

IgG4-related disease as an unusual cause of biliary stenosis and lymphadenopathy

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IgG4-related disease encompasses a range of conditions characterized by diffuse or focal organ infiltration by lymphocytes and IgG4-positive plasma cells, storiform fibrosis, and often increased serum IgG4 concentrations.¹ It was first recognized in patients with pancreatitis but can affect virtually any organ, including the biliary tree and lymph nodes.^{2,3}

We present a case of a previously healthy 43-year-old man who was transferred to the Department of Gastroenterology and Hepatology at the Medical University of Gdańsk (Gdańsk, Poland) from a regional hospital, where he had undergone a cholecystectomy with choledochotomy and Kehr drainage for obstructive jaundice thought to be related to gallstone disease. Subsequent endoscopic biliary stenting did not improve hyperbilirubinemia in this patient. On admission, he reported abdominal pain, subfebrile temperatures, and a recent weight loss of 10%. A physical examination revealed jaundice, a recent cholecystectomy scar, and an outlet of biliary drainage catheter. The liver and spleen were not enlarged. Laboratory tests showed a bilirubin concentration of 5.64 mg/dl with mixed hepatocellular and cholestatic pattern of liver damage (aspartate aminotransferase, 247 U/l; alanine aminotransferase, 353 U/l; γ -glutamyl transpeptidase, 362 U/l; and alkaline phosphatase, 340 U/l) as well as elevated C-reactive protein levels (27 mg/l). Coagulation parameters and albumin levels were normal.

A repeat endoscopic cholangiography was performed (FIGURE 1A–1C), showing stenosis of the common bile duct in the lower third with dilation of the proximal common bile duct and the right and left biliary ducts as well as segmental narrowing within the bile ducts of the right liver lobe. The previously inserted stent was found

to be occluded and was replaced by 2 new double-pigtail biliary stents. Within a broad differential diagnosis, we determined an elevated IgG4 concentration (3.33 g/l; reference range, 0.03–2.0 G/l), suggesting possible IgG4-related disease. After stent exchange, the patient's symptoms and laboratory results rapidly improved; therefore, no steroid therapy was initiated and the patient was discharged.

Within 2 weeks, the patient was readmitted with jaundice, hepatomegaly, and generalized lymph node enlargement. Multiple lymph node conglomerates were found in the thorax and abdomen by computed tomography. An axillary lymph node excision and a pathological examination were performed. The histological appearance suggested early infiltration by an angioimmunoblastic T-cell lymphoma. Due to an earlier suggestion of IgG4-related disease, a second opinion was obtained. The consulting hematopathologist diagnosed reactive follicular hyperplasia, T-cell (CD3⁺) and immunoblast (CD30⁺) infiltration, and plasmacytosis (FIGURE 1D–1G) with increased expression of IgG4. T-cell receptor analysis by flow cytometry revealed polyclonal infiltration. Steroid therapy with prednisone (20 mg) led to complete resolution of symptoms, including resolution of lymphadenopathy and normalization of IgG4 levels and liver enzymes. Follow-up endoscopic cholangiography was normal and biliary stents could be removed. Steroids were slowly tapered over 2 years. More than 3 years after initial presentation, the patient is symptom free, with normal laboratory results without steroids.

This clinical case illustrates the importance of including IgG4-related disease in the differential diagnosis of cholestatic liver disease, especially followed by lymph node enlargement. If

