

## Development of Sclerosing Cholangitis During Long-Term Interferon-Alpha-2b Therapy

Treatment of hemato-oncologic and chronic viral hepatitis with alpha-interferon (IFN) is usually safe. Common side effects are bone marrow suppression and a flu-like syndrome. More serious undesirable effects are the induction of autoimmune-related phenomena, such as a positive rheumatoid factor (RF), islet cell-, antinuclear (ANA)-, smooth muscle (SMA)-, antimitochondrial (AMA)-, adrenal medullary and antineutrophil cytoplasmic (ANCA) autoantibodies, as well as the development of interstitial pneumonia, autoimmune hemolytic anemia and cholestatic liver disease (1,2).

In 1993 a 56-year-old male patient underwent resection of a renal cell carcinoma. IFN treatment (10 million IU/day 5 days a week) was started immediately because of multiple lung metastasis. In May 1995 the patient developed an intrahepatic cholestasis with positive p- and c-ANCAs, a macrocytic anemia with positive antiparietal cell autoantibodies (PCA) and a type A gastritis with a decreased Vitamin B12 serum level. A positive RF, positive SMA and thyroidal autoantibodies (TAK) without dysthyroidism were detected. On endoscopic retrograde cholangiopancreatography (ERCP) the cholangiogram imitated a primary sclerosing cholangitis (PSC) (Figure 1). Infectious and other autoimmune causes of cholestatic liver disease were excluded by several serological tests and a liver biopsy. Three months after discontinuation of IFN all liver enzymes, the Vitamin B12 and the hemoglobin levels were in the normal range, the cholangiogram had completely normalized (Figure 2) and all other autoimmune phenomena had disappeared.

We conclude that IFN can induce an intrahepatic cholangitis imitating PSC. IFN is an immune-modulating drug, inducing autoantibody production, the deterioration of preexisting autoimmune disorders and even the development of autoimmune diseases. In one patient, treated with IFN for chronic hepatitis C, interstitial pneumonia, haemolytic anaemia and cholestatic liver disease occurred; an ERCP was not performed (2). Five to ten percent of patients treated with IFN develop TAK; dysthyroidism is rare. One of the following autoantibodies – SMA, PCA, ANA, AMA – or adrenal medullary autoantibodies appeared in 32.8% of patients under IFN



**Figure 1:** ERCP in May 1995: During IFN treatment the intrahepatic bile ducts showed an irregular wall; they are incompletely filled.



**Figure 2:** ERCP in August 1995: Three months after discontinuation of IFN therapy the cholangiogram is normal.

treatment (3–5). The occurrence of diabetes mellitus with or without detectable islet cell antibodies or ANA-positive arthritis is rare (3,5). To our knowledge our patient is the first case developing cholestatic liver disease imitating PSC documented by ERCP during and after IFN treatment.

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