Acute liver injury with special clinical phenotype after use of herbal Runzaozhiyang capsules

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Running Head: Liver injury caused by Runzaozhiyang capsules

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Introduction

Runzaozhiyang capsules (RZZYC) are commonly used over-the-counter Chinese patent medicines containing *Polygonum multiflorum* (PM), which have been approved for the urticaria. RZZYC are generally well tolerated and, liver injury associated with its use has not been previously described. A 25-year-old female patient was initially referred to our service due to urticaria, and she was started on levocetirizine (LCZ) oral solution, compound glycyrrhizin (CG) and RZZYC. Hepatic enzymes were normal at that time and there was no prior history of hepatic disease. At two weeks, she had jaundice, generalized rash, pruritus and fatigue. Laboratory investigation revealed aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin (T-BILI) and bile acid (BA) were increased to 46 U/L, 80 U/L, 10.12 mg/dL and 197.9 μmol/L, respectively. Hepatitis A, B, and C, CMV, EBV and HSV serologies were all negative. Serum anti-mitochondrial antibody, anti-smooth muscle antibody, anti-nuclear antibody, antidsDNA antibody, anti-neutrophil cytoplasm antibody and anti-liver kidney microsome antibody were all negative. Serum ceruloplasmin, laminin, hyaluronic acid and collagen type IV concentrations were within normal limits. Ferritin, complement C3 and C4 concentrations slightly exceeded normal concentrations. An abdominal CT and cardiac uhrasonography were unremarkable. RZZYC was discontinued on the first day on admission, her rash and pruritus improved and serum transaminase was normalized after one week of treatment. Her bilirubin recovered slowly and jaundice was still apparent, and BA was higher than that on the first day of admission. She was started on dexamethasone (10 mg, qd) from day 9 to 10, and dexamethasone was subsequent tapered over the course of her hospital stay as her clinical condition was improved and she was discharged on day 20. A liver biopsy was performed on day 16, which revealed cholestasis with mild hepatic cell watery degeneration and mild portal inflammation. (Figure 1). She continued on outpatient medications, after four-month follow-up, all liver tests were returned to normal (Table 1). She restarted LCZ oral solution and had normal serum transaminase and bilirubin through six months of follow-up.

Discussion

Based on the patient's medication history, RZZYC-induced liver injury was considered, which belonged to

the category of herb-induced liver injury (HILI) [1]. Laboratory tests fail to meet diagnostic criteria for HILI in our patient, though liver biopsy suggested that the clinical presentations of liver injury is cholestatic injury. The reported special clinical types that could not be confirmed by liver function index were excluded [2]. The reason for the special clinical phenotype may be related to the improvement of liver function index by CG [3], and the genetic differences of body factors, especially immune-related factors. In the presence of liver protectors, RZZYC still caused severe liver damage, suggesting that RZZYC has a strong ability to damage liver. We were unable to locate articles and clinical etiology attributing acute liver injury to RZZYC. The underlying mechanisms of RZZYC-associated acute liver injury with special clinical phenotype are unknown.

Controversial glucocorticoid treatment is empirically used by clinicians to treat hepatic injury, but it has not demonstrated benefits in survival in patients with specific clinical types of drug-induced liver injury [4,5], and it can also increase mortality in patients with poor liver function [6]. Our case showed that glucocorticoid therapy was effective for acute liver injury with special clinical phenotype, but there is still a lack of randomized controlled studies of glucocorticoid therapy in liver injury[6]. Glucocorticoids are not recommended for the treatment of hepatic injury in the absence of clear clinical indications.

Conflict of interest

No potential conflict of interest was reported by the author(s).

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

1. Wang, J B, Zhu Y, Bai Z F et al. Guidelines for the Diagnosis and Management of Herb-Induced Liver Injury. Chinese Journal of Integrative Medicine, 2018, 24(09):58-68.
2. European Association for the Study of the Liver. EASL clinical practice guidelines: drug–induced liver injury. J Hepatol, 2019, 70(6): 1222–1261
3. Karkhanis J, Verna E C, Chang M S, et al. Steroid use in acute liver failure. Hepatology, 2014, 59(2): 612-621.
4. Liang SB, Hou WB, Zheng RX, Liang CH, et al. Compound glycyrrhizin injection for improving liver function in children with acute icteric hepatitis: A systematic review and meta-analysis. Integr Med Res 2022 Mar;11(1):100772.
5. Peeraphatdit T B, Wang J, Odenwald M A, et al. Hepatotoxicity From Immune Checkpoint Inhibitors: A Systematic Review and Management Recommendation. Hepatology, 2020, 72(1): 315-329.
6. Bonkovsky H L, Kleiner D E, Gu J, et al. Clinical presentations and outcomes of bile duct loss caused by drugs and herbal and dietary supplements. Hepatology, 2017, 65(4): 1267-1277.

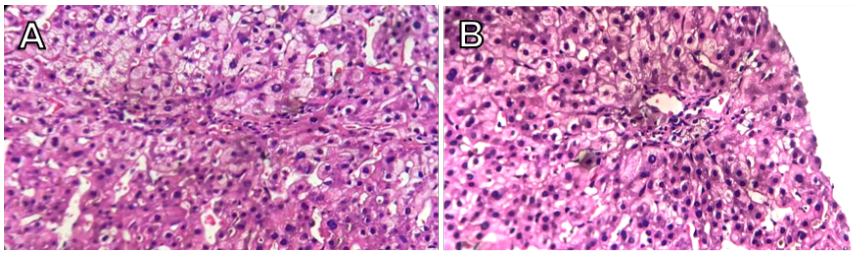

Figure 1. Liver biopsy tissue after hormone therapy on day 16 (H&E, ×200) show that mild watery degeneration of hepatocytes with hepatic cord disorder and cholestasis (A), and portal area is infiltrated with a few scattered lymphocytes (B).

	Day1	Day2	Day7	Day12	Day17	Day25	Day31	Day39	Day51	Day79	Day96	Normal
T-BILI (mg/dL)	10.18	8.09	7.21	6.32	4.61	3.46	2.58	1.93	1.15	1.69	1.00	0.1-1
AST (U/L)	46	33	26	21	20	24	29	19	15	27	11	13-40
ALT (U/L)	80	63	33	28	29	34	44	31	14	18	9	7-45
BA (μmol/L)	197.9	168.2	200.6	120.7	22.6	16.4	9.1	7.5	6.7	7.6	3.1	0-20
GGT (U/L)	22	19	13	15	16	21	19	14	14	35	24	7-45
ALP (U/L)	123	112	95	89	80	64	87	62	65	60	49	35-135

Table 1. Changes in laboratory parameters over time