

# Successful Liver Transplantation in a Patient with Hypereosinophilic Syndrome Treated with Mepolizumab

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## Aims

- Hypereosinophilic syndrome (HES) is a multisystem disorder characterized by peripheral blood eosinophilia and organ impairment due to eosinophil infiltration.<sup>1</sup> Mepolizumab, an anti-interleukin (IL)-5 monoclonal antibody has been used on a compassionate basis (GSK study #104317) to treat life threatening HES.
- We describe a case of HES with sclerosing cholangitis leading to cirrhosis of the liver who underwent a successful living donor liver transplantation while on treatment with high dose IV mepolizumab for over 10 years.

## Case Description

- A 66 year-old Caucasian male was seen in the hepatology clinic in November 2016 for evaluation of elevated alkaline phosphatase. Work-up revealed multiple biliary strictures requiring chronic stenting (see Procedures). He was diagnosed with primary sclerosing cholangitis.
- Past medical history
  - Significant for a diagnosis of HES obtained in 2004 when he presented with peripheral blood eosinophilia and multiple organ system involvement:
    - Liver involvement with elevated liver enzymes and alkaline phosphatase. He reported a history of hepatitis with jaundice occurring 10 years prior and treated with oral corticosteroids with improvement.
    - Cardiac involvement: congestive heart failure with shortness of breath, orthopnea and peripheral edema and elevated serum troponin levels.
    - Central nervous system involvement: motor imbalance and speech disruption. Unable to drive.
  - He was initially treated with oral prednisone with decrease in peripheral blood eosinophilia and improvement of liver enzymes. In 2005, he was started on compassionate use mepolizumab at 750 mg IV every 4 weeks.
  - Peripheral blood eosinophilia was controlled (Figure 1)
  - Liver enzymes returned to normal but alkaline phosphatase remained elevated (Figure 2)
  - Troponin level normalized
  - CNS symptoms resolved
- Liver biopsy in 2019 revealed cirrhosis. He underwent living related donor liver transplant in July 2019.
- Since then, the patient has continued to do well while on maintenance therapy with tacrolimus (dose tapered to 1 mg BID) and mepolizumab (dose tapered to 500 mg IV every 6 weeks in December 2013).

## Results

### Tissue Biopsies

- Liver Biopsy
  - 2001. Eosinophils seen in the portal tract and liver sinusoids. No fibrosis.
  - 2006. Patchy bile duct proliferation with acute pericholangitis, chronic portal inflammation, focal bridging fibrosis, suggesting impairment of bile flow. Few eosinophils.
  - 2019. Cirrhosis with features of sclerosing cholangitis. Bile duct with chronic cholangitis. No eosinophils.
- Bone marrow biopsy 2004. Hypocellular with increased eosinophils at 15%. No blast cells
- Terminal ileum/ Colon
  - 2017. Focal active ileitis. Colon normal
  - 2019. Normal cecum as well as right, left, transverse, splenic flexure and terminal ileum

### Imaging

- 2004 CT scan of the abdomen. Prominent liver with slightly lobulated contour with prominence of the left lateral lobe and the caudate lobe.
- 2007 MRCP. Minimal irregularity of intrahepatic ducts suggestive of early sclerosing cholangitis and cirrhotic liver.
- July 2019 MRI of abdomen with contrast. Cirrhotic liver morphology with numerous bands of fibrosis. Irregular structuring and dilatation of the intrahepatic and extrahepatic bile ducts. Splenomegaly and esophageal varices.

### Laboratory Tests

- Genetic testing for FIP1L1/PDGFRα fusion mutation: negative
- Tryptase level: normal
- B12 level: normal
- T cell clonality: positive on multiple occasions in October 2014, October 2015 and May 2018
- Lymphocytosis panel negative in October 2015 and May 2018
- IgG4 level normal at 61 mg/dL.

Figure 1. Blood eosinophils

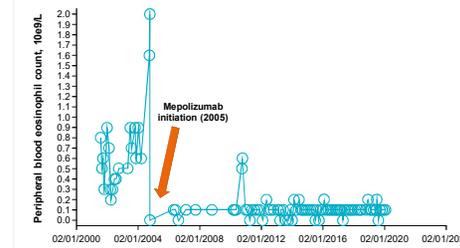
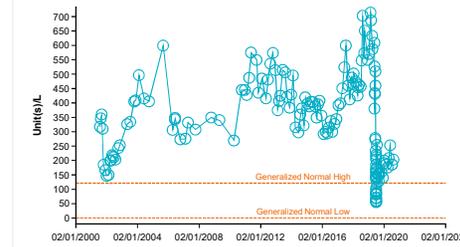


Figure 2. Alkaline Phosphatase



## Procedures

- He underwent multiple endoscopic retrograde cholangiopancreatography procedures:
  - July 2017 for dilation of bile ducts and stone removal
  - September 2017 for stent placement
  - December 2017 for stent replacement
  - March 2018 for stent replacement
  - June 2018 for dilation of bile ducts and stent replacement
  - Sept 2018 for dilation of bile ducts and stent replacement
- Liver transplant, July 2019. Living donor transplant from his son.

## Conclusions

- To our knowledge, this is the first case report of successful liver transplantation in a patient with HES on long-term therapy with mepolizumab.
- Concomitant use of mepolizumab and immunosuppressive therapy used for transplantation was well tolerated in this patient.
- This case also illustrates the heterogeneity of organ system involvement in patients with HES. Although the patient was diagnosed with primary sclerosing cholangitis, this condition has also been reported in the setting of HES.<sup>2</sup>
- Biliary strictures were present prior to initiating mepolizumab therapy. If we assume that the sclerosing cholangitis was due to HES, this case also illustrates the possibility of permanent organ damage due to untreated HES and the importance of early diagnosis and therapy.
- Mepolizumab is now approved by the Food and Drug Administration for the treatment of HES in patients 12 years of age and older.

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- AMI declares the following real or perceived conflicts of interest during the last 3 years in relation to this presentation: GSK employee March 2019-October 2020. CP is a GSK employee and owns stock and shares. LS is on the safety monitoring board for the AstraZeneca study of benralizumab in HES and

receives a share of VCU's royalties from Thermofisher for the Tryptase assay. BB and VL report no conflicts of interest to declare.

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## References

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