



Brief Report

Drug reaction with eosinophilia and systemic symptoms syndrome secondary to Chinese oral herbal paste: a case report

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Introduction

Herbal and dietary supplements (HDS)-induced liver injury has garnered interest in recent years for the increasing trend worldwide [1]. Chinese oral herbal paste, a popular herbal formula to enhance immunity as HDS in a Chinese medicine clinic, has been less reported to induce liver injury. Here we reported a case of drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome with abrupt transaminitis, which was caused by daily consumption of herbal formulas for 4 weeks.

Case report

A 54-year-old man presented to our hospital with a 20-day history of liver injury (Supplementary Figure 1). He reported a recent history of HDS use, taking Chinese oral herbal paste (Supplementary Table 1) to strengthen his immune system 2 months prior to this admission. One month after starting the oral herbal paste, he developed a fever of 39.3°C and a rash that was particularly noticeable on his back and hips. Intravenous dexamethasone 5 mg daily for three times and oral levofloxacin were prescribed by a community health center and the herbal paste was withheld. His fever and cutaneous symptoms gradually disappeared within a few days, although he developed severely multiple arthralgia, which led him to a local hospital for help. An acute liver dysfunction was accidentally discovered on 6 January 2021 when the levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were markedly elevated at 560 and 1,440 U/L, respectively. Laboratory investigations showed leukocytosis of $14.98 \times 10^9/L$ with eosinophilia of $2.04 \times 10^9/L$, a C-reactive protein level of 61.18 mg/L, and a fasting plasma glucose level of 10.10 mmol/L, but no evidence of jaundice and coagulopathy. He underwent an 8-day treatment consisting of piperacillin, reduced glutathione, etoricoxib, and dapagliflozin, which resulted in remission of his symptoms, including arthralgia, transaminitis (ALT, 620 U/L; AST, 211 U/L), and glycemia (fasting plasma glucose 7.3 mmol/L). He was

admitted to our Hepatology Unit for transaminitis (ALT, 246 U/L; AST, 130 U/L) 10 days later.

During hospitalization, he experienced mild pain in both knees and a recurring rash on the neck, which were treated effectively using topical diclofenac and steroids, respectively. Except for an erythematous eruption that appeared on the anterior neck region on the fifth day, other physical examination findings were normal. The ultrasonography showed the present of multiple enlarged lymph nodes in the cervical, axillary, and inguinal regions, with a maximum long-axis diameter measuring 12 mm. Abdominal magnetic resonance imaging did not demonstrate any signs of chronic liver disease. The main laboratory results are shown in Figure 1. Fasting plasma glucose ranged from 6.06 to 7.39 mmol/L. The levels of creatinine, electrolytes, and immunoglobulin including IgG, IgA, IgM, and IgE were within the normal range. No active infection was detected for hepatitis viruses, cytomegalovirus, or Epstein-Barr virus. Competing causes of liver disease were further excluded by negative antinuclear antibodies, normal levels of ceruloplasmin, and ferritin and its saturation.

The patient had a medical history of essential hypertension and had been on amlodipine besylate and atorvastatin calcium treatment for 3 years. He consumed 12 drinks of wine weekly with no other social- or family-related history.

Based on the findings above, the patient was diagnosed with DRESS syndrome according to the European Registry of Severe Cutaneous Adverse Reactions (RegiSCAR) criteria (scored 9 points) [2]. The herbal paste was further considered the "probable" culprit agent as evidenced by the adverse drug reaction probability scale of Naranjo (scored 5 points) [3].

We provided the patient with supportive care, including glycyrrhizic acid, dietary education for glycemia, etc., which resolved the aforementioned laboratory abnormalities and gradually brought about a near-complete recovery.

After 1 year, a health check showed no indications of liver injury, eosinophilia, glycemia, or superficial lymphadenopathy. The patient reported no recurrence of fever and rash in the entire follow-up.

