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LETTER TO THE EDITOR

Medical dilemma: Programmed death 1 blockade (sintilimab) therapy in patients suffering from tumours combined with psoriasis

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Abstract

Tumour immunotherapy represented by immune checkpoint inhibitors (ICIs) has greatly improved the overall prognosis of patients with malignant tumours, and is regarded as an important breakthrough in the field of medicine in recent years. ICIs have gradually become the core of tumour therapy and are increasingly used in the clinic. In order to achieve early clinical prediction and management of immune-related adverse events (irAEs), it is still necessary to perform further research on the mechanisms, risk factors, and predictors of irAE occurrence in the future. Zhou *et al* describe the consultation of a patient with advanced gastric cancer combined with chronic plaque psoriasis. This case provides an important reference for the use of programmed cell death protein-1 (PD-1) inhibitors in patients of tumours combined with chronic plaque psoriasis. This case also highlights that screening of high-risk groups for irAEs is critical before applying PD-1 inhibitors to patients with chronic psoriasis combined with tumours. PD-1 inhibitors are new and potent antineoplastic agents that can cause serious immune-related adverse events such as toxic epidermal necrolysis release and psoriasis. Glucocorticosteroids are the first-line agents for irAEs. The incidence of rheumatic irAEs may be higher in reality, which will inevitably become a new challenge for rheumatologists and dermatologists.

Key Words: Immune checkpoint inhibitors; Tumor immunotherapy; Immune-related adverse events; Cytokine release syndrome; Psoriasis

Core Tip: The major strategies for dealing with immune-related adverse events should include scientific awareness, early diagnosis and graded management. The important direction of tumour immunotherapy research is how to reduce the adverse effects of immunotherapy and can improve the quality of patient survival. The correlation between programmed cell death protein-1 inhibitors and chronic psoriasis is gradually receiving more and more attention, and how to screen high-risk populations in the future, as well as to give the necessary and effective preventive therapeutic measures still need to be further explored.

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TO THE EDITOR

Tumor immunotherapy, using immune checkpoint inhibitors (ICIs), has greatly improved the prognosis of patients with malignant tumors. ICIs are regarded as essential breakthroughs in recent years[1]. With the outstanding therapeutic effects of immunotherapy in clinical practice and the gradual expansion of its applications, a series of immune-related adverse events (irAEs) have become increasingly common[2]. Currently, ICIs mainly target cytotoxic T lymphocyte-associated antigen 4 (CTLA-4), programmed cell death protein-1 (PD-1), and programmed cell death ligand-1 (PD-L1). The latest data from the United States show that almost half of the patients with malignant tumors meet the indications for ICIs therapy[3]. Therefore, ICIs have gradually become the core of tumor therapy and are increasingly used in clinical settings. To achieve early clinical prediction and management of irAEs, further research on their mechanisms, risk factors, and predictors is necessary.

PD-1 INHIBITORS IN TUMOR-PSORIASIS

Zhou *et al*[4] described the consultation of a patient with advanced gastric cancer and chronic plaque psoriasis. The patient developed a severe rash with cytokine release syndrome (CRS) after sintilimab treatment. In the present case, the patient presented with a recurrent rash as the first manifestation, followed by acute hyperthermia, hypoxia, and progressive exacerbation of skin lesions, which were life-threatening and resulted in CRS. The patient was treated effectively with glucocorticoids, tolizumab, and acitretin. The glucocorticoid dose was gradually reduced, and the rash did not recur. This case provides an essential reference for using PD-1 inhibitors in patients with tumors and chronic plaque psoriasis. This case also highlights the importance of screening high-risk groups for irAEs among patients with chronic psoriasis.

IrAEs are similar to the pathogenesis of rheumatic immune diseases and can mimic most rheumatic immune diseases, such as arthritis, rheumatic polymyalgia, myositis, and psoriasis. Previous clinical trials have shown that 54%–76% of patients have different degrees of irAEs. Therefore, ICI-related irAEs have gradually become a topical and challenging issue in tumor immunotherapy[3]. The risk factors for irAEs include gender, body mass index, tumor type, drug type, and history of autoimmune disease. Predictive factors include immune cells, cytokines, chemokines, autoantibodies, the genome, and intestinal flora. For example, sex hormones lead to sex differences in immune responses, and women are more likely to develop autoimmune diseases. Bui *et al*[5] conducted a retrospective analysis of 235 patients with melanoma and found that women were more prone to skin irAEs. Cortellini *et al*[6] found a significant correlation between a high BMI and the occurrence of irAEs. Patients who are overweight (25 kg/m^2 ≤ BMI ≤ 29.9 kg/m^2) are more likely to develop irAE related to the skin, endocrine system, gastrointestinal tract, and liver. A meta-analysis of 5560 patients in clinical trials showed that 18.4% of patients treated with ICIs developed rheumatic irAEs[7]. Almost all clinical trials excluded patients with comorbid rheumatological diseases (*e.g.*, rheumatoid arthritis, spondyloarthritis, and vasculitis). Therefore, the incidence of rheumatic irAEs may be high, which will inevitably become a new challenge for rheumatologists and dermatologists.

