ULTRASTRUCTURE OF ALCOHOLIC HYALINE FILAMENTS IN ALCOHOLIC HEPATITIS

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Summary

Ultrastructure of alcoholic hyaline (AH) in alcoholic hepatitis was observed to demonstrate the relationship between AH filaments and intermediate filaments (IFs). Type 1, Type 2 and Type 3 AH were noted in hepatocytes, and the filaments in these types of AH showed similar ultrastructural findings as already reported. Two different kinds of filaments were noted in the Type 2 AH. The large one showed 160 to 200 Å in diameter and the small one showed around 100 Å in diameter. Of the 29 cases with alcoholic hepatitis, a new type of AH was noted in the rosette forming hepatocytes in 2 cases of alcoholic hepatitis. The filaments of this AH in rosette forming hepatocytes showed 40 to 60 Å in diameter and shorter length compared with Type 2 AH. These filaments with 40 to 60 Å diameter were quite different from IFs. Our results indicate that AH in alcoholic hepatitis is not induced by the simple accumulation of the IFs.

Key Words: alcoholic hyaline, intermediate filament, cytoskeleton, alcoholic hepatitis.

Introduction

Alcoholic hyaline (Mallory body) was first described in patients with alcoholic liver disease by Mallory in 19111). Alcoholic hyaline (AH) was observed in the hepatocytes and also in the biliary epithelial cells in alcoholic hepatitis2,5), and AH was noted in some cases of various kinds of diseases including hepatocellular carcinoma4,5). Recently much attention has been paid to the mechanism of AH formation and the pathogenesis of AH in alcoholic hepatitis because there are three current hypotheses regarding pathogenesis of AH, namely, the microtubular failure hypothesis6), vitamin A deficiency hypothesis7,8) and the preneoplasia hypothesis9,10). AH filaments in hepatocytes have been considered to be derived from intermediate filaments (IFs) of hepatocytes according to the results from experimental studies11–13), but this theory is not definitive. To demonstrate the relationship between the filaments in various types of AH and the cytoskeleton of hepatocyte, we examined hepatocytes containing AH in patients with alcoholic hepatitis by electron
Materials and Methods

Twenty six (26) liver biopsies and 3 autopsy specimens from 29 patients of alcoholic hepatitis with AH were studied. 21 biopsies were performed for clinical indications and obtained after informed consent under protocols approved by the Human Studies Committees of the Harbor General Hospitals and the Martinez Veterans Administration Medical Center California, USA. Five biopsies were performed in the 3rd Department of Internal Medicine, Kyoto Prefectural University Hospital. The diagnosis of alcoholic hepatitis was based on the findings of necrosis, ballooning hepatocyte, neutrophilic infiltration and AH. Of the 29 cases with alcoholic hepatitis, 14 cases also showed alcoholic hepatitis with cirrhosis. The liver tissues were fixed for light and electron microscopic examination. Hematoxylin-eosin and Masson-trichrome stains were performed to determine the histologic diagnosis.

Specimens for electron microscopy were cut into 1mm cubes and fixed in a solution of 2.5% glutaraldehyde in 0.1 M sodium cacodylate buffer. The tissues were postfixed in 1% osmium tetroxide in sodium veronal buffer or in phosphate buffer, dehydrated and then embedded in either Spurr's low viscosity resin or Epon 812. Thin sections were stained with uranyl acetate and lead citrate, and examined by electron microscopy.

Results

In light microscopic examination, AH was chiefly noted in centrolobular areas, particularly in the cases of alcoholic hepatitis without cirrhosis; however, they were noted anywhere in the lobule in the cases of alcoholic hepatitis in the advanced stage.

Three ultrastructural variants of AH were observed as Yokoo had reported. Type 1 AH (Fig. 1) consisted of bundles of filaments aligned in parallel arrays which showed fingerprint-like appearance; however, Type 1 AH...