Comparative Study on Acute Gastric Mucosal Lesion in Experimental Obstructive Jaundice and Biliary Drainage Models*)

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ABSTRACT

The authors prepared obstructive jaundice models by cannulation into the common bile duct, using Wistar-strain rats, and examined active amines in the gastric wall and the incidence of AGML before and after biliary drainage.

1) The incidence of AGML was comparatively high in the group of 1–3 weeks’ obstruction, while the incidence was greatly reduced after biliary drainage in the groups of 1–2 weeks’ obstruction.

2) HA and 5-HT contents in the gastric walls were significantly high in the group of 1–3 weeks’ obstruction, while biliary drainage succeeded in gradually reducing the levels down to the control values in the group of 1–2 weeks’ obstruction.

3) In 3 weeks’ obstruction, the increase in HA was not improved after biliary drainage and the incidence of AGML was similar to 1 week’s obstruction on the 5th day after biliary drainage.

It was suggested therefore that there was an intimate relationship between the changes in the active amines contents in gastric walls and the incidence of AGML, and the obstructive jaundice was a pathological state where active amines in the gastric walls were markedly increased, and that such a state was associated with the mechanism of onset of AGML in obstructive jaundice.

INTRODUCTION

In recent years, the release of jaundice with Percutaneous Tranchoaptic Cholangiodrainage (PTCD) has been gaining ground for the purpose of radical operation for obstructive jaundice, and the results of operations in these cases have been improving.

It is not rare, however, that the delayed cases of obstructive jaundice are sometimes complicated with acute gastric mucosal lesions (AGML). The mechanism of onset of AGML has been studied from both the aggressive factors and defensive factors, but many points have remained unclarified, so that no definite views have been obtained yet.

In particular there have been very few reports examining the mechanism of AGML in terms of the changes in active amines in tissue in obstructive jaundice. The authors, therefore, prepared an obstructive jaundice model using Wistar-strain rats, and examined the mechanism of onset of AGML complicated with obstructive jaundice. The findings are presented in this paper.

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MATERIALS AND METHODS

1) Animals and preparation of the model
Wistar-strain male rats (weight 200-250 g) were anesthetized with Nembutal (50 mg/kg, ip), and the following procedures were taken:

The animals were laparotomized with median incision, and the common bile duct within the hepatoduodenal mesenterium was exposed. A polyethylene tube, 1 m/m in outer diameter (Atom venous catheter, 3 Fr), was inserted into a region about 1/3 of the common bile duct on the liver side, i.e., the region where the great pancreatic duct converges into the common bile duct, and the tube is fixed. Then the other end of the tube is led to the back from the right abdominal wall through the subcutaneous tunnel. The end of the tube is heated and compressed to make the obstructive jaundice model (obstructive group) (Fig. 1), and the animals were bred for 3 weeks in a thermostat room and were used for the following experiments. During the period from 1 to 3 weeks, the tube was opened each week, and biliary drainage was performed for 1, 3 and 5 days to make the biliary drainage model (drainage group).

2) Observation of AGML and changes in standard liver function
The animals were starved for 24 hours, and beheaded to extract blood. After the stomach was removed, changes in the incidence of AGML was observed macroscopically. For the markers of liver function, serum total bilirubin (T.B), alkaliphosphatase (Al-p) and serum transaminase (GOT, GPT) were determined.

3) Determination of histamine (HA) content in fundic mucosa and serotonin (5-HT) content in antrum tissue. The fundic mucosa and antrum tissue were taken under iced-cooled state and homogenized according to the method of Wada, after which HA and 5-HT were extracted. Fluorescent quantitation of HA was performed by the Shore method and that of 5-HT by the Maickel-Miller method.

RESULTS

1) Incidence of AGML
The incidence of AGML in the obstructive group was gradually increased by 17% in the 1-week group, 26% in the 2-week group and...
Fig. 3. Changes of standard liver function in rats with experimental obstructive jaundice and biliary drainage (n=6, M±SD)

○ Control, ○ Jaundice 1W, △ Jaundice 2W, □ Jaundice 3W
39% in the 3-week group. On the other hand, the incidence of AGML in the drainage group was gradually decreased in all groups, showing 0% in the 1-week group, 8% in the 2-week group and 15% in the 3-week group on the 5th day after biliary drainage (Table).

