HYPOKALEMIC MYOCARDITIS
REPORT OF TWO CASES*

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It is our purpose to report two instances of focal necrosis and inflammation of the myocardium produced in patients presumed to have potassium deficiency associated with diabetic acidosis.

We have used the term "hypokalemic myocarditis" to indicate a lesion occurring in patients with potassium deficiency. The loss of the main cellular cation, potassium, has been found in the following conditions: fasting, diarrhea, diabetic coma and dehydration. It has also been found experimentally in animals on a low-potassium, high-sodium diet which was ingested at the expense of the replenishment of the extracellular compartment; in animals treated with desoxycorticosterone acetate; and in subjects in alkalosis. Furthermore, it has been found that the administration of potassium as well as sodium is beneficial in some of these conditions.

In 1942 Darrow and Miller experimentally produced potassium deficiency in rats by repeated injections of desoxycorticosterone. The myocardial lesions were described as focal areas of necrosis of myocardial fibers with macrophagic and fibroblastic proliferation surrounded by lymphocytes. These observers found that high doses of desoxycorticosterone replaced potassium in the muscle fiber by sodium. The lesions were prevented by the administration of potassium chloride in water. The work of Darrow and Miller was substantiated by Follis and associates, who described similar lesions in the kidneys and myocardium of rats in which potassium deficiency was induced by a low-potassium, high-sodium diet. They also found that it took eight days before the characteristic picture was produced in the myocardium. Recently Perkins and associates, in a report of a man suffering from protracted diarrhea, demonstrated characteristic electrocardiographic findings, low serum-potassium levels and described myocardial lesions identical with those reported by Darrow and Miller. In 1944 Goodof and McBryde described typical myocardial changes in a patient with Addison’s disease who was receiving desoxycorticosterone by pellet implantation but discontinued taking the prescribed fluid and food.

Frenkel, Groen and Wallebrands, Holler, and Nicholson and Branning reported recovery of patients from diabetic acidosis following the administration of potassium.

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REPORT OF CASES

Case 1

Clinical data. A well nourished two-year-old white boy was admitted to the hospital in coma. Two weeks prior to admission he exhibited polydypsia and polyuria, and two days before entry he developed anorexia, vomiting, drowsiness, and incontinence of urine. He was in fairly deep coma, his respiratory movements were deep and rapid and his pulse weak and fast. The skin was hot, dry and pale. The breath had a faint odor of acetone. The chest was clear and resonant. The reflexes were hypoactive. On the day of admission the blood glucose was 409 mg. per 100 ml. blood and the CO₂ combining-power was 18 volumes per 100 ml. blood plasma. Urinalysis revealed 4-plus sugar, albumin and a trace of acetone. The patient was placed in an oxygen tent, and was given fluids, glucose in saline intravenously and insulin. During the first nine hours there was slow recovery of consciousness. Despite the administration of 3075 ml. of 5 per cent glucose in saline in twenty-four hours the urinary output was 700 ml.

On the following day the extremities were cold, the patient again lapsed into coma and a complete flaccid paralysis became apparent. The respirations were rapid, shallow and occasionally grunting in type. Cyanosis became apparent and two hours later the child expired.

Autopsy was performed one and one-half hours after death. External examination revealed a well developed, well nourished child exhibiting cyanosis of fingertips and lips. Postmortem rigor was absent. Each pleural cavity contained about 75 ml. of clear straw-colored fluid; 200 ml. of similar fluid was present in the peritoneal cavity. The heart weighed 50 Gm. and was of normal color and soft consistency. The epicardial surface was smooth and glistening. The right ventricle was dilated. The lungs contained several small areas of consolidation. The other essential organs appeared normal except for small atrophic fatty pancreas.

Microscopic sections of the heart (Fig. 1) revealed marked edema and fragmentation of the myocardial fibers. There were widely distributed foci of necrosis with fibroblastic proliferation and lymphocytic infiltration. That these areas represented early lesions was shown by the lack of formation of collagen and new capillaries. Sections of the lungs showed patchy areas of atelectasis. The liver exhibited fatty degeneration of the parenchyma. The pancreas was characterized by marked hypoplasia of the islands of Langerhans with nearly complete absence of the beta cells. Occasional collections of lymphocytes were seen.

Case 2

Clinical data. A 77-year-old white woman had been known to have diabetes for many years. The history as obtained from a member of the family indicated that the patient had refused to take insulin or food during the ten days preceding entry. Previously she had regularly taken insulin and diuretics, and digitalis had been prescribed for relief of a cardiac condition. She was admitted to the hospital in a stuporous state and later lapsed into deep coma. The skin was cold to touch and there was marked cyanosis. The pulse was feeble and rapid; the blood pressure at the time of admission was 80/60. Respirations were shallow and grunting. Marked ankylosis of various joints was attributable to a long-standing rheumatoid arthritis. The blood sugar at the time of admission was 409 mg. per 100 ml. blood. In spite of all supportive efforts the patient expired shortly after admission.
Necropsy was performed three and one-half hours after death. The serous cavities were free of fluid and their surfaces were smooth and glistening. The heart weighted 575 Gm. It was markedly enlarged and its apex approached the left lateral thoracic wall. The right atrium and ventricle were moderately dilated. The left ventricular wall measured 1.2 cm. in thickness and in its anterior wall was palpated an area of softening measuring 1.5 cm. in diameter which grossly was assumed to be a recent infarct. The myocardium was otherwise of normal color though of slightly soft consistency. The coronary vessels were carefully inspected and no evidence of thrombotic occlusion was seen. There was some sclerosis and narrowing but it was felt that there was enough patency for adequate blood flow. The valves were normal. The right lung weighed 525 Gm. and the left 375 Gm. There was some hypostatic congestion of both lower lobes. Purulent material exuded from the smaller bronchioles in the upper lobes, but from the lower lobes only frothy material was expressed. The liver was normal in weight and color. The wall of the gallbladder was thickened and the lumen contained stones. The spleen, adrenals and pancreas were not remarkable. The kidneys were of normal weight but the capsules stripped with difficulty revealing granular surfaces. On sectioning, pale areas of fibrosis were seen alternating with the normal parenchyma. The cortex was thin and irregular in contour. The other organs were not unusual.

