Case Report

Fatal Fulminant Hepatitis Associated with *Ganoderma lucidum* (Lingzhi) Mushroom Powder

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Hepatotoxic effect related to Ganoderma lucidum (Lingzhi) mushroom powder was first described in a patient from Hong Kong in 2004. In 2005, the authors experienced a case of fatal fulminant hepatitis associated with such a preparation. Both patients had taken other therapeutic agents and traditionally boiled Lingzhi without any toxic effect. After switching to taking Lingzhi in powder form for 1-2 months, the hepatotoxic episode occurred in both patients. The toxic role of Lingzhi powder needs close monitoring in the future, especially in combination with other drugs.

Keywords: *Toxic hepatitis, Ganoderma lucidum, Lingzhi powder*

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During the last decade, the use of traditional or herbal medicines has expanded globally because of an increased in popularity within the industrialized society. This society is choosing complementary medicines as health supplements or alternative medicines as remedies for various conditions[1,2]. The hepatotoxicity by these agents has been closely monitored in some particular industrialized countries. No toxic effect from Lingzhi, a Chinese herbal medicine, has been recognized[1,2]. The first case of hepatotoxicity by Lingzhi in powder preparation was reported from Hong Kong[3] in 2004. The patient was a 78-year-old Chinese lady having hypertension treated by felopidine for two years. She used to have regular intakes of traditionally boiled Lingzhi slices for at least one year as a health supplement and changed the agent to powder form for one month before having the hepatotoxic episode. In 2005, the authors experienced a case of fatal toxic hepatitis associated with Lingzhi powder as reported in this communication.

Case Report

The patient was a 47-year-old female with a history of schizophrenia on treatment with lithium, perphenazine, and trihexyphenidil long-term. She took traditionally boiled Lingzhi slices for several years without any untoward effect. She changed to taking Lingzhi powder, one capsule containing 400 mg of Lingzhi extract per day, for two months before having the episode of jaundice and coma due to fulminant hepatitis.

Her previous liver biochemical profiles were within normal limits. On admission, the biochemical profiles included albumin 30.4 g/l (normal 43.1-53.3), total bilirubin 690.3 mmoles/l (normal 0-17.1), direct bilirubin 504.9 mmoles/ l (normal 0-5), alkaline phosphatase 132 U/l (normal 50-136), gamma glutamyltranspeptidase 59 U/l (normal 5-55), aspartate aminotransferase 280 U/l (normal 15-37), alanine aminotransferase 276 U/l (normal 30-65) and prothrombin time 55.3 seconds (normal 10-13), international normalized ratio (INR) 4.66 (normal 0.85-1.10). The serological tests for anti HAV IgM, anti-HBcIgM and anti-HCV were negative. Acute hepatic failure was considered. N-acetyl cysteine 100 mg/kg/day with lactulose was given. Endotracheal intubation with mechanical ventilator and gastric intubation were performed. Antibiotic prophylaxis with third generation cephalosporin (Cefotaxime) was prescribed. Fresh frozen plasma and

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vitamin K were given to correct coagulopathy.

Her consciousness became progressively deteriorated. The blood levels of lithium, acetaminophen, and perphenazine were below the toxic levels. Liver transplantation was considered. On day 4 of admission she developed localized seizures controlled by diphenylhydantoin and diazepam. On day 5 the blood culture grew out *Klebsiella pneumoniae*. She expired on day 6 with the prothrombin time being 82.5 seconds (INR 6.91).

The autopsy revealed a shrunken liver of 600 g in weight. Microscopically, there were extensive zonal liver-cell necroses involving more than 70 percent of the parenchymal cells. Many hepatic lobules showed centrilobular necrosis (acinar zone 3 necrosis) extending to the middle zone (acinar zone 2). Some lobules revealed panlobular necrosis (Fig. 1). The absence of lymphocyte infiltration in portal tracts was not in favor of neither acute nor chronic viral hepatitis due to any hepatitis virus[4]. The bile-ductular reaction secondary to panlobular necrosis[5] was prominent in some lobules (Fig. 1). The pathological features were interpreted as toxic or drug-induced hepatitis causing acute hepatic failure[6].