PD-1 inhibitors can cause serious irAEs, such as toxic epidermal necrolysis and psoriasis[8]. The pathogenesis of psoriasis induced by PD-1 inhibitors has not yet been clearly defined. The presence of a genetic susceptibility gene for psoriasis may also be a contributing factor. Morelli *et al*[9] investigated the immunological and genetic profiles of two patients with metastatic melanoma and one patient with lung cancer who developed severe psoriasis after receiving PD-1 inhibitor therapy. NGS analysis revealed that all patients carried several allelic variants in psoriasis susceptibility genes,

such as HLA-C, ERAP1, and other genes of the significant psoriasis susceptibility PSORS1 locus. Previously, there were relatively few case reports on PD-1 inhibitors inducing psoriasis activity. Sui *et al*[10] reported a case of a 56-year-old man with a 25-year history of psoriasis who was first injected with sintilimab (200 mg) for lung adenocarcinoma. Two weeks later, the patient's skin showed generalized red and swollen plaques accompanied with severe itching without obvious cause. A dermatological examination revealed many plaques, scales, scratches, crusts, and pigmentation on the scalp, trunk, and limbs. The patient presented with an acute exacerbation of the typical cutaneous features of plaque psoriasis. The mechanism of PD-1 inhibitors in psoriasis exacerbation may be related to the down-regulation of PD-1 on the surface of the T-cells, which indirectly activates the downstream cytokines, such as interleukin (IL)-1, IL-17, and IL-22[11]. However, for patients who develop severe manifestations of psoriasis, the continuation of PD-1 inhibitors remains a controversial issue, and the future treatment of these patients is highly challenging. The Sui *et al*[10] recommends that the patient should discontinue sintilimab.

The main therapeutic approaches in the treatment of gastric cancer are based on surgery and chemotherapy. Thus, ICIs provide new therapeutic options for patients with gastric cancer[12]. Immune-related skin reactions are the most common side effects of ICI treatment, with an incidence rate of > 50%. Skin lesions are usually mild and do not affect the continuation of immunotherapy. The clinical manifestations vary greatly, and nonspecific macular papules are common[13]. Early diagnosis and timely intervention for irAEs are essential to improve the quality of life of patients with malignant tumors. Glucocorticosteroids are the first-line agents for irAEs, with the dose set according to the criteria for evaluating common adverse event grades and clinical severity. Individualized tapering is performed according to the patient's therapeutic response to glucocorticoids, and some patients may require tumor necrosis factor inhibitors and other monoclonal antibodies to prevent opportunistic infections and reduce the side effects of glucocorticoids.

CONCLUSION

In conclusion, the major strategies for managing irAEs should include scientific awareness, early diagnosis, and graded management. An important direction in tumor immunotherapy research is to reduce the adverse effects of immunotherapy and improve the quality of patient survival. The correlation between PD-1 inhibitors and chronic psoriasis is receiving increasing attention, and further research is required to identify high-risk populations.

FOOTNOTES

Author contributions: Jin D and Wang YW prepared the manuscript and contributed equally to this article, ensuring a cohesive presentation of the research findings; Jin D and Lin ZM were responsible for the meticulous analysis and interpretation of the case, providing essential insights that underpinned the study's conclusions; Li C and Li M were at the helm of conceptualizing and designing the research ideas, setting the stage for the study with their innovative and well-defined framework; All authors have read and approved the final manuscript, with Jin D and Wang YW recognized as co-first authors for their significant contributions to the manuscript preparation, and the collaborative efforts of the team were instrumental in bringing the research to fruition.

