JGH Journal of Gastroenterology and Hepatology
JGHF
doi:10.1111/jgh.14136

EDUCATION AND IMAGING

Hepatobiliary and Pancreatic: Nivolumab-related cholangiopathy

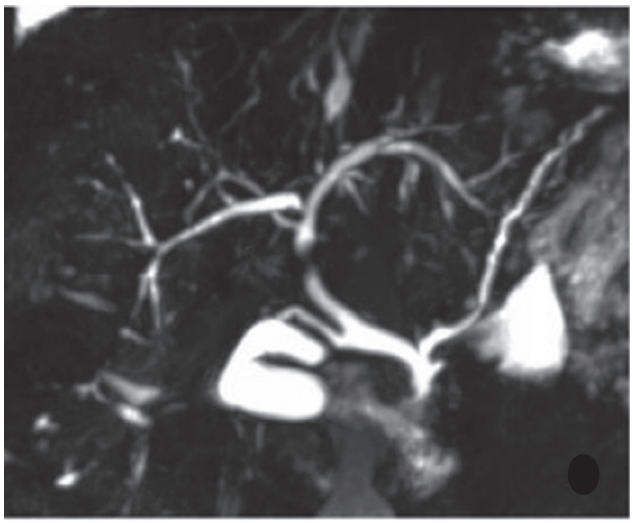

Figure 1 MRCP showing an abnormal visibility of intrahepatic small bile ducts with irregular walls and stenosis.

A 71-year-old Caucasian man developed a new-onset cholestasis of unknown origin. His medical history includes non-small-cell lung cancer with cerebral metastasis treated by surgery 24 months ago, cisplatin–pemetrexed-based chemotherapy during 10 months, stopped 11 months ago, and nivolumab immunotherapy (started 12 weeks ago and still effective). Blood analysis showed dominant cholestasis with high alkaline phosphatase level (558 U/L, normal $<$ 130 U/L) and gamma-glutamyl transpeptidase levels (984 U/L, normal $<$ 60 U/L) together with a low increase in liver transaminases (aspartate aminotransferase level 129 U/L, normal $<$ 40 U/L and alanine aminotransferase level 135 U/L, $<$ normal 45 U/L). International normalized ratio and bilirubin levels were normal. Serological tests for viral hepatitis and autoimmune hepatitis or cholangitis were negative. Abdominal computed tomography with contrast was normal. Magnetic resonance cholangiopancreatography (MRCP) demonstrated an abnormal visibility of intrahepatic small bile ducts with irregular walls and stenosis (Fig. 1).

A transjugular liver biopsy and hepatovenous pressure gradient were performed, showing a normal pressure gradient. Histological findings revealed severe portal inflammation, mainly composed of $CD8^+$ T lymphocytes infiltration, and cholangitis (Fig. 2). Nivolumab was stopped and was followed by a slow decrease of liver enzymes. Unfortunately, an increase in cerebral metastasis size was then observed 5 weeks after the cessation of nivolumab, justifying the introduction of oral methylprednisolone (0.5 mg/kg). Ursodeoxycholic acid (10 mg/kg) was finally started 8 weeks after the cessation of nivolumab and was followed by a complete normalization of liver enzymes 12 weeks after the end of nivolumab.

Nivolumab, used for the treatment of several solid tumors including melanoma and non-small-cell lung cancer, is an anti-programmed cell death-1 monoclonal antibody leading to the recovery of immune competence against tumor cells. Five cases of biliary tests abnormalities due to nivolumab have been described recently. We present the first case of nivolumab-related cholangitis with magnetic resonance imaging features of intrahepatic cholangitis. Time to resolution of liver enzymes can be long, and response to steroid administration is disappointing, which is due to the long half-life ($t_{1/2}$) of nivolumab (17–25days). Whilst ursodeoxycholic acid was used with apparent normalization of the liver enzymes, its true effectiveness remains unknown in this condition. Further studies will be important to establish the optimal management of patients developing cholangitis when taking nivolumab.

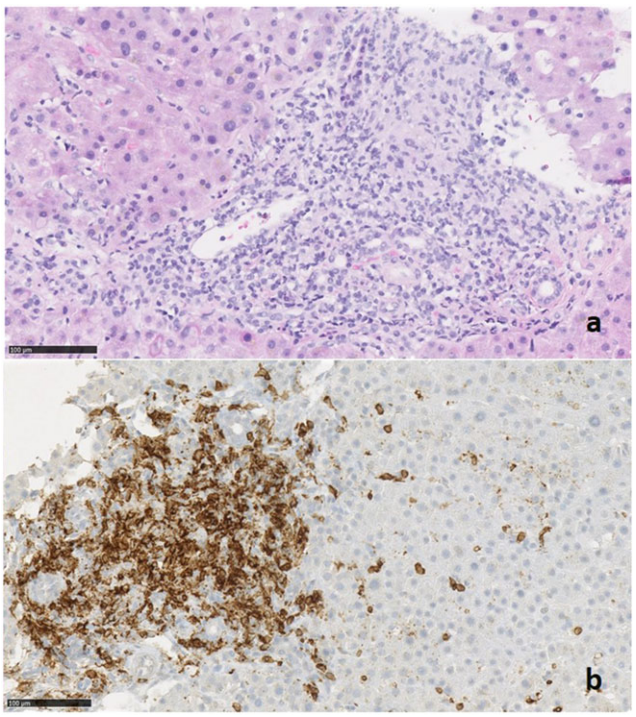

Figure 2 (a) Hematoxylin and eosin staining showing portal inflammation with biliary damages. Lymphocytic portal infiltration is $CD8^+$ predominant (b—CD8 immunohistochemistry).

Contributed by
C Hamoir,* M deVos,† F Clinckart,‡ G Nicaise,§ M Komuta¶ and N Lanthier*

*Departments of *Hepatogastroenterology, ¶Pathology, Cliniques universitaires Saint-Luc, Université catholique de Louvain, Brussels and Departments of †Hepatogastroenterology, ‡Pneumology, §Radiology, Jolimont Hospital, La Louvière, Belgium*