ULTRASONOGRAPHIC CHANGES OF THYROID GLAND IN DIABETES MELLITUS

THESIS

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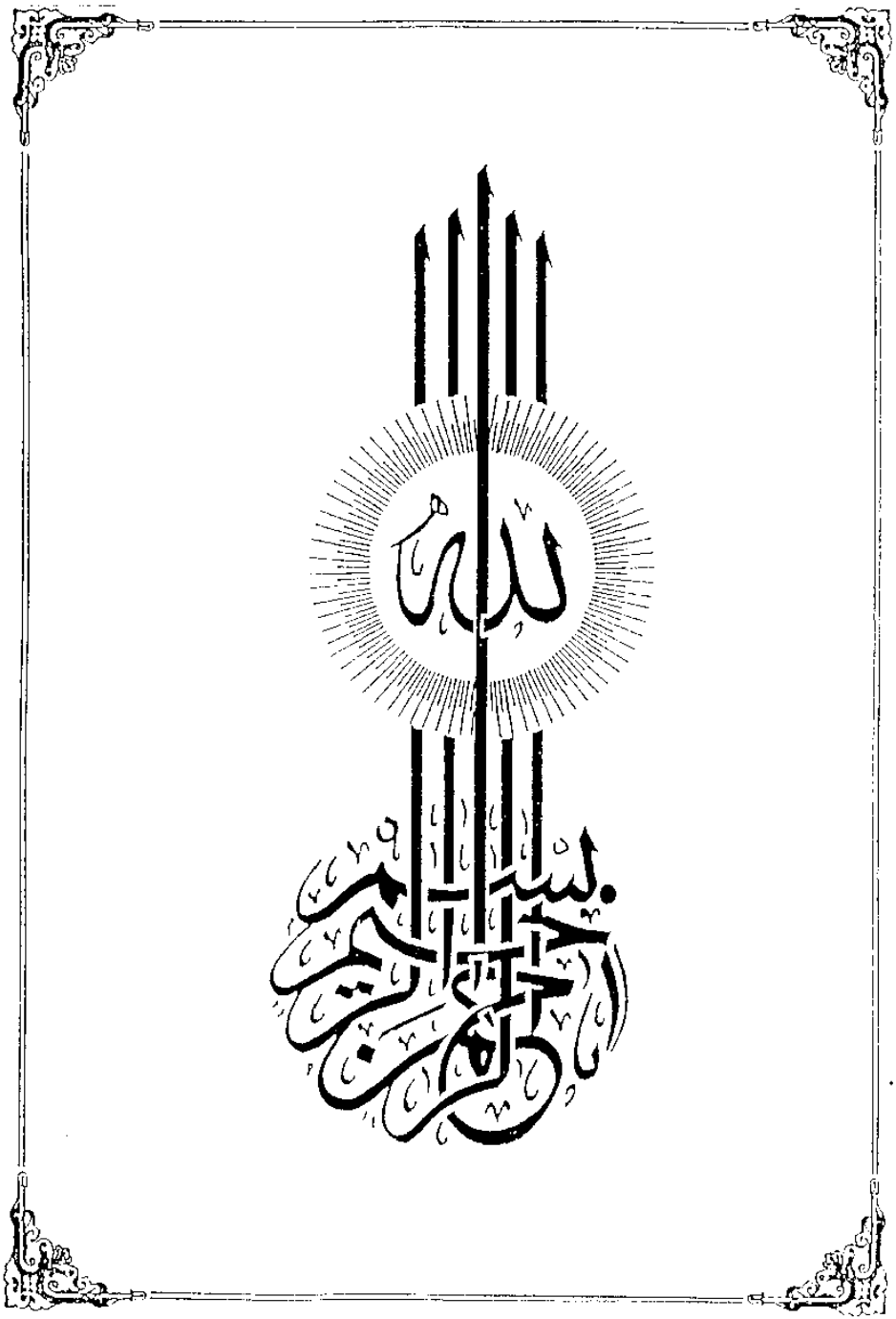

