40.2 pg/mL (≤5.4 pg/mL), an IL-8 level of 33.6 pg/mL (≤20.6 pg/mL), and a thyrotropin level of 9.82 mIU/I (0.27–4.2 mIU/I). The patient had a prothrombin time of 13.7 seconds (9.8–12.1 seconds), a plasma D-dimer level of 7.30 mg/LFEU (0–0.55 mg/LFEU), and a plasma fibrin level of 21.4 μg/mL (0.0–5.0 μg/mL). The patient's skin symptoms were not relieved, and red rashes were observed covering his skin, some of which had fused into patches, especially on the head, face, and limbs (see *Figure 1*). The rash area was 40%, and the adverse reaction was grade 3. A coagulation function test showed that the patient's d-dimer level was high, and the patient received a droparin calcium injection (0.4 mL, qd) for anticoagulant therapy, methylprednisolone (70 mg, qd) for hormone pulse therapy, and a kushen injection (20 mL, qd) for TCM treatment.

On March 10, 2022, the red rash on the skin of the patient's body partially subsided, and the symptoms of edema and pruritus were relieved, but the patient reported a burning sensation in his stomach and heartburn. On March 16, 2022, the red rash on the skin of the patient's body had subsided, the symptoms of edema and pruritus disappeared, but the symptoms of acid regurgitation and heartburn remained. The patient's symptoms were significantly

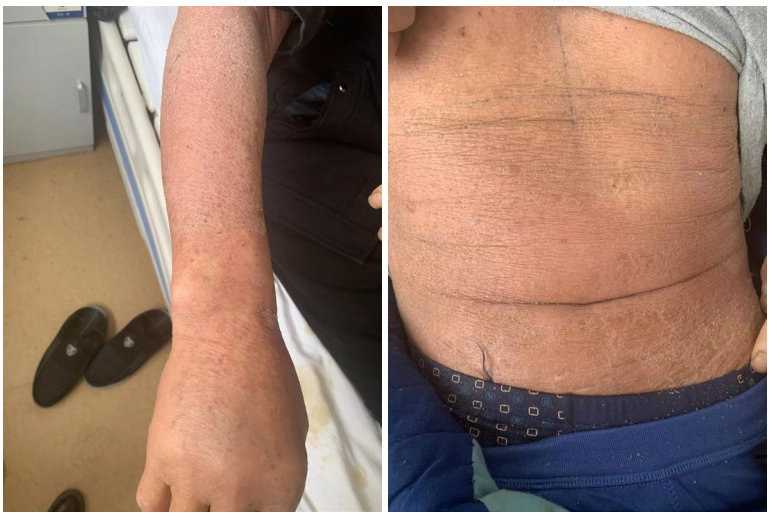

Figure 2 Symptoms of rash on patient's body after treatment.

improved, and the dose of methylprednisolone was adjusted to 50 mg, and TCM was administered at the same time. The TCM prescription was based on the Xiaofeng powder. The specific prescription was as follows: Schymba chinensis (10 g), windstorm (10 g), morning cattle seed (10 g), Cicatricide ghost (10 g), silkworm (10 g), atractylodes (10 g), Kushen (15 g), Rhizoma atractylodes (10 g), gypsum (30 g), anemarphoid (20 g), Angelica sinensis (15 g), raw land (24 g), fire maren (15 g), licorice (10 g), salvia miltiorrhiza (30 g), Xu Changqing (10 g), white Tribulus (10 g), fried malt (10 g), chicken internal gold (10 g), yam (12 g), paeony (30 g), red peony (15 g), danpi (10 g), Bupleurum (10 g), Fructus aurantii (10 g), astragalus (30 g), plantain (30 g), and motherwort (30 g). The doctor prescribed 7 doses of the above Chinese medicine to the patient, which had to be boiled in an amount of water sufficient to make 400 mL, and the patient took 200 mL in the morning and evening.

