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Iron Accumulation in Hepatocellular Carcinoma and the Role of Hepatitis B Core Antigen

Masachika SENBA[1] and **Kioko KAWAI**[2]

[1]Department of Pathology, Institute of Tropical Medicine, Nagasaki University, Nagasaki 852, Japan, [2]Department of Pathology, Nagasaki University School of Medicine

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Summary. **Histochemical and immunohistochemical analyses were carried out to determine the relationships of iron accumulation in hepatocellular carcinoma and hepatitis B virus antigens using 300 autopsy cases obtained from Nagasaki University Hospital. Iron accumulation in hepatocellular carcinoma was studied with Prussian blue reaction, and a positive reaction for hepatitis B core antigen and hepatitis B surface antigen were investigated by immunoperoxidase methods. Two cases of iron positive were observed in the cancerous tissue. These cases were hepatitis B core antigen-positive in the cancerous tissue, but hepatitis B surface antigen was negative in the same area. Therefore, hepatocellular carcinoma with hepatitis B surface antigen does not show iron accumulation, whereas the same tumor with hepatitis B core antigen is accompanied by iron accumulation. These findings suggest that hepatitis B core antigen produces the degeneration or collapse of the genes of hepatocellular carcinoma resulting in an iron metabolism disorder.**

INTRODUCTION

Iron accumulation could not be identified in hepatocellular carcinoma of siderosis in humans[1)] or experimental animals.[1-3)] However, Hirota and his colleagues[4)] reported on two iron-positive cases of hepatocellular carcinoma with cirrhosis combined with primary hemochromatosis where one case was hepatitis B surface antigen-positive in non-cancerous tissue and the other was negative. On the other hand, there was a strong correlation between the presence of hepatitis B surface antigen and iron deposition in Kupffer cells and spleen cells. Thus, it is suggested that the hepatitis B surface antigen affects the iron metabolism in cells of the reticuloendothelial system.[5)] The authors further tested for iron accumulation in hepatocellular carcinoma tissue using the Prussian blue reaction, and for the hepatitis B core antigen and hepatitis B surface antigen by immunoperoxidase methods. The purpose of this study is to find the relationship between iron accumulation, hepatitis B core antigen and/or hepatitis B surface antigen in hepatocellular carcinoma tissues.

MATERIALS AND METHODS

Specimens of hepatocellular carcinoma from 300 autopsy cases at Nagasaki University Hospital were used. The specimens were fixed in 10% formalin and embedded in paraffin. Sections were cut at 4 micron and stained-by Gomori's method, for iron with Prussian blue reaction. These materials were stained with hepatitis B core antigen (Dako PAP Kit: 511, Lot. 025-3) and hepatitis B surface antigen (Dako PAP Kit: 523, Lot. 063-3) using immunoperoxidase methods.

RESULTS

In two of 300 cases, iron accumulation was observed not only in the cytoplasms but also in the nuclei and the nucleoli of hepatocellular carcinoma (Fig. 1; upper and lower). In non-cancerous siderotic human liver, almost all iron accumulation was observed as granular deposition. In hepatocellular carcinoma, two iron-accumulated cases were hepatitis B core antigen-positive (Fig. 2) and hepatitis B surface antigen-negative. On the other hand, three cases were hepatitis B core antigen-negative and hepatitis B surface antigen-positive in hepatocellular carcinoma and did not show iron accumulation.

