Species Specificity of Serum Factors from Rabbits with Acute Pancreatitis in Stimulation of B-cell Regeneration in Pancreatic Islets in Experimental Diabetes

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The humoral aspects of regulation of reparative processes in the liver [1-3], salivary glands, and exocrine part of the pancreas [1] have been studied in detail. However, the problems relating to stimulation of the regeneration of islet cells have received little attention. Earlier we found enhanced mitotic activity of B-insulocytes in rabbits following triplicate injection of serum from animals with acute pancreatitis obtained 12 hours after the disease was induced (unpublished data).

The aim of the present study was to establish the species specificity of the influence of serum factors from rabbits with acute pancreatitis on compensatory processes in experimental diabetes.

MATERIALS AND METHODS

The experiments were carried out on 78 male and female albino rats weighing 180-200 g. Experimental diabetes was induced in the rats by single intraperitoneal injection of alloxan (200 mg/kg). The animals of the first group were injected i.v. on the 7th day with 5 ml/kg serum obtained from rabbits 12 hours after mechanical trauma of the pancreas. The rats of the second and third groups were injected with serum from sham-operated and intact rabbits, respectively. The injections were performed once a day during 3 days. The animals were killed by ether overdose 1, 3, 7, 14, and 21 days after the last injection. Histological slices were stained with hematoxylin-eosin and aldehyde-fuchsin after Gomori, and with Phenaph dye, and impregnated after Grimelius. The fasting blood glucose concentration was determined by the orthotoluidine method, and in the urine by the Glucotest semiquantitative method.

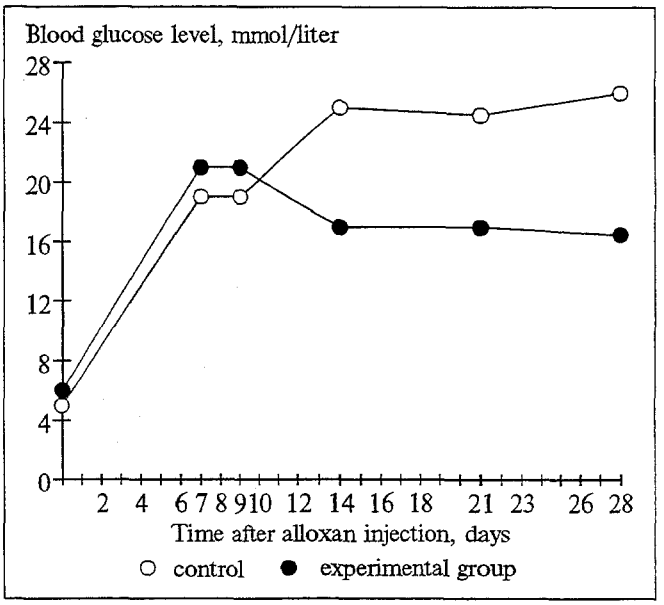

Fig. 1. Blood glucose level in rats with alloxan-induced diabetes without treatment (control) and after serum injection.

