CASE REPORT

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Acute liver failure due to trovafloxacin: CT findings

Abstract Symptomatic drug-induced hepatic adverse events due to trovafloxacin, a new fluoroquinolone antibiotic, are uncommon, but recent severe reactions have led to restriction on its use. We report the clinical course and computed tomography findings in a patient who developed acute liver failure shortly after commencing treatment with trovafloxacin. Extensive hepatic necrosis occurred and the patient ultimately died of her liver disease.

Key words Computed tomography – Hepatic necrosis – Trovafloxacin

Introduction

Drug-induced liver disease accounts for 2–3% of hospital admissions and 15–30% of cases of fulminant liver failure [1]. Trovafloxacin (Trovan, Pfizer Inc., New York), a relatively new fluoroquinolone antibiotic, has recently been restricted in its use due to several reports of adverse hepatic events. We report the CT findings in a patient treated with trovafloxacin who developed acute liver failure.

Case report

A 48-year-old woman presented to her physician with nausea and pain in her upper abdomen radiating to her back. On physical exam she was evidently ill, with a temperature of 104 °F. A CT scan showed a contracted gallbladder filled with stones and a large liver abscess. The abscess was drained percutaneously and an endoscopic retrograde cholangiopancreatogram was negative for common bile duct stones. As the patient’s condition did not improve, an open cholecystectomy was performed. Pathological study of the gallbladder found evidence of cholelithiasis and acute and chronic cholecystitis. Biopsy of the abscess revealed acute inflammation and necrosis. A surgical drain was placed in the abscess. The patient initially did well postoperatively and the drain was removed. However, 2 weeks later she again developed fevers. CT showed reaccumulation of fluid in the abscess (Fig. 1), which was percutaneously drained but persisted for several months. Cultures of the drainage fluid grew vancomycin-resistant Enterococcus and Pseudomonas aeruginosa and the patient was treated with multiple antibiotics without improvement. Trovafloxacin treatment (Trovan, Pfizer Inc., New York) was therefore started and all other antibiotics were discontinued. CT performed during the 2-week treatment period with trovafloxacin revealed new extensive necrosis in the liver without change in the abscess (Fig. 2). The right lobe enhanced heterogeneously and appeared swollen. There were ill-defined areas of low attenuation compatible with edema and/or fatty infiltration. Low attenuation in the left lobe of the liver was compatible with infarction. Angiogram revealed occlusion of the celiac axis with reconstitution of the hepatic artery and cavernous transformation of the portal vein. White blood cell count increased from 14.1 × 1000 cells/μl to 20 × 1000 cells/μl (normal 3.8–10.8 × 1000 cells/μl). The bilirubin increased from 1.2 mg/dl to 2.1 mg/dl (normal 0–1.3 mg/dl). The necrosis in both lobes of the liver was treated by percutaneous drainage. No biopsy was attempted. The trovafloxacin treatment was discontinued and the patient initially improved slowly, but died 6 months later from hepatic failure.

Discussion

The patient in our report had been on a regimen of multiple antibiotics for resistant organisms in a liver abscess without significant change for several months. However, soon after being placed on trovafloxacin, the amount of necrosis in the liver rapidly increased. Although no biopsy was obtained to confirm eosinophilic infiltration and the necrosis may, in part, have been secondary to vascular occlusion, extensive hepatic necrosis leading
to vascular thrombosis is more likely. Worsening of the patient’s underlying condition is also unlikely as there was no change in the abscess cavity itself. The liver disease involved previously normal liver. The temporal association raises the possibility of trovafoxacin-induced liver damage, and Trovan has since been shown to cause massive hepatic necrosis and acute liver failure.

Drug-induced liver disease has variable manifestations and the prognosis depends on the particular type of adverse reaction. The case fatality rate is 5% overall but may approach 50% for agents that produce acute hepatic necrosis similar to that of acute viral hepatitis [1]. Idiosyncratic hepatotoxins produce an unexpected injury, usually while a dose in the therapeutic range is being administered [1]. The liver is diffusely involved by necrosis and usually a significant inflammatory reaction is present.

Trovafoxacin is a synthetic fluoroquinolone antibiotic that has been on the market since 1998. It has a broad antimicrobial spectrum that enables it to be used for community-acquired as well as nosocomial infections [2]. Unlike most other fluoroquinolones, this drug undergoes extensive hepatic metabolism and is primarily excreted in bile [3, 4].

Dizziness is the most common side effect of Trovan, occurring in 11% of patients [5]. Other side effects occurring in >1% of patients were nausea, vomiting, headache, vaginitis, diarrhea, and mild phototoxicity. During pre-marketing trials, the incidence and magnitude of liver function abnormalities were similar to those associated with other agents except for one study in which patients were administered the drug for 1 month (personal communication, Adrian Vega, Pfizer, NY). Nine percent of these patients had greater than three-fold elevation of serum transaminases without elevation of other liver markers. Patients were asymptomatic and laboratory tests returned to normal within 1–2 months after treatment was discontinued. Abnormalities of liver function tests were observed in <1% of patients in clinical trials. During the post-marketing period, however, liver enzyme increases and/or symptomatic hepatitis have been noted. Liver failure including acute hepatic necrosis has also been reported (personal communication, Adrian Vega, Pfizer, NY). One hundred forty cases of adverse hepatic events have occurred from February 1998 to May 1999, during which approximately 2.5 million prescriptions for Trovan were issued (statement by Pfizer Inc., NY, to health care professionals, 6 October 1999). These ranged from elevation of serum liver function tests to serious liver injury. The latter occurred in 14 patients, 4 of whom needed liver transplantation and 5 of whom died. The events do not appear to be related to length of dose administration. The