On March 18, 2022, the patient had a D-dimer level of 0.94 mg/LFEU (0–0.55 mg/LFEU), and his prothrombin time and plasma fibrin levels had returned to normal. On March 19, 2022, the rash on the patient's skin had subsided, the burning sensation in the stomach had disappeared, and the dose of methylprednisolone was adjusted to 30 mg. On March 22, the methylprednisolone dose was adjusted to 25 mg. On March 25, the methylprednisolone dose was adjusted to 20 mg. On March 27, the erythema on the skin of the patient had subsided (see *Figure 2*), and the methylprednisolone was adjusted to methylprednisolone tablets (16 mg, QD), and reduced to 1 tablet every 7 days. The methylprednisolone tablets were discontinued on April 24.

On April 26, 2022, the patient's IL-6 level returned to normal. The patient was hospitalized in the Department of Respiratory and Critical Care medicine for the treatment of severe pneumonia, and the treatment regimen was piperacillin sodium (4 g, tid) and methylprednisolone sodium succinate (80 mg, bid). The patient's sputum culture was positive for streptococcus pneumoniae. On April 30, piperacillin sodium was adjusted to piperacillin tazobactam sodium (4.5 g, bid) combined with levofloxacin sodium chloride (0.5 g, qd). Methylprednisolone was adjusted to 60 mg, on May 4. Methylprednisolone was adjusted to 40 mg, on May 7, and the treatment was continued. On May 9, imaging and biochemical studies showed improvement, and the patient was discharged. Oral medication was prescribed, and treatment was continued. The treatment regimen of the patient was moxifloxacin tablets (0.4 g, qd), acetylcysteine effervescent tablets (1 tablet, bid), theophylline sustained-release tablets (1 tablet, bid), and prednisone (6 tablets, qd, reduced to 1 tablet every 7 days and stopped on June 20). In the course of the treatment of the diseases and the adverse reactions, the patient showed good compliance and took the medication in a timely manner.

On June 21, 2022, the imaging examination results of the patient showed that the lung infection lesions were significantly smaller than before. The patient had developed severe pneumonia and immune-related rash, so the use of sintilimab was not considered, and the albumin-paclitaxel plus cisplatin regimen was continued to treat lung cancer

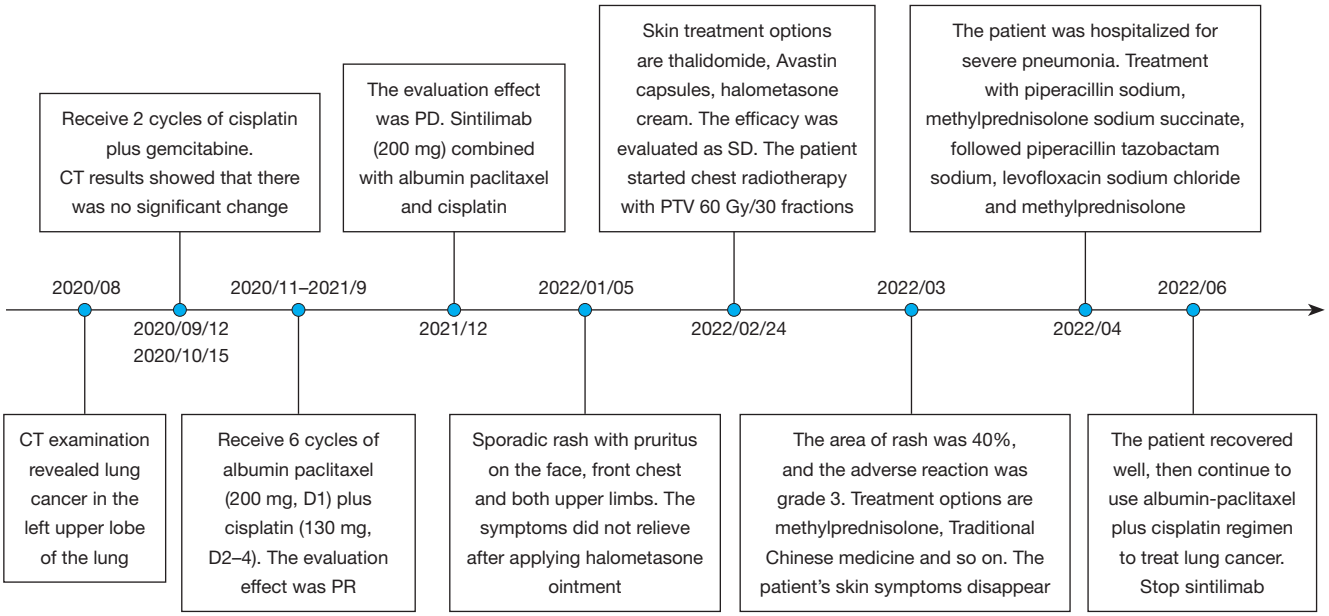

Figure 3 The timeline for diagnosis, treatment, and follow-up. CT, computed tomography; PR, partial response; PD, progressive disease; SD, stable disease; PTV, planning target volume.

