Nodular regenerative hyperplasia of the liver

Author: Dr. Ricard Cervera
Creation date: September 2003
Updated: March 2005

Scientific editor: Prof. Josep Font

Servei de Malalties Autoimmunes, Hospital Clinic, Villarroel 170, 08036 - Barcelona, Catalonia, Spain.
rcervera@clinic.ub.es

Abstract
Nodular regenerative hyperplasia of the liver (NRHL) is a rare disorder characterized by diffuse micronodular transformation of the hepatic parenchyma without fibrous septa between the nodules. It has been described in association with a variety of conditions; most of them are systemic autoimmune diseases or hematological disorders. Pathogenesis is unknown but seems related to abnormalities of hepatic blood flow. Clinically, it is usually silent, although many patients have been found to have mildly abnormal liver function tests with progressive symptoms and signs of portal hypertension. The diagnosis of NRHL requires histological evaluation and treatment should be focused on the underlying condition. The disease was diagnosed in 0.52% of the liver biopsies and 0.72% of the autopsies.

Keywords
Nodular regenerative hyperplasia of the liver, antiphospholipid antibodies, portal hypertension

Disease name and synonyms
Nodular regenerative hyperplasia of the liver (NRHL) was first described by Ranström (Ranström, 1953) in 1953 under the name of “miliary hepatocellular adenomatosis” in a patient with Felty’s syndrome. NRHL has also been called “nodular transformation”, “non-cirrhotic nodulation”, “hepatocellular adenomatosis” and “adenomatous hyperplasia”. Steiner (Steiner, 1959) coined the currently accepted term “nodular regenerative hyperplasia”.

Diagnosis criteria / definition
NRHL is characterized by diffuse micronodular transformation of the hepatic parenchyma without fibrous septa between the nodules.

Associated diseases
NRHL has been described in association with a variety of conditions. Most of them are systemic autoimmune diseases or hematological disorders, and, less frequently, solid neoplasms, Crohn’s disease and Hashimoto’s thyroiditis are also reported.
The pathogenesis of NRHL is unknown, but seems related to abnormalities of hepatic blood flow (Pérez-Ruiz et al., 1990). In 1981, Wanless et al. proposed that the vascular lesions in NRHL could be due to recurrent embolization of the portal vein radicals by platelet aggregates and thrombi originating in the portal venous system or in the spleen, the so-called “portal oblitative venopathy”. Recent thrombi in portal veins were observed in some cases of NRHL (Ranström, 1953; Wanless et al., 1981). NRHL may be the morphological response to atrophy of the liver parenchyma caused by vascular obstruction of small hepatic arteries or portal veins; hyperplastic nodules might arise in those acini with maintained blood supply (Pérez-Ruiz et al., 1991).

In 1990, Pérez-Ruiz et al. suggested a possible role of the antiphospholipid antibodies (aPL) in the pathogenesis of NRHL. The aPL have been associated with venous and arterial thrombosis, whether the patient presents with systemic lupus erythematosus or primary antiphospholipid syndrome. Although the coagulopathy associated with the aPL was originally thought to be associated with large- or medium- size vessel occlusions (Lie, 1989), it recently became evident that small vessels may also be involved and the liver is not an exception to this process (Minoshima, 1990; Cadranel et al., 1996).

**Diagnostic methods**

The diagnosis of NRHL requires histological evaluation that is characterized by the presence of nodules of hyperplastic hepatocytes diffusely distributed without significant fibrosis.

**References**


Keegan AD, Brooks LT, Painter DM. Hepatic infarction and nodular regenerative hyperplasia...


Lie JT. Vasculopathy and the antiphospholipid syndrome: Thrombosis or vasculitis or both? J Rhumatol 1986; 16: 713-715.


