Nivolumab-related Sclerosing Cholangitis in Gastric Cancer

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In this issue of Internal Medicine, Kono et al. reported a case of gastric cancer presenting with sclerosing cholangitis during nab-paclitaxel plus ramucirumab following treatment with nivolumab, an immune checkpoint inhibitor (1). This is the first case report on nivolumab-related sclerosing cholangitis in gastric cancer. Interestingly, a clinical anti-tumor effect of nab-paclitaxel plus ramucirumab regimen was recognized in addition to the adverse event of sclerosing cholangitis after nivolumab, whereas the same regimen showed no antitumor effect nor adverse events when administered before nivolumab.

As the authors described, ischemia due to ramucirumab (with anti-angiogenic action) and the effects of cytotoxic agents such as nab-paclitaxel are also involved in the occurrence of sclerosing cholangitis. Tumor antigens are released from tumors that have been destroyed by cytotoxic agents and then exposed to immune systems activated by nivolumab. Recently, the efficacy and safety of the combination of immune checkpoint inhibitors and radiation has been discussed (2).

Kawashima et al. (3) reported three cases of nivolumab-related cholangitis associated with diffuse hypertrophy of the extrahepatic bile duct wall in non-small cell lung cancer. Gelsomino et al. (4) also described four cases of nivolumab-related cholangitis in non-small cell lung cancer. However, these reported cases in non-small cell lung cancer were not described as sclerosing cholangitis, although bile duct wall lesions may have been induced by immunological mechanisms.

There seem to be two issues in the present case. First, what are the characteristics of nivolumab-related sclerosing cholangitis? The imaging findings of the present case appear to be more representative of immune-related sclerosing cholangitis than of cases with small-cell lung cancer where the main lesion is located at the extrahepatic bile duct. Second, is the sequential use of ramucirumab plus nab-paclitaxel and nivolumab implicated in the development of sclerosing cholangitis? More clinical studies are warranted to answer this question.

If sclerosing cholangitis becomes recognized as a rare immune-related adverse event, we should be more careful when dealing with hepatic dysfunction after the administration of nivolumab.

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References