Mast Cell Degranulation with Special Reference to the Effect of Lipid Administration upon the Mesenteric Mast Cell of Albino Rats

Kook Lee*, Yong Hae Lee* and Soo Yun Pak

Department of Anatomy, Yonsei University College of Medicine
Seoul, Korea
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ABSTRACT

Morphological effects of degranulation upon mesenteric mast cells of albino rats (Sprague-Dawley strain) by means of lipid administration were studied.

An evident degranulation of metachromatic granules from mesenteric tissue mast cells was observed in more than half of experimental rats which were intraperitoneally given 10 cc of stearic monoglyceride suspension in warm Tyrode solution (50 mg. of stearic monoglyceride in 10 cc of Tyrode solution). A fairly light degranulation of metachromatic granules from mesenteric mast cells was also displayed by the rats fed ad libitum with butter for 6 hours after being deprived of food for 24 hours.

INTRODUCTION

Tissue mast cells, containing metachromatic or orthochromatic granules in the cytoplasm have been described in the literatures as a source of heparin by Holmgren and Wilander (1937), histamine by Riley and West (1953), 5-hydroxytryptamine by Benditt et al. (1955) and hyaluronic acid by Ashoe-Hansen (1952).

It has been suggested that heparin, in addition to its well-known function as an anticoagulant, may be related to the mobilization of lipid in the metabolic and absorptive processes. Hahn (1943) first observed that the importance of plasma lipoproteins in normal and abnormal fat metabolism has stimulated interest in the heparin-induced lipemia clearing system. Anderson and Fawcett (1950) and Brown et al. (1953) reported that upon the administration of heparin to animals of many different species an enzyme appears in the blood which is able to clear lipemic serum in vivo or in vitro.

Korn (1955 a) suggested that clearing factor, the enzyme present in postheparin plasma, can be extracted from acetone powders of normal rat hearts and that it catalyzes the hydrolysis of the neutral fat of chylomicrons, which is activated by heparin and inhibited by salt and protamine. Korn (1955 b) added that lipoprotein lipase prepared by extracting rat heart acetone powder, will catalyze the hydrolysis of triglycerides only when they are associated with protein.

Korn (1955 a, b) and Korn and Quigley (1955) reported that the clearing factor of postheparin plasma has been identified with a lipoprotein lipase obtained from rat, rabbit and calf hearts and rabbit adipose tissue. Korn and Quigley (1957) also added that lipoprotein lipase has been isolated from chicken adipose tissue and the hydrolysis of lipoproteins by this enzyme has been shown to occur in two stages: the
formation of an enzyme-substrate complex and the actual hydrolysis. Lynn and Perryman (1960) reported that the purified lipase obtained from a pig adipose tissue, is the same as lipoprotein lipase, and the role of lipoprotein and heparin on the activity of the lipoprotein lipase is that of an emulsifying agent, both for the substrate as well as the enzyme.

Considering these results presented by others, the authors were interested in the effect of lipid administration to the tissue mast cell and have studied the morphological reaction of the tissue mast cell in which heparin is contained, when certain lipids were administered in various ways to the experimental animal.

MATERIALS AND METHODS

26 healthy mature albino rats (Sprague-Dawley strain) of about 250 grams in body weight were used and treated as follows:

1. An experimental group injected with stearic monoglyceride suspension intraperitoneally:

   10 albino rats were intraperitoneally injected with 10 cc of stearic monoglyceride suspension in Tyrode solution in which 50 mg of stearic monoglyceride was contained. Each injecting suspension was preheated to 37°C.

2. A control group for the former experimental group:

   5 albino rats were intraperitoneally injected with 10 cc of warm Tyrode solution preheated as in the former group.

