CASE REPORT

GLYCOGEN STORAGE DISEASE

BY

MARY CRAGO, M.B. Ch.B.

Late House Physician, Hospital for Sick Children, Great Ormond Street, London

The diagnosis of glycogen storage, or von Gierke's disease, is frequently made only at autopsy, particularly if the clinical picture presents an unusual aspect of the disease. The most common clinical finding is enlargement of the liver associated with a low fasting blood sugar, a defective or absent rise in the blood sugar following an injection of adrenaline, and ketonuria. Many other features, however, have been described, and the clinical picture may be varied. This is not surprising in view of the underlying factor in the pathology of the disease, namely, that there is an excessive accumulation of glycogen, which is difficult of mobilization, in various organs. These organs vary from the liver, kidney, heart, intestines, stomach, pylorus and oesophagus, to the brain, spinal cord, blood vessels and striped muscles. It is because the present case shows unusual aspects of the disease that it seems worth while to report it.

The pathogenesis of the disease had not been finally settled. Ellis and Payne (1934) consider that the enzyme responsible for the breakdown of glycogen is missing within the liver cell. They also point out the possibility of anterior pituitary dysfunction as a cause, since Houssay and Biasotti (1931) have shown that extirpation of the pituitary results, among other things, in an increased resistance on the part of the liver to liberate glucose from its glycogen stores.

Clinical record

P. M., male, aged three and a half months, was admitted to hospital on March 17, 1942, on account of feeding difficulties. He was the fifth child, full term, born by normal labour, and his birth weight was 6½ lb. He was breast fed for the first three weeks, but he vomited occasionally, and failed to gain weight. He was then changed from cow's milk and water to national dried milk, and then to a proprietary full-cream dried milk, but without success, and the vomits which were at first regurgitations now 'shot out.'

On examination he was found to be wasted (weighing 6 lb. 1 oz.) and dark skinned. He was intelligent and took considerable notice of what was going on around him. The abdomen was prominent due to enlargement of the liver which extended

4 inches below the costal margin, and was firm and smooth, with a well defined edge. The spleen was not enlarged. There were no changes to be found in the central nervous system, or other systems.

Progress. Soon after admission the child had a 'fit.' He went a greyish-white colour, his respirations increased, there were slight generalized twitchings of his limbs, and he seemed exhausted. Nikethamide was given and he recovered shortly afterwards. In the following days he had several such attacks. During this time the child vomited occasionally but this was not projectile in character.

Investigations. Lumbar puncture showed no abnormality of the cerebro-spinal fluid.

A single blood sugar estimation was done two hours after a feed, and this showed 235 mgm. per cent. of sugar; the urine on two occasions contained sugar in small quantities, on the first occasion no acetone was present, and on the second acetone was found.

The Wasserman reaction was negative.

The blood count showed a mild hypochromic anaemia, but was otherwise within normal limits.

On the assumption that this was an unusual case of diabetes mellitus, insulin was given, one unit half an hour before his feed. Half an hour after the insulin had been given, however, he had another attack similar to the previous ones, but recovered on being given his feed. He died the following day.

Post-mortem findings (less than twenty-four hours after death.):

EXTERNAL—small wasted, male child.

BRAIN—slight congestion, otherwise normal.

CARDIOVASCULAR SYSTEM—heart muscle pale, but firm and of average thickness. Ductus arteriosus admitted a fine probe and foramen ovale slightly patent.

RESPIRATORY SYSTEM—a few areas of atelectasis in posterior parts of both lower lobes. Lungs slightly congested.

DIGESTIVE SYSTEM—tonsils, oesophagus, stomach, intestines, pancreas: nil abnormal. Liver: 10 oz., enlarged, smooth, pale yellow, fairly firm. Pattern: clear outline, with fine grey markings. Gall bladder etc.: normal. Light yellow bile.

HAEMATOPOIETIC SYSTEM—spleen: nil abnormal. Lymph glands: mesenteric slightly swollen.

URINARY SYSTEM—kidneys: slight congestion. Bladder: nil abnormal.

DUCTLESS GLANDS—nil abnormal.

