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CONGENITAL PERMANENT DIABETES MELLITUS WITH HYPOPLASIA OF THE PANCREAS: REPORT OF 2 CASES AND REVIEW OF THE LITERATURE

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ABSTRACT

Two siblings (a girl and a boy) with intrauterine growth retardation and early-onset insulin dependent diabetes mellitus, who had a clinical syndrome consistent with congenital pancreatic hypoplasia will be reported.
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INTRODUCTION

Insulin dependent diabetes mellitus occurring during the neonatal period is a rare event, and the majority of the reported cases are transient.[1,2] Permanent diabetes mellitus has been reported in approximately 40% of all cases of neonatal diabetes.[3]

Infection, hypothalamic or adrenocortical dysfunction, resistance to insulin, and beta cell hypoplasia have been suggested causes.[4] Disorders of pancreatic organogenesis that lead to IDDM range from isolated islet cell aplasia to pancreatic agenesis.[5] Pancreatic hypoplasia is an uncommon developmental defect that has not been well documented in association with type-I diabetes mellitus.[6] Two siblings with IDDM who had a clinical syndrome consistent with congenital pancreatic hypoplasia are presented in this paper. To our knowledge, 11 such cases have been reported in the literature to date.

CASE REPORTS

Case 1

A male infant was born weighing 2100 g after a 38-week gestation period to a 27 year old gravida 2, para 2, abortion 0 healthy mother. A previous sibling was a normal girl. There was a family history of permanent neonatal diabetes mellitus in his maternal cousin who died at 9 months of age due to severe gastroenteritis.

The patient developed weight loss, fever, dehydration, tachypnea and persistent hyperglycemia requiring insulin therapy at the end of the first week of life. Abdominal distension and frequent loose stools were first noted 5 months later. Fecal fat analysis at 7 months of age confirmed the presence of steatorrhea. On two occasions the sweat chloride level was normal and he showed no evidence of chronic lung disease. Intestinal mucosal function appeared normal by the D-xylose test. At the age of 9 months he was on 4 units of NPH insulin each day. At about the same age he developed ascites, hepatomegaly, and jaundice with severe hepatic enzyme elevation (SGPT=2735 IU).

He was managed as a case of septicemia and hepatic failure without any benefit and the patient expired one week later.

Case 2

The sister of case 1 (a 1.5 year old girl) was also small for gestational age with a birth weight of 2 kg. At the age of 2 days she was referred for unexplained irritability. Hyperglycemia and glucosuria were detected and insulin therapy was begun.

At the age of one year she developed steatorrhea. D-xylose absorption, sweat chloride test, and neutrophil count were normal. She had no evidence of chronic pulmonary disease or abnormal susceptibility to infections. CT scan of the pancreas showed pancreatic hypoplasia. She was treated with pancreatic enzyme extracts. Her diabetes remained stable with a daily dose of 3 to 4 units of NPH insulin, and she had no episode of ketoacidosis up to 1.5 years of age.

DISCUSSION

In contrast to the course of the patients presented, transient neonatal diabetes resolves within the first few months of

life.[1] In the literature several cases of permanent diabetes mellitus appearing in the first months of life are reported.[2] A variety of etiologic factors have been suggested for this syndrome, including hypothalamic imbalance, infection, adrenocortical disturbance, insulin resistance or absolute hypoinsulinemia due to hypoplasia of beta cells.[4]

The findings of intrauterine growth retardation, onset of IDDM in early infancy and biochemical evidence of pancreatic exocrine insufficiency in these siblings were consistent with pancreatic hypoplasia. Because insulin is a major intrauterine growth factor, intrauterine insulin deficiency leads to growth retardation.[8] The absence of elevated sweat chloride test results, chronic lung disease, severe or recurrent infections and neutropenia ruled out the possibility of cystic fibrosis or Schwachman syndrome.

The cause of death in the first case seems to be hepatic failure. Involvement of two siblings (both sexes) and a close relative would strongly suggest the possibility of an autosomal recessive mode of inheritance of the disease.

A severe disruption in normal cellular differentiation is the presumed cause of pancreatic hypoplasia or agenesis.[7] There is considerable experimental evidence that insulin is necessary for maintenance of normal hepatic architecture and for regeneration after injury.[9]

The liver in normal humans is exposed to much higher insulin concentrations in portal blood than are found in the systemic circulation; if this is important in maintaining liver structure, insulin treated diabetic subjects would be expected to show a high incidence of hepatic abnormalities. Fatty infiltration of the liver is the most consistent change in diabetes mellitus, but liver function tests in well controlled diabetes reveal little difference from those of normal subjects.[11]

Cirrhosis follows viral hepatitis more frequently in diabetics than in non-diabetics.[12] Nevertheless, there is little evidence in man that pancreatic hyposecretion in diabetes leads to serious loss of hepatic integrity in the absence of further liver insult.[13] It is conceivable that a hepatic cellular insult was the cause of subsequent liver failure in the first case reported here.

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