The experimental and control animals of both groups were sacrificed 8 hours after the injection by means of occipital blows. Absolute methanol was directly infused into the peritoneal cavity through a small incision made in the anterior median abdominal wall of the rat and then fixed for 20 minutes in situ with the rats in supine position in order to reduce the direct mechanical injury to the mesenteric mast cell. A few pieces of the mesentery were carefully excised and stained for 3 minutes for histological preparation with Pugh solution containing toluidine blue used by LeBlanc and Rosenberg (1957).

3. An experimental group given commercial butter orally:

   5 albino rats were fed ad libitum with butter after being deprived of food for 24 hours. In the course of this experiment the rats were always accessible to water. The amount of butter taken by rats for 6 hours, ranged approximately from 1.9 to 6.0 grams.

4. A control group for the previous experimental group given butter orally:

   5 albino rats deprived of food 24 hours were allocated for this control group. However, the rats were allowed to take water as well. Both rats of the experimental and the control groups were sacrificed and histological preparations of the mesenteric mast cells were carefully made as in the similar procedures mentioned previously.

In order to confirm morphologically lipid absorption through the intestinal mucosa of the experimental animals given butter orally, a few pieces of the jejunal mucosa fixed in 10% formalin, were prepared in thin frozen section and stained in Oil red O. All of the frozen sections showed fairly demonstrable pictures of lipid absorption through the intestinal mucosa.

RESULTS

In the experimental group injected with stearic monoglyceride suspension intraperitoneally, 6 out of 10 experimental rats showed an evident degranulation of metachromatic granules from mesenteric tissue mast cells. However, the degree of the degranulation was fairly light. In the control rats, all appeared to be without any morphological phenomena of degranulation in mesenteric tissue mast cells (Table 1., Fig. 1 and 2).
Degranulation of Mast Cells Due to Lipid Administration

Table 1. The degranulation of mesenteric mast cells by the intraperitoneal injection of stearic monoglyceride suspension in Tyrode Solution

<table>
<thead>
<tr>
<th>Rats in the experimental group</th>
<th>Degranulation of mast cells</th>
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<th>Degranulation of mast cells</th>
<th>Rats in the control group</th>
<th>Degranulation of mast cells</th>
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<tbody>
<tr>
<td>1.</td>
<td>+</td>
<td>6</td>
<td>−</td>
<td>1</td>
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<tr>
<td>2.</td>
<td>+</td>
<td>7</td>
<td>−</td>
<td>2</td>
<td>−</td>
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<tr>
<td>3.</td>
<td>+</td>
<td>8</td>
<td>−</td>
<td>3</td>
<td>−</td>
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<tr>
<td>4.</td>
<td>+</td>
<td>9</td>
<td>+</td>
<td>4</td>
<td>−</td>
</tr>
<tr>
<td>5.</td>
<td>−</td>
<td>10</td>
<td>+</td>
<td>5</td>
<td>−</td>
</tr>
</tbody>
</table>

+: Slight degranulation of mesenteric mast cells in about more than half of the cells observed.
−: No degranulation or intact mast cells in the majority of the cells observed.

Table 2. The degranulation of mesenteric mast cell by the oral administration of commercial butter

<table>
<thead>
<tr>
<th>Rats in the experimental group</th>
<th>Degranulation of mast cells</th>
<th>Rats in the control group</th>
<th>Degranulation of mast cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>+</td>
<td>1</td>
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<td>5</td>
<td>+</td>
<td>5</td>
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</table>

+: Slight degranulation of mesenteric mast cells in more than half of the cells observed.
−: No degranulation or intact mast cells in the majority of the cells observed.

In the experimental group given commercial butter orally, 4 out of 5 rats showed a light degranulation of metachromatic granules from mesenteric tissue mast cells. In some case tissue mast cells which were adjacent to the small blood vessels of the mesentery, displayed a fairly evident degranulation which was somewhat light in degree. As with the previous control rats, most rats of this control group were found to be without any changes of degranulation (Table 2., Fig. 3 and 4).

