Hepatotoxicity Associated With Herbal Does Not At All Mean Innocuous: The Sixth Case of Hepatotoxicity Associated With Morinda Citrifolia (Noni)

TO THE EDITOR: Up to two-thirds of the population report using complementary and alternative self-medication (1) without consulting health-care professionals (2). We are concerned about this since we have seen two cases of hepatotoxicity related to the consumption of noni juice (Morinda citrifolia), one of which required liver transplantation (3). Three further cases have been reported in the literature to date (4–6). We herein report another patient with hepatotoxicity related to the ingestion of noni juice and provide a summary of all cases reported to date in order to make hepatologists aware of the potential of noni juice to cause liver damage.

Our patient is a 43-yr-old white male who was diagnosed with a glioblastoma in September 2007 after suffering two seizures. He underwent surgery and was scheduled for radiation and chemotherapy in early December 2007. To aid his recovery, he started to drink noni juice (Tahitian Noni, Tahitian Noni International UK Ltd, London, UK) in the recommended dose of 20 mL twice daily. Two weeks later, routine prechemotherapy blood tests were performed; these revealed elevated transaminases: aspartate-aminotransferase (AST) 192 U/L (normal <35 U/L), and alanine-aminotransferase (ALT) 516 U/L (normal <45 U/L). Bilirubin remained normal (0.58 mg/dL [normal 0.1–1.2 mg/dL]). Liver function tests had, however, been completely normal 3 days before the patient started to drink noni juice (AST 17 U/L, ALT 34 U/L) and the patient did not report any symptoms at that time. He had had no liver-related problems in the past and had abstained totally from alcohol following the diagnosis of glioblastoma; previously he had consumed an occasional glass of wine. Viral hepatitis, autoimmune hepatitis, hemochromatosis, α1-antitrypsin deficiency, and Wilson’s disease were ruled out. The patient was treated with levetiracetam (500 mg twice daily) for his tumor-related epilepsy. Since liver function tests were normal after 3 weeks’ therapy with levetiracetam (see above), we did not consider this medication to be the cause of the deranged transaminases. Transaminases dropped as soon as the patient stopped drinking noni juice. After 6 wk, AST had decreased to 34 U/L and ALT to 70 U/L. The patient remained on treatment with levetiracetam throughout this period. A liver biopsy was not taken because of the patient’s rapid recovery.

Drug-related hepatotoxicity is the most frequent reason for postmarketing warnings or drug withdrawal, since hepatotoxicity is such a rare event that premarketing studies often fail to detect it (7). Herbal hepatotoxicity is even more difficult to diagnose: herbal preparations are sold over the counter; patients do not consider them to be medication and so do not report their use (7). Scoring systems have been developed to assess the likelihood that a drug will cause hepatic toxicity. The two most common ones are the CIOMS (Council for International Organizations of Medical Sciences) score (8) and the Maria & Victorino score (9). Both scores in our case gave the result “probable” (CIOMS +8, Maria & Victorino +4). So far, the mechanism of noni-induced hepatotoxicity is only speculative. Anthraquinones, which are known to be hepatotoxic (10) and have been found in the fruit of Morinda citrifolia, have come under suspicion (11, 12).

With this case report, we would like to increase awareness of herbal hepatotoxicity, especially related to the use of noni juice. Although this case shows the mildest clinical presentation reported so far, the occurrence of hepatotoxicity most likely related to the ingestion of noni juice had important implications for our patient, because chemotherapy could not be started as planned and had to be delayed by 4 wk. We think that six reported cases are more than just chance and would like to emphasize the importance of a detailed history including self-medication when patients present with unexplained high transaminases. We also hope that health authorities will...
<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age</th>
<th>Ingestion Duration</th>
<th>Amount Ingested</th>
<th>Delay Between Ingestion and Onset of Symptoms</th>
<th>Laboratory Tests (Maximum)</th>
<th>Concomitant Medication</th>
<th>Outcome</th>
<th>Presentation</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>45</td>
<td>Few weeks</td>
<td>1 glass per day</td>
<td>Few weeks</td>
<td>AST 604 U/L, ALT 195 U/L, Bilirubin 0.82 mg/dL</td>
<td>None</td>
<td>Spontaneous recovery</td>
<td>Malaise, thoracic discomfort</td>
<td>(5)</td>
</tr>
<tr>
<td>2</td>
<td>Male</td>
<td>29</td>
<td>3 weeks</td>
<td>1.5 L</td>
<td>3 weeks</td>
<td>AST 1557 U/L, ALT 1626 U/L, Bilirubin 45.3 mg/dL</td>
<td>Chinese herbs</td>
<td>Liver transplantation</td>
<td>Acute liver failure</td>
<td>(3)</td>
</tr>
<tr>
<td>3</td>
<td>Female</td>
<td>62</td>
<td>4 months</td>
<td>2 L</td>
<td>4 weeks</td>
<td>ASL 2020 U/L, ALT 3570 U/L, Bilirubin 3.9 mg/dL</td>
<td>None</td>
<td>Spontaneous recovery</td>
<td>Diarrhea</td>
<td>(3)</td>
</tr>
<tr>
<td>4</td>
<td>Female</td>
<td>24</td>
<td>4 weeks</td>
<td>1-1.5 L</td>
<td>3 weeks</td>
<td>AST 2818 U/L, ALT 3648 U/L, Bilirubin 43.5 mg/dL</td>
<td>Interferon beta-1a</td>
<td>Spontaneous recovery</td>
<td>Subacute liver failure</td>
<td>(4)</td>
</tr>
<tr>
<td>5</td>
<td>Female</td>
<td>33</td>
<td>2 weeks</td>
<td>Not stated</td>
<td>1 weeks</td>
<td>AST 3382 U/L, ALT 2740 U/L, Bilirubin 8.1 mg/dL</td>
<td>None</td>
<td>Spontaneous recovery</td>
<td>Abdominal pain, nausea, vomiting, anorexia</td>
<td>(6)</td>
</tr>
<tr>
<td>6</td>
<td>Male</td>
<td>43</td>
<td>2 weeks</td>
<td>2 × 20 ml per day</td>
<td>2 weeks</td>
<td>AST 192 U/L, ALT 516 U/L, Bilirubin 0.58 mg/dL</td>
<td>Levitiracetam</td>
<td>Spontaneous recovery</td>
<td>Routine laboratory check-up</td>
<td>This report</td>
</tr>
</tbody>
</table>

Table 1. Reports on Noni-Related Hepatotoxicity

consider these reports when assessing the risk of “novel food” and add appropriate warnings to the labels of such products.

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REFERENCES


An Unusual Cause of Colonic Obstruction

TO THE EDITOR: Medications with anticholinergic properties have long been recognized as having numerous side effects, including urinary retention, constipation, decreased secretion, and tachycardia (1, 2). The differential diagnosis of acute colonic obstruction has traditionally been relatively