The AGML thus formed was all found at the fundus of the stomach, being mostly either gastric hemorrhage alone or shallow multiple lesions of the degree of UL-I, II (Fig. 2).

2) Changes in standard liver function

The serum T. B levels in the obstructive group were, as compared with the level of 0.3±0.1 mg/dl in the nontreated group (Control), 7.1±0.8 mg/dl in the 1-week group, 7.4±1.7 mg/dl in the 2-week group and 9.0±1.4 mg/dl in the 3-week group, all groups showing remarkable high levels.

In the drainage group, the level was decreased almost to the control level on the 5th day after biliary drainage in all-week groups (Fig. 3-A). A similar tendency was noted with the serum Al-p, GOT and GPT levels before and after biliary drainage (Fig. 3-B, C and D).

3) i) Changes in HA content

The HA contents in the obstructive group were, as compared with 22.8±1.2 µg/g of the control level, 33.3±8.6 µg/g in the 1-week group, 34.4±8.7 µg/g in the 2-week group and 35.1±5.4 µg/g in the 3-week group, all showing significantly high levels (p<0.05, p<0.01, Fig. 4).

In the drainage group, on the other hand, the level dropped to the control level in the 1-week group on the 3rd day and in the 2-week group on the 5th day, after biliary drainage. In the 3-week group, however, HA content still remained high even on the 5th day after biliary drainage. (p<0.01, Fig. 4).

ii) Changes in the 5-HT content

The 5-HT contents in the obstructive group were, as compared with 8.3±1.1 µg/g of the control level, 11.8±1.9 µg/g in the 1-week group, 13.0±2.7 µg/g in the 2-week group,
and 13.3±3.1 µg/g in the 3-week group, all showing significantly high levels (p<0.01, Fig. 5).

In the drainage group, on the other hand, the contents in all week groups dropped to the control level on the 5th day after biliary drainage (Fig. 5).

**DISCUSSION**

Not a few reports have been made on experimental obstructive jaundice with rats, examining liver function after the release of obstructive jaundice and the recovery of liver regenerative capacity, but very few have been made on the mechanism of onset of AGML often complicated with the disease in terms of the changes in active amines in tissue before and after the release of jaundice.

The authors accordingly prepared the obstructive jaundice model by cannulation into the common bile duct with a view to examining the changes in pathological states of gastric mucosa before and after biliary drainage. As seen in terms of the changes in standard liver function, hyperbilirubinemia or liver disorder were aggravated with the delay of obstruction, which was greatly improved, however, by biliary drainage on the 5th day. It is considered consequently that the external biliary drainage model prepared by the authors was, as compared with the internal biliary drainage model, though non-physiological, a method whereby a good jaundice reducing effect can be expected with little intervention, clinically nearer to PTCD.

The properties of AGML occurring on the gastric mucosa of the obstructive jaundice rats closely resembled comparatively multiple acute gastric ulcers observed clinically. As an acute gastric ulcer model complicated with obstructive jaundice, it is considered useful.

Incidentally, HA and 5-HT and other active amines exist abundantly on the gastric walls of mammals. It is to be noticed in particular that HA exists much in the EC-like cells and atypical mast cells in the fundic mucosa, whereas 5-HT is said to exist much mainly in EC cells in the antral mucosa, and these active amines have been known as vasoactive amines, and microcirculation disturbance in the gastric mucosa due to the gastric vascular action have been regarded as important factors in the mechanism of onset of AGML in the experimental stress ulcer models and obstructive jaundice.

On the examination of the authors' results, it was found that the contents of HA and 5-HT in the gastric walls in obstructive jaundice rats were significantly increased, and with it the incidence of AGML became rather high.

On the other hand, both active amines were gradually decreased to the normal level after biliary drainage for 2 weeks' obstruction, and the occurrence of AGML was markedly inhibited. In 3 weeks' obstruction, however, the increase in HA was not improved after biliary drainage, and the incidence of AGML was similar to that of 1 week. It was suggested therefore that an apparent relationship must exist between the changes in the contents of both active amines and the incidence of AGML before and after biliary drainage. It was further suggested, therefore, that in obstructive jaundice HA and 5-HT in gastric walls must be markedly increased, and such a pathological state may be strongly associated with the mechanism of onset of AGML. A brief reference to the prophylaxis of AGML from the present study is that biliary drainage at an early stage might inhibit the occurrence of AGML.

**REFERENCE**

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