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CORRESPONDENCE
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Hepatitis B virus Reactivation During Steroid Treatment of IgG4-Related Disease

Dear editor:

Despite recommendations on the prevention of HBV reactivation in patients receiving immunosuppressive therapy,[1] those treated with ≥ 4 weeks of corticosteroids remain at significant risk of HBV reactivation but are frequently overlooked. Here we describe the first two reported cases of HBV reactivation in the context of corticosteroid induced immunosuppression for treatment of IgG4-related disease.

CASE REPORT

Patient 1 is a 64 year old East Asian man who was seen in our clinic for relapsed IgG4-related autoimmune pancreatitis (AIP) and elevated liver enzymes. He was diagnosed with AIP 8 years prior when an ultrasound performed for hepatocellular cancer screening in the setting of chronic HBV revealed a lesion in the head of the pancreas which was confirmed to be consistent with AIP on MRI. Serum IgG4 level was elevated at 2.91 g/L. At that time he was referred to a hepatobiliary surgeon who initiated treatment with prednisone 40 mg daily for 1 month with subsequent taper over 11 weeks, resulting in radiographic and serologic remission. His history was also significant for envelope antigen (eAg)-positive chronic HBV treated with Tenofovir. Five years prior to assessment, he had seroconversion to eAg-negative and envelope antibody (eAb)-positive chronic HBV. After 10 months of consolidation therapy, Tenofovir was discontinued by his gastroenterologist and he remained surface antigen (sAg)-positive and eAb-positive with normal liver enzymes and minimal fibrosis on Fibroscan.

Eight months prior to presentation, he was noted to have radiographic recurrence of AIP with 3 hypodense pancreatic lesions noted on MRI and serum IgG4 rising to 2.5 g/L, prompting re-initiation of prednisone 40 mg daily by his treating surgeon. On presentation to our clinic 3 months ago, his previously normal liver enzymes were found to be elevated with ALT 82 U/L and AST 43 U/L; ALP, bilirubin, albumin, and INR were normal. HBV DNA levels had risen to 7 logs IU/mL with positive HBV sAg (2,226 IU/mL), negative HBeAg, and positive HBeAb. Transient elastography showed stage 0-1 fibrosis (4.8 kPa) and repeat MRI showed resolution of the pancreatic lesions. Treatment was promptly initiated for HBV reactivation with Tenofovir 300 mg daily. Repeat laboratory tests 1 month later showed improvement in ALT and AST with decreased HBV DNA to 3 logs IU/mL.

Patient 2 is a 65 year old man of Southeast Asian origin with a 3 year history of biopsy-proven IgG4-related disease with sclerosing cholangitis, pancreatic lesions, and paraspinal lymphadenopathy, with stable disease on long-term azathioprine. He also had previous HBV exposure with positive HBV total core antibody (cAb) and surface antibody (sAb) with negative sAg. Two months prior to presentation, he developed progression of IgG4-related sclerosing cholangitis with increased ductal wall thickening and dilation in the right liver lobe on MRI as well as elevations of GGT at 130 U/L and IgG4 at 5.29 g/L. Azathioprine was increased from 150 mg daily to 200 mg daily and he was started on prednisone 40 mg daily. On re-assessment at our clinic after prednisone initiation, he was found to have newly elevated AST 65 U/L and ALT 103 U/L secondary to HBV reactivation with HBV DNA 4 logs IU/mL. Interestingly, HBV sAg remained undetectable despite the elevated viral load and positive HBV eAg. HBV sAb and cAb remained positive. Prednisone was decreased to 30 mg daily and he was started on Tenofovir 300 mg daily with a plan to continue treatment for at least 6 to 12 months following the completion of a prednisone taper.

DISCUSSION

IgG4-related autoimmune pancreatitis is an uncommon disorder now recognized worldwide, but first described in East Asia where the prevalence is estimated at 1:100,000,

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predominantly among middle aged men.[2] This population is also at high risk of chronic HBV with an estimated HBsAg seroprevalence of 7-9%.[3]

High-dose corticosteroids represent the cornerstone of treatment for IgG4-related disease and pose a high risk of HBV reactivation (> 10%) in sAg positive patients and a moderate risk (1-10%) in sAg negative/cAb positive patients. Current practice guidelines recommend screening patients undergoing immunosuppression who are at moderate-to-high risk for HBV, and providing antiviral prophylaxis to patients receiving any dose (if HBsAg-positive) or moderate-to high doses (if HBsAg-negative/anti-HBcAb positive) of corticosteroids for ≥ 4 weeks.[2] A recommendation that is frequently overlooked in day-to-day practice.

HBV reactivation is a potentially life threatening complication in chronically infected patients. Given that IgG4-related disease is a multisystem condition treated by different specialists including gastroenterologists, hepatologists, hepatobiliary surgeons, and rheumatologists, our case report emphasizes the importance of screening for HBV in this high risk group, initiating antiviral prophylaxis per recommendations, and highlighting this need to multidisciplinary team members involved in patients' care.

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