

Introduction

- Drug induced liver injury (DILI) commonly leads to mild elevations in liver enzymes but on rare occasions they can cause severe liver injury.
- DILI is regarded as one of the most common cause of acute liver failure.
- Leflunomide is a disease-modifying antirheumatic agent approved for rheumatoid arthritis (RA) and psoriatic arthritis (PA).
- Mild elevations in the liver enzymes is a common side effect but rare severe hepatotoxicity and fatalities have been reported.

Case Presentation

- A 57-year-old female who was started on Leflunomide for uncontrolled RA was referred to our clinic due to elevated liver enzymes and jaundice.
- The patient endorses the associated symptoms of pruritus, nausea, and diarrhea 5 weeks after starting Leflunomide
- She denied any history of prior liver enzyme elevation, alcohol use, intravenous drug use, or recent travel.
- Her only other medications were Olmesartan and Ketorolac.
- Physical exam was remarkable for significant bilateral scleral icterus. Abdomen was soft, non-tender, non-distended with no signs of hepatomegaly.
- Labs revealed AST 253, ALT 810, Alkaline Phosphatase of 466 and bilirubin of 4.0.
- Work up showed negative hepatitis serologies and autoimmune markers (anti-smooth muscle/anti-mitochondrial)
- Abdominal ultrasound was ordered and revealed no hepatic or biliary pathology.
- MRI w/ MRCP was performed and showed no acute abnormalities

Liver Enzyme Trend

Laboratory Values	Week 7	Week 8	Week 9	Week 10	Week 13
AST	253	193	66	60	27
ALT	810	600	220	167	38
Alk Phos	466	413	368	286	142
Total Bilirubin	4	5.7	7.5	4.7	1.4

Figure 1. Weeks corresponded to the time from initiation of Leflunomide. Leflunomide was discontinued at week 7.

Management

- The patient was told to discontinue Leflunomide
- The following week liver enzymes were remarkable for AST 193, ALT 600, Alkaline Phosphatase 413, and total bilirubin of 7.5.
- The patient at this time reported that she was still experiencing pruritus.
- Due to her persistent symptoms and rising bilirubin, the patient was started on ursodeoxycholic acid(udca)
- A week later the bilirubin decreased to 4.7 and the persistent pruritus resolved.
- Figure 1 illustrates the downtrend of liver enzymes in weeks after the cessation of Leflunomide.
- She remained consistent with her follow ups and did not have any recurrence of her symptoms following the cessation of the medication.

Discussion

- Drug induced liver injury can be defined as inflammation of the hepatic system secondary to a medication or herbal supplement.
- Leflunomide is commonly used for rheumatoid arthritis and psoriatic arthritis and can be associated with symptomatic severe liver injury.
- The liver injury arises after 1 to 6 months of therapy and can present with a cholestatic or hepatocellular pattern.
- On weeks 5-6 of starting Leflunomide for her rheumatoid arthritis, our patient was symptomatic with diarrhea, nausea, and pruritus.
- A mixed hepatocellular and cholestatic pattern was noted on week 7, with an improvement of liver enzymes within a week of stopping treatment.
- However, bilirubin remained persistently elevated and the patient still complained of persistent pruritus which promptly improved with the initiation of UDCA.
- This case underscores the importance of monitoring liver enzymes in patients on Leflunomide, at least once monthly for the first six months, and immediate discontinuation when liver enzymes increase more than three times upper normal.
- In our patient, worsening jaundice and persistent pruritus responded promptly to UDCA which supports data that shows possible benefits of UDCA in the treatment of DILI.

