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LETTER TO THE EDITOR

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A case of malignant melanoma with shrinking metastases after sequential severe irAEs

Dear Editor,

While immune checkpoint inhibitors (ICIs) have changed the treatment paradigm for advanced malignant melanoma,[1,2] they have the potential to cause various immune-related side effects, including—but not limited to—enteritis, interstitial pneumonia, and liver dysfunction. A 58-year-old man with acral lentiginous melanoma on the right sole was diagnosed with pT4bN3M0 Stage IIIC. At seven months after tumor resection and inguinal lymph node dissection, multiple liver metastases were detected, and a subcutaneous nodule was identified in the right femoral and groin region. No *BRAF* gene mutation was detected. Although he was treated with seven doses of nivolumab, the metastatic liver lesions showed progression (Figure 1A). Although he was administered with relatlimab as a clinical trial, subsequently requested to switch to ipilimumab due to his own financial issues, a week after the 1st administration of ipilimumab, he noticed general fatigue and watery diarrhea with blood clot. The diarrhea had not improved, even after the initiation of treatment with prednisolone (30 mg/d) based on the diagnosis as colitis (grade I). Subsequently, a month later, acute pancreatitis developed with a sudden decrease in blood pressure and increase in pancreatic amylase and lipase levels (917 and 1283 IU/L, respectively). Because the colitis was exacerbated to grade IV, even under treatment with high-dose methylprednisolone (Figure 1B), we introduced infliximab (1.5 mg/kg). The colitis ceased and his general condition improved after three additional doses of infliximab (Figure 1C). Although severe colitis was successfully cured, the subsequent development of grade IV pancreatitis necessitated ICU management and continuous systemic steroid treatment. At the same time, there was a noticeable reduction in the size of the metastatic lesion in S6 of the liver (Figure 1D), which continued to shrink for 6 months without further use of any antitumor agents.

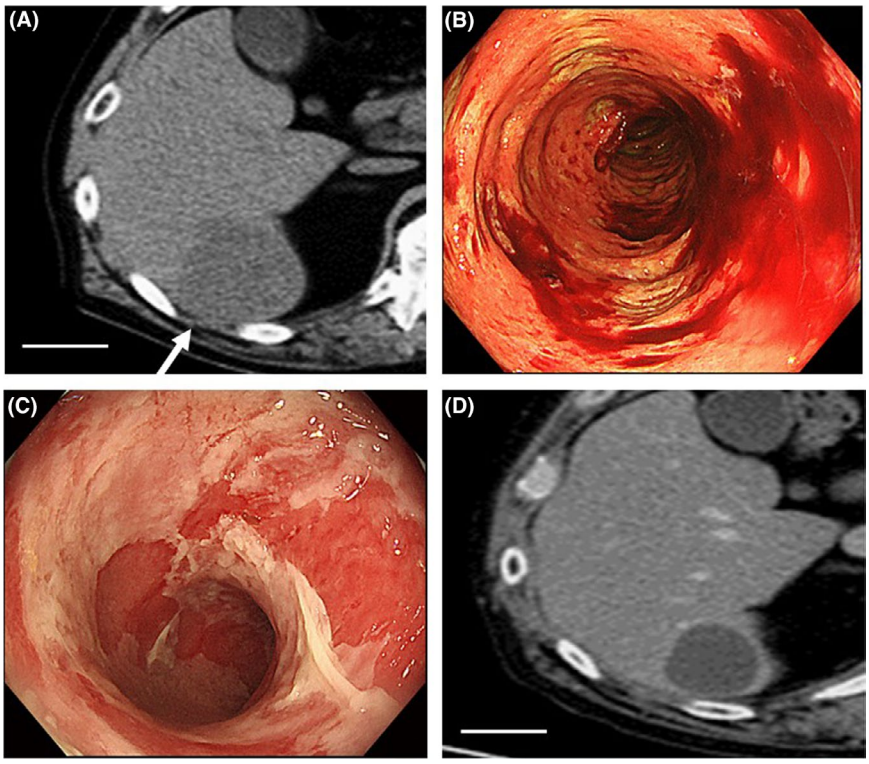

FIGURE 1 A, Computed tomography detected a growing metastatic lesion in S6 of the liver (arrow). Scale bar indicates 5 cm. B, Endoscopic observation showed multiple mucosal ulcers and bleeding. C, White re-epithelization was noticed after the administration of three doses of infliximab. D, The lesion shown in A shrank was well defined. Scale bar indicates 5 cm

Stephanie et al reported that all melanoma patients with complete responses developed severe irAEs, indicating a correlation between the antitumor effects of ICIs and complications associated with the administration of ICIs.[3] They noted that the use of high-dose steroids against severe irAE was not associated with tumor enlargement and that it did not affect the prognosis. Reportedly, the use of systemic corticosteroids or immunosuppressive agents did not influence either overall survival or the duration of antitumor treatment.[1] The median duration of response extended to 34 months in patients with grade 3-4 irAEs, but only 11 months in patients with grade 1-2 irAEs.[4] Cumulative analysis of Japanese melanoma patients demonstrated that nivolumab followed by ipilimumab treatment induced high frequency of irAE including colitis.[5] Immune-related severe colitis requires the exclusion of colorectal infection and the immediate induction of high-dose steroid therapy. If it is not effective within 1 week, physicians should not hesitate in using infliximab.[6] In the present case, three doses of infliximab were indispensable for treating colitis, while the subsequent administration of continuous systemic steroids was required to treat sequential acute pancreatitis. The present case is valuable, as it indicates that the occurrence of severe irAEs is a pivotal sign of augmentation of the antitumor effect in patients with malignant melanoma.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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