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Methotrexate induced hepatitis-A case report

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ABSTRACT

Methotrexate is a folic acid antagonist with cytotoxic and immunosuppressant activity. Drug-induced liver injury is greatly variable in the nature of reactions seen and individual patient susceptibility. Here we report a case of hepatitis which was induced by methotrexate, have been rarely implicated in the causation of hepatitis. 55 years old man was visited to dermatology with pain in the mouth, throat, and abdomen of 2 days duration leading to a diagnosis of drug induced hepatitis. The differential diagnosis (psoriasis) was found in the documents provided by the patient, he was prescribed methotrexate. Cutaneous examination showed skin lesions over the scalf, abdomen, upper & lower limbs. He was administered intravenous fluids, folic acid, antibiotic, ondansetron, paracetamol, Syp. Muconine Gel. This adverse reaction is dose-related and can be labeled as Type-A class of adverse effect. Most drug hepatotoxicity is facilitated by a phase I toxic metabolite, but glutathione depletion, barring inactivation of harmful compounds by glutathione S-transferase, can contribute as well. The magnitude of the elevations and the enzymes involved depend on the offending agent and the severity and stage of the liver damage. The most important step that can be taken in a suspected clinically significant drug-induced liver injury is discontinuation of the offending agent.

Keywords: Liver injury, Methotrexate, Psoriasis, Stevens Johnson syndrome

INTRODUCTION

Methotrexate is a folic acid antagonist with cytotoxic and immunosuppressant activity. It has a more rapid onset of action than other DMARDs, but treatment has to be closely monitored because of some fatal adverse drug reactions. Nausea and mucosal ulcers are the most common toxicities. Progressive dose-related hepatotoxicity in the form of enzyme elevation occurs frequently, but cirrhosis is rare (< 1%).[1] Liver injury possibly will follow the inhalation, ingestion, or parenteral administration of a number of pharmacologic agents used in medical therapy. Drug-induced liver injury is greatly variable in the nature of reactions seen and individual patient susceptibility. Drug-induced liver injury is most often asymptomatic until widespread damage is done. For some agents, elevations in serum aminotransferases can be transient despite continuation of therapy. Several different types of hepatitis have been reported as adverse drug reactions. Habitually, the pharmacist is enquired to evaluate if the patient's medications could be contributing to liver disease. Even though this is challenging to govern with any level of certainty, the first step in the evaluation is to determine for each medication (prescription and over-the-counter) the scope of liver injury that has been reported in the literature. Here we report a case of hepatitis which was induced by methotrexate, have been rarely implicated in the causation of hepatitis.[2]

Case Report: 55 years old man was visited to dermatology with pain in the mouth, throat, and abdomen of 2 days duration leading to a diagnosis of drug induced hepatitis. Prior to this visit, he had presented to a dermatologist with symptoms of skin lesions over the scalf, abdomen, upper & lower limbs of 2 year duration. The differential diagnosis

(psoriasis) was found in the documents provided by the patient, he was prescribed methotrexate. After 2 years, he developed pain in the throat, mouth and abdomen. On presentation, he was conscious and cooperative. Cutaneous examination showed skin lesions over the scalf, abdomen, upper & lower limbs. Investigations revealed the following: Total bilirubin-1.58 mg/dl, direct bilirubin-0.44 mg/dl, indirect bilirubin-1.14 mg/dl, SGOT-55 IU/L, SGPT-62 IU/L and ESR-45 mm/hr. He was administered intravenous fluids, folic acid, antibiotic, ondansetron, paracetamol, Syp. Muconine Gel.

DISCUSSION

This adverse reaction is dose-related and can be labeled as Type-A class of adverse effect. Hepatotoxic drugs can injure the hepatocyte directly, through a free-radical or metabolic intermediate that causes peroxidation of membrane lipids and finally results in liver cell injury. On the other hand, the drug or its metabolite can falsify cell membranes or other cellular molecules, bind covalently to intracellular proteins, stimulate apoptotic pathways, impede with bile salt export proteins, or block biochemical pathways or cellular integrity. [3]Interfering with bile canalicular pumps can allow endogenous bile acids, which can injure the liver, to accumulate. Such injuries, consecutively, may lead to necrosis of hepatocytes; injure bile ducts, fabricating cholestasis; or block pathways of lipid movement, constrain protein synthesis, or impair mitochondrial oxidation of fatty acids, causing in lactic acidosis and intracellular triglyceride accumulation. Most drug hepatotoxicity is facilitated by a phase-I toxic metabolite, but glutathione depletion, barring inactivation of harmful compounds by glutathione S-transferase, can contribute as well. [4] Several different types of hepatitis have been reported as adverse drug reactions. The signs and symptoms of drug-induced hepatitis are highly variable and can present as acute or chronic disease. Some patients may have only asymptomatic transient elevations in their serum aminotransferases, while others progress to fulminant hepatic failure. All patients have elevations in at least some liver tests (AST, ALT, alkaline phosphatase, and bilirubin). The magnitude of the elevations and the enzymes involved depend on the offending agent and the severity and stage of the liver damage. The diagnosis of drug-induced liver injury requires exclusion of other causes because the symptoms of drug-induced hepatitis can be quite similar to those of hepatitis from other origins.[5]

CONCLUSION

A comparison between the time course, frequency, and type of injury the patient is exhibiting and those that have been reported in the literature is helpful in determining the likelihood that a particular reaction is drug induced. The most important step that can be taken in a suspected clinically significant drug-induced liver injury is discontinuation of the offending agent.

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