Prolonged Oliguria with Survival in Acute Bilateral Cortical Necrosis

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Summary: Survival is uncommon in cases of acute bilateral cortical necrosis. Three cases admitted to the renal unit at Newcastle have regained useful renal function after oliguric phases of 38, 46, and 120 days.

Prolonged periods of intermittent dialysis are justified in patients in whom a firm diagnosis of acute cortical necrosis is made.

Introduction

Acute bilateral cortical necrosis of the kidney is a clinical entity which was first described by Juhel-Rénoy in 1886. Since then numerous clinical and pathological studies have suggested that it has an almost universally fatal outcome. However, in the past four decades there have been 14 individual reported survivors, two before the days of dialysis (Crook, 1927; Groen and Lindeboom, 1940; Gormsen *et al.*, 1955; Alwall *et al.*, 1957; Boucot *et al.*, 1957; Lauler and Schreiner, 1958; Dérot *et al.*, 1960; Milne, 1961; Effersøe *et al.*, 1962; Oram *et al.*, 1963; Vernon-Parry and Williams, 1963; Chervony *et al.*, 1965; Rieselbach *et al.*, 1967; Riff *et al.*, 1967). We here report three further survivors who, after prolonged periods of oliguria (less than 400 ml./24 hours), recovered sufficient renal function to maintain life. Case 1 has previously been reported (Walls *et al.*, 1966).

Case 1

A 13-year-old schoolboy was admitted to the Royal Victoria Infirmary unconscious after being involved in a motor accident on 3 December 1964. No bony injury was found, and 200 ml. of dark blood-stained urine was obtained by catheterization. During the next 24 hours he complained of increasing abdominal pain, and at laparotomy a large retroperitoneal haematoma was found and drained. Postoperatively he was noted to be anuric. By the second post-trauma day his blood urea had risen to 322 mg./100 ml. and he was transferred to the renal unit. The next day he had his first haemodialysis, which was repeated according to his rising blood urea.

On the 28th post-trauma day a retrograde pyelogram showed normal caliceal outlines and ureters. A percutaneous renal biopsy on the 51st day showed the changes of acute cortical necrosis (Fig. 1). Neither renal biopsy nor x-ray examination of the abdomen showed calcification in the kidneys. Because of the biopsy findings he was placed on regular outpatient haemodialysis therapy.

As time went by his pre-dialysis blood urea estimations gradually decreased (Fig. 2) and his urine output increased. In view of these facts and the difficulty in maintaining a satisfactory arteriovenous shunt it was decided to withhold his dialysis therapy on 16 September 1965—nine months after the onset of anuria. His blood urea gradually stabilized (80–100 mg./100 ml.) on a 40 g. protein diet and free fluids with a urinary output of about 1,500 ml./24 hours. During this period he required Resonium-A (sodium polystyrene sulphonate) 15 g. daily because of hyperkalaemia. He was normotensive. A creatinine clearance at one year post trauma was 8 ml./min. with a blood urea of 68 mg./100 ml., though he had become hypertensive (B.P. 160/100) and was treated with methyl dopa 250 mg. t.d.s.

Since then he has remained well and is able to carry out light work. When last seen in the outpatient department in February

1968 the results of investigations were: blood urea 65 mg./100 ml.; serum sodium 142 mEq/l.; serum potassium 5.5 mEq/l.; serum chloride 106 mEq/l.; bicarbonate 15 mEq/l.; serum creatinine 3.1 mg./100 ml.; creatinine clearance 24.5 ml./min.; midstream specimen of urine sterile; haemoglobin 90%; W.B.C. 9,000/cu. mm.; serum calcium 9.1 mg./100 ml.; serum phosphate 4.3 mg./100 ml.; alkaline phosphatase 139 i.u. He is still mildly hypertensive. Repeat x-ray examination of the abdomen again failed to show renal calcification. He is on a free diet and unrestricted fluids and has achieved normal growth and development.

FIG. 1.—Case 1. Photomicrograph of renal biopsy showing acute cortical necrosis of the kidney. (H. and E. $\times 85$.)

FIG. 2.—Case 1. Blood urea estimations showing gradual decrease while on regular outpatient haemodialysis therapy.

Case 2

This patient, a 53-year-old miner, had a long history of intermittent claudication in both legs. On 26 October 1967 he had a Dacron graft to the aortic bifurcation, below the renal arteries, in a four-hour operation, complicated by prolonged hypotension. His kidneys at the time of operation were noted to be normal and his preoperative blood urea was 38 mg./100 ml. During the first postoperative 24 hours he passed 700 ml. of dark blood-stained urine but then became totally anuric for the next 20 days. He was transferred to the renal unit on the third postoperative day with a rising blood urea. Maintenance haemodialysis therapy was continued throughout his postoperative period, and on the 21st day a percutaneous renal biopsy revealed outer cortical infarction but with a few juxtamedullary glomeruli well preserved. No calcium deposits were noted.