(see *Figure 3*).

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 Declaration of Helsinki (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.

Review of the literature

By searching the literature, a total of 23 case reports of adverse reactions caused by sintilimab were retrieved, including 5 cases of skin-related adverse reactions (see *Table 1*). Among the 5 cases, there was 1 case of bullous dermatitis, 1 case of rare purpura like cutaneous vasculitis, and 3 cases of toxic epidermal necrolysis. After treatment, the skin symptoms of 4 of the patients were basically completely relieved; 1 patient died after treatment. Sintilimab was discontinued in all patients in the later stages of treatment.

Discussion

On February 27, 2022, the National Cancer Center released statistics on cancer incidence and mortality in China in 2016. The most common cancer in men is lung cancer, which accounts for about 24.6% of all cancers in men (7), and of which, about 85% is NSCLC. About 30% of NSCLC patients have lung squamous cell carcinoma in China. At present, traditional platinum-based chemotherapy is still the main treatment for lung squamous cell carcinoma, but the survival benefit is limited. In recent years, following research progress in the area of immunotherapy in lung cancer, advances in chemotherapy in the treatment of lung squamous cell carcinoma have been made, and clinical study of first-line treatments have shown survival benefits (8). However, while immunotherapy improves the survival of patients, it also causes immune-related adverse reactions.

ICIs include PD-1/PD-L1 inhibitors and Cytotoxic T-lymphocyte antigen 4 (CTLA-4) inhibitors. Sintilimab is an immune drug that was independently developed in China and has been shown to have efficacy in the treatment of a variety of malignant tumors (9). It binds to PD-1 receptors and blocks its interaction with PD-L1 and PD-L2, thereby restoring endogenous antitumor T cell responses (10). In related studies, PD-1 inhibitors have been shown to have significant survival benefits in the treatment of some patients with advanced driver-negative NSCLC, with few toxic and side effects and durable efficacy (11-13). Zhang *et al.* (14) showed that ICI blockade therapy has a significant

Table 1 Case analysis of literature on adverse skin reaction caused by sintilimab

Number	Sex	Age (years)	Cancer	Immunotherapy regimen	Dose	Occurrence time	Initial symptom	Treatment	Stop/start sintilimab	Outcome of adverse event
1 (2)	Male	55	Lung adenocarcinoma	Sintilimab, pemetrexed, carboplatin	200 mg, q21d	44 days after the first cycle	Dermatitis bullosa	Piperacillin tazobactam, fusidic acid cream, and cetirizine, prednisone tablets	Stop	Survived
2 (3)	Male	64	Cancer of the esophagogastric junction	Sintilimab	200 mg, q21d	5 days after the first cycle	Purpura like cutaneous vasculitis	Methylprednisolone and diphenhydramine	Stop	Death
3 (4)	Male	72	Lung cancer, hepatopulmonary metastases	Sintilimab, paclitaxel liposome, carboplatin	200 mg/kg, q21d	23 days after the first cycle	Toxic epidermal necrolysis	Methylprednisolone sodium succinate injection and prednisone acetate tablets	Stop	Survived
4 (5)	Male	65	Lymphoma	Sintilimab, gemcitabine, oxaliplatin	200 mg, q21d	11 days after the first cycle	Toxic epidermal necrosis	Oral cetirizine, methylprednisolone, immunoglobulin, piperacillin sodium/tazobactam, and parenteral nutrition	Stop	Survived
5 (6)	Female	72	Gallbladder carcinoma	Sintilimab, anlotinib	Not mentioned	2 weeks after receiving 1 dose of sintilimab	Toxic epidermal necrolysis	Methylprednisolone, immunoglobulin, albumin, encapsulation, tapering of glucocorticoid, and oral nystatin	Stop	Survived

clinical effect in the treatment of NSCLC. Currently, phase I, II, and III clinical trials are being conducted in China for a variety of solid tumors, including NSCLC and advanced liver cancer tumors (15).

