A CASE OF VENOPLANT®-INDUCED HEPATIC INJURY

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Summary

The first case of hepatic injury induced by Venoplant®, extracts of Aesculus Hippocastanum, having anti-inflammatory activities, was described. A 37 yr-old man was admitted for treatment of pathological fracture of the left brachial bone. He had been received 65 mg Venoplant® at another hospital several hours before admission. 17 days later, a liver function test showed mild abnormality and 60 days after injection, he complained of pruritus and jaundice. Laboratory studies revealed moderate elevation of total bilirubin, ALP, γ-GTP and mild eosinophilia. CT studies and ERC showed no signs of extrahepatic obstructive jaundice. The lymphocyte stimulation test was positive. The liver biopsy demonstrated marked cholestasis with zonal necrosis in the centrilobular areas but showed little or no changes in the portal tracts. These features are consistent with drug-induced hepatic injury.

Key Words: Venoplant®, Drug-induced hepatic injury.

Introduction

Venoplant®, extracts of Aesculus Hippocastanum, has been used in the treatment of peripheral circulatory disorders in Europe1), and since 1967, it has been used as an antiinflammatory drug after surgery or trauma in Japan2,3). In this study we describe the first documented case of Venoplant®-induced hepatic injury.

Received 00, 1985. Accepted 00, 1985.
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The authors are very grateful to Professor Toshihiko Namihisa in Tokyo who kindly provided us much information concerning the side effects of Venoplant®.

Case Report

A 37 yr-old man was admitted to the orthopedic service of Takaoka City Hospital on Dec. 26, 1983, because of pathological fracture of the left brachial bone. Several hours before admission, he received an i.m. injection of 65 mg Venoplant® at another hospital, and liver function tests were normal at the time of his admission to our institution. He received no other medication until January 12, 1984, when liver function tests showed mild abnormality including an elevation of serum ALP and γ-GTP levels. An orthopedician made a diagnosis of giant cell tumor of bone (grade 2) by bone biopsy, and treated by curettage and bone allograft on January 20, 1984.
On Feb. 14, 1984, the patient was admitted to our service because of pruritus and jaundice. There was no history of atopy, jaundice, exposure to hepatitis, blood transfusion or excessive alcohol. There was no family history of hepatic diseases. On physical examination, he was well nourished and afebrile. Mild scleral icterus was present and no skin rash, lymphadenopathy or hepatosplenomegaly were noted. Examinations of the chest and neuromuscular system were normal. On his admission to our clinic, laboratory studies revealed the following values: hemoglobin, 13.2 g/dl; hematocrit, 40%; white blood cell count 6000/mm³, with 8% eosinophils; blood platelets 26 × 10⁴/mm³; total bilirubin, 2.9 mg/dl, and direct 1.1 mg/dl; SGOT, 19 IU/l; SGPT, 31 IU/l; ALP, 649 IU/l (normal <280); y-GTP, 155 IU/l (normal <20); total cholesterol, 230 mg/dl; total protein, 6.6 g/dl, and albumin and -globulin, 3.8 and 0.9 g/dl, respectively. Prothrombin time was 12.8 seconds (control <13.5). HBs-antigens, and anti-HBs and HA antibodies, as determined by radioimmunoassay, were negative.

Hepatic scintiscan showed hepatosplenomegaly (Fig. 1). Computed tomography suggested no evidence of intrahepatic tumor or dilatation of the intrahepatic bile ducts (Fig. 2). A endoscopic retrograde cholangiography (ERC) showed no abnormality of the bile ducts or gallbladder (Fig. 3). Two months later, the lymphocyte transformation test was positive (lymphocyte stimulation index; 290%) when Venoplant® was added to the culture medium of the peripheral mononuclear cells.

A needle biopsy of the liver, performed on May 7, 1984, showed marked intrahepatic cholestasis with zonal necrosis in the centrilobular area and several focal liver cell damages with mobilization of Kupffer cells in each lobule (Fig. 4). Portal tracts did not show significant changes except minimal inflammatory cell infiltration. Bile duct damage was not seen. These features were consistent with a diagnosis of drug-induced hepatic injury.

In spite of supportive care, such as bed rest, high-protein diet and vitamin supplement, total bilirubin gradually increased in value and reached a maximum level of 9.0 mg/dl on the 73rd day after admission (Fig. 5). From May 7, 1984, he was started on prednisolone 40 mg/day, tapering down over several weeks. Six months after admission, as he was feeling well and total bilirubin had decreased to 2.2 mg/dl, he was discharged. There has not been a recurrence of the giant cell tumor of bone.