A Rare Case of Refractory Drug Induced Liver Injury Following Ocrelizumab Use for Multiple Sclerosis

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Background

- Ocrelizumab, a humanized anti-CD20 monoclonal antibody, has been recently approved for use in Multiple Sclerosis (MS).
- Thus far, it has not been associated with liver enzyme elevations during therapy or idiosyncratic liver injury, but has been linked to cases of reactivation of Hepatitis B in susceptible patients.
- We present a case of severe liver injury in a patient with relapsing-remitting MS who received Ocrelizumab.

Case Presentation

- A 34-year-old Hispanic woman with newly diagnosed MS was started on treatment with Ocrelizumab.
- Pre-treatment acute and chronic Hepatitis B labs were negative.
- Three weeks after infusion, patient presented to the ED with abdominal pain, nausea, fatigue, diminished appetite, and dark urine.
- Lab work revealed ALT 2209 U/L, AST 2261 U/L, Tbili 10.6 mg/dL, ALP 232 U/L (LFTs two months prior were all within normal limits). INR was elevated to 1.5, but she had no signs of hepatic encephalopathy.
- Viral and toxic etiologies of acute hepatitis were thoroughly ruled out. Autoimmune markers, including those specific for autoimmune hepatitis, were negative.
- Abdominal US and MRCP revealed no abnormalities other than a surgically absent gallbladder.

Case Presentation

- As LFTs continued to rise despite drug withdrawal, she was started on IV steroids. INR further rose to 1.8, and inpatient liver transplant evaluation was initiated.
- Liver biopsy revealed acute hepatitis with hepatocyte trabecular disarray and parenchymal collapse, perivenular zone 3 confluent necrosis, and mixed inflammatory infiltrate with no lymphocytes/plasma cells identified, suggestive of drug-induced liver injury (DILI).
- Considering the above workup and timeline of symptoms and lab abnormalities in relation to initiation of Ocrelizumab, DILI secondary to Ocrelizumab was favored as the culprit.
- The patient's symptoms resolved and LFTs steadily improved with IV steroids. She was discharged on PO steroids with close follow-up and monitoring.

Tables and Images

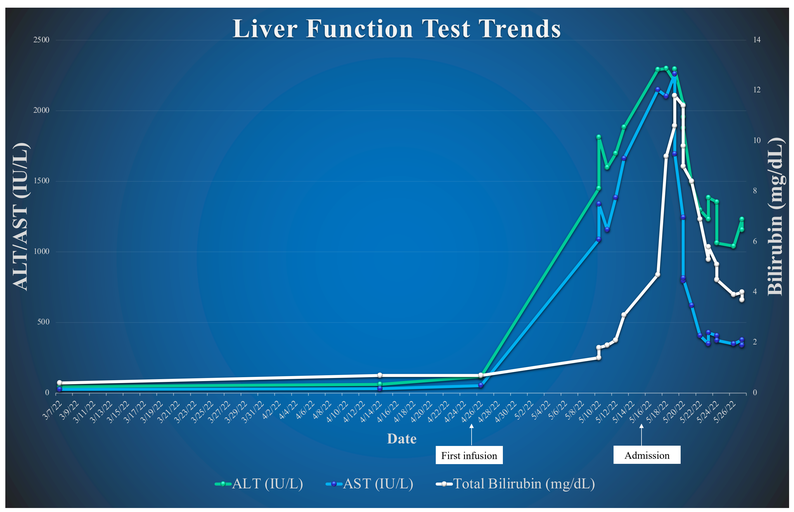

Table 1. LFT trends in period preceding and following initiation of Ocrelizumab infusion.

Tables and Images

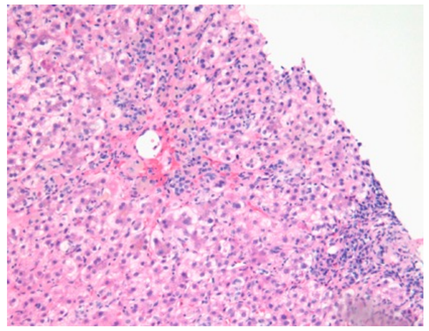

Figure 1. Confluent perivenular necrosis. The hepatocytes around the central vein toward the upper left have all been lost, replaced by pigment-laden macrophages.

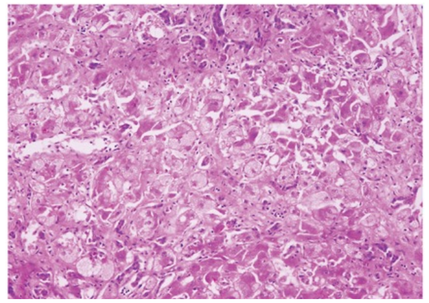

Figure 2. Acute hepatitis with parenchymal collapse and trabecular disarray. Ballooned cells and cholangiolar proliferation present as well.

Discussion

- We report what is, to our knowledge, the first case of DILI (4+ on DILI Network severity scale) related to Ocrelizumab.
- Characterizing, monitoring, and reporting Ocrelizumab-related hepatotoxicity is important as its use in MS continues to increase.
- Responsiveness to steroids may point towards an underlying autoimmune component.
- Further studies are needed to shed light on the mechanisms underlying DILI from Ocrelizumab.