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Case Report

Rifaximin-induced Neutropenia in Patients with Cirrhosis

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Abstract

Rifaximin is an antibiotic of the rifamycin family. In healthy individuals, it is very poorly absorbed into the blood stream. In patients with liver damage, however, the systemic effect increases as the severity of liver damage increases. This case is presented to highlight the fact that neutropenia can develop due to rifaximin use in patients with hepatic cirrhosis.

Keywords: Cirrhosis; neutropenia; rifaximin.

Hepatic encephalopathy is a neuropsychiatric disorder seen in association with a portosystemic shunt or liver cirrhosis. Hepatic encephalopathy may be seen in 10% to 14% of patients with compensated cirrhosis, and in 16% to 21% of decompensated cirrhosis cases [1]. Lactulose has been used as the primary treatment in the management of hepatic encephalopathy since 1970, and since 2010, rifaximin has been used in patients with persistent neuropsychiatric symptoms or in individuals who cannot tolerate lactulose treatment despite adequate intestinal motility [2]. Rifaximin is regarded as a nonabsorbable antibiotic of the rifamycin family that binds to beta-subunits of DNA-dependent RNA polymerases. Rifaximin is used in hepatic encephalopathy to prevent the development of encephalopathy by decreasing the concentration of urease-producing bacteria in the colon [3]. Bass et al. [4] compared rifaximin and a placebo and observed a decrease in the number of hepatic encephalopathy episodes in rifaximin users.

Presently described is a case of neutropenia that developed secondary to rifaximin used as an adjunct to lactulose treatment in a cirrhotic patient.

Case Report

A 53-year-old female patient was admitted to the clinic with the diagnosis of Child-Pugh score Class C hepatic cirrhosis. Diuretic treatment was initiated as the patient had tense ascites. Prophylactic propranolol was added to the treatment due to the presence of large, F3 esophageal varices. Diuretic treatment was discontinued upon an increase in the serum creatinine level, and Glypressin (Ferring Pharmaceuticals Ltd., Caesarea, Israel) treatment was initiated. Portal vein Doppler US performed upon patient complaints of abdominal pain revealed the presence of portal thrombosis, and renal doses of enoxaparin were administered. As a result of the development of cloudy consciousness, lactulose, and rifaximin (200 mg 3x2) was added to the treatment. At the start of rifaximin therapy, the white blood cell (WBC) count was 5.200/uL, and the neutrophil count was 2.830/uL. Five days later, neutropenia began to develop (WBC: 4444/µL; neutrophil: 2.130/µL). No change was observed in the hemoglobin value or the platelet count. Infectious (Brucella, Epstein-Barr virus, cytomegalovirus,

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HIV, procalcitonin level), hematological (vitamin B12, folic acid), and malignant causes and markers were investigated, and all results were normal. On the 10th day of rifaximin treatment, the WBC was 1.060/uL and the neutrophil count was 0.44/µL. The onset of neutropenia after rifaximin use, the status of hemoglobin and platelet counts, and the inability to detect any other etiology suggested drug-related neutropenia. Two days after cessation of the drug, the neutrophil level began to gradually increase. On the eighth day the WBC was 3.250/uL and neutrophil count was 1.180/uL. Neutropenia did not recur before discharge or during 8 months of follow-up.

Discussion

Rifaximin is a nonsystemic antibiotic of the rifamycin group. In various case reports, the development of leukopenia due to the use of subgroups of rifamycin, especially rifabutin and rifampin, has been described. Rifamycin group antibiotics have been reported to lead to neutropenia after 7 to 10 days of drug use. Rifaximin has the same systemic absorption pattern as the other members of the rifamycin family [5-6]. Some studies have demonstrated that less than 0.4% of a single daily dose of 400 mg rifaximin given to healthy volunteers was systemically absorbed [7]. In individuals with liver injury, a greater percentage of the drug enters into systemic circulation. The effect of rifaximin in the area under concentration-time curve increases 10-, 13-, and 20-fold with increased severity of hepatic injury according to the Child-Pugh classification (A, B, C) [8]. As was the case with our patient, Hynicka et al. [9] reported the development of neutropenia 4 days after the initiation of rifaximin treatment in the first instance of rifaximin toxicity cited in the literature in a case of ulcerative colitis and hepatic injury. The development of neutropenia 5 days after rifaximin was added to the treatment, the worsening of neutropenia during rifaximin treatment, the inability to detect any etiology reflecting infectious or hematological disease, and the use of other drugs without the side effect of neutropenia, suggested to us that in our case, neutropenia developed secondary to rifaximin use. Rapid normalization of the neutrophil count and recovery from neutropenia upon termination of the drug therapy support our argument.

Informed Consent: Approval was obtained from the patient.

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