METABOLISM OF RENAL LESION OF DIABETIC GLOMERULOSCLEROSIS

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In order to study the metabolism of diabetic glomerulosclerosis (DGS) we examined the metabolism in the kidney and the reaction of substances in the blood during GTT. Also we investigated the cause of the DGS as related to metabolism.

Results

The source of energy in the kidney is the oxidation of fatty acid in the cortex and anaerobic glycolysis in the medulla. The greater part of this energy in the kidney is used for the active transport within the kidney.

First using normal rabbit we measured renal Na-K ATPase activity and observed high level activity progressing from the medulla to the cortex to the papilla. Very similar high level activity was observed in microsome and mitochondria in the cortex.

There was no change of Na-K ATPase activity when 5% glucose was administered by drip infusion, but the addition of 0.2 unit/kg of insulin decreased the activity. This decrease was especially evident in the mitochondria. It has been reported that insulin is not connected with the reabsorption of glucose in the kidney, but in our experiment we observed that to some extent insulin is involved in the active transport. In our experiment concerning renal diabetic state we used rats that had been injected with alloxan (A) and aminonucleoside (AN). The renal glucose level of the A-treated rat increased, but in the A-AN treated rat the glucose level in the cortex and medulla of the kidney decreased. The enzyme activity which is involved in gluconeogenesis (G-6-Pase, PEPCK) increased in the kidney of
the A-treated rat but decreased in the cortex and medulla of the A-AN treated rat. The enzyme activities (Hexokinase, PFK) which belonged to glycolysis pathway, decreased in the A-treated rat but on the other hand, increased in A-AN treated rat. (Fig. 1)

As mentioned above, the metabolic pattern in the kidney treated with A and AN is suitable for a model of human DGS. And the enzyme activities which are involved in gluconeogenesis decreased when there are pathological change in the kidney. These findings suggest that the blood sugar level of a patient suffering

The activities of the gluconeogenetic enzymes in the kidney of the diabetic rat.

- G-6-Pase
- PEP Carboxykinase

The activities of the glycolytic enzymes in the kidney of the diabetic rat.

Hexokinase
- PFK

Fig. 1.
Metabolism of Renal Lesion of Diabetic glomerulosclerosis

from DGS is lower than that of a patient suffering only from diabetes mellitus (DM) and that the dosage of insulin used for the treating patient suffering from DGS should be decreased.

The changes of several substances in the blood during 50 g OGTT were measured to analyse the effect on the metabolism in human DGS.

The response of serum IRI to glucose administration, decreased in the cases of DGS. But the change of serum NEFA in the patients with DGS, were the same as those in the patients suffering only from DM.

The serum amino acid did not change in the cases of DGS, and the blood ATP level did not change either. The serum glycerol level of the patient with DGS decreased most remarkably, and did not recover even after 180 minutes. (Fig. 2)

In the cases of DGS the reaction to the administration of glucose was minimum and was similar to the pattern of severe DM.

These findings reveal that hepatic metabolism and general organic metabolism have an effect on the levels of several substances in the blood.

Next, two experiments were made to investigate the cause of glomerulosclerosis. At first, the serum blood sugar level of KK mice which were known to have the same pathological change in the kidneys as in human glomerulosclerosis, were measured. FBS reached a high level 5 months after the birth of the animal, the maximum level was reached at 7-8 months.

There was a decrease of direction to normal level at 24 months.

The glucose tolerance curve revealed a almost typical diabetic pattern at 4 and
6 months. Elctromicroscopic figure revealed thickened glomerular basementmem- 
brane, proliferation of mesangial matrix.

Those findings were especialy remarkable at 24 months.

The electrophoretic pattern of the serum protein in the KK diabetic mice. The serum protein pattern of these mice showed that albumin decreased and β and 7 globulin increased remarkably. (Fig. 3) This was in the same pattern as that of the patient with DGS. Uronic acid was measured by means of extraction from the urine by the Discheś Carbazol method and Brown's Orcinol method.

Uronic acid level of acid–mucopolysaccharide in the normal urine was about 0.0096 μM/ml by both methods. But that in the urine of the patients with DGS was 0.0180 μM/ml by means of Carbazol (C) method and was 0.0272 μM/ml which was higher than normal level by means of Orcinol (O) method.

C/O ratio in the normal urine was 0.97 and it was 0.63 in the urine of the patients with DGS. The uronic acid level of acid–mucopolysaccharide in the kidney cortex was higher than level in the medulla. The uronic acid of acid–mucopolysaccharide level in the kidney cortex and medulla of the patients with DGS was remarkably higher than normal.

**Conclusion**

1) The metabolism of diabetic glomerulosclerosis was examined from the stand point of renal enzyme activity, and response of blood substances during 50 g OGT. From our experiments we observed that there was an inhibition of the diabetic state, and in DGS the pathological states were affected by general organic metabolism.
2) Concerning of the causes of glomerulosclerosis, pathological figure in the kidney and serum protein pattern were similar to the human diabetic glomerulosclerosis, therefore we suggest that KK mice are related to hereditary factor of metabolic disorder (decreased action of insulin) and the factor of angiopathy and are progressed by the both factors separately.

Uronic acid of acid–mucopolysaccharide increases in the urine and in the diabetic glomerulosclerosis, so we suggest that this finding is related closely to diabetic glomerulosclerosis.