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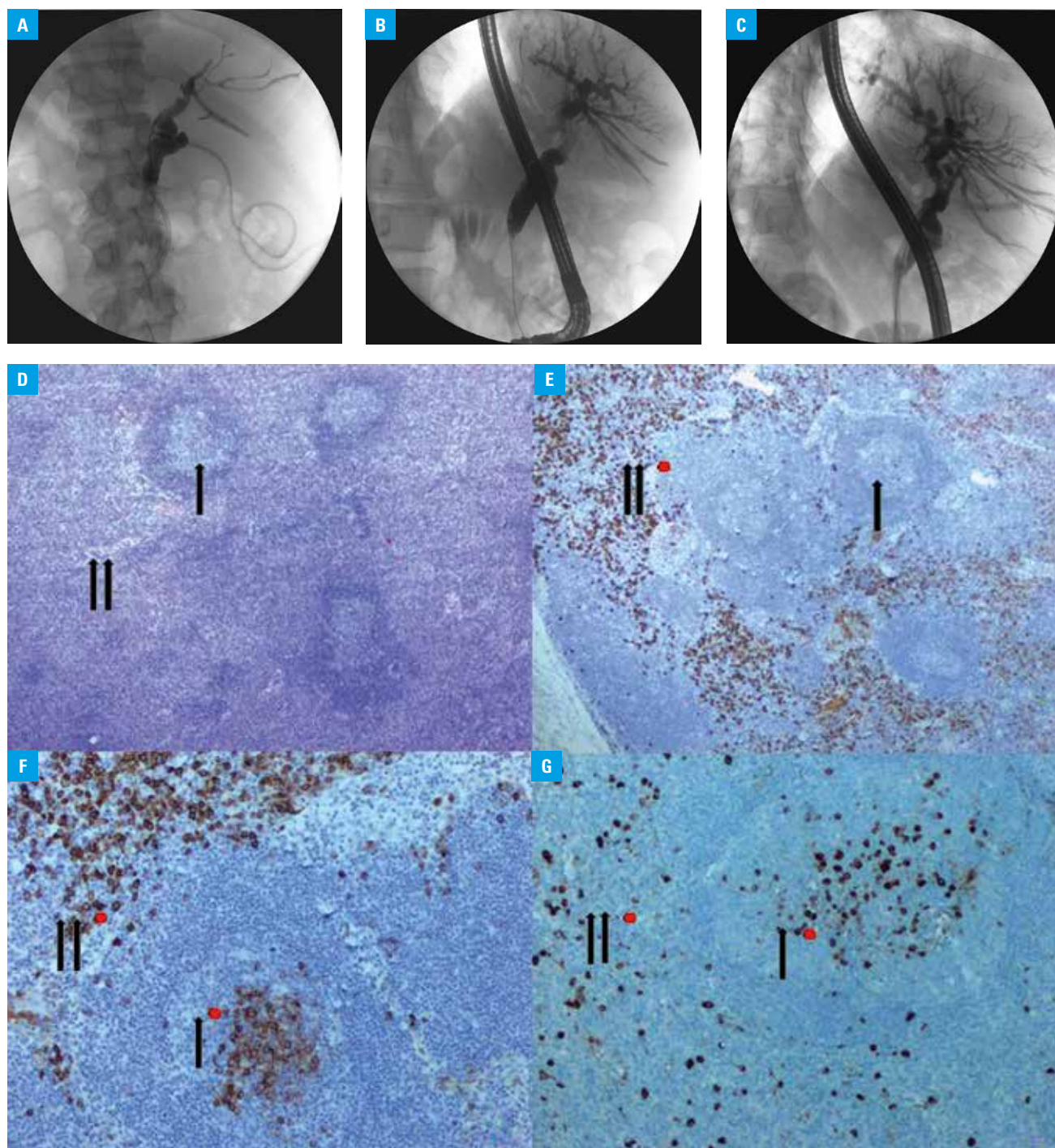


FIGURE 1 **A** – transcutaneous cholangiography showing dilated common bile duct and intrahepatic ducts; a biliary stent is visible in the lumen of the common bile duct; **B** – endoscopic retrograde cholangiography showing stenosed distal third of the common bile duct; **C** – endoscopic retrograde cholangiography showing dilated bile ducts of the left hepatic lobe and stenosis of the intrahepatic bile ducts of the right hepatic lobe; **D–G** – IgG4-related lymphadenopathy; histopathological and immunohistochemical findings of reactive follicular (arrow) and paracortical (double arrows) hyperplasia with plasmacytosis (red dot) with increased expression of IgG4 in the enlarged lymph nodes; hematoxylin and eosin staining (**D**), CD138 (**E**, **F**) and IgG4 (**G**) immunostaining. Numerous IgG4-positive plasma cells in the follicular and paracortical space were identified, and the ratio of IgG4-positive plasma cells to CD138-positive plasma cells exceeded 40%; original magnification $\times 40$ (**D**, **E**) and $\times 100$ (**F**, **G**).

technically feasible, the diagnosis can be aided by cholangioscopy-guided bile duct biopsy or, if not possible, by biopsy of the duodenal papilla, with staining for IgG4 in either case. To our knowledge, this is a unique case report of lymphadenopathy in the context of IgG4-related biliary disease.

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