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SCIENTIFIC LETTERS

Red yeast rice extract: The risky trend of natural products

Extracto de arroz rojo: los riesgos de los productos naturales

Case description

A 40 year-old man was referred to the Hepatology outpatient clinic due to the detection of abnormal liver blood tests. He had a history of acute lymphoblastic leukemia requiring standard chemotherapy and an autologous stem-cell transplantation, achieving complete remission. He did not smoke, nor consume alcohol or any illicit drugs. He did not take any prescribed medication. Additionally, he did not report any liver disease, neither in his family. Previous laboratory tests throughout these years showed normal liver enzymes.

During a follow-up visit in December 2019 high cholesterol levels were detected, and the patient was told to start statins. However, he rejected the prescribed drug and decided to start over-the-counter red-yeast rice (RYR) 600 mg/day (Rice Plus Q10 Nadiu©, Spain). A month later, the patient developed progressive weakness and tiredness, which finally lead to a consult to the general physician. Physical examination was unremarkable. Laboratory tests revealed marked hypertransaminasemia with normal GGT, alkaline phosphatase, total bilirubin, prothrombin time and albumin (Table 1). Creatine kinase levels, renal function and complete blood count were within the normal range as well. A week later, laboratory tests showed further increase in the transaminases levels and the patient was instructed to stop RYR pills and transferred to our Liver Disease Clinics.

Laboratory work-up excluded acute viral hepatitis (HAV, HBV, HCV and HEV), auto-antibodies were negative and IgG levels were within the normal range. Abdominal ultrasound was unremarkable. CIOMS/RUCAM score for RYR was 8 points (probable), therefore, diagnosis of drug-induced liver injury (DILI) due to RYR was established.

Just a week after discontinuing RYR the patient referred improvement in his general condition and laboratory tests revealed a decrease of transaminases levels, which returned to normal levels 3 months later (Table 1).

Discussion

Herbal and dietary supplementation (HDS) are commonly used around the world, either in association or in substitution of prescribed drugs. Importantly, patients assume that these products are safe and their use is generally over-the-counter without any medical supervision. The increasing use of such products, the lack of rigorous surveillance in their preparation and marketing and the low awareness of their potential liver toxicity by physicians are relevant problems. Indeed, drug-induced liver injury (DILI) represents one of the most frequent causes of acute liver failure in Western countries,[1] and some studies have showed that almost 10% of all DILI-related acute liver failure are due to HDS.[2]

RYR is a traditional Chinese medicine used to improve digestion and also as a revitalizing agent. In addition, it has been shown to reduce cholesterol levels and thus, its use has been popularized in recent years as a natural way for treating hypercholesterolemia. RYR is produced by the fermentation of white rice by the yeast *Monascus purpureus*. Its active agent is monacolin K, a secondary metabolite with cholesterol-synthesis inhibiting properties because of its

Table 1 Evolution of liver enzymes.

	AST (*N* < 40 U/L)	ALT (*N* < 40 U/L)	AP (*N* < 116 U/L)	GGT (*N* < 40 U/L)	Bilirubin (*N* < 1.2 mg/dL)	Prothrombin time (*N* 80–100%)
19/06/2019	–	31	58	28	–	–
START RYR 19/12/2019						
11/02/2020	269	619	83	48	–	–
20/02/2020	345	805	71	63	0.7	100%
STOP RYR 20/02/2020						
26/02/2020	161	518	55	69	1.2	100%
19/05/2020	33	44	69	24	1	100%

identical chemical structure to lovastatin.[3] Thus, although RYR is claimed to be a safer alternative to regular statins, structural similarity with lovastatin implies that similar adverse reactions can be expected. Furthermore, monacolin content is not standardized among marketed products and are generally not depicted on labels.[4] Indeed, a study assessing monacolin content in 12 commercial RYR formulations labeled as ''600 mg/capsule of active product'' found marked variability, ranging from 0.10 to 10.09 mg of monacolin per capsule, challenging the efficacy and safety of the product.[5] In our case, the label stated that monacolin K content was at least 10 mg per capsule.

The U.S. Food and Drug Administration (FDA) has ruled that RYR with more than trace amounts of monacolin K cannot be sold as dietary supplements, which is not the case of the European Food Safety Authority (EFSA).

There are isolated case-reports of over-the-counter RYR hepatotoxicity, all of them are mild-to-moderate in severity and self-limited in course, which are consistent with the one presented in this report. For this reason, taking into account that HDS are easy-to-obtain products, considered safe for most people, contain multiple active ingredients in poorly specified amounts and with incomplete labeling, safety can very well be compromised. Therefore, physicians must remain alert that HDS might be the cause of acute liver injury in some patients.

Conflict of interest

XF has acted as advisor for Abbvie and Gilead. GS has nothing to report.

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Surgery and emergency gastrointestinal endoscopy during the Covid-19 pandemic

Cirugía y endoscopia gastrointestinal de emergencia durante la pandemia de Covid-19

Urgent gastrointestinal endoscopy (UGE) is a worldwide extended medical procedure, being the most frequent the upper and lower gastrointestinal bleeding and impaction of a foreign body the most common emergencies that require this technique.[1,2] The activity in endoscopy units has been deeply affected by Covid-19 pandemic. In order to decrease the risk of infection, elective endoscopy has been stopped since ''State of Alarm'' was declared. However this restriction does not apply to UGE.

We analyzed the UGEs that have been performed from March 1st 2020 to April 30th 2020 and compared with those performed during the same period in the previous year (2019; pre-Covid period).

The UGE is usually performed in our hospital (Donostia University Hospital) from Monday to Friday between 3 p.m and 8 p.m and saturday/sunday during all the day. UGE are usually requested by the Emergency Department and less frequently from hospitalization rooms or intensive care unit. Regarding our protocol, we routinely perform the UGE within the 12h after admission to patients with gastrointestinal bleeding and within 6 h to those with impaction of foreign bodies.

In total 126 UGE were included of which 107 (85%) were upper endoscopy. Upper bleeding was the most common clinical indication in 56 patients (44%), while impaction of a foreign body was the second most common reason for indication reported in 47 cases (37%) (Table 1). On the other hand, lower gastrointestinal bleeding was the main indication for urgent colonoscopy, performed in 11 (9%) cases, followed by 6 patients (5%) who needed stenting due to colonic obstruction related with colorectal cancer. Sixty-four procedures (51%) were performed either in Saturday or Sunday (Table 1).

Comparing the two periods, a reduction of 44% in UGE procedures was observed in the Covid period (45 Covid period vs. 81 pre-Covid). In addition, upper endoscopy was significantly more common in proportion than colonoscopy in the Covid period, 89% (40/45) vs. 83% (67/81). The number of UGE by upper gastrointestinal bleeding fell from 33 patients in the pre-Covid period to 23 patients in the Covid period, therefore constituting a reduction in 30%. In impaction of foreign bodies, a 58% decrease was observed: from 33 in the pre-Covid period to 14 during the pandemics. The percentage of emergency endoscopies that required some therapeutic procedure went from 47% (40/85) in the pre-Covid period to 47% (21/45) in the Covid period (Table 1). The number of colonoscopies needed for colonic stents in obstructive colorectal cancer decreased by half during the Covid period. It is to be noted that the decrease in the num-