DIABETIC KETOSIS COMPLICATED BY ACUTE RENAL FAILURE

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A DEGREE of nitrogen retention is the rule in diabetic ketosis (Lyall and Anderson 1932) but despite this there are very few reported cases in which the uræmia has become clinically important nor has the pathogenesis of this change been fully elucidated. Aoyama and Kolff (1958) have reported a case of diabetic coma in which hæmodialysis was used first to correct the acidosis and on a second occasion a few days later to combat the electrolyte upset of associated acute renal failure. A similar case, treated with hæmodialysis, has been described by Lasch (1960). Other cases of acute renal failure complicating diabetic ketosis are on record (Gastineau, 1959; Chao, 1959) but most were of mild degree and responded to conservative treatment. Parsons (1959) mentions diabetic ketosis as a cause of acute renal failure, but gives no details.

The present case of diabetic ketosis complicated by acute renal failure is reported for several reasons. Since there are few such cases on record, it is important to draw attention to renal function in diabetic ketosis; failure to recognize the development of renal complications might be disastrous. The combination of renal failure and diabetic ketosis presents a complex electrolyte upset, the management of which requires very careful thought. This case demonstrates that hæmodialysis can offer a speedy solution to such problems, and indeed it may be the only satisfactory answer to electrolyte upsets of this kind.

Case Report

The patient was a female, aged 61 years, with diabetes of 30 years' standing, which was previously well controlled on 36 units of soluble insulin daily, in divided doses. On July 3, 1961, she developed profuse diarrhoea and was admitted to the Victoria Infirmary, Glasgow. Severe diabetic ketosis was found to be present, and she was in coma, with the blood pressure unrecordable for several hours. Blood sugar was 1,400 mg./100 ml.; Na 41 mEq./l, K 5.1 mEq./l and HCO₃ 7 mMol./l. Blood urea was 150 mg./100 ml., this being attributed to dehydration.

She was treated with the usual regime of massive doses of insulin intravenously and intramuscularly, with large amounts of intravenous saline and glucose. Potassium supplements were given the next day, and she appeared to improve. It was noted that after the first day the blood-sugar levels were extremely labile, and that the urine volume failed to rise even after rehydration was complete. This pattern persisted until July 10, 1961, at which time the daily urine volume had fallen to less than 200 ml./24 hours. Serum Na 133 mEq./l, K 4.2 mEq./l and urea 340 mg./100 ml. The acidosis had been corrected, but the blood sugar

varied from 30 mg./100 ml. to 600 mg./100 ml. within a few hours.

On July 11, 1961, the patient was transferred to the Artificial Kidney Unit, Glasgow Royal Infirmary. On admission her general state was very poor. Physical examination revealed mental confusion, considerable sacral œdema and hypotension (B.P. 90/50 mm. Hg). Scattered moist sounds were heard throughout the chest. There was mild diabetic retinopathy, but no evidence of neuropathy.

Investigations: Blood sugar 417 mg./100 ml.; Na 134 mEq./l, K 6.8 mEq./l, HCO₃ 30 mMol./l; blood urea 350 mg./100 ml. Urine volume 300 ml./24 hours; it contained no sugar, a moderate amount of protein, occasional red cells and hyaline casts. Urinary urea 0.56 g./100 ml., PCV 36%.

A diagnosis of acute oliguric renal failure was made based upon the high blood urea and the poor urine volume and concentration. It was uncertain whether this was superimposed on chronic diabetic nephropathy, although scrutiny of the notes made at the diabetic clinic which the patient attended revealed previous albuminuria, hypertension or renal symptoms. It was therefore assumed that at least part of the damage was acute, and potentially reversible. Although the daily rise in blood urea was relatively slow (20 mg./100 ml./day), and the daily urine volume was slowly improving, the serum potassium was rising quickly, she was overhydrated and control of blood-sugar levels was difficult. The final and overriding indication for immediate hæmodialysis was provided by her very poor clinical condition.

Hæmodialysis was undertaken on July 11, 1961 using a modified rotating drum machine of the Kolff-Brigham type with a high efficiency (Kennedy, Gray, Dinwoodie and Linton, 1961). The dialysing fluid used was of standard composition with regard to electrolytes. Normally, with this machine, glucose is added to the dialysing fluid to a concentration of 320 mg./100 ml., in order to compensate for the osmotic pressure of the plasma proteins. In this case, where the patient's blood sugar was 417 mg./100 ml., this effect would have been lost and further overhydration might have occurred. The bath glucose concentration was therefore doubled. An arterio-venous circuit was used, and a flow rate of 150 ml./min. was obtained only with the assistance of L-noradrenaline, the patient's blood pressure remaining very low. Aggravation of the hypotension led to the procedure being discontinued after three hours. The clinical condition of the patient was unchanged, but the serum potassium had been reduced to normal and the blood urea lowered to 160 mg./100 ml.

The patient's further progress is shown in Fig. On the day following hæmodialysis her condition was much improved. Diuresis had begun, and her diabetes was well controlled on four-hourly doses of soluble insulin. The usual conservative regime of dietary and fluid restriction was enforced, and recovery was typical

of that seen in resolving acute renal failure due to acute tubular necrosis. Blood urea rose again for a few days in the early diuretic phase, then levelled off and began to fall. Features of note in the recovery phase were that the urine sugar content continued to be no guide to the blood-sugar levels, the continued hypotension and the recurrence of diarrhoea. She required continuous L-noradrenaline for four days after dialysis, and no cause for this hypotension was found. ECG showed no evidence of myocardial infarction. Stool cultures were repeatedly negative for pathogens, and the diarrhoea, too, remained unexplained.