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INTRODUCTION

ENDOCRINAL CHANGES IN DIABETES MELLITUS

The development of an endocrinopathy in a patient with preexisting diabetes may be heralded by substantial alterations in diabetic control. Acromegaly, Cushing's disease, pheochromocytoma and hyperthyroidism can produce a marked increase in hypoglycemia, ketonuria, and insulin requirement. Alternatively, loss of growth hormone, thyroid, or adrenal function may cause a marked reduction in blood glucose, insulin requirement,and propensity to hyperketonemia. More importantly, these patients may suddenly develop bouts of severe hypoglycemia on small doses of insulin.

Correction of the endocrinopathy usually restores the premorbid state.

The occurrence of genetic diabetes mellitus and another endocrinopathy would be expected for a variety of reasons.

These include the usual risk for diabetes occurring independently in many patients the fact that these patients are very likely to undergo careful metabolic scrutiny as a part of their evaluation, and the ability of several endocrine conditions to bring out latent diabetes by specific hormonal effects.

Further,the diabetic state and other endocrinopathies may be linked by common etiologies, such as polyglandular immune destruction or immune-mediated hormone resistance.

On occasion, it will not be possible to distinguish the glucose intolerance caused by an endocrinopathy from coexistent diabetes mellitus.(Flier and Roth,1979).

Anderson (1968) reported that the disorders of the pituitary, adrenal and thyroid glands which cause hypersecretion are not invariably associated with loss of carbohydrate tolerance, and it is therefore possible that they precipitate the onset of diabetes only in patients rendered susciptible by genetic or other factors, such as obesity.

In favour of this view is the observation that successful treatment of endocrine disease is more often followed by disappearance of diabetes in patients without family history of diabetes than in those with one.

PANCREAS IN DIABETES MELLITUS

Pancreatic pathology in diabetes:

The pathology of pancreas varies greatly in diabetics. Four types of lesions have been observed:

1. Glycogen infilteration of B-cells.
2. Hydropic degeneration in B-cells.
3. Hyalinization of islets.
4. Lymphocytic infilteration of islets.

Since more than 80% of the normal pancrease must be removed for frank and permanent hyperglycemia to be produced, it is difficult to relate the metabolic findings in most patients to the pathology. Wrenshall found that in the normal individuals the amount of insulin extractable from the pancreas correlates best with the body surface area and is greatest in the most obese individuals. The amount of extractable insulin and the number of B-cells increase with the age from early childhood until they reach the adult level at the age 12-16 years.

In general diabetic subjects had lesser amounts of pancreatic insulin than non diabetic controls.This reduction averaged 40%,but most of the difference

was in subjects under the age of 20 with IDDM.*

Among other pancreatic pathology changes associated with diabetes,the most common is vaculoization of B-cells. These vacules give positive PAS reaction suggesting glycogen within them.Such alterations are found at autopsy in untreated hyperglycemia, and they do not occur in the treated diabetic syndrome. Similar findigns are observed in untreated experimental diabetes, in which there may also be an increase in glycogen of the ductular epithelium. Occasionally these vacuoles become complex and contain lipids as well as carbohydrates,such lesion have been called "hydropic degeneration" and have been considered by some to be precursors of the B-cell death. Hyalinization of the islets is relatively common occurring in 30-40% of diabetics.The hyaline material consists of deposits of a homogeneous subendothelial, acidophilic substance. A similar material may be found in non diabetic subjects. There is a considerable evidence that this hyaline material is or closely resembles, amyloid.Such idea somewhat strengthened by the lymphocyte infilterations observed in the absence of generalized pancreatic inflammatory disease in insulin dependent diabetes mellitus.This

* Insulin dependent diabetes mellitus.

finding has been termed insulitis and is of interest since viral and autoimmune etiologies have been proposed for juvenile-onset-type diabetes mellitus (Daniel et al., 1981).

