Published in final edited form as:

Clin Gastroenterol Hepatol. 2019 March ; 17(4): 789–790. doi:10.1016/j.cgh.2018.06.035.

Sclerosing Cholangitis Like Changes on Magnetic Resonance Cholangiography in Patients with Drug Induced Liver Injury

Jawad Ahmad, M.D., Simona Rossi, M.D., Shuchi K. Rodgers, M.D., Marwan Ghabril, M.D., Robert J. Fontana, M.D., Andrew Stolz, M.D., Paul H. Hayashi, M.D., Huiman Barnhart, Ph.D., David E Kleiner, M.D., and Einar S. Bjornsson, M.D.

Division of Liver Diseases, Icahn School of Medicine at Mount Sinai, New York, NY 10029

Summary

Drug induced liver injury can lead to changes of the biliary tree that resemble sclerosing cholangitis. These changes can be seen on magnetic resonance cholangiopancreatography.

Keywords

Sclerosing cholangitis; drug-induced liver injury; magnetic resonance cholangiopancreatography

Introduction

Idiosyncratic drug induced liver injury (DILI) has a variable presentation including cholestatic liver injury (1) in which case, magnetic resonance imaging (MRI) is often performed to exclude pancreatobiliary causes of obstruction. Sclerosing cholangitis (SC) like changes on imaging have been described anecdotally with DILI (2, 3). A recent study of 25 consecutive, unselected DILI patients found that 10% had SC-like changes on magnetic resonance cholangiopancreatography (MRCP) (4). The aim of the current study was to identify the clinical features of patients enrolled in the U.S. Drug Induced Liver Injury Network (DILIN) prospective study who had SC-like changes on MRCP.

Methods

The DILIN prospective study is a multicenter observational cohort study that enrolls patients with suspected DILI from prescription drugs and herbal and dietary supplements (HDS) (5).

Correspondence and reprint requests to: Jawad Ahmad, M.D., Professor of Medicine, Division of Liver Diseases, Icahn School of Medicine at Mount Sinai, New York, NY 10029, Phone: 212 241 8035, Fax: 212 731 7340, jawad.ahmad@mountsinai.org.

Author contributions: All authors contributed to the collection of clinical data, data analysis, and initial and final drafting of the manuscript. DEK provided expert review of the available liver histopathology.

Conflicts of interest:

JA, SKR, MG, AS, HB, PHH, ESB. No disclosures

RJF: I have received research support from Gilead Sciences and BMS. I have provided consulting services to Alynam and Abbvie.

SR: BMS, Gilead

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Patients must meet predefined laboratory criteria for study entry and be enrolled within 6 months of onset. All patients undergo testing to exclude other causes of liver injury, and causality is assessed by expert opinion and the standardized Roussel Uclaf Causality Assessment Method (RUCAM).

In this study, all patients with abdominal MRI performed as part of the diagnostic evaluation were identified and available studies were reviewed centrally in a blinded manner using a structured cholangiographic assessment tool (2).

Results

Between 2004–2014, 233 of 1487 subjects enrolled in the DILIN Prospective Cohort underwent MRI and 83 had MRCP images available for review. Four of 56 patients (7%) with adequate quality images had SC-like changes (4 with intrahepatic strictures and 1 with a common hepatic duct stricture as well). An example is shown in Figure 1. All 4 patients developed jaundice (mean peak bilirubin 18.8 mg/dL), 3 had cholestatic liver tests (mean peak ALT 982 U/L, Alk P 573 U/L) and hepatocellular injury in the other. The latency of drug exposure to DILI onset was 1 to 17 weeks and the time from onset to MRCP was within 2 weeks in 3 and at 20 weeks in 1 case. Implicated agents included moxifloxacin, atorvastatin and 2 HDS products (Chinese herbs and a weight loss supplement). During follow-up, 3 had persistent laboratory abnormalities 6 months after onset and 1 patient underwent liver transplantation. The age (mean 56 years), gender (50% female), and liver injury patterns were similar to those without SC-like changes. Liver biopsy available in 2 patients demonstrated ductular reaction and ductopenia in 1 and bridging necrosis in another who later developed cirrhosis (the patient with initial hepatocellular injury).

Discussion

Current guidelines recommend MRI in patients with unexplained cholestatic liver injury or jaundice (6). In this study SC-like changes were noted in 7% of those with adequate imaging but only 24% of MRIs performed were available for central review, and the reports of some unavailable images suggested cholangiographic abnormalities. Most patients who underwent MRI were jaundiced and hospitalized and they were more likely to have cholestatic and prolonged liver injury than the overall DILIN cohort (7). Nevertheless, these results suggest that MRI should be considered in patients with suspected DILI and cholestatic liver tests.

