Case Report

A Case Report of Ivermectin-Induced Prolonged Liver Dysfunction in an Elderly Patient with Scabies

Mikako HIROTA[*1,*2], Tosifusa TODA[*2], Hiraku MORISAWA[*2] and Satoru MINESHITA[*3]

[*1] Faculty of Pharmaceutical Sciences, Teikyo Heisei University, Chiba, Japan
[*2] Research Team for Mechanism of Aging, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan
[*3] Department of Medicine, Funado Hospital, Tokyo, Japan

Among 30 elderly patients who received ivermectin for the treatment of scabies, we observed a case of possible ivermectin-induced liver dysfunction in an 85 year-old patient. He developed liver dysfunction after the second dose of the drug. While elevated serum ALT and AST subsided to normal levels 2 months after discontinuation of the drug, increased serum ALP and γ-GPT persisted. Ivermectin was effective in all patients for the eradication of scabies.

Key words : scabies, ivermectin, liver dysfunction, geriatric patients

Introduction

Approximately 300 million people worldwide are considered affected by infestation of the ectoparasite *Sarcoptes scabiei* var. *hominis* (*Sarcoptes scabiei*). Particularly immunologically compromised hosts are prone to suffer from profound infestation with the scabies mites and develop severe discomforts due to intense itching, hyperkeratosis and skin crusting[1,2]. Recent studies of scabies are mainly from India, Iraq, Brazil and other developing countries[3,4], and reports from Japan are very scarce. At present oral administration of ivermectin is recommended for the treatment of scabies. In contrast to the general belief that ivermectin is safe based upon the 10-year experience with the treatment of onchocerciasis[6], here we report an elderly patient who developed prolonged liver dysfunction after administration of a standard dose of ivermectin for the treatment of scabies.

Clinical course of patients receiving ivermectin for the treatment of scabies

We have treated a series of 30 elderly patients with scabies (15 males, mean age 76 [range, 50-96] years ; and 15 females, mean age 82 [range, 70-93] years by a single oral administration of ivermectin (Stromectol®) at a dose of 0.2 mg/kg body weight. In all patients ivermectin was effective in eradicating mites and alleviating clinical symptoms. No scabies mites were observed in scrapings taken from the patients' skin specimens at 2 weeks from the commencement of treatment. The treatment resulted in no discernible adverse drug reactions except for one patient described below.

An 85-year-old homeless man (160 cm, 45 kg) was brought to our hospital with fever and chills. He had been homeless for several years and appeared severely ill and malnourished upon admission. He had dry skin and a few macular lesions over the trunk. He complained of severe itching at night. *Sarcoptes scabiei* was identified by microscopic examination of skin specimens taken from the patient. He also complained of low back pain and was diagnosed as having hypertension and mild cognitive dysfunction. The patient had taken an oral antihypertensive drug, enalapril maleate (Renivace®), for several years. While he had drunk alcohol, he abstained from drinking recently. On admission, blood biochemistry showed no abnormalities in liver and kidney functions. Routine abdominal ultrasonography identified a cyst in the right kidney, but detected no abnormal findings in the pancreas, liver and biliary tracts (cholelithiasis was excluded). He had no detectable antibodies against HCV and HBV. He was given an oral dose of ivermectin (Stromectol® ; 0.2 mg/kg body weight) to be repeated at 2-week intervals if

Address for Correspondence : Hirota M. Faculty of Pharmaceutical Sciences, Teikyo Heisei University, 4-1 Uruidominami, Ichihara, Chiba 290-0193, Japan E-mail : mhirota@thu.ac.jp