Microscopic examination of the heart revealed myocardial lesions in practically all stages of development. The earliest was characterized by edema of the muscle fibers with fragmentation, necrosis and lymphocytic infiltration. This appeared to be followed by a more diffuse infiltration with lymphocytes. In older lesions fibrosis and collagen formation became evident. There was an abundance of lymphocytes but few or no macrophages. The lesions were found in all parts of the myocardium, including the area of softening noted grossly (Figs. 2 and 3).

The lungs were characterized by edema and congestion with many pigmented macrophages in the alveoli. The liver presented chronic passive congestion with periporal lymphocytic infiltration. The kidneys were the seat of arteriosclerosis with glomerulosclerosis. The convoluted tubules were widened and there was cloudy swelling of the epithelium. Sections of the pancreas revealed hyalinization of many islands with occasional compensatory hyperplasia of others. There was also a mild chronic pancreatitis.

It seems unlikely that the myocardial lesions in either case were due to ischemia. Neutrophils are characteristically predominant in early ischemic lesions, while lymphocytes predominated to the exclusion of neutrophils in the early lesions of the cases presented. The older lesions showed an abundance of lympho-

Fig. 1. Case 1. Early lesion. Note the separation of the myocardial fibers secondary to interstitial edema. There is fragmentation and beginning lymphocytic infiltration. X 100.

Fig. 2. Case 2. Focal area of necrosis with lymphocytic infiltration of the adjacent interfibrillar spaces. Neutrophils are absent. This lesion shows fibroblastic proliferation but slight fibrosis.

Fig. 3. Case 2. Typical myocardial lesion of a later stage. There is fibrosis with collagen deposition and an abundance of lymphocytes. Macrophages are absent.
FIGS. 1-3

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cytes and differed from infarcts in the lack of macrophagic infiltration and a lesser amount of fibrosis and collagen formation. There was no suggestion of rheumatic fever and little evidence of infectious disease in either case.

**DISCUSSION**

Hypokalemia is usually manifested by hypoactive reflexes, respiratory embarrassment and flaccid paralysis. A characteristic flattening or absence of the T wave and a depressed S-T segment in the electrocardiogram has also been recorded. A history of recovery from diabetic acidosis is quite typical in such cases. Diabetic acidosis was present in the patients of Frenkel and associates and those reported by Holler.

Elkinton, Winkler and Danowski described diminution in serum potassium levels in association with hypertonicity and dehydration resulting from water restriction or diuresis induced by urea. With hypotonicity there may be loss of cell potassium without associated increase in the serum potassium. However, in cases with oliguria or anuria or when the renal mechanism is impaired, potassium may not leave the cells. The ability to excrete extracellular potassium is one factor in the movement of this cation from the cells. Leaf and Camara found that in man during the nephrotic phase of renal insufficiency the tubules were capable of excreting potassium. This serves to prevent extracellular accumulation but leads ultimately to a deficiency of the cation in those cases lacking an exogenous supply.

The deficit of the cation is at the expense of the intracellular element since the body attempts at all times to maintain a normal level of extracellular potassium. Danowski and associates and Elkinton and associates have concluded that the entry of the cation into the cells depends upon the availability of an exogenous supply of the cation. The reverse holds true only in familial periodic paralysis.

One must conclude, therefore, that several factors enter into the production of hypokalemia in diabetic acidosis. Dehydration and insufficient exogenous supply of potassium due to an improper diet are probably of prime importance. The diuretic and dilution effect of the intravenous therapy of glucose and saline without replacement of intracellular potassium is another factor. Finally, insulin has a potassium-fixing effect, which is probably due to the transformation of glucose into potassium hexose-phosphate. This further depletes the available ionic substance.

In Case 1 the four factors listed for the production of potassium deficiency were present. These were dehydration and a deficient supply of exogenous potassium, dilution of the extracellular fluids by intravenous therapy and the fixing-effect of the insulin on glucose and potassium. The myocardial lesions were identical with those described in experimental potassium deficiency and in the proven cases of clinical hypokalemia. In Case 2, so far as can be determined, the patient received no therapy except diuretics. However, prolonged coma, acidosis and dehydration might well have produced the hypokalemic lesions. In this patient, a negative potassium balance was further enhanced by renal insufficiency.
Myocardial damage of this nature in diabetic acidosis would appear to be of permanent nature and all patients in diabetic acidosis should be evaluated from the point of view of negative potassium balance.

**SUMMARY**

Two cases of diabetic acidosis exhibiting myocardial lesions similar to those described in experimental and clinical potassium deficiency are presented. The lesions are characterized by focal necrosis with a related lymphocytic reaction.

**REFERENCES**