Fluorouracil/calcium folinate

Liver injury: 2 case reports

Two men developed liver injury following treatment with fluorouracil and calcium folinate [leucovorin calcium].

A 66-year-old man received a 30-week course of once weekly fluorouracil 750mg by IV bolus and calcium folinate 35mg, for Duke’s C colonic carcinoma. Six weeks after completing the course, he presented with jaundice. Laboratory tests showed the following levels: AST 644 U/L, ALT 866 U/L, ALP 170 U/L, γ-glutamyltransferase 114 U/L and bilirubin 525 µmol/L. His hepatocellular presentation (R ratio = 15) quickly changed to a mixed picture (R = 2 to 4) and returned to normal 4 months after presentation. A liver biopsy was consistent with a drug reaction, showing typical features of intrahepatic cholestasis.

A 62-year-old man received one cycle of bolus IV fluorouracil 750mg and calcium folinate 36mg, daily for 5 days, after resection of a rectal Duke’s C carcinoma. Two weeks later, he presented with dark urine and jaundice. Laboratory tests showed the following levels: AST 187 U/L, ALT 433 U/L, ALP 425 U/L and γ-glutamyltransferase 487 U/L, suggesting a mixed picture (R = 3). His transaminase levels had normalised within 2 weeks, leaving a cholestatic pattern (R < 1). Within 4 months, his ALP, bilirubin and albumin levels normalised; he had a persistently increased γ-glutamyltransferase level of 3–4 times normal.

Author comment: Causality was assessed using the Naranjo and Roussel Uclaf causality assessment methods. For these patients, both algorithms indicated that it was ‘probable’ that liver injury was due to fluorouracil and calcium folinate. "It is possible that our patients had a genetic predisposition to enhanced fluorouracil effect."