Our results are similar to those from an Icelandic DILI cohort (4) where only 25% of patients had an MRI/MRCP so that the actual percentage of SC-like changes could have been higher. One patient in the current study had resolution of the biliary changes at repeat MRCP 18 months later despite persistence of liver test abnormalities suggesting that these changes can resolve. The pathogenesis of SC-like changes are unclear and may reflect true biliary injury or perhaps extrinsic compression from architectural distortion as in the patient who underwent liver transplantation where the explant demonstrated marked ductular cholestasis and submassive collapse.

The patients with SC-like changes had a more severe initial injury and were more likely to develop chronic injury (using 6 months rather than 12 months as the cut-off for persistent laboratory abnormalities) than the average patient in the DILIN cohort (75% vs 18%) (8).

The main limitations of the current study are the small number of cases showing SC-like changes, precluding assessment of any risk factors and the lack of MRCPs performed in most patients, perhaps underestimating the reported frequency of biliary abnormalities. However, strengths of the study are prospectively enrolled, well characterized patients with prolonged follow-up and standardized, expert, central review of MRCPs.

In conclusion, SC-like changes were associated with severe and chronic DILI. Initial MRCP should be considered in patients with suspected cholestatic DILI. Further studies of follow up imaging in patients with chronic cholestatic DILI are warranted.

Acknowledgments

Funding source: The Drug Induced Liver Injury Network (DILIN) is structured as an U01 cooperative agreement supported by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health (NIH) with funds provided by the following grants: U01DK065211 (Indiana University [Purdue]), U01DK065184 (University of Michigan [Ann Arbor]), U01DK065201 (University of North Carolina [Chapel Hill], Asheville, Wake Forest Baptist Medical Center), U01DK083020 (University of Southern California, University of California-Los Angeles [Pfleger Liver Institute]), U01DK083027 (Albert Einstein Medical Center), U01DK100928 (Icahn School of Medicine at Mount Sinai), U01DK065176 (Duke Clinical Research Institute). Additional support was provided by the Intramural Division of the National Cancer Institute (NCI), NIH.

Financial Support: DILIN

Abbreviations

ALT	Alanine aminotransferase
ANA	Antinuclear antibody
Alk P	Alkaline phosphatase
AST	Aspartate aminotransferase
DILI	Drug induced liver injury
DILIN	Drug Induced Liver Injury Network
HDS	Herbal and Dietary Supplements
INR	International normalized ratio
MRCP	Magnetic Resonance Cholangiopancreatography

References

1. Chalasani N, Björnsson E. Risk factors for idiosyncratic drug-induced liver injury. *Gastroenterology* 2010;138:2246–59. [PubMed: 20394749]
2. Sandrasegaran K, Alazmi WM, Tann M, et al. Chemotherapy-induced sclerosing cholangitis. *Clin Radiol*. 2006;61:670–8. [PubMed: 16843750]

3. Horsley-Silva JL, Dow EN, Menias CO et al. Docetaxel Induced Sclerosing Cholangitis. *Dig Dis Sci* 2015;60:3814–6. [PubMed: 26501143]
4. Gudnason HO, Björnsson HK, Gardarsdottir M, et al. Secondary sclerosing cholangitis in patients with drug-induced liver injury. *Dig Liv Dis* 2015;47:502–7.
5. Fontana RJ, Watkins PB, Bonkovsky HL, et al. Drug-Induced Liver Injury Network (DILIN) prospective study: rationale, design and conduct. *Drug Saf* 2009;32:55–68. [PubMed: 19132805]
6. Kwo PY, Cohen SM, Lim JK. ACG Clinical Guideline: Evaluation of abnormal liver chemistries. *Am J Gastroenterol* 2017;112:18–35. [PubMed: 27995906]
7. Chalasani N, Bonkovsky HL, Fontana R, et al. Features and outcomes of 899 patients with drug-induced liver injury: The DILIN Prospective Study. *Gastroenterology* 2015;148:1340–52. [PubMed: 25754159]
8. Fontana RJ, Hayashi PH, Gu J et al. Idiosyncratic drug-induced liver injury is associated with substantial morbidity and mortality within 6 months from onset. *Gastroenterology* 2014;147:96–108. [PubMed: 24681128]

Figure 1:
Coronal MRCP image demonstrating a focal hilar stricture and left hepatic duct stricture