Drug-induced Hepatitis due to Repeated Use of Hair Dye

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Abstract

A 27-year-old Japanese man with no past history of liver disease was admitted to our hospital due to liver abnormalities. The patient was diagnosed with drug-induced hepatitis, as the three episodes of hepatitis occurred just after repeated use of hair dye. After cessation of the hair dye use, abnormal liver function tests improved to within the normal range. Although hair dyes contain various hepatotoxic compounds, hair dye is not known to cause drug-induced hepatitis. Thus, in cases of liver abnormality of unknown origin, the history of hair dye use should be investigated.

(Key words: hair dye, drug-induced hepatitis, acute hepatitis

Introduction

While various drugs can cause hepatotoxicity, identification of the causative drug can sometimes be difficult (1, 2). Recently, Chinese herbal medicines and dietary supplements have been found to contain hepatotoxic agents (3–6). However, to date, there have been no reported cases of drug-induced hepatitis due to hair dye. In this report, we describe a patient with drug-induced hepatitis due to repeated hair dye use.

Case Report

A previously healthy 27-year-old Japanese male was admitted to a local hospital due to general fatigue in June 2001. Laboratory data on admission showed liver abnormalities. White blood cell count was 4,700/mm³, aspartate aminotransferase (AST) was 951 IU/l, while alanine aminotransferase (ALT) was 307 IU/l. The patient had no family history of liver disease and denied exposure to hepatitis, mononucleosis, or blood transfusions. He had no history of taking drugs, Chinese herbal medicines, or dietary supplements, and showed no evidence of alcohol abuse, consumption of acetaminophen, or food allergies during the preceding months. On admission, the patient had no fever, anemia, jaundice, or skin rash.

Laboratory tests showed a total white blood cell count of 1,700/mm³, which while relatively low, was without abnormal differentiation or atypical lymphocytes (neutrophil 61.0%, lymphocyte 31.0%, monocyte 8.0%, basophil 0.0%, eosinophil 0.0%). The red blood cell count was 439x10⁶/mm³, the hemoglobin level was 15.8 g/dl, hematocrit was 44.6%, the platelet count was 17.9x10⁵/mm³. Serum total bilirubin was 0.8 mg/dl, AST 112 IU/l (normal <37), ALT 547 IU/l (normal <49), alkaline phosphatase (ALP) 110 IU/l (normal <147), gamma-glutamyl transpeptidase (GGT) 131 IU/l (normal <71), and leucine aminopeptidase (LAP) 126

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Figure 1. The first liver biopsy showed condensation of the reticulin fibers and a variation in nuclei size predominantly in zone 3 (Silver stain, ×200).

IU/l (normal <71). Serology was negative for IgM anti-hepatitis A virus antibody, hepatitis B surface antigen (HBsAg), IgG anti-hepatitis B core antibody (anti-HBc), IgM anti-HBc, and anti-hepatitis C virus antibody. While the patient was positive for herpes simplex virus (HSV) IgG, cytomegalovirus (CMV) IgG, and Epstein-Barr virus (EBV) IgG antibodies, herpes virus-6 (HHV-6) IgG was negative. HBV DNA, HCV RNA, TT virus (TTV) DNA and hepatitis G virus (HGV) RNA were negative in serum by polymerase chain reaction. Copper, iron and porphyrin studies were negative, serum immunoglobulins were normal, and antinuclear antibody (ANA), anti-smooth muscle antibody (ASMA), and anti-mitochondrial antibody (AMA) were negative. Fecal parasite eggs were absent and antibodies for parasites in serum were negative.

Ultrasonography and computed tomography (CT) of the abdomen revealed no significant changes. Drip infusion cholangiography (DIC)-CT and magnetic resonance cholangiopancreatography (MRCP) revealed no abnormalities of the common bile duct, gall bladder or intrahepatic ducts.

The drug-induced hepatitis was considered due to the coincidence of repeated hair dye use and episodes of hepatitis. Histopathology on a third liver biopsy was performed on March 2002 and showed condensation of the reticulin fibers, variable nuclei size, and degeneration of hepatocytes in the centrilobular area, but with well-preserved hepatocyte arrangement. While a mild mononuclear cell infiltrate was present in the lobular parenchyma and portal tracts, there was no fibrotic expansion in the portal tracts (Fig. 3).

Lymphocyte stimulation tests with and without a test drug were performed, with the data expressed as a stimulation index (SI) of cpm of cultures containing the drug to cpm of cultures without the drug. A SI of 180% was considered to represent a positive response. Hair dye gave a positive response with a SI of 187%. On the basis of these results, the patient was diagnosed as having drug-induced hepatitis due to hair dye use. Cessation of hair dye use led to improvement of the liver abnormalities, and the patient has now had normal liver tests for 5 months (Fig. 2).

Discussion

Hair dye is a commonly used cosmetic treatment and is well recognized to cause contact dermatitis (7, 8). While rhabdomyolysis (9) and anaphylactic shock (10) have been reported as rare adverse reactions, hair dye has been overlooked as a cause of liver abnormalities, with no reported cases until the present report. The patient had used hair dye
over a prolonged period of time but had no recognized risk factors for liver disease, and was negative for liver disease-associated viral markers and autoantibodies. While liver function tests were markedly elevated, values returned to normal after cessation of hair dye use.

Hair dye consists of various components, including a base, surface-active agent, antiseptic and emulsifier. Some of these compounds may exhibit hepatotoxicity, hematotoxicity, cardiotoxicity, renal toxicity, or carcinogenicity. In the present case, the hair dye contained the hepatotoxic agents PEG, PG, and p-hydroxy benzoic acid ester. Recent study has demonstrated that hair dye use is not a risk of hematopoietic neoplasm (11, 12). However, our case revealed leukocytopenia, which may be associated with hematotoxicity due to hair dye. It is necessary to follow the patient to confirm whether leukocytopenia will recover or not.

These compounds can be absorbed into the body through a wound or damaged skin, or via the airways by spray aspiration during dyeing. As the patient appeared not to have broken skin when he used the hair dye, it is probable that the agents were absorbed by aspiration.

Hair dye is an uncommon cause of hepatotoxicity. Although a re-challenge test was not considered dangerous due to the high risk of fulminant hepatic failure and shock, an accidental re-challenge test was in effect performed due to the patient’s unawareness of the positive hepatotoxicity test. Along with the lymphocyte stimulation test performed using the hair dye, this result supported the diagnosis of drug-induced hepatitis. This chronological course and laboratory tests predicted that the mechanism of hepatotoxicity was an allergic reaction.

The clinical diagnosis of drug-induced hepatitis commonly uses two scales: Criteria of the Council for International Organizations of Medical Sciences (CIOMS) (13–15) and a scale reported by Maria and Victorino (16). These criteria were applicable to the present case, with the CIOMS criteria classifying our case as “likely” and the Maria and Victorino criteria as “possible” with a score of 12. Both sets of criteria made a point of chronological change. As the latter criteria requires a previous report of the causative drug in the literature, our patient received a relatively light score as the present paper represents the first case report of hair dye as a hepatotoxin (17, 18).

In conclusion, the present patient showed that hair dye could act as the causative agent in drug-induced hepatitis. Early identification of the hepatotoxic agent is such cases is important as removing exposure to the causative drug can lead to a rapid recovery. In cases where the cause of the liver abnormality is unknown, hair dye should be recognized as a possible source of hepatotoxin to avert diagnostic errors.

References