CLINICAL VIGNETTE

A Popular Supplement Leads to Acute Liver Injury

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Abstract

We present a case of hepatocellular injury from a herbal supplement called kratom. This herbal supplement has been advertised for patients seeking relief from chronic pain and for those trying to avoid chronic opioid use. Due to the active ingredient, mitragynine, patients may experience both stimulant and sedative effects. There are multiple complications associated with this drug with 26 published case reports and 50 additional reports in other databases of liver injury. Unlike the majority cases derscribed in the literature, our case was not cholestatic in nature but rather hepatocellular. Our patient admitted to chronic use and recovered within days of stopping the supplement. There is currently no regulation for this product and although it has been banned in Southeast Asia, it is still available in the United States on the internet in unregulated doses.

Case Review

A 35-year-old Caucasian male with back pain on hydrocodone presented via televideo visit with recurrent episodes of diffuse abdominal pain and nausea during televisit appointment. Symptoms usually lasted 24 hours and occured intermittently about once a month, over the last few months. This episode's abdominal pain has lasted over 48 hours prompting evaluation. Usually symptoms were self-limited. Patient denied heartburn, dysphagia, odynophagia, or vomiting. There was no dark urine, light stool, or itching, nor changes in bowel movements, melena, rectal bleeding and no fever or chills. Presence of dizziness, seizures, loss of conciousness, and confusion was denied by his spouse.

Patient acknowledged social use of alcohol and did not use tobacco or IVDU use, or marijuana. His only medication was hydrocodone, and he denied new supplements.

PE: Vital signs were stable. Patient was alert, oriented without icterus. His abdomen was mildy obese, as seen on the monitor.

Abdominal ultrasound was normal. Laboratory work showed normal CBC, but AST 4200, ALT 6700, Tbili 1.9.

Additional testing was ordered with negative acute hepatitis A, B, C; no evidence of HSV, EBV. Negative ANA, normal ceruloplasmin, and iron studies. PT/INR was slightly prolonged at 15.5/1.6. Repeat labs 2 days later, showed normal INR, CBC and improvement of AST and ALT to 94/600 respectively. Resolution of symptoms also occured almost immediately.

Upon additional questioning the patient reported stopping all medications when he felt sick, except for occasionally use a supplement called Maeng Da. He failed to mention the supplement previously although he chronically used it to decrease hydrocodone use and to treat his back pain. He usually stopped the supplement when he was not feelling well. This supplement, contained kratom, however, the exact composition is unclear as supplements are not FDA regulated.

Discussion

Our patient developed drug induced liver injury due to a popular supplement, named kratom. Kratom is derived from Mitragyna speciosa, a tree in the coffee family indigenenous to Southeast Asia. It is also known as kratom tree, biak-biak, ketum, and Maeng Da, thom, mambog, ithang depending on the country of origin.[1] The main active component is mitragynine, which as a natural indole alkaloid, serves as an agonist of mu opiod receptors and has higher affinity and potency than morphine.[2] Similar to opiod drugs, it is used to relieve pain and has been used for withdrawal from heroine and morphine. This substance is unique in that it has dose dependent effects,with stimulant effects noted at lower concentrations and sedative effects at higher concentrations.[3]

In Western countries, herbal supplements containing this product are used for self management of chronic pain. The reported adverse effects include abdominal pain, itching, nausea, vomiting, mouth and throat numbness, seizures and coma.[4]

Retrospective review of the National Poison Data System of associated toxicities due to kratom, as well as records from the medical examiner's office noted that this supplement caused agitation, tachycardia, drowsiness, vomiting, confusion as well as hallucinations, seizures, withdrawal. In 2,300 patients, less than 3% kratom exposures reported respiratory, distress, coma and cardia arrest.[5]

In many Southeast Asian countries, planting, selling and buying of kratom is illegal. This product is banned in Australia. In USA, one can still buy online in the form of gum, leaves, tablets,capsules with no documented dose content. There is no safe dose established for this medicine.[4]

Persistent users develop tolerance and dependence, but withdrawal symptoms resolve within 1 to 3 days. Chronic use, mostly in Southeast Asian countries, is associated with weight loss, fatigue, hyperpigmentation, constipation as well as neurological symptoms of hand tremor, headache.[6]

Although it is unclear which subgroup of users is at higher risk for clinially apparent liver disease, most laboratory tests show mixed liver injury with liver biopsies showing predominantly cholestatic injury. Recent comprehensive literature review regarding kratom liver injury noted 26 case reports and abstracts. This study unlike prior case reports, used Roussel Uclaf Causality Assessment Method (RUCAM). Among the reviewed cases and biopsy findings, the most common presentations were abdominal pain as well as evidence of jaundice, pruritis and dark urine. Most of the cases were cholestatitic liver injuries, and only one other case had normal initial bilirubin which increased to 11.2 within 48 hours and with increased in INR. On day 5, this patient received a liver transplant with, ALT 6869 and AST >14000, whereas other cases AST and ALT remained between 200-300. Total Bilirubin varied from 2.3 to 30.9, with AST and ALT varying from 49 to >14,000. There was latency in presentation with mean of 21 days to symptom onset. No uniform data for the duration of use or the amount consumed was documented.[1]

Review of publications from Malaysia show that kratom users with >5 year of daily use with mitragyne content 76.3-114.8mg, show no difference in biochemic or hematological values compared with healthy controls.[7]

Our patient, like most of the patients, had vague symptoms at presentation and detection of elevated liver enzymes greater than 1000 enabled diagnosis of liver injury. This case reminds us that DILI and its subset, HILI – herb induced liver injury, need further investigation.

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