Cytochrome P450 2E1 genotype and the susceptibility to antituberculosis drug-induced hepatitis
Drug-induced liver injury is a common, but often unrecognized cause of liver damage that continues to fascinate and challenge clinicians. Isoniazid, rifampicin and pyrazinamide have been observed to have hepatotoxic potential and drug-induced hepatotoxicity (DIH) is an important adverse effect with antituberculosis treatment. Idiosyncratic damage, dose-dependent toxicity, induction of hepatic enzymes, drug-induced acute hepatitis and allergic reactions have all been implicated as the pathogenetic mechanisms of DIH. 37. Huang YS, Chern HD, Su WJ, Wu JC, Chang SC, Chiang CH, et al. Cytochrome P450 2E1 genotype and the susceptibility to antituberculosis drug-induced hepatitis. Hepatology 2003;37:924-30. Most cases with antituberculosis drug-induced hepatitis have been attributed to isoniazid. Isoniazid is metabolized by hepatic N-acetyltransferase (NAT) and cytochrome P450 2E1 (CYP2E1) to form hepatotoxins. However, the role of CYP2E1 in this hepatotoxicity has not yet been reported. After adjustment for acetylator status and age, the CYP2E1 c1/c1 genotype remained an independent risk factor for hepatotoxicity (OR, 2.38; P = .017). Furthermore, under the administration of isoniazid, the volunteers with CYP2E1 c1/c1 genotype had higher CYP2E1 activity than those with other genotypes had and, hence, might produce more hepatotoxins.