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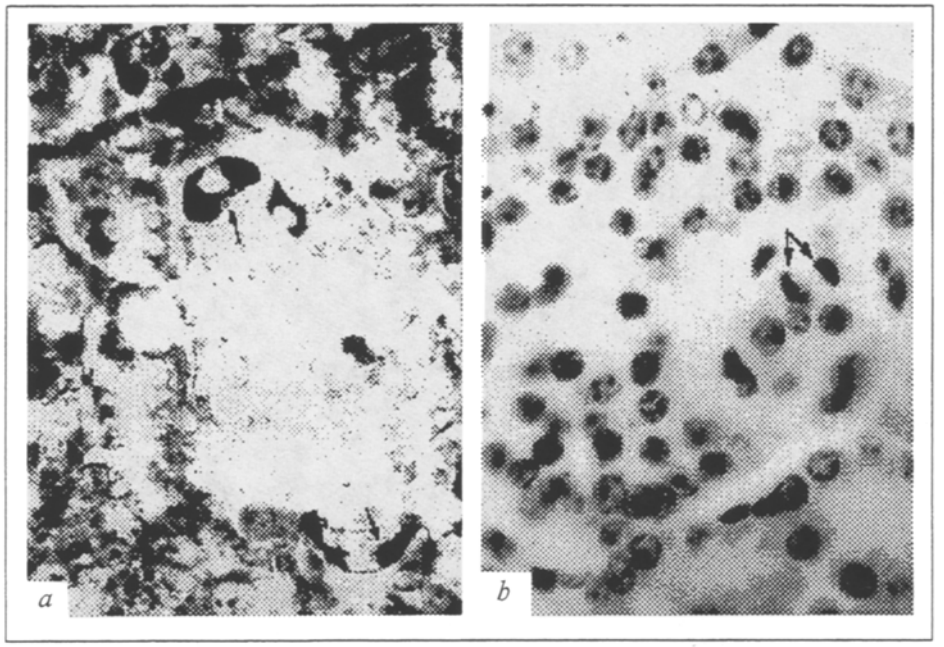

Fig. 2. Pancreatic islets from rats with alloxan diabetes. *a*) 7 days after alloxan injection (extensive necrosis of B-cells, solitary A-cells in peripheral zone of islet), impregnation after Grimelius; *b*) one day after three injections of 12-hour serum (anaphase of islet cell), staining with hematoxylin and eosin; magnification ×280.

RESULTS

One week after the alloxan injection we observed a distinct picture of acute diabetes mellitus in the rats, manifested as adynamia, weight loss, polydipsia, and polyuria. Fasting hyperglycemia reached 25.5 mmol/liter (normal value 4.0±0.5 mmol/liter), glucosuria being 5.0% (Fig.1). Histological study reveal marked dystrophic and necrotic changes in the islets, accompanied by massive B-cell mortality (Fig. 2, *a*).

One week following the last injection of serum from rabbits with acute pancreatitis, a considerably enhanced mitotic activity was found in the insular B-cells in rats with experimental diabetes (Fig. 2, *b*). The mitotic index (MI) reached 1.62‰ (versus 0.01‰ in intact and untreated animals). However, it should be noted that MI in the rats was reliably lower than that observed in rabbits treated with the same serum (2.15‰). At the same time, the serum from intact and sham-operated aminals had no stimulatory effect on the islet cells of rats with alloxan diabetes.

In the succeeding days the dynamics of mitotic activity of the B-cells was similar to that observed in rabbits, the values of MI being lower in the rats. After just 3 days a two-fold decrease of MI occurred (0.81‰). Meanwhile, in the rabbits this index was 1.09‰. After 7 days the mitotic activity continued to drop and reached 0.31‰, whereas in rabbits it was 0.76‰. The correlation between the level of glycemia and the mitotic activity of the endocrine cells is worthy of note. For example, 14 days after the last serum injection the MI dropped to the control value. At the same time, the drop of the blood glucose concentration, which started the very first days after serum injection, gradually reached a stable level (Fig. 1). The synchronous dynamics of the mitotic activity and glycemia level seems to reflect the differentiation and functional specialization of newly formed insular B-cells. The resulted is a partial compensation of the endocrine function of the pancreas in the rats. The general state of the animals improves and diuresis decreases. During the following days in the islet structures the compensation of damaged endocrine tissue through acino-insular transformation manifested in the proliferation of single B-cells as well as in the appearance of new small islets in the acini, becomes the major event.

The above data suggest the presence of factors in the serum of rabbits with acute pancreatitis which stimulate the repair processes in alloxan-damaged islets of the rat pancreas. They are, moreover, relatively species-specific, as seen from their lower effect in rats than in rabbits. This difference in the stimulation of regeneration in animals of another species may be attributed to partial inactivation of the serum components with antigenic properties, as well as poorer recognition of these humoral factors by insular B-cells or intermediate regulatory elements.

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