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Immune checkpoint inhibitors for patients with pre-existing autoimmune diseases

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Maeda O, Yokota K, Atsuta N, Katsuno M, Akiyama M, Ando Y. Nivolumab for the treatment of malignant melanoma in a patient with pre-existing myasthenia gravis. *Nagoya J Med Sci.* 2016;78(1):119–122.

A 79-year-old man with lymph node recurrence of malignant melanoma received nivolumab, an antiprogrammed death 1 (PD-1) monoclonal antibody. He had pre-existing ocular myasthenia gravis (MG) and a continued small amount of corticosteroid. Grade 3 creatine phosphokinase elevation appeared after two doses of nivolumab, and the treatment was postponed until it improved to grade 1. After three doses of nivolumab, he experienced diplopia and facial muscle weakness which were consistent with an acute exacerbation of MG, and the symptoms relieved without additional treatment for MG. He achieved shrinkage of metastasis after ten doses of nivolumab. Although a case who died due to MG after administration of nivolumab was reported recently, pre-existing MG is considered not to be always a contraindication of nivolumab.

Keywords: malignant melanoma, nivolumab, anti-programmed death 1 (PD-1) monoclonal antibody, myasthenia gravis, creatine phosphokinase

In an earlier case report, we described the use of the immune checkpoint inhibitor nivolumab to treat a patient with malignant melanoma who was comorbid with myasthenia gravis.[1] During this course of treatment, the patient's myasthenia gravis symptoms worsened, improving only with the temporary withdrawal of nivolumab. Nevertheless, the malignant melanoma decreased in size.

Patients with pre-existing autoimmune diseases are usually excluded from the clinical trials of immune checkpoint inhibitors based on the study's exclusion criterion.[2] However, in clinical practice, the administration of immune checkpoint inhibitors in such patients is still controversial. The mentioned case report has been cited in other publications, a few of which discussed cases of myasthenia gravis induced by immune checkpoint inhibitors,[3,4] while the others elaborated on the

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pros and cons of administering immune checkpoint inhibitors to cancer patients with autoimmune diseases.[5] In clinical cases of cancer, treatment decisions take risk–benefit ratio into account. However, for certain cancers, other therapies were frequently used when these were available as alternative options to immune checkpoint inhibitors. Moreover, immune checkpoint inhibitors are often administered with caution in diseases like malignant melanoma for which few therapeutic options are available. The indications for immune checkpoint inhibitors are broadening for many types of cancer. As a result, weighing the choice to use immune checkpoint inhibitors in patients with pre-existing autoimmune diseases is likely to become more challenging for clinicians.

We extend our congratulations to the *Nagoya Journal of Medical Science* on its 100th anniversary and hope that the journal will continue to grow and develop by publishing interesting and significant findings.

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