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Acute Liver Injury Induced by Red Yeast Rice Supplement

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Background

Red yeast rice is a commonly used supplement made by fermenting steamed rice with a food fungus, M. purpureus. Patients may use this supplement to lower low-density lipoprotein (LDL) as an alternative to statins. Red yeast rice contains monacolin K, a fungal product that is biochemically equivalent to lovastatin, and hence carries the same risk of hepatotoxicity.

Case Presentation

A 64-year-old female was transferred to our hospital for assessment. She had presented to another hospital's emergency room with a 2-week history of fatigue, bloating, and early satiety; a 1-week history of darker urine and lighter stools; and a recent development of jaundice. She did not report any liver disease, blood transfusion, contact with anyone ill, or recent travel. She had a history of pernicious anemia treated with monthly B12 injections but no other acute or chronic conditions. She was a non-smoker, drank 2 glasses of red wine every night, and had an active lifestyle. At a routine visit with her primary care physician 6 weeks earlier, she was alerted that she had hyperlipidemia. Hesitant to start taking statins, she opted to use red yeast rice supplement to lower her lipids. She reported using 1200 mg/d of red yeast rice supplement with a concentrated 10:1 extract from NOW Foods (Bloomindale, IL).



Figure 1. Liver core biopsy sample showing lobular inflammation, cholestasis, and steatosis with hepatocyte drop out. Magnification 40x.

Acute Hepatic Injury Caused by Red Yeast Rice

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Investigations

• On admission to our hospital, serum liver function tests revealed high alanine transaminase (ALT) 2488 U/L, aspartate transaminase (AST) 1643 U/L, alkaline phosphatase (ALP) 268 U/L, and total bilirubin 12.8 mg/dL.

DAY	ALT/SGPT (IU/l)	AST/SGOT (IU/l)	Total Bilirubin (mg/dl)	Direct Bilirubin (mg/dl)	Alkaline Phosphatase (mg/dl)
1	2188	1643	8.9		368
(admission)					
2	2488	1643	12.8		268
3	2843	2015	12.8		414
4	2018	1154	13.2	8.2	319
5	2149	1284	15.1	9.4	343
6	2033	1297	16.3	12.9	317
7	2042	1357	17.2	9.9	305
8 (steroids initiated)	2200	1340	19.7	14.7	346
9	1869	890	16.7	9.2	325
10	1805	784	13.7	7.8	360
32	584	208	2.3	1.5	99

Table 1. Progression of liver function tests preceding and following steroid treatment. Transaminases peaked early in hospitalization, while total bilirubin peaked a week later. Transaminases and bilirubin began to decrease following initiation of steroid treatment but had not completely resolved one month later.

Differential Diagnosis

- Viral serologies negative (Hepatitis A IgM antibodies, Hepatitis B Surface antigen, Hepatis B core IgM antibodies, Hepatitis C RNA, Hepatitis C antibodies, Ebstein Barr virus DNA, and Cytomegalovirus DNA)
- Autoimmune hepatitis panel negative (anti-smooth muscle antibodies, antinuclear antibodies, anti-liver kidney microsomal type 1 antibodies)
- No alpha-1 antitrypsin antibodies detected
- Hemochromatosis ruled out given normal transferrin saturation and total iron binding capacity and the absence of fibrosis on liver biopsy (also genetic testing negative for C282Y and H63D mutations)
- Wilson's disease ruled out based on normal ceruloplasmin level and the absence of liver fibrosis
- addition, CA 19-9 and alpha fetoprotein levels were normal)
- Malignancy was not suspected (no masses were seen on abdominal CT; in • MRCP revealed no biliary obstruction, ruling out cholestatic causes • The patient denied taking medications apart from monthly B-12 injections
- and red yeast rice supplements
- Acetaminophen level less than 10mg/dl and salicylate levels less than 4mg/dl eliminated an analgesic overuse etiology



- discharge)

- ALT 2843 U/L and AST 2015 U/L
- bilirubin decreased (Table 1)

As this case demonstrates, red yeast rice has the potential to cause severe adverse effects such as acute liver injury. These effects are difficult to pre-empt in part because the concentration of monacolin K in red yeast rice is not regulated. A recent study found that monacolin K concentrations ranged from 0.09 to 10.94 mg per daily manufacturer recommended dose (2). Of note, 5-7 mg of monacolin is as effective as 20-40 mg of pure lovastatin (1). Multiple reports globally of red yeast rice hepatotoxicity and myopathy have been previously documented by the Italian Surveillance System of Natural Health Products, which determined that hepatic reactions occurred in 10 patients between April 2002 and September 2015, nine of which were compatible with the definition of drug induced liver injury (3). As previous cases have also documented, recovery may take months after discontinuing red yeast rice (4).

- jaundice and malaise.

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Treatment and Outcome

• Red Yeast Rice supplement was discontinued and the patient was prescribed high-dose IV methylprednisolone (15mg every six hours for three days, followed by oral prednisone 40mg on

• Liver function was monitored by weekly labs upon discharge • Transaminases peaked shortly after admission at levels of • Total bilirubin peaked five days later at 19.7 mg/dL • With initiation of steroid treatment, transaminases and

Discussion

Take Home Points

• Red yeast rice contains monacolin K which is biochemically equivalent to lovastatin and carries the same risks of adverse effects. • Those choosing to use red yeast rice supplements should be educated about the risk of hepatotoxicity and to recognize symptoms such as

• Supplements are not necessarily safer than prescription medications, and physicians and patients should be aware of their adverse effect profile before using them or approving their use.

Bibliography