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It was thought that recovery of renal function was unlikely, and he was changed to regular outpatient haemodialysis therapy on the 26th day, the urine volumes at that time being less than 100 ml./24 hours. By the 46th day he noted that his urine volumes had increased to 400 ml. on the day before dialysis. On the 52nd day the urine volume had increased to 1,340 ml./24 hours with a creatinine clearance of 3.8 ml./min., and haemodialysis was discontinued. During the period of regular haemodialysis therapy he has remained normotensive. Over the next four months he made a gradual clinical and biochemical improvement with a creatinine clearance of 6.8 ml./min. (see Table) and was on unrestricted fluids and a 60 g. protein diet. Routine straight x-ray examination of his abdomen failed to show evidence of renal calcification.

Decrease in Serum Creatinine and Increase in Creatinine Clearance Over 108 days in Case 2.

Days Postoperative	Serum Creatinine (mg/100 ml.)	Creatinine Clearance (ml./min.)
0-46	14.2*	—
52	16.9	2.2
56	17.4	3.8
72	11.4	—
86	10.5	—
100	9.4	—
160	7.4	6.8

* Mean pre-dialysis serum creatinine.

Case 3

A 22-year-old primigravida was admitted to the Princess Mary Maternity Hospital, Newcastle upon Tyne, following a concealed accidental haemorrhage when she was 36 weeks pregnant. After the haemorrhage she had an eclamptic fit and became anuric. On admission her blood urea was 78 mg./100 ml., serum potassium 6.8 mEq/l., and haemoglobin 59%. Three days later she had an induced normal delivery of a stillborn infant, during which she lost a further 800 ml. of blood. She was transferred to the renal unit on the fifth day of anuria, when her blood urea was 192 mg./100 ml., serum sodium 127 mEq/l., serum potassium 4.2 mEq/l., serum bicarbonate 16 mEq/l., and haemoglobin 44%.

She was treated by haemodialysis on four occasions, and by the tenth day had begun to pass small quantities of urine, 10-30 ml. On the 20th day a percutaneous renal biopsy revealed necrosis of glomeruli, tubules, interstitium, and vessels in the cortex. Occasionally the vessels contained recent thrombi. The medulla was spared. However, there were moderate amounts of calcified material in the interstitium and in some tubules. A diagnosis of acute bilateral cortical necrosis was made.

The urine volumes gradually increased until by the 40th day she was consistently passing over 1,000 ml./24 hours, with a creatinine clearance of 0.36 ml./min. The last dialysis was on the 43rd day, and by the 50th day her creatinine clearance had increased to 2 ml./min. She was able to maintain her blood urea below 200 mg./100 ml. on a 20 g. protein diet. During this period in hospital her progress was complicated by several epileptiform convulsions, which were eventually controlled by phenobarbitone and phenytoin sodium. Nephrotomography on the 43rd day showed bilateral cortical tram-line calcification (Fig. 3). She was eventually discharged on the 76th day, with a blood urea of 178 mg./100 ml., to continue on a 40 g. protein diet, 22 mEq sodium diet, Resonium-A 15 g. daily, and anticonvulsant therapy.

During the next three months she was admitted for blood transfusions on two occasions, and at one year her blood urea was 226 mg./100 ml., serum creatinine 11.7 mg./100 ml., and mid-stream specimen of urine sterile. Moderately severe hypertension (B.P. 175/125) found at this time was treated with methyl dopa. She then ceased to attend outpatient clinics but was readmitted at 15 months with a two-month history of vomiting, diarrhoea, dyspnoea, and ankle-swelling. At this time she admitted to considerable dietary indiscretion. Her blood urea had risen to 426 mg./100 ml., her haemoglobin was 26%, and her blood pressure was 165/100, so she was started on regular outpatient haemodialysis therapy.

As suspected from her previous outpatient behaviour she was a difficult patient to manage, and became severely hypertensive (B.P. 240/140) and hyperkalaemic (serum potassium 7.2 mEq/l.) on several occasions, despite drug therapy and warnings from the

medical staff. She died suddenly on 16 April 1967 while walking in the street near her home. The most significant necropsy findings were: (1) A large heart (weight 500 g.) with considerable left ventricular enlargement but no infarction or fibrosis. The coronary arteries were also enlarged. (2) Both kidneys were shrunken (weight 55 g. each). The capsule was adherent to the surface, and the cut surface showed complete absence of cortex in both kidneys. The most striking feature was the yellow stippled calcification of the outer rim of the kidney at the site of the defunct cortex. This dipped

Fig. 3.—Case 3. Straight abdominal x-ray film showing renal calcification.

down between medullary pyramids, and in many places there was a definite tram-line pattern of double lines. On histological examination there were very occasional normal-looking glomeruli. Marked hypertensive changes were noted in the large and small vessels and in the tufts of several glomeruli.