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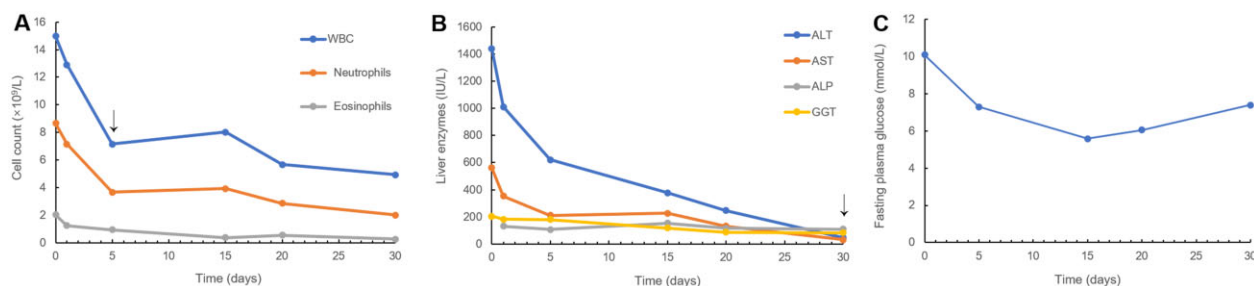


Figure 1. Changes in granulocytes, liver enzymes, and fasting plasma glucose. (A) Changes in absolute WBC, neutrophils, and eosinophils. (B) Changes in liver enzymes. (C) Changes in fasting plasma glucose. Day 0 designates the date when the transaminitis was noticed. The downward arrow denotes the date on which the granulocytes (A) and liver enzymes (B) returned to the normal range. WBC, white blood cells; ALT, alanine aminotransferase; AST, aspartate aminotransferase; GGT, glutamyl transpeptidase; ALP, alkaline phosphatase.

Discussion

DRESS syndrome is a severe, multi-organic and potentially life-threatening drug-induced hypersensitivity reaction that typically develops within 2–6 weeks of exposure to several common drugs such as clozapine, yet is less recognizable in daily practice considering the protean clinical manifestations [4, 5]. To date, few cases of DRESS syndrome caused by HDS, especially oral Chinese herbal paste, have ever been reported [4].

Here we provided a vignette of HDS-induced liver injury with DRESS syndrome, presenting with fever and rash. Additional to the typical presentation of DRESS syndrome, hyperglycemia occurred to our patient. A transit immune-based involvement of the pancreas would be the most likely explanation for the infrequent complication of this entity [6].

The initial signs and symptoms of DRESS syndrome have usually been mistaken as infection. Just like our case, ~4 weeks' delay of diagnosis was seen regretfully. But fortunately, the Chinese herbal paste was immediately withdrawn in the community health center since adverse drug reactions were suspected. The following dexamethasone therapy altogether resulted in an overall benign outcome, although the patient somehow experienced a transit relapse of rash and a liver injury lingering for 1 month, as suggested by the comprehensive review [7]. As a matter of fact, it is a pity for the current report that we missed the opportunity to take pictures and biopsies of the skin lesions.

The practical significance of the present case is that oral Chinese herbal paste, as a special type of HDS, has the potential risk to induce DRESS syndrome. In patients with herb-induced liver injury who present with fever, rash, and eosinophilia, it is important to consider the possibility of a multisystem disorder and a detailed screening for other organ disorders is suggested. Hepatologists should be aware of this possibility and a judgment can be made based on RegiSCAR criteria. Given the traditional culture of strengthening the immune system by taking Chinese oral herbal paste as HDS in winter and the perception of its safety among the masses, this rare but severe adverse effect has to be noticed. In future studies, it is important to investigate the incidence and risk factors of this injury, identify the specific causative chemical in the herbal formula, and elucidate its underlying mechanisms.

Supplementary Data

Supplementary data are available at *Gastroenterology Report* online.

Authors' Contributions

W.J. and Y.X. were involved in caring for the patient and writing, reviewing, and revising the manuscript. Written consent for publication was obtained from the patient.

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Not applicable.

Conflict of Interest

None declared.

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