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 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).

Liver Biopsy

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

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.

<table>
<thead>
<tr>
<th>DAY</th>
<th>ALT/SGPT (IU/L)</th>
<th>AST/SGOT (IU/L)</th>
<th>Total Bilirubin (mg/dL)</th>
<th>Direct Bilirubin (mg/dL)</th>
<th>Alkaline Phosphatase (mg/dL)</th>
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<tr>
<td>1 (admission)</td>
<td>2188</td>
<td>1643</td>
<td>8.9</td>
<td>368</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>2488</td>
<td>1643</td>
<td>12.8</td>
<td>268</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>2843</td>
<td>2015</td>
<td>12.8</td>
<td>414</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>2018</td>
<td>1154</td>
<td>13.2</td>
<td>8.2</td>
<td>319</td>
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<tr>
<td>5</td>
<td>2149</td>
<td>1284</td>
<td>15.1</td>
<td>9.4</td>
<td>343</td>
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<tr>
<td>6</td>
<td>2033</td>
<td>1297</td>
<td>16.3</td>
<td>12.9</td>
<td>317</td>
</tr>
<tr>
<td>7</td>
<td>2042</td>
<td>1357</td>
<td>17.2</td>
<td>9.9</td>
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<tr>
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<td>19.7</td>
<td>14.7</td>
<td>346</td>
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<tr>
<td>9</td>
<td>1869</td>
<td>890</td>
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<tr>
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<td>584</td>
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<td>2.3</td>
<td>1.5</td>
<td>99</td>
</tr>
</tbody>
</table>

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, Hepatitis B core IgM antibodies, Hepatitis C RNA, Hepatitis C antibodies, Elstein Barr virus DNA, and Cytomegalovirus DNA)
- Autoimmune hepatitis panel negative (anti-smooth muscle antibodies, anti-nuclear 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
- Malignancy was not suspected (no masses were seen on abdominal CT; in addition, CA 19-9 and alpha fetoprotein levels were normal)
- MRCP revealed no biliary obstruction, ruling out cholestatic causes
- The patient denied taking medications apart from monthly B12 injections and red yeast rice supplements
- Acetaminophen level less than 10mg/dl and salicylate levels less than 4mg/dl eliminated an analgesic overuse etiology
- Transaminases peaked shortly after admission at levels of ALT 2843 U/L and AST 2015 U/L
- Total bilirubin peaked five days later at 19.7 mg/dL
- With initiation of steroid treatment, transaminases and bilirubin decreased (Table 1)

Discussion

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).

Take Home Points

- 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 discharge)
- Liver function was monitored by weekly labs upon discharge
- Transaminases peaked shortly after admission at levels of ALT 2843 U/L and AST 2015 U/L
- Total bilirubin peaked five days later at 19.7 mg/dL
- With initiation of steroid treatment, transaminases and bilirubin decreased (Table 1)

Bibliography