Discussion

To the authors' knowledge, the hepatotoxicity by traditionally boiled Lingzhi slices has never been reported in the English literature. Hepatotoxicity due to the powder form has only been described very recently[3]. Of all the psychotropic agents administered to the patient, only perphenazine can induce cholestasis but not extensive zonal necrosis in the liver[6].

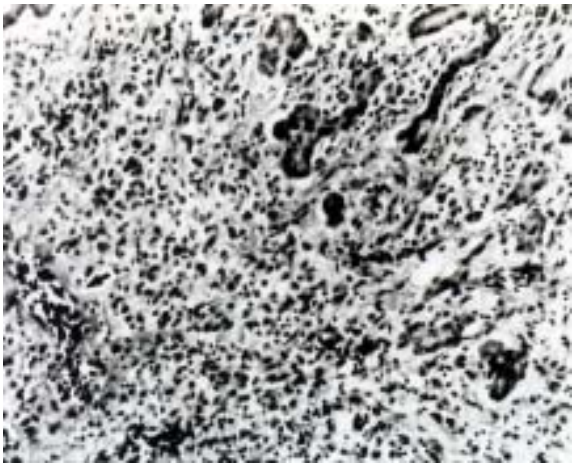

Fig. 1 Bile-ductular reaction in the right upper quadrant. The remaining area of photograph shows panlobular necrosis of the liver cells in the lobule with central vein marked by the arrow. Hematoxylin and eosin staining. X 150

In a controlled human supplement study, four capsules of Lingzhi powder (totally 1.44 g of Lingzhi extract) per day were given to a group of volunteers for one month without any hepatotoxic effect or drug accumulation[7]. The cumulative dosage is unlikely to be a risk factor in hepatotoxicity by the agent in the presented case with the patient taking only 400 mg per day. The induction of cytochrome P 450 enzymes by other therapeutic agent(s) in the previous and present cases may synergistically enhance the production of toxic metabolite derived from Lingzhi powder[1]. The possibility of adverse or idiosyncratic reaction by the individual to the agent cannot be ruled out. The early symptoms of hepatitis may not be detected due to the difficulty in verbal communication with the psychotic patient. The prolonged intake of the agent may lead to repetitive injuries of liver cells followed by extensive zonal necrosis. The hepatotoxic role of Lingzhi powder needs close monitoring in the future since the preparation in powder form is getting an increasing popularity due to the convenience in consumption without any tedious prolonged boiling.

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ตับอักเสบรุนแรงถึงตายอันอาจมีสาเหตุมาจากเห็ดหลินจือผง *(Ganoderma lucidum)*

หริรักษ์ วานม่วง, ยุวดี เลี่ยวไพรัตน์, โฉมศรี โฆษิตไชยวัติ, วินัย วนานุกูล, สุขุม บุณยะรัตเวช

ตับอักเสบร่วมกับการใช้เห็ดหลินจือผงได้ถูกรายงานเป็นครั้งแรกในปี พ.ศ. 2547 จากฮ่องกง ในปี พ.ศ. 2548 ผู้นิพนธ์ได้พบผู้ป่วยหนึ่งรายที่มีตับอักเสบรุนแรงถึงตายจากการบริโภคเห็ดหลินจือผง ผู้ป่วยทั้งสองรายเคยได้รับยาอื่นเพื่อการรักษาโรคร่วมกับการบริโภคเห็ดหลินจือตุ๋นด้วยไฟอ่อนโดยไม่มีอาการเป็นพิษ หลังจากเปลี่ยนเป็นการบริโภคเห็ดหลินจือผงเป็นเวลา 1-2 เดือนผู้ป่วยทั้งสองเกิดอาการตับอักเสบ การเกิดพิษต่อตับโดยเห็ดหลินจือผงสมควรได้รับการเฝ้าระวังอย่างใกล้ชิดในอนาคต โดยเฉพาะในการเกิดร่วมกับยารักษาโรคอื่น ๆ