ICIs not only enhance the body's normal immune response, but also lead to the occurrence of immune-related adverse reactions, often involving the skin, gastrointestinal tract, endocrine system, liver, and heart. Rash, pruritus and vitiligo are the most common symptoms and signs of ICI-related skin toxicity, which often occurs on the trunk and limbs of patients, and is accompanied by erythema, edema, maculopapular rash and other manifestations. Other more severe skin toxicity symptoms include toxic epidermal necrolysis (16), and Stevens-Johnson syndrome (17).

For skin immune-related adverse reactions, rash and pruritus usually occur in the first to second cycle of immunotherapy. In the early stage, ICI-mediated adverse reactions do not usually have typical symptoms, and thus are difficult to identify and easy to ignore. The median time to onset of skin toxicity is 4 weeks, but the time to onset may range from 2 weeks to 150 weeks. In this case, the patient developed systemic rash with pruritus after 1 month of immunotherapy with sintilimab, which showed progressive aggravation, and the adverse reaction was grade III. This patient had no previous underlying skin-related conditions, and the lung cancer itself would not have caused a severe rash. No adverse skin reactions had been observed when the patient was previously treated with cisplatin, gemcitabine, and albumin paclitaxel. Following a consultation, a dermatologist recommended a skin biopsy, but the patient declined. At the same time, the multiple rashes on the whole body subsided completely after treatment with hormones, TCM, and other drugs. Based on the analysis of the above factors, the doctor determined that the rash in this patient was directly related to the use of sintilimab.

Under the "Management of toxicities from immunotherapy: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up," published by the European Society of Clinical Oncology (EMSO), the treatment methods for immune-related adverse skin reactions mainly include symptomatic treatment, and the local or systemic application of glucocorticoids; the use and dosage of hormones are adjusted according to the severity of the disease. Changes to medication are not required in cases of primary adverse skin reactions; only local symptomatic treatment is required. Grade 2 adverse skin reactions can be observed while using medication, and if there is no remission, the drug should be suspended. If a patient has an

adverse skin reaction > grade 3, the medication should be stopped immediately, and systemic corticosteroids should be used until the reaction drops to a grade 1. Grade 4 adverse skin reactions are rare, but if they occur, the drug should be stopped immediately, and the patient hospitalized as soon as possible for dermatological assistance. Our patient was treated with avastine capsules, halometasone cream, methylprednisolone, prednisone tablets, and other drugs, and at the same time, the TCM prescription was used as an auxiliary treatment. The patient was treated in accordance with the guidelines.

In this case, the TCM prescription mainly composed Xiaofeng powder, and the addition and subtraction of TCM was carried out based on the prescription. After treatment with TCM, the patient's skin symptoms were relieved. There are as many as 31 books about Xiaofeng powder, and there are 39 versions of different prescriptions. *Prescriptions of the Bureau of Taiping People's Welfare Pharmacy* and *WaiKeZhengZong* record that the most widely used prescription is Xiaofeng powder. In the *WaiKeZhengZong*, Xiaofeng powder is most widely used in dermatology. Xiaofeng powder has a good effect in the treatment of urticaria, eczema, pityriasis rosea, facial hormone-dependent dermatitis, seborrheic dermatitis, acne, neurodermatitis, herpes zoster, and other diseases in dermatology. Li *et al.* used Xiaofeng powder to treat acneiform rash caused by cetuximab and it achieved a good curative effect (18).

It should be noted that in this case, the patient did not immediately inform the doctor when the rash first appeared. The doctors did not pay special attention to skin immune-related adverse reactions during the first treatment, did not invite the Departments of Pharmacy and Oncology to carry out a multidisciplinary consultation and did not treat the reaction in time in accordance with the standards.

Conclusions

The early diagnosis and appropriate management of immune-related adverse events (irAEs), including active prevention, baseline evaluation, early detection, timely treatment, and dynamic monitoring, are crucial and require attention. The early identification and correct treatment of irAEs play an important role in maximizing the anti-tumor effect of immune therapy and improving patient outcomes.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-5925/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-22-5925/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 Declaration of Helsinki (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.

