

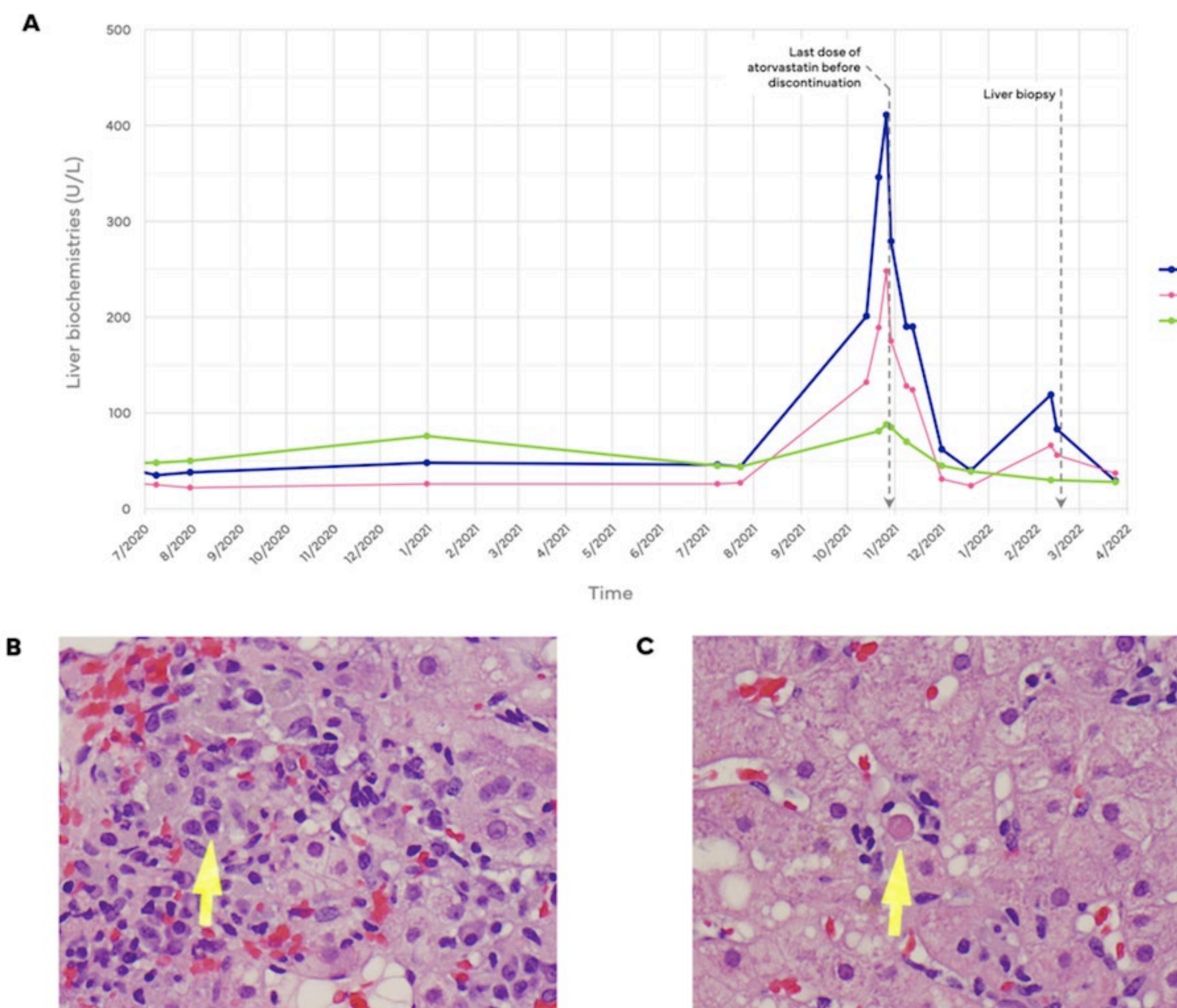
INTRODUCTION

- Statin are amongst the most common drugs prescribed in the U.S., prescribed for almost 40 million individuals
- Well-recognized adverse effects (AE) of statins are in the liver and muscle
- Atorvastatin and simvastatin are the most common of statins to cause AE
- Abnormal liver enzyme elevations are observed in <3% of cases
- We describe a rare case of drug-induced liver injury (DILI) resembling autoimmune hepatitis attributed to a statin

CASE PRESENTATION

- A 74-year-old woman was evaluated for elevated liver enzymes of hepatocellular pattern of injury
- Past medical history included: overweight status, hypertension, hyperlipidemia, diabetes mellitus type II, endometrial carcinoma stage IIIC with metastasis to lung and peritoneum
- Prior treatment included megestrol and tamoxifen; she was still actively taking atorvastatin 40 mg/d
- She was previously evaluated for the elevated liver enzymes which had naturally normalized when she had paused taking her statin
- Laboratory results: ALT peak 411 U/L, AST peak 248 U/L, with normal alkaline phosphatase level (**Fig. A**); a high ANA titre of 1:640, positive anti-smooth muscle antibody (ASMA), and positive anti-mitochondrial antibody (AMA); serum IgG was also elevated
- CT abdomen and ultrasound liver were unrevealing for liver pathology
- Due to elevated liver enzymes, she was not yet eligible for additional cancer treatment until the diagnosis can be resolved

STATIN-RELATED AUTOIMMUNE HEPATITIS



(A): Timeline of liver enzyme trends from July 2020—March 2022. Atorvastatin was discontinued on 10/29/21. The delayed-onset of transaminase elevations while on statin therapy may in retrospect represent also an idiosyncratic form of drug-induced liver injury. Liver enzymes naturally improved after discontinuation of statin medication, without the need for systemic corticosteroid therapy. (B): Liver biopsy histology (H&E, 400x) - Moderately portal chronic inflammation consisting of mainly lymphocytes, admixed with eosinophils and occasional plasma cells (arrow: plasma cell). (C): Liver biopsy histology (H&E, 400x) - Minimal steatosis and single cell necrosis (Councilman body) of hepatocytes (arrow: Councilman body). Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase.

MANAGEMENT & CLINICAL COURSE

- Patient underwent liver biopsy with revealed features resembling autoimmune hepatitis (AIH) (**Fig. B and C**)
- Liver biochemistries were observed over time while off atorvastatin, without starting corticosteroids; liver enzymes eventually normalized without the need for immunosuppression, supporting a diagnosis of DILI, rather than chronic idiopathic AIH
- Patient was then deemed eligible for additional treatments for her endometrial cancer

DISCUSSION

- AIH-like DILI is a subtype of DILI^[1-3], a diagnosis supported by removing the offending agent, in this case the statin; in most cases, liver biopsy itself may be inconclusive but still required to exclude other acute or chronic liver diseases
- Diagnostic strategies for AIH-like DILI have been proposed^[1]
- Management of AIH-like DILI can be challenging as it is a rare entity almost indistinguishable from AIH; AIH is treated with long-term steroids which bears important implications due to potential AE related to steroids
- 67% cases of AIH-like DILI present with elevated ANA titres and positive AMA^[2], similar to our case
- The exact mechanism of this phenotype is unclear
- In our case, liver enzymes spontaneous improved across 1 month after discontinuation of atorvastatin
- In clinical practice, a case-by-case decision about statin rechallenge should be formulated in a multidisciplinary fashion in conjunction with the strength of indications for prescribing a statin

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