Discussion

Acute bilateral cortical necrosis is an uncommon cause of acute renal failure. Previous authors (Swann and Merrill, 1953; Lauler and Schreiner, 1958) have reported a 2% incidence of the lesion in cases of acute renal failure. From January 1961 to December 1967 352 cases of acute renal failure were admitted to the renal unit of the Royal Victoria Infirmary. Of these, six had histological proof of acute bilateral cortical necrosis, which is in agreement with the previous estimates. Pregnancy, complicated by antepartum haemorrhage or eclampsia, is the commonest precipitating cause in adults (Sheehan and Moore, 1952). There are numerous other causes, including diabetes mellitus, trauma, surgery, snake-bites (Oram *et al.*, 1963), and even spontaneous (Gormsen *et al.*, 1955). In children the most common cause is dehydration due to diarrhoea and vomiting, followed by infections—that is, pneumonia, tonsillitis, peritonitis, and tuberculosis (Williams, 1963). In previously reported survivors, 11 out of 14 cases were in the obstetric group, though in the present series only one was an obstetric accident, the others being post-traumatic and postoperative.

The diagnosis of acute bilateral cortical necrosis is usually considered in cases of acute renal failure when the period of oliguria has exceeded 21 to 28 days. In the reported survivors the period of oliguria (less than 400 ml./24 hours) has varied from 7 to 60 days (Groen and Lindeboom, 1940; Alwall, 1957), with a mean duration of 28 days. Two further survivors were reported to have urinary outputs of 1,000 ml. or more per 24 hours by the 25th and 32nd days respectively (Boucot *et al.*, 1957; Chervony *et al.*, 1965). The surviving patients in this series were oliguric for 38, 46, and 120 days. Confirmation

of the diagnosis can be made by either renal biopsy or finding renal cortical calcification on x-ray examination.

Renal biopsies in all reported cases, as with the present patients, have revealed necrosis of the glomeruli, tubules, interstitium, and vessels of the cortex. In some vessels there has been evidence of recent thrombosis. The renal medulla is spared and normal juxtamedullary glomeruli are occasionally found. Renal calcification is occasionally commented on. If needle biopsy shows findings compatible with the diagnosis of acute bilateral cortical necrosis one is still unable to predict the survival of the patient, owing to the patchy nature of the lesion and the sampling error of needle biopsies. This is illustrated by Case 1, which showed no surviving glomeruli, whereas in Case 2 not only was cortical necrosis present but juxtamedullary glomeruli with a normal appearance were shown.

Calcification of the renal cortex as a consequence of acute bilateral cortical necrosis has been reported in 5 of the 14 survivors (Groen and Lindeboom, 1940; Gormsen *et al.*, 1955; Boucot *et al.*, 1957; Oram *et al.*, 1963; Vernon-Parry and Williams, 1963). As both the presence and the absence of calcification have been noted in the survivors it appears to have diagnostic rather than prognostic value. Calcification is found on biopsy as early as the fifth day and radiologically by 49 days (Moëll, 1957). In Case 3 calcification was present on renal biopsy by the 20th day, the tram-line calcification, as described by Lloyd-Thomas *et al.* (1962), was noted by nephrotomography by the 43rd day.

Of the three non-surviving cases seen in this unit two showed some return of renal function after delivery. One patient, after 53 days of oliguria, achieved a urinary output of 1,000 ml./24 hours and dialysis was stopped at this point. However, her renal function deteriorated and she died in renal failure on the 143rd day. The second patient, who also had untreated myxoedema (^{131}I uptake was 8% at 24 hours), was anuric for 35 days. Following this her urinary output gradually increased but never exceeded 500 ml./24 hours and dialysis was stopped on the 70th day. Her blood urea rose to 470 mg./100 ml. by the 120th day, shortly after which she died. These two patients were admitted to the unit before the establishment of regular outpatient haemodialysis therapy. The third patient was a male with acute hepatic failure who died 48 hours after admission to hospital while still anuric.

Considering the length of the oliguric period followed by a return of some renal function in the present series, we feel that prolonged dialysis is justified in this group of patients. Once renal function is re-established continued improvement may occur, as seen in Cases 1 and 2. Other authors (Rieselbach *et al.*, 1967) have noted the improvement in renal function over a long period of observations and suggested that improvement

was due to functional adaptation of the nephron rather than to increase in the nephron population. The improvement in renal function, as seen in Case 1, is striking