

INTRODUCTION

- Voxelotor is a HbS polymerization inhibitor approved by FDA in 2019 for treatment of sickle cell disease.
- Drug-induced liver injury (DILI) is one of the most common causes of acute liver injury and accounts for approximately 10% of all acute hepatitis. We present a rare case of DILI associated with Voxelotor at the dose of 1500mg which has not been previously reported.

CASE REPORT

- A 37 year old male with a past medical history of HbSC disease who was on Hydroxyurea 1.5g daily for 2 years which was discontinued due to pancytopenia.
- He was started on Voxelotor 1500mg daily with improvement in sickle cell symptoms, indirect bilirubin, hemoglobin, and reticulocyte count. He tolerated Voxelotor well.
- He had elevated liver enzymes- ALT 47 U/L after 4 months of therapy.
- Both AST and ALT were trending upwards at monthly follow-ups.
- A thorough review of history and physical examination was performed, however the patient remained asymptomatic.
- BMI was 23.8 kg/m² and he drank alcohol socially.
- He was not on any other hepatotoxic over-the counter or herbal medications.
- Acute hepatitis panel was negative.
- The R factor was 3.6, indicating a mixed hepatocellular-cholestatic pattern.
- Chronic liver disease workup including ceruloplasmin, A1AT, IgG, LKMA, AMA, ASMA were negative. FibroScan showed no fibrosis or steatosis (F0S0). US gallbladder noted cholelithiasis with normal bile ducts. Liver biopsy showed mild sinusoidal congestion, normal architecture, no steatosis, hepatitis, or necrosis (Fig 1).

