Hepatotoxicity induced by celecoxib and amlodipine

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Introduction
We report two cases with severe hepatotoxicity induced by celecoxib and amlodipine respectively. In both patients the observed liver damage was of the mixed cytoltyic/cholestatic type and was entirely reversible.

Case reports
Case 1
A 58-year old woman received celecoxib (Celebrex®) for 2 years to treat fibromyalgia. Pathological liver enzyme levels were discovered incidentally. Abdominal sonography showed no cholelithiasis, the bile ducts were normal, and there were no signs of chronic liver disease. At admission the patient was icteric and physical examination revealed no signs of chronic liver disease. Her history confirmed that she was taking celecoxib more or less regularly but no other medication within the last three months. She tested negative for anti-HAV, anti-HCV, HBs-antigen, antimitochondrial antibody and antinuclear antibodies. Laboratory tests showed (upper limit of normal): bilirubin 151 (20) umol/L, ASAT 1032 (37) U/L, ALAT 1058 (40) U/L, alkaline phosphatase 391 (37) U/L, thromboplastin time 76 (>70) %, albumin 35 (38) g/L.

A percutaneous liver biopsy revealed severe, acute hepatitis with marked, mixed inflammatory infiltrates of the portal fields, and confluent, focal necrosis. After discontinuation of celecoxib, the cholestatic parameters normalised during the following 3 months. The transaminases however returned to normal only after 1 year (Fig. 1).

Case 2
A 87-year-old woman was treated with amlodipine (Norvasc®) for several years for hypertension. One month before she was admitted to the hospital, she developed pruritus and 2 weeks later painless jaundice. Abdominal CT revealed a normal, homogeneously structured liver without focal injury and abdominal sonography excluded cholelithiasis. Laboratory tests excluded viral or autoimmune hepatitis and showed (upper limit of normal): bilirubin 336 (20) umol/L, ASAT 291 (37) U/L, ALAT 300 (40) U/L, alkaline phosphatase 1019 (270) U/L, gamma-GT 323 (61) U/L, thromboplastin time 76 (>70) %, albumin 30 (38) g/L. A liver biopsy showed severe intra-hepatocellular and canalicular cholestasis with moderate inflammatory infiltrates without necrosis, compatible with drug-induced liver damage.

After discontinuation of amlodipine, the transaminases and parameters of cholestasis decreased markedly within 2 weeks (Fig. 2). The transaminases however returned to normalised during the following 3 months.

In summary drug induced liver disease should not be underestimated in everyday clinical practice, even if this side effect may not be listed in current reference books as it is in the case of amlodipine [1].

References

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Figure 1
a: values of bilirubin and SGPT after withdrawal of celecoxib (case 1).
b: values of bilirubin and SGPT after withdrawal of amlodipine (case 2).
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