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REFERENCES

1 **Robert C**. A decade of immune-checkpoint inhibitors in cancer therapy. *Nat Commun* 2020; **11**: 3801 [PMID: 32732879 DOI: 10.1038/s41467-020-17670-y]
2 **Fan Y**, Geng Y, Shen L, Zhang Z. Advances on immune-related adverse events associated with immune checkpoint inhibitors. *Front Med* 2021; **15**: 33-42 [PMID: 32779094 DOI: 10.1007/s11684-019-0735-3]
3 **Johnson DB**, Nebhan CA, Moslehi JJ, Balko JM. Immune-checkpoint inhibitors: long-term implications of toxicity. *Nat Rev Clin Oncol* 2022;

19: 254-267 [PMID: 35082367 DOI: 10.1038/s41571-022-00600-w]

4 **Zhou MH**, Ye MF, Zhang ZX, Tao F, Zhang Y. Cytokine release syndrome triggered by programmed death 1 blockade (sintilimab) therapy in a psoriasis patient: A case report. *World J Clin Cases* 2024; **12**: 3555-3560 [PMID: 38983424 DOI: 10.12998/wjcc.v12.i18.3555]

5 **Bui AN**, Bougrine A, Buchbinder EI, Giobbie-Hurder A, LeBoeuf NR. Female sex is associated with higher rates of dermatologic adverse events among patients with melanoma receiving immune checkpoint inhibitor therapy: A retrospective cohort study. *J Am Acad Dermatol* 2022; **87**: 403-406 [PMID: 34252467 DOI: 10.1016/j.jaad.2021.06.885]

6 **Cortellini A**, Bersanelli M, Buti S, Cannita K, Santini D, Perrone F, Giusti R, Tiseo M, Michiara M, Di Marino P, Tinari N, De Tursi M, Zoratto F, Veltri E, Marconcini R, Malorgio F, Russano M, Anesi C, Zeppola T, Filetti M, Marchetti P, Botticelli A, Antonini Cappellini GC, De Galitiis F, Vitale MG, Rastelli F, Pergolesi F, Berardi R, Rinaldi S, Tudini M, Silva RR, Pireddu A, Atzori F, Chiari R, Ricciuti B, De Giglio A, Iacono D, Gelibter A, Occhipinti MA, Parisi A, Porzio G, Fargnoli MC, Ascierto PA, Ficorella C, Natoli C. A multicenter study of body mass index in cancer patients treated with anti-PD-1/PD-L1 immune checkpoint inhibitors: when overweight becomes favorable. *J Immunother Cancer* 2019; **7**: 57 [PMID: 30813970 DOI: 10.1186/s40425-019-0527-y]

7 **Zhang S**, Zhou Z, Wang L, Li M, Zhang F, Zeng X. Rheumatic immune-related adverse events associated with immune checkpoint inhibitors compared with placebo in oncologic patients: a systemic review and meta-analysis. *Ther Adv Chronic Dis* 2021; **12**: 2040622320976996 [PMID: 33633822 DOI: 10.1177/2040622320976996]

8 **Di Altobrando A**, Bruni F, Alessandrini A, Starace M, Misciali C, Piraccini BM. Severe de-novo palmoplantar and nail psoriasis complicating Nivolumab treatment for metastatic melanoma. *Dermatol Ther* 2020; **33**: e13363 [PMID: 32239596 DOI: 10.1111/dth.13363]

9 **Morelli M**, Carbone ML, Scaglione GL, Scarponi C, Di Francesco V, Pallotta S, De Galitiis F, Rahimi S, Madonna S, Failla CM, Albanesi C. Identification of immunological patterns characterizing immune-related psoriasis reactions in oncological patients in therapy with anti-PD-1 checkpoint inhibitors. *Front Immunol* 2024; **15**: 1346687 [PMID: 38495872 DOI: 10.3389/fimmu.2024.1346687]

10 **Sui CL**, Lin XF, He L, Zhu W. Dermoscopic features of acutely exacerbated plaque psoriasis induced by anti-programmed death-1 for lung cancer. *Chin Med J (Engl)* 2020; **133**: 2123-2125 [PMID: 32769492 DOI: 10.1097/CM9.0000000000000958]

11 **Bartosińska J**, Zakrzewska E, Purkot J, Michalak-Stoma A, Kowal M, Krasowska D, Chodorowska G, Giannopoulos K. Decreased blood CD4+PD-1+ and CD8+PD-1+ T cells in psoriatic patients with and without arthritis. *Postepy Dermatol Alergol* 2018; **35**: 344-350 [PMID: 30206445 DOI: 10.5114/ada.2018.75609]

12 **Sun J**, Zheng Y, Mamun M, Li X, Chen X, Gao Y. Research progress of PD-1/PD-L1 immunotherapy in gastrointestinal tumors. *Biomed Pharmacother* 2020; **129**: 110504 [PMID: 32768978 DOI: 10.1016/j.biopha.2020.110504]

13 **Haanen J**, Obeid M, Spain L, Carbonnel F, Wang Y, Robert C, Lyon AR, Wick W, Kostine M, Peters S, Jordan K, Larkin J; ESMO Guidelines Committee. Management of toxicities from immunotherapy: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up. *Ann Oncol* 2022; **33**: 1217-1238 [PMID: 36270461 DOI: 10.1016/j.annonc.2022.10.001]

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