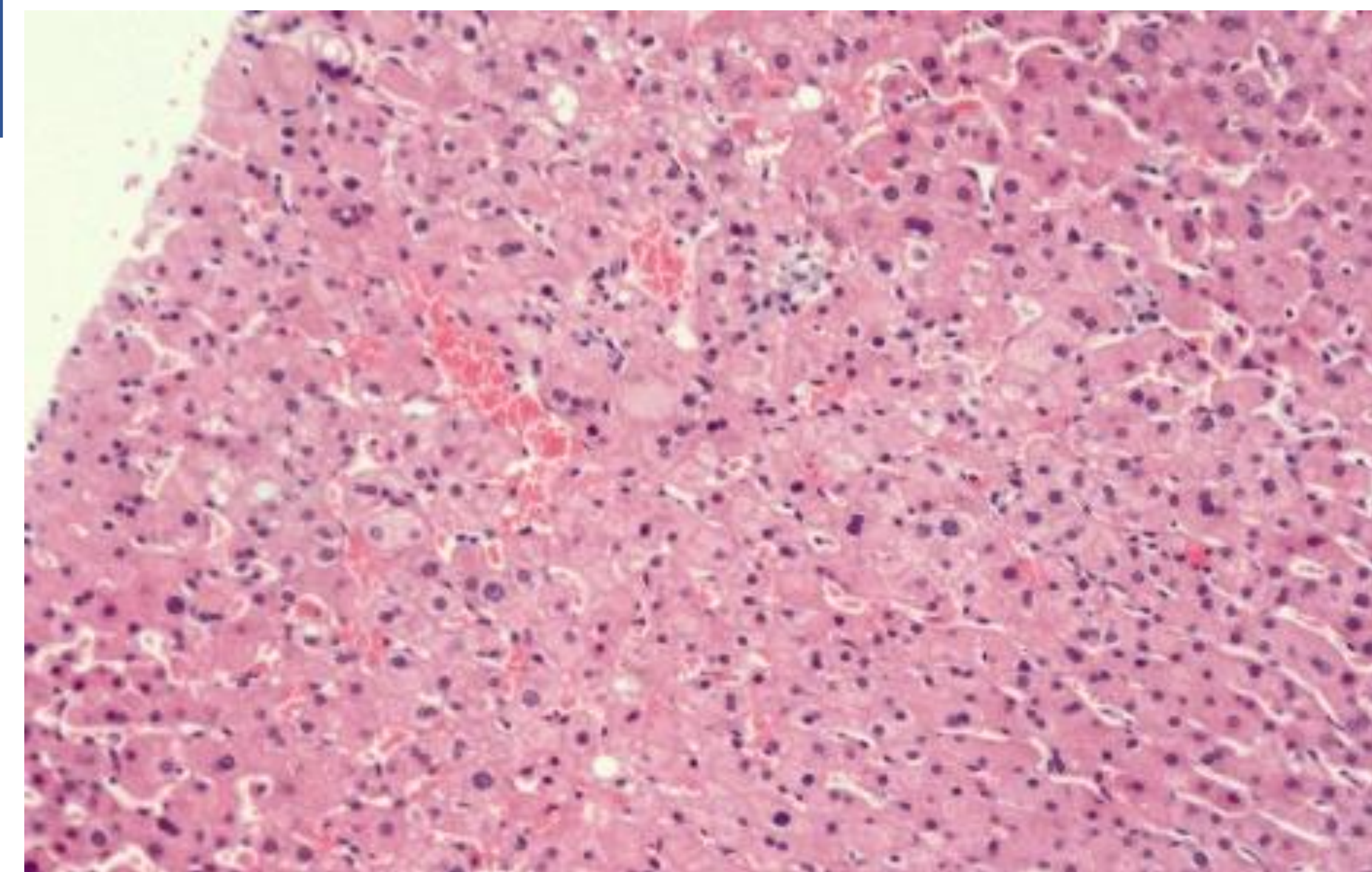


Figure 1- Liver biopsy- Mild sinusoidal congestion

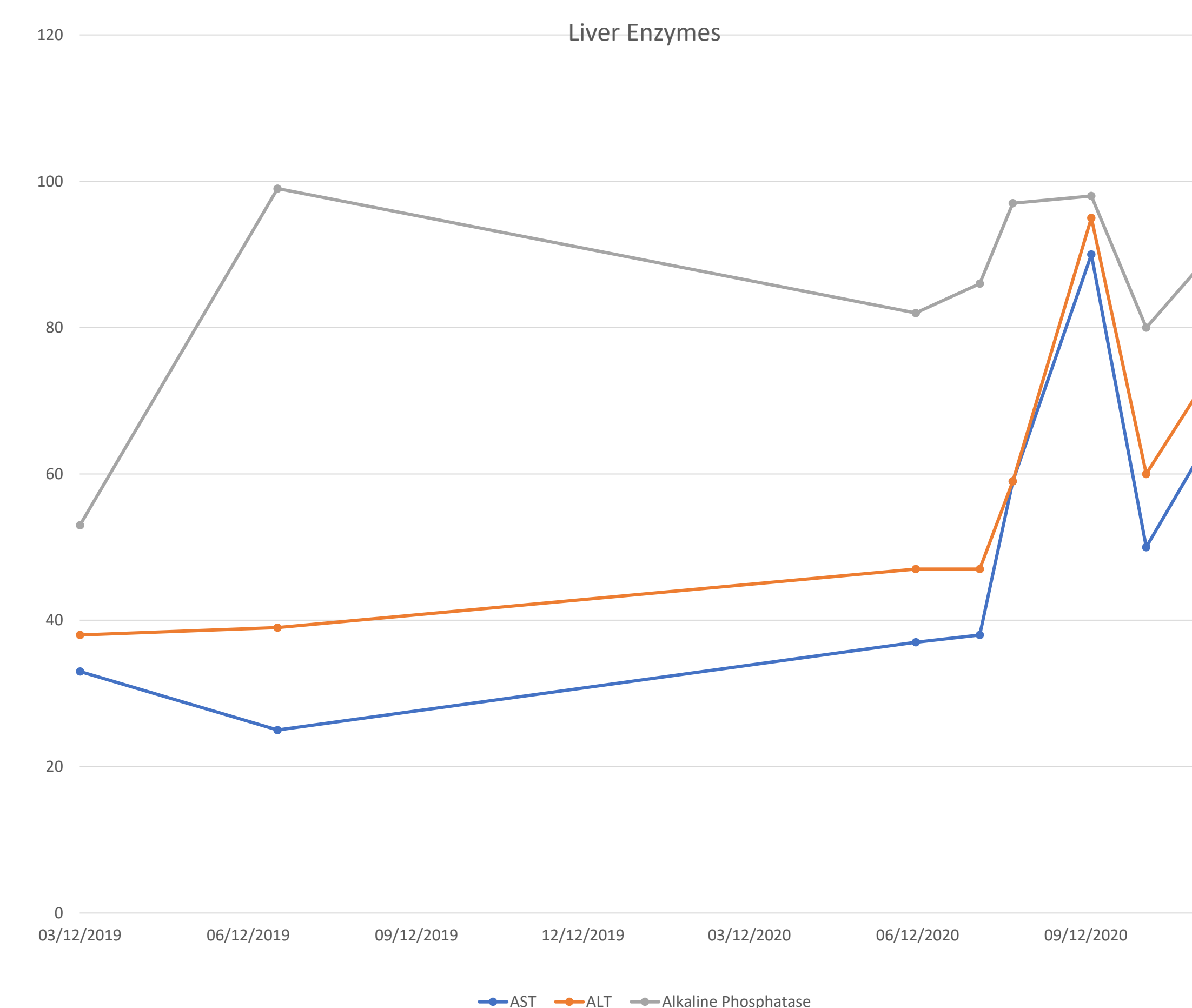


Figure 2- Trend of liver enzymes

CLINICAL COURSE

- Liver enzymes peaked at 6 months with AST 90U/L and ALT 95 U/L. Alkaline phosphatase and total bilirubin were normal. (Fig 2)
- Voxelotor 1500mg daily was held for a week with improvement in liver enzymes (AST 35 U/L, ALT 45 U/L)
- Given the benefits of Voxelotor for sickle cell disease and negative workup, it was restarted at a lower dose of 1g. We recommended monitoring liver enzymes every 3-6 months and repeating Fibroscan in 1 year.

CONCLUSION

- DILI can be diagnosed based on correlation with exposure and improvement with cessation of the drug.
- Voxelotor inhibits RBC sickling and extends the half life of RBCs, improving anemia, hemolysis, and hemoglobin levels.
- Only 2.2% of patients were reported to have elevated AST with a dose of 900mg in the Voxelotor randomized control trial. However, liver injury with Voxelotor at a dose of 1500mg was not reported.
- Providers should be aware of this potential DILI and consider the risk and benefits of withdrawing treatment.

REFERENCES

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