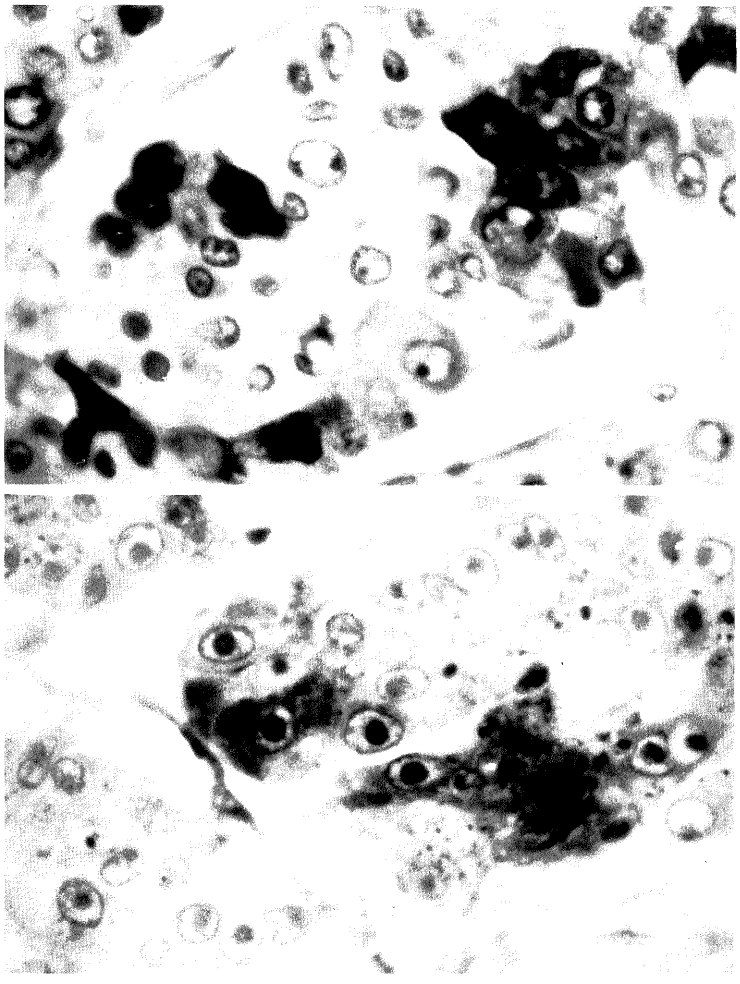

Fig. 1. Iron accumulation is seen in the cytoplasms, nuclei (upper) and nucleoli (lower) of hepatocellular carcinoma. (Prussian blue reaction; ×320).

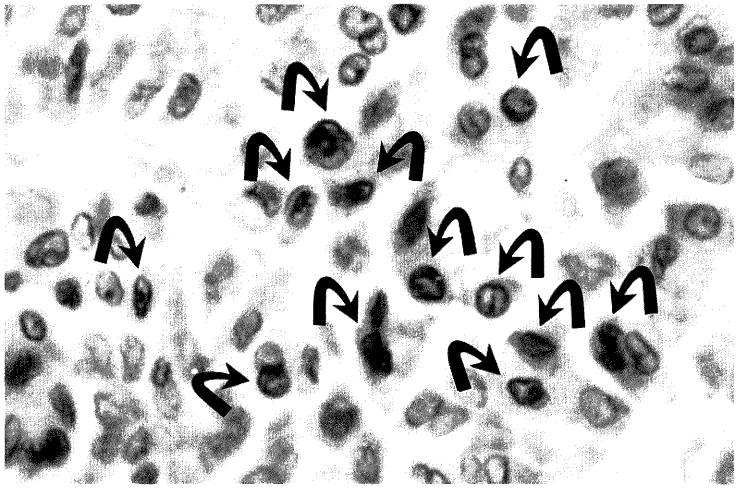

Fig. 2. Positive immunoperoxidase staining for hepatitis B core antigen is identified in the nuclei of hepatocellular carcinoma. The arrows indicate hepatitis B core antigen. (Immunoperoxidase for hepatitis B core antigen; ×320).

DISCUSSION

The reasons for the coexistence of iron accumulation and hepatitis B core antigen in hepatocellular carcinoma tissue are not known. A possible explanation may be that hepatitis B core antigen causes degeneration and/or collapse of the genes of hepatocellular carcinoma cells, which results in iron accumulation in the cytoplasms, nuclei and nucleoli of hepatocellular carcinoma tissue. Thus, hepatitis B core antigen might possibly give rise to disorders of iron metabolism in hepatocellular carcinoma. On the other hand, iron accumulation could not be found in hepatocellular carcinoma tissue of siderotic human.[6] Williams stated that the altered foci and preneoplastic and neoplastic nodules were readily identifiable by the resistance to iron accumulation in the siderotic rat livers, and they reported that the resistance to iron accumulation is a steady and sensitive morphological marker of the preneoplastic as well as neoplastic changes in animals.[1-3] The process of iron metabolism of the hepatocellular carcinoma tissue might be different from that of the normal tissue, because hepatocellular carcinoma tissue might take up much iron and then release it rapidly to non-cancerous tissue of the same liver.[7-9] Thus, no stainable iron could be found in hepatocellular carcinoma lesions.

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