877

Muscle Carnitine Deficiency in a Patient with Persistent Neonatal Diabetes and Hypokalemia.

J. McLAUGHLIN, P. OZAND, L. KOSKI, N. MACLAREN*, M. GUMBINAS, R. BEJAR and M. CORNBATH, Baltimore, MD

A 3 year old Cuban female with persistent neonatal diabetes mellitus developed corneal opacities, photophobia, hirsutism and failure to thrive following a prolonged episode of hypoglycemia with coma and seizure at 8 months of age. Generalized myopathy with marked proximal muscle weakness was noted at 2 years of age. Persistent hypokalemia was noted from 2½ years of age. Electromyography and nerve conduction velocities at 3 years of age showed mild non-specific changes but the creatine-phosphokinase was elevated at 197mU/ml (N<45mU/ml) and the muscle biopsy showed increased intrafiber (type I fibers) fat droplets. The serum carnitine was normal at 79.2µM/L (mean of 26 age control sera 53±21µM/L) but the muscle free carnitine and short chain acyl carnitine were markedly reduced at 0.29 (N>1.6) and 0.09 (N>1.1) µM/gm muscle respectively. Additionally hyperaldosteronism and hyperreninemia were also noted in face of a normal blood pressure.

This case appears to show a previously undescribed association between insulin requiring diabetes and muscle carnitine deficiency. An underlying defect of cellular membrane transport involving muscle, cornea and perhaps pancreatic β cells is suggested by the findings. Supported NIH grants A.M. 19256 and A.M. 05745.

880

THE HYPERGLYCEMIA OF CYSTIC FIBROSIS L.W. Matthews, H. Rodman, & E. Nussbaum Case Western Reserve University, Rainbow Babies & Childrens Hospital, Cleveland.

Oral glucose tolerance tests (OGTT) separated 30 cystic fibrosis (CF) patients into those with normal OGTT (Group I-8), normal fasting but abnormal OGTT (Group II-14) and manifest hyperglycemia treated with insulin (Group III-8). Mean peak glucose in OGTT was 153 mg% and 229 mg% at 90' and 526 mg% at 150' in Groups I(G₁), G₂, and G₃ respectively (p<0.0005). Insulin response was delayed with mean peaks of 56 µU/ml at 120' in G₁, 72 µU/ml at 150' in G₂ and 10.9 µU/ml at 240' in G₃. Insulin responses to OGTT were higher than to intravenous glucose tolerance tests (IVGTT) for G₁. In G₂ the mean plasma glucagon was suppressed by 25 pg/ml at 60' during both OGTT and IVGTT suggesting that abnormal OGTT may occur in the presence of normal glucagon suppression. Unlike previous studies G₃ showed mean glucagon increase by 53 pg/ml at 120' suggesting a paradoxical rise with significant insulin deficiency. Mean glucagon increased by only 66 pg/ml during arginine TT (ATT) in G₃ which differs from previous reports for C.F. and from juvenile diabetes whose plasma glucagon rises excessively during ATT. At 120' OGTT suppressed mean human growth hormone (HGH) by 5.08 ng/ml in G₁ and by only 0.8 ng/ml in G₃ (p<0.05). At 40' IVGTT suppressed mean HGH by 1.0 ng/ml in G₂ and increased by 0.5 ng/ml in G₃ (p<0.05). During ATT HGH was higher in G₃ (p<0.05). In spite of impairment of their carbohydrate metabolism C.F.'s maintain peripheral tissue sensitivity to insulin resulting in significant decreases in glucose at 10' during insulin TT in all groups. The difference from juvenile diabetes mellitus is probably due to the multi-hormonal abnormalities in C.F.

878

FAILURE TO ISOLATE A TRANSMISSIBLE AGENT FROM THE PANCREAS OF A CHILD WITH NEWLY DIAGNOSED DIABETES MELLITUS. Melvin I. Marks, Alan Soneji, Robert

Bolande, Elizabeth Rapaport, Hy Goldman. McGill University, Montreal Children's Hospital, Department of Pediatrics, Montreal.

A 9 year old girl died in ketoacidotic coma that developed less than two weeks after her first symptoms of diabetes mellitus. Electron microscopic examination of pancreatic tissue showed acute beta cell necrosis associated with myxoparameyovirus-like particles in islet, acinar and ductal cells. We attempted to isolate a virus from the pancreas of this patient by several techniques. Primary inoculation and passage of pancreas onto Hep 2, cerco (CMK) and rhesus monkey kidney, and human embryonic lung (HEL) tissue culture were negative for cytopathic effect (CPE), hemadsorption with guinea pig red blood cells (HA), challenge with echovirus 11 and electron microscopy (EM). Whole islet and pancreatic suspension cultures were adapted to monolayer cultures and maintained for 20 passages. These materials were also co-cultivated with CMK Hep 2 and HEL for 6 passages and with Hela and Vero cells for 20 passages. All passages (cell contents and supernatant) of pancreas and co-cultivations remained negative for CPE, HA, hemagglutination, echovirus 11 challenge and EM after ultra-centrifugation. Late passages treated with 5-iodo-2-deoxyuridine for 24 and 48 hours also remained negative. Conventional and "rescue" techniques failed to detect complete or latent viruses in the pancreas of a child with recent onset diabetes mellitus.