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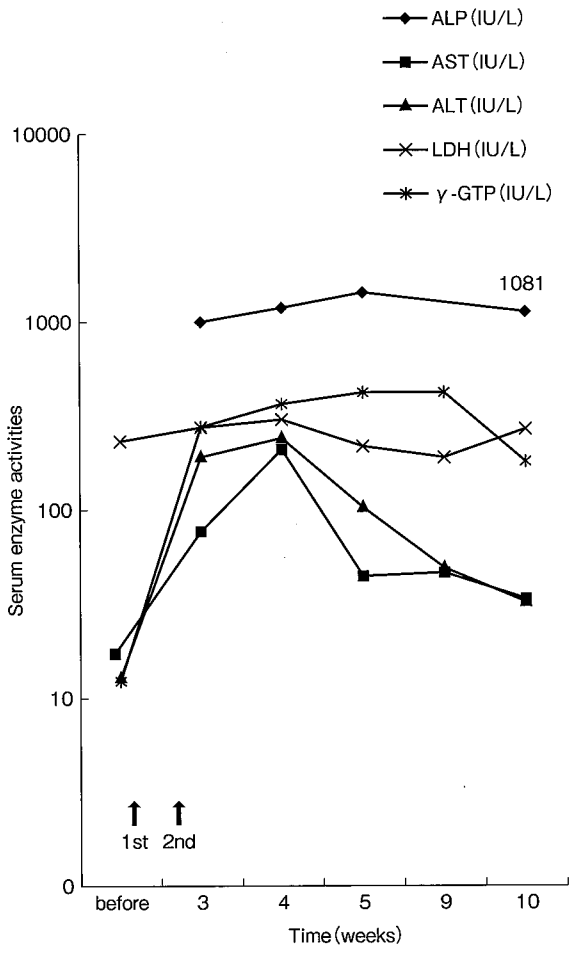

Fig. Time courses of liver function tests in an 85-year-old patient who developed liver dysfunction during ivermectin therapy for scabies

necessary, according to the instructions on the package insert. The patient required a second dose of the drug at two weeks after the first dose and was cured by the time of the four-week follow-up evaluation. However, skin eruptions and itching were not relieved completely at 3 weeks after the first ivermectin dose. Blood chemistry and urinary tests performed during the treatment revealed liver dysfunction (Fig.) manifested by elevated serum AST (GOT), ALT (GPT), ALP and LDH. As a result, a third dose of the drug was withheld and liver function tests were repeated thereafter. Total ALP level was extremely high (1081 vs. normal level of 100–325 IU/L at 37 ℃). Electrophoresis of the blood sample showed that ALP 1 and 2 fractions (11.1% and 77.9%, respectively) were predominantly elevated as compared with ALP 3 and 5. Although all other laboratory values including total and direct/indirect bilirubin levels returned to normal after 3 months, γ-GTP and ALP remained elevated at 8 weeks after the last dose of ivermectin. These laboratory data suggested that the hepatocellular damages manifested by elevated serum ALT and AST levels were resolved faster than those of the biliary tract enzyme abnormalities. After 10 weeks from the commencement of therapy, serum ALP and γ-GPT were still elevated above the normal levels. The patient provided written informed consent to undergo treatment and agreed to the publication of this report. The Ethics Committee of our hospital approved the study and also agreed to the publication of this report.

Discussion

We observed a case of possible ivermectin-induced liver dysfunction in an 85 year-old male patient. He received no other drugs that might have caused liver dysfunction. He had no hepatitis viral infections and was not drinking alcohol. Cytochrome P4503A4 (CYP3A4) is the predominant isoform responsible for the metabolism of ivermectin by human liver microsomes[7]. The patient received no concomitant drugs that may have either induced or inhibited CYP3A4 activity. No genetic polymorphism associated with defective enzyme activity of CYP3A4 has been reported[8]. Thus, we cannot give any reasonable explanation for altered pharmacokinetics of ivermectin that might have been associated with the liver dysfunction. Further investigational examinations (e. g., liver biopsy) were not performed, because the patient moved to another hospital.

While ivermectin is considered extremely safe[6], Barkwell and Shields[5] reported that 15 of 47 elderly patients (mean age 73 years) treated with ivermectin for scabies died within 6 months. Whether or not these deaths were associated with the administration of ivermectin was unclear, nevertheless they recommended that elderly patients should not be treated with ivermectin for scabies. However, many researchers have criticized their methodology and their conclusion. A FDA review of the study found no causal relationship between the deaths and ivermectin[10]. In addition, Meinking et al.[6] reported that a single administration of oral ivermectin at a dose of 0.2 mg/kg of body weight was safe and effective in 11 patients with scabies (age range, 18–80 years). They reported that ivermectin administered at doses of 0.1 to 0.4 mg/kg body weight did not affect blood cell counts, blood chemistry and urine tests[6,9]. In good agreement with Meinking's report, no abnormalities were observed in 29 of our 30 patients, and ivermectin cured skin eruption and itching in all of them within weeks with no discernible adverse drug reactions.

In conclusion, we consider that ivermectin would be safe in most elderly patients but may cause severe and prolonged liver dysfunction. Because the present study

included only elderly patients, caution should be exercised to extrapolate our data to younger patients.

Conflicts of Interest

The authors have no conflicts of interest with the manufacture providing ivermectin (Maruho Co., Ltd.).

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