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Fulminant Hepatitis Caused by Pioglitazone, Paraquat or Both?

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OBJECTIVE: Hepatotoxicity is one of common manifestations of severe paraquat poisoning. It is mostly comes after renal injury. However, fulminant hepatitis without renal injury is seldom reported. Pioglitazone is one of thiazolidinedione and rarely cause hepatotoxicity. Here we present a case under pioglitazone treatment drunk little amount of paraquat and encountered fulminant hepatitis in 24 hours.

CASE REPORT: This 58-year-old female with medical history of diabetes, hypertension, coronary artery disease suffered from drinking 5 ml paraquat and throwing up. Throat pain and vomiting were the first symptoms and activated charcoal was used for decontamination. Laboratory data showed serum creatinine: 0.78, serum lactic acid: 61, normal liver function, and negative urine and serum paraquat test. However, jaundice developed within 24 hours. The followed laboratory data showed serum creatinine: 0.76, ALT: 2233, AST: 9240, total Bilirubin: 4.7, direct bilirubin: 2.8, ammonia: 107, and INR: 2.59. There is no structural abnormality found by computer tomography. Reviewing her drugs history, she used pioglitazone every day. Therefore pioglitazone induced hepatitis was suspected. We added N-acetylcysteine to treat hepatitis and her liver function improved after one-week therapy.

DISCUSSION: In paraquat poisoning, lung and kidney are often the organs primarily affected. Most toxic hepatitis was subacute followed by acute renal injury after paraquat exposure and the course was mild and transient. Mechanism of hepatotoxity might be disturbing glutathione homeostasis and altering bile acid amidation. Troglitazone and pioglitazone were both thiazolidinedione-type anti-diabetes drugs. Troglitazone inhibits both bile acid amidation and the bile salt export pump (BSEP) but pioglitazone only inhibit BSEP. That induced high toxic, non-amidated bile acid instead of amidated bile acid accumulation. While combined exposure of pioglitazone and paraquat may induce hepatotoxicity through bile acid retention as troglitazinoe, even though serum paraquat concentration is under detective level.