References

1. Ruggiero R, Fraenza F, Scavone C, et al. Immune Checkpoint Inhibitors and Immune-Related Adverse Drug Reactions: Data From Italian Pharmacovigilance Database. Front Pharmacol 2020;11:830.
2. Yan QX, Fang C, Pan Y, et al. A case of dermatitis

bullosa caused by sintilimab in treating advanced lung adenocarcinoma. Chin J New Drugs Clin Rem 2022;41:253-6.
3. Wu YP, Zhang LN, Yi YS. A case report: rare purpuric skin vasculitis induced by sintilimab. Chin J Hosp Pharm 2022;42:1290-2.
4. Shan B, Lu YL, Hou J, et al. One case of toxic epidermal necrolysis caused by tumor immune checkpoint inhibition sintilimab. Herald of Medicine 2022;41:263-5.
5. Yang W, Xu X, Xia D, et al. Toxic epidermal necrolysis associated with chemoimmunotherapy for lymphoma: case report and literature review. Immunotherapy 2022;14:275-82.
6. Zhao Y, Cao Y, Wang X, et al. Treatment of PD-1 Inhibitor-Associated Toxic Epidermal Necrolysis: A Case Report and Brief Review. Onco Targets Ther 2022;15:345-51.
7. Zheng RS, Zhang SW, Zeng HM, et al. Cancer incidence and mortality in China, 2016. Journal of the National Cancer Center 2022;2:1-9.
8. Griesinger F, Pérol M, Girard N, et al. Impact of immune checkpoint inhibitors on the management of locally advanced or metastatic non-small cell lung cancer in real-life practice in patients initiating treatment between 2015 and 2018 in France and Germany. Lung Cancer 2022;172:65-74.
9. Jia R, Li Y, Xu N, et al. Sintilimab in Patients with Previously Treated Metastatic Neuroendocrine Neoplasms. Oncologist 2022;27:e625-32.
10. Zhang B, Qi L, Wang X, et al. Phase 2 study of camrelizumab (anti-PD-1 antibody) combined with apatinib and chemotherapy for the first-line treatment of advanced esophageal squamous cell carcinoma. J Clin Oncol 2019;37:abstr 4033.
11. Gao P, Chen H, Zeng T, et al. A pathological complete response to neoadjuvant chemotherapy and immunotherapy in a non-small cell lung cancer patient. Transl Lung Cancer Res 2020;9:2157-60.
12. Yang ZR, Liu MN, Yu JH, et al. Treatment of stage III non-small cell lung cancer in the era of immunotherapy: pathological complete response to neoadjuvant pembrolizumab and chemotherapy. Transl Lung Cancer Res 2020;9:2059-73.
13. Jiang L, Huang J, Li C, et al. Immuno-based therapeutic strategies for initial unresectable locally advanced non-small cell lung cancer: a case report. Transl Lung Cancer Res 2020;9:803-6.
14. Zhang Y, Song L, Zeng L, et al. Sintilimab plus docetaxel as second-line therapy of advanced non-small cell lung cancer without targetable mutations: a phase II efficacy and biomarker study. BMC Cancer 2022;22:952.
15. Zhang W, Gong C, Peng X, et al. Serum Concentration of CD137 and Tumor Infiltration by M1 Macrophages Predict the Response to Sintilimab plus Bevacizumab Biosimilar in Advanced Hepatocellular Carcinoma Patients. Clin Cancer Res 2022;28:3499-508.
16. Weber JS, Dummer R, de Pril V, et al. Patterns of onset and resolution of immune-related adverse events of special interest with ipilimumab: detailed safety analysis from a phase 3 trial in patients with advanced melanoma. Cancer 2013;119:1675-82.
17. Nie FF, Fu J. Adverse reactions of tumor immune checkpoint inhibitors and their treatment: skin. Chinese Journal of Radiation Oncology 2018;27:331-4.
18. Li HD, Hu LJ. One case of acneiform rash caused by cetuximab was treated by Hu Lingjing with Xiaofeng powder. Forum on Traditional Chinese Medicine 2021;36:62-3.

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