881

PLASMA LIPID LEVELS IN INSULIN DEPENDENT DIABETES: CORRELATION TO CONTROL. W.V. Moore, W.G. Perkins, J. Knapp and R. Kauffman (Spon. by C. Cho), Kans. Med. Ctr., Sect. of Ped. Endocrinol., Kansas City, Kans.

Recent reports observed that 20-50% of insulin dependent diabetic children have hyperlipidemia. A study of the insulin dependent diabetic population at this center detected an incidence not significantly different from the general population. The reason for the discrepancy was investigated. Forty-seven diabetics (age 2.5-19.3 yr) had a mean plasma triglyceride of 55±33 mg/dl compared to 56±38 mg/dl for a normal control population. The mean cholesterol was 164±38 mg/dl, significantly less than the 183±26 mg/dl of normal controls. Three patients had cholesterol >220 or triglyceride >140 mg/dl giving an incidence of hyperlipidemia of 6.4% compared to 5.7% for the normal controls. The patients were divided into groups based on adequacy of control of the diabetes. The poor control group was older but the duration of diabetes, male/female ratio, % of ideal body weight, insulin dosage, and excess caloric and carbohydrate intake did not differ among the groups. The poor control group's diet was characterized by higher fat, lower protein and higher cholesterol intake. The major distinction between this diabetic population and those with elevated lipids was prescribed versus "free" diet. We conclude that: 1) hyperlipidemia is not necessarily a concomitant of insulin dependent diabetes, and 2) composition of the diet is the major determinant of plasma lipid levels in insulin dependent diabetics maintained in a reasonable degree of control.

879

FRUCTOSE-1,6-DIPHOSPHATASE ACTIVITY IN HUMAN TERM PLACENTA. Reuben Matalon, Parvin Justice, Kimberlee Michals and Minerva Deanching. University of

Illinois Hospital, Department of Pediatrics, Chicago, Illinois. Fructose-1,6-diphosphatase (FDPase) is a liver gluconeogenic enzyme. FDPase deficiency has been described which is characterized by severe hypoglycemic episodes, metabolic acidosis, and hepatomegaly. FDPase deficiency may be diagnosed by the enzyme assay only if liver tissue is utilized. For the study of FDPase activity in tissues other than liver, human term placentas were used. Placental slices were washed with cold 0.15 M NaCl then sonicated in 0.2 M glycine buffer, pH 9.2, containing 0.1 M MnCl₂, then centrifuged at 10,000 xg for 10 min. The supernatant fractions were assayed for FDPase activity using fructose-1,6-diphosphate as substrate. The hydrolyzed phosphate was estimated by the method of Fiske and Subbarow. Extracts from normal human placentas hydrolyze 1.5 µM phosphate/mg protein/hr. In order to ascertain that the phosphate hydrolyzed is from Fructose-1,6-diphosphate, a labeled substrate U-(14C)-Fructose-1,6-diphosphate was used and the hydrolysis products were determined by thin layer chromatography using 80% propanol as solvent. Full term placental extracts hydrolyze 40% of the radioactive substrate per 100 µg of protein per hour. These data indicate the presence of FDPase in placental tissues which may prove useful in the study of pregnancies at risk for FDPase deficiency. This assay may be used for the study of the gluconeogenesis in human placenta. Supported by Nat'l Foundation Grants - 244-39-66-321 and 244-39-66-317

882

THE OUTCOME OF DIABETIC PREGNANCIES, A PROSPECTIVE STUDY. Richard L. Naeye, Pennsylvania State University, College of Medicine, Dept. of Pathology, Hershey, Pa.

The perinatal mortality rate was 71/1000 for diabetic and 34/1000 for the nondiabetic in a prospective study of 53,518 pregnancies. Placentas from the diabetics had twice the frequency of atheromata, fibrinoid change and thrombi in decidual arteries as the nondiabetics. 40% of the excess perinatal deaths in offspring of diabetics were due to the consequences of these lesions, i.e. large infarcts and marked growth retardation of placentas. The diabetic placentas showed an excess of lesions characteristic of underperfusion, excessive syncytial knots and retained cytotrophoblast. 17% of the excess perinatal deaths in offspring of diabetics were related to maternal acidosis or insulin shock, 4% to hydramnios, 12% to severe congenital anomalies, 12% to the complications of Caesarean section and 5% to amniotic fluid bacterial infections. These latter infections were only half as frequent but their mortality was 2.6 times greater in offspring of diabetics than of nondiabetics.

Histologic grading demonstrated normal lung maturation for neonates of diabetic mothers when they were compared with offspring of nondiabetics in the same fetal growth percentile. Low IQ values and excessive neurologic abnormalities in 4 year old offspring of ketotic diabetic gravaida were related to amniotic fluid bacterial infections and their complications rather than to the ketoacidosis.