DISCUSSION

Robinson and French (1960) suggested that the turbidity of the plasma in alimentary lipaemia is due to the presence of large numbers of visible lipid particles or chylomicra. It is now generally accepted that plasma obtained after heparin injection (post-heparin plasma) clears this turbidity in vitro because it contains an enzyme which hydrolyses the triglycerides of chylomicra. The effect of exogenous heparin in inducing clearing activity in the blood was established in earlier experiments.

It is also known that heparin is not unique in this respect and many sulphated polysaccharides act in the same way. Iselin and Schuler (1957), and Korn and Quigley (1955) have demonstrated that exogenous heparin can increase the activity of the enzyme extracted from heart and adipose tissue in the clearing activity of lipid. Iselin and Schuler (1957) have suggested that, in extracting the enzyme from the heart, heparin may release the enzyme of lipase from its binding site in the tissue.

Korn (1955) has suggested that the clearing activity mentioned previously is also inhibited by pyrophosphate and other phosphate derivatives, and this inhibition can be reversed by heparin. Brown (1953) has suggested that the
inhibition of post-heparin plasma activity upon the clearing activity of lipid by mean of protamine sulphate, a known heparin antagonist, is not conclusive since protamine sulphate also has a direct effect on the chylomicron substrate.

Fredrickson and Gordon (1958) have suggested that under conditions where carbohydrate utilization by the tissues is minimal, as for instance in starvation and in diabetes, there is a net movement of fatty acids away from the depots, which seems to be under hormonal and nervous control.

It is well known that heparin acts in the clearing activity of lipid or the mobilization of lipid in vitro and in vivo. The authors were interested in the morphological changes of tissue mast cells, in which metachromatic granules contain heparin. The degranulation of metachromatic granules may cause a heparin release into the tissue space, when lipid absorption and mobilization were undertaken in the experimental rats after depriving of the food for 24 hours.

In the rats given butter orally after such a short period of the food deprivation, more than half of the experimental animals displayed a fairly remarkable degranulation of metachromatic granules of mesenteric mast cells. In such rats positively showing a degranulation, the degree was slight as shown in the figure. The degranulation of metachromatic granules due to an intake of butter orally may implicate a heparin-release to facilitate lipid mobilization or clearing activity in the course of fat metabolism. However, there is no direct biochemical proof to account for a heparin release associated with the facilitation of lipid mobilization in this experiment.

In the control group deprived of food, rats fasted for 48 hours readily showed a visible degranulation of mesenteric mast cells so that deprivation of the food undertaken for more than 24 hours, was not taken into account. Under this condition the degranulation of mesenteric mast cells was thought due to the stress from the fast for 48 hours or the facilitation of lipid mobilization from tissue depots for metabolic compensation if the degranulation of the mast cell is associated with a heparin-release.

In the rats injected with monoglyceride suspension in Tyrode solution intraperitoneally, more than half of the rats showed a positive reaction of degranulation of mesenteric mast cells. From this result, the degranulation of mesenteric mast cells caused by the intraperitoneal injection of the monoglyceride suspension in Tyrode solution was morphologically established in this experiment. However, the direct cause of the degranulation of mesenteric mast cells whether due to the foreign body reaction of the injected suspension, the facilitating action of emulsification of the suspension, or the promoting action of lipid mobilization was not determined in this experiment.

ACKNOWLEDGEMENT

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REFERENCES

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Fig. 1. Degranulation of rat’s mesenteric mast cells caused by injection of stearic monoglyceride suspension intraperitoneally. Stained in Pugh solution. 400 ×

Fig. 2. Intact mast cells of the rat’s mesentery given Tyrode solution intraperitoneally. Stained in Pugh solution. 400 ×

Fig. 3. Degranulation of rat’s mesenteric mast cells caused by an oral administration of butter after food deprivation for 24 hours. Stained in Pugh solution. 400 ×

Fig. 4. Intact mast cells of the rat’s mesentery deprived of food for 24 hours. Stained in Pugh solution. 400 ×