Six days after dialysis (July 17, 1961) the patient was well enough to be returned to the Victoria Infirmary. The blood urea was 150 mg./100 ml. and falling; daily urine volume was in excess of 2.5 l., with a urea concentration of 0.67 g./100 ml.; the serum electrolytes were all normal. From then on, so far as renal function was concerned, progress was good. The blood urea was less than 40 mg./100 ml. after four weeks, and did not rise again. Electrolyte and fluid balance remained completely normal. It had been intended to readmit her for assessment of renal function, but further unexplained diarrhoea and eventually alimentary bleeding prevented this. Comprehensive investigation revealed no cause for this, and the patient died on November 19, 1961. Postmortem examination showed only severe atrophy of the colonic wall, and it was thought that non-specific colitis was the cause of the bleeding. There was no evidence of cerebrovascular or cardiac disease, and the adrenals were normal. The kidneys showed some tubular atrophy with increase in interstitial tissue consistent with recovery from acute tubular necrosis. The glomeruli showed little change.

There seems little doubt that her death was unrelated to her episode of ketosis, and that she had made a good recovery from the superimposed acute renal failure, with restoration of adequate renal function.

Discussion

There are few reports in the literature of acute renal failure complicating diabetic ketosis. However, closer study of papers dealing with series of patients in diabetic coma suggests that renal damage of some degree is probably not uncommon. For example, Cohen, Vance, Runyan and Hurwitz (1960) report 73 cases of diabetic acidosis, with four deaths. Acute renal failure was prominent as a contributory cause in two of the four fatal cases, and temporary oliguria and azotæmia were present in a third. Trever and Cluff (1958) reviewed 476 cases of diabetic ketosis, and found 24 cases where increasing azotæmia was observed; of these, 21 were found to have infection or chronic renal disease, but in three there was no obvious cause beyond the ketosis. There remains an appreciable mortality in diabetic ketosis, and it seems possible that at least some of this is due to acute renal damage, often superimposed on chronic renal disease. It is also possible that some cases of azotæmia complicating diabetic ketosis are not recognized, for the finding of an elevated blood urea may be ascribed to dehydration. It seems reasonable to suggest that closer supervision of renal function during and after diabetic ketosis is desirable.

The cause of acute renal failure in diabetic ketosis is difficult to decide, since many possible factors are present in such a complex electrolyte

FIG. 1.

upset. Hypotension offers an aetiology common to many other types of acute renal failure, but acidosis and hypokalaemia may also play a part in damaging the tubules. Various disturbances of renal function have been reported during and after diabetic ketosis. It has been suggested that the azotæmia of diabetic ketosis is more usually due to renal disturbance than to dehydration, and a marked fall in RBF, RPF, GFR and urea clearance has been demonstrated during diabetic ketosis (Reubi, 1953). In most cases, PAH extraction values showed no evidence of renal vasoconstriction, but this did appear occasionally and the patient developed a true tubular necrosis. Bernstein, Foley and Hoffman (1952) performed clearance studies in six patients with diabetic coma—they demonstrated a reduction of C_M , C_{pah} , and Tm_{pah} , but all these values returned to normal on correction of dehydration and electrolyte upsets. In contrast, two other patients showed progressive azotæmia and reduction in the above values, suggesting that mild tubular necrosis had occurred. It has been suggested that hypotension is the essential causative feature of this renal upset (Knowles and Alverson, 1956) but Shields (1958) reports a case of ketosis causing acute renal failure in which there was no hypotension, but severe hypokalaemia. There is other evidence that hypokalaemia may be important in the tubular damage in the demonstration of both glomerular and tubular damage following a phase of hypokalaemia (Relman and Schwartz, 1956). It should also be pointed out that serum potassium levels in diabetic ketosis are no indication of total body potassium—radioactive studies have shown a loss of one-third of the total body potassium with a serum

level of 8 mEq./l. (Holler, 1946). Finally, acidosis may also be involved in the renal damage which is often present, though only occasionally progressing to the stage of requiring specific therapy.

Our findings in this case throw no light on the causation of the acute renal failure, since hypotension, hypokalaemia and acidosis were all present. It does, however, serve to highlight some points of general management. Close watch should be kept on the blood urea and the urine output in diabetic ketosis. Should azotæmia develop, then it is unsafe to assume that this is due to dehydration or to chronic diabetic nephropathy, and the patient should be given the benefit of the doubt with adequate treatment, including hæmodialysis if necessary. This procedure will give time for more precise diagnosis which might be obtainable only by renal biopsy. In the presence of severe renal damage, it is well to remember that urinary sugar content is no guide to the blood levels. It seems

also that blood sugar levels are extremely labile when acute renal failure complicates diabetic ketosis, and this may be due to the fact that no sugar is being excreted. Finally, the electrolyte upset due to diabetic ketosis complicated by acute renal failure is extremely severe, and it is probable that hæmodialysis offers the best hope of successful treatment.

Summary

A case of acute renal failure complicating diabetic ketosis is reported. The number of similar cases previously described is small, but review of several large series of patients with diabetic ketosis suggests that some renal damage is common. This case serves to draw attention to the need for careful watch on renal function in diabetic ketosis, and demonstrates that hæmodialysis may be invaluable in management of such cases.

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