PANCREATIC HORMONES IN DIABETES MELLITUS

A. Juvenile-Onset Type Diabetes Mellitus

Insulin

The form of diabetes is clearly associated with a deficiency of insulin secretion. For many years it was believed that complete destruction of the islets had occurred at the time of diagnosis. This belief appeared to be confirmed by the inability of such patients to secrete insulin in response to any islet challenge. However, it has been observed that basal insulin levels are often maintained near normal (but probably only because of severe hyperglycemia) and ketoacidosis does not always lead to permanent insulin therapy. Furthermore,there is the peculiar phenomenon of the honey moon period which is frequently observed during the first year or two of treatment Marked improvement in the carbohydrate tolerance is observed during this period, sometimes to the point where insulin therapy may be stopped for a short period of time. Insulin measurements at this time in patients without antibodies have demonstrated a partial restoration of insulin secretion, indicating that some of the

damage to the islets is reversible.

Because of circulating antibodies to insulin and their ability to bind endogenous and exogenous insulin,it was for a long time impossible to further assess insulin secretion during insulin therapy. (Daniel et al.,1981).

Glucagon

Secretion of this hormone is also abnormal in Juvenile onset diabetes. Basal levels are particularly high during ketoacidosis or in very poorly controlled patients.When tested with arginine, these subjects hyperrespond.When such patients are injected with glucose there is no suppression of the elevated level. Insulin treatment will usually reverse the abnormality and restore basal glucagon concentrations to the normal range.

If glucose is infused with insulin treatment, glucagon will be suppressed but only to about 50% of the normal response. However, if insulin is added to the glucose infusion, glucagon suppression may become normal. This may require very large injection of insulin,giving plasma concentrations higher than those found in normal subjects after a glucose without

insulin. If sufficient insulin is given to prodcue hypoglycemia, the normal glucagon elevation in response to this hypoglycemic stimulus is not observed.

This glucose is perceived poorly when it is elevated, while non glucose stimuli such as arginine produce at least normal and perhaps supernormal glucagon response.

Similarly, fatty acids elevations are capable of suppressing the A-cell normally.

During meal feeding the usual balance between stimulatory and inhibitory forces in normal subjects after mixed meals may be converted into hyperglucagonemic response in Juvenile-onset diabetic, while these responses can be normalized by insulin injection.If insulin treatment is stopped experimentally, glucagon levels rise quite rapidly.The prevention of this rise by the infusion somatostatin has been shown to delay hyperglycemia and ketonemia.However,these studies were complicated by the fact that growth hormone levels were also suppressed. Thus, it is possible that their may be an interaction between these two counterregulatory hormones rather than the effect due solely to glucagon

suppression. (Daniel et al 1981).

Somatostatin

Little is known about the role of somatostation in this syndrome,however, increased somatostation content and increased number of D-cells have been reported in pancreases of Juvenile-onset-type diabetics, and in alloxan or streptozotocin induced diabetes. If this finding is indicative of increased or inappropriate somatostatin release, its suppressive effects on the small amounts of residual B-cells could contribute significantly to the state of insulin deficiency in insulin dependant diabetics.(Daniel et al 1981).

MATURITY-ONSET-TYPE DIABETES MELLITUS

Insulin:

Insulin secretion in the basal state is normal in patients with modest fasting hyperglycemia (115-200 mg/dl). Basal insulin levels may in fact be elevated owing to the frequent presence of obesity in this group of patients. However, in both normal subjects and maturity-onset diabetes, basal insulin levels are not correlated with basal glucose but instead increase or decrease with changes in relative adiposity. Presumably this is a compensatory change related to the insulin resistance of obesity. This compensation remains nearly intact in patients with mild to moderate fasting hyperglycemia. Since the higher islet gain of obesity is reflected in the increased basal insulin levels in an increased insulin response to glucose. Daniel et al, 1981).

Glucagon:

Abnormalities of glucagon secretion can also be demonstrated in maturity-onset-type diabetes. The precise nature of the abnormality and whether it is independent change contributing to hyperglycemia or whether it is secondary to the hypoinsulinemia is