Microscopic examination. Liver : sections of formalin-fixed material, stained with Best's carmine, show large quantities of glycogen in the liver cells abnormally resistant to post-mortem autolysis. There is a moderate increase of fibrous tissue producing the appearance of an early portal cirrhosis. A narrow rim of liver cells adjacent to the fibrous tissue at the periphery of the lobules contains less glycogen than the remainder of the lobules, but shows a slight degree of fatty change in addition (fig. 1).

HEART : myocardium of left ventricle contains a moderate amount of glycogen. The myocardial fibres do not appear enlarged. Glycogen cannot be demonstrated in the right ventricle but the fibres are somewhat vacuolated.

KIDNEYS : glycogen can only be demonstrated in an occasional cell of the renal tubules, but many of the tubular epithelial cells are pale and foamy and possibly may have contained this substance.

DUODENUM : a large amount of glycogen is demonstrable in the villi and mucosal glands.

Discussion

The following are points of interest.

Age. It seems likely that glycogen storage disease is congenital since in patients described by Schall (1932), Unshelm (1931), and Kimmelsteil (1933), the large size of the abdomen was noted within the first few weeks of life, and those of van Creveld (1933), Bischoff (1932), and Holt (1932), probably from birth. In the majority of patients, however, symptoms are delayed until about three to five years, though the patient described by Holt was two days

old at the onset, and the case here described had symptoms within the first few weeks of life.

Vomiting. This has been described by Worster-Drought (1923), Holmes á Court and Bray (1934), van Creveld and others, but has been cyclical in character. The significance of the presence of glycogen accumulation in the pylorus as a possible cause of pyloric stenosis in infants has been discussed by van Creveld.

Although none was found in the pylorus in the present case, the presence of glycogen in the duodenum may have been responsible for the projectile vomiting with which the infant suffered during the first few weeks of life.

Hypoglycaemic attacks. That the 'fits' were really attacks due to a lowered blood sugar seems probable since they occurred before meals, and were relieved by taking a feed. Hypoglycaemic attacks are surprisingly rare, having been described in only four cases up to the present.

Other case reports

Holt describes the case of a female infant who developed respiratory distress two days after birth, and went into a state of collapse. Her liver was found to be greatly enlarged and there was acetone in her urine. The blood sugar level was 16 mgm. per cent. and she recovered on being given glucose saline infusion. There was no rise in the blood sugar level after an injection of adrenaline. She improved, and during the second month the glucose tolerance test showed a blood sugar level of 382 mgm. per cent at 1 hr., and 150, 121, 58 mgm. per

FIG. 1.

cent. at 2, 3, and 4 hours respectively. At the age of 2½ months she died of a respiratory infection, and autopsy showed a high percentage of abnormally stable glycogen in the liver.

Solomon and Anderson's (1933) case came under observation at the age of 22 months on account of failure to grow and gain weight. The liver was found to be enlarged, the blood sugar was within normal limits; the urine contained a trace of sugar. Almost a year later the child began to have 'turns' resembling epileptiform seizures, which always occurred between five and six in the morning. Acetone was found in the urine on one occasion. The fasting blood sugar was 56 mgm. per cent. and this rose to 88 mgm. per cent. after glucose ingestion. On feeding the child with an abundance of glucose at night the attacks did not occur.

Worster-Drought's patient came under observation at the age of ten years with a history of epileptiform attacks from one to four years. Then these attacks ceased, but she had been subject to attacks of cyclical vomiting. On examination she was found to be undersized and had an enlarged liver. The fasting blood sugar was within normal limits, there was no glycosuria, but the urine contained acetone and diacetic acid.

Holmes á Court and Bray's case was first observed at the age of three and a half years, having had liver enlargement from the age of six months. She had a history of recurrent fits and attacks of vomiting since she was three months old, which had diminished in frequency. She was mentally

retarded. The urine showed persistent acetonuria but no glycosuria. The fasting blood sugar was low, and the adrenaline response was negative.

Summary

The case report of a child aged three months suffering from glycogen storage disease is described: the main symptoms were projectile vomiting, and hypoglycaemic attacks.

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