Organizing Pneumonia Induced by Nivolumab in a Patient with Metastatic Melanoma

Kazuhisa Nakashima, MD,a Tateaki Naito, MD,a,* Shota Omori, MD,a Shusuke Yoshikawa, MD,b Masahiro Endo, MD,c Yoshio Kiyohara, MD,b Toshiaki Takahashi, MDa

Division of Thoracic Oncology, Shizuoka Cancer Center, Shizuoka, Japan
Department of Dermatology, Shizuoka Cancer Center, Shizuoka, Japan
Division of Diagnostic Radiology, Shizuoka Cancer Center, Shizuoka, Japan

Received 30 September 2015; accepted 1 October 2015

A 70-year-old woman with a 7-month history of recurrent postoperative malignant melanoma with pulmonary metastases (Fig. 1A) presented with fever, anorexia, exertional dyspnea, and productive cough. The patient had never smoked and had no underlying pulmonary disease. Eleven weeks before presentation, she enrolled in a clinical trial of nivolumab, an anti–programmed death 1 monoclonal antibody, during which she received four doses of nivolumab (2 mg/kg every 3 weeks). Computed tomography of the chest revealed multiple ground-glass opacities surrounded by consolidations of air bronchograms in the lower lung fields (reversed halo sign, Fig. 1B). Each lesion had a shrunken tumor at its center. The bronchoalveolar lavage fluid was sterile and contained 770 white cells/mm³ (43.5% lymphocytes, 38.5% macrophages, 13.0% neutrophils, and no eosinophils). A transbronchial biopsy sample contained fibroblast plugs within the alveolar spaces (Fig. 2). Nivolumab-induced organizing pneumonia was diagnosed. The patient’s symptoms and radiographic abnormalities resolved rapidly (Fig. 1C) after nivolumab had been discontinued and oral prednisolone initiated at a daily dose of 0.5 mg/kg; the prednisolone was gradually tapered over a 2-month period.

Recently, accumulating evidence has shown that antibodies against immune checkpoint inhibitors are effective in the treatment of advanced cancers. In a phase III study of treatment of metastatic melanoma, nivolumab was associated with significant improvement in overall survival compared with that obtained from chemotherapy, and it is now used as a standard treatment for melanoma. Two phase III studies have reported several immune-related adverse events, including pneumonitis in 1.5% to 5% of patients. Little is known regarding the clinicopathologic features of nivolumab-induced pneumonitis. Nishino et al. reported three cases of nivolumab-induced pneumonitis in patients with melanoma. The onset of pneumonitis in these cases occurred 7.4 to 24.3 months after initiation of therapy. Two cases were radiographically classified as acute interstitial pneumonia/acute respiratory distress syndrome, and one case was classified as nonspecific interstitial pneumonia. Bronchoalveolar lavage or transbronchial biopsy was not performed in those patients. In our case, computed tomography of the chest showed the typical reversed halo sign, a finding that differed from those reported by Nishino et al. Organizing pneumonia was diagnosed in our patient both radiographically and pathologically. Like patients with cryptogenic organizing pneumonia, our patient had a favorable response to corticosteroid therapy.

The increasing use of immune checkpoint inhibitors will necessitate the establishment of a standard algorithm

*Corresponding author.

Disclosure: The authors declare no conflict of interest.

Address for correspondence: Tateaki Naito, MD, Division of Thoracic Oncology, Shizuoka Cancer Center 1007, Shimonagakubo, Nagatzumicho, Sunto-gun, Shizuoka, 411-8777, Japan. E-mail: t.naito@scchr.jp

© 2015 International Association for the Study of Lung Cancer. Published by Elsevier Inc. All rights reserved.

ISSN: 1556-0864
http://dx.doi.org/10.1016/j.jtho.2015.10.004
for early detection and intervention against common immune-related adverse events. Further compilation of cases with detailed clinical information will expand our knowledge and improve recognition of and therapy for such adverse events.

References

Figure 1. Computed tomography of the chest revealed multiple pulmonary nodules before nivolumab therapy (A) and multiple ground-glass opacities surrounded by consolidations of air bronchograms in the lower lung fields at the onset of pneumonitis (B). The radiographic abnormalities resolved rapidly after nivolumab had been discontinued and oral prednisolone initiated (C).

Figure 2. Hematoxylin and eosin staining demonstrates fibroblast plugs within the alveolar spaces (magnification ×20).