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A Case of Living Donor Liver Transplantation due to Hepatic Failure Cause of Isotretinoin Therapy

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ABSTRACT

Observation: Isotretinoin is a widely used in acne treatment. It has been some side effects. This drug may rarely cause severe liver failure. Thirty-five year old woman, liver function tests significantly increased 25 days after start to using isotretinoin. Other reasons that cause acute liver failure was investigated and there was not found any other reason. During follow-up period in our hospital, the bilirubin and international normalized ratio levels was not decreased. The liver biopsy showed that widespread necrosis. Finally, the patient underwent living donor liver transplantation. Isotretinoin treatment may not be innocent. We recommend that the medicine be used only in well-selected patients and by monitoring.

Keywords: Hepatic failure, Isotretinoin, Liver transplantation

Introduction

Isotretinoin is a widely used agent for the treatment of severe persistent nodular acne when topical treatment is unresponsive. It is known that this agent which is good in acne treatment is teratogenic; in addition side effects such as cheilitis, dryness on skin and mucosal membranes, increased risk of cutaneous staphylococcus aureus infection, myalgia, hyperlipidemia and increased liver function tests can be seen. This case report has been published with the written consent of the patient.

Case Report

Thirty-five years old female patient with no previously known disease history has begun using isotretinoin therapy for approximately 45 days. Complaints of abdominal pain, nausea and vomiting started 20 days ago. Liver function tests was found

to be high in examinations. Patients who detected negative viral markers were referred to our center because of increased bilirubin and international normalized ratio (INR) values that may require liver transplantation. At the first examination of the patient at our center; aspartate aminotransferase (AST): 848 U/L, alanine aminotransferase (ALT): 593 U/L, total bilirubin: 21 mg/dL, direct bilirubin: 16 mg/dL, creatinine (Cr): 0.6 mg/dL, albumin: 4.1 g/dL, INR: 2.4, C-reactive protein: 3, white blood cells: 9160/μL, platelet: 203 000/μL, ammonia: 190 was detected. N-acetyl cysteine infusion and ursodeoxycholic acid treatment were started. The viral and autoimmune markers were negative. Immunoglobulin G, seruloplasmin and alpha-1-antitrypsin were found to be normal. The patient had triphasic computed tomography scan; no evidence of chronic liver disease, and vascular structures were evident. On the 6th day of



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hospitalization, liver-tre-cut biopsy was performed cause of poor response to medical treatment. The histopathological findings were sentinelobular, bridging, panasinine necrosis areas as active acute hepatitis. In this process, the patient who had prepared live donor, bilirubin and INR values were not regressed on the follow-up and living donor liver transplantation was performed on the 15th day of hospitalization. Histopathologic evaluation of explant liver revealed diffuse centrilobular and panasyner necrosis, mild portal inflammation.

Discussion

Although isotretinoin is known to have side effects, it is often used because of its good efficacy in acne treatment and rarely can cause life-threatening side effects [1]. For this reason, monitoring of some tests is generally recommended during the use of the drug. The frequency with which monitoring should be done is still controversial. Some authors have defined liver enzymes and lipid profile control as weekly or biweekly until the time when the relevant response is received after the onset of the drug, which is usually defined as a 4-week period; some sources suggest baseline and monthly monitoring of blood count, lipid profile, and liver function tests [2,3].

With the treatment of ISO, elevation in liver function tests is detected in 15-20% of patients. When interrupted for drug use, they usually fall within normal limits and are usually insignificant [4,5,6]. In fact, some authors state that the risk of developing liver disease is low, if the liver function tests are normal before the treatment [5]. In our patient, the liver function tests had been elevated 25 days after begun the treatment.

In the study of Hansen et al. [7], which included 515 patients using ISO cause of acne, investigated the frequency, timing and severity of side effects. High ALT level was found 19 (3.3%) of patients and the most severe case was found to be 264 U/dL in the second month (after vitamin replacement); in another case ALTX4 NUS increased in the first month. The mean time to detect elevation in ALT was 61.9 days. Therefore, it is recommended that patients with normal baseline liver function tests before treatment, take a two-month follow-up of control tests and if they are normal, they should not be controlled again. It is emphasized that blood count monitoring is not necessary in the same study.

In Lee et al.'s [8] systematic review and meta-analysis, it is suggested that less frequent laboratory monitoring is safe for most patients, laboratory anomalies are likely to occur according to the patient's clinical and additional disease status (preexisting liver disease, additional hepatotoxic drug use, Metabolic syndrome) it is stated that more frequent control can be made in patients, in summary monitorisation can be individualized.

Ataseven et al.'s [9] in retrospective analysis of 110 patients included, there was statistically significant increase in total cholesterol, triglyceride and AST values, no significant increase in low-density lipoprotein-cholesterol, no increase in high-density lipoprotein-cholesterol, Cr and ALT values when baseline-to-third-month laboratory tests were evaluated.

Ucak et al.'s [10] study that evaluated 40 patients, a statistically significant increase was detected in AST and no significant increase was detected in ALT. The increase in AST value was also reported to be correlated with the dose and a significant difference was found between baseline and 3rd month values at >0.51 mg/kg/day.

It has been stated that ISO therapy may be associated with hepatitis, but in some studies there is no relationship between ISO and chronic liver toxicity [6]. If the liver function tests were normal during two months after the treatment started, it was observed that they stayed in the normal limits in the later period [11].

Conclusion

From a liver perspective, ISO treatment may not be innocent, as stated in the literature. It is recommended that the medicine be used only in well-selected patients and by monitoring. Patients with serious hepatitis should be directed to the transplant center in time.

Ethics

Informed Consent: Consent form was filled out by all participants.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Ş.A., Ş.Y., A.K., R.D., S.A., K.Y.P., Ç.A., M.A., Concept: Ş.A., M.A., Design: Ş.A., M.A., Data Collection or Processing: Ş.A., M.A., Analysis or Interpretation: Ş.A., M.A., Literature Search: Ş.A., Ç.A., M.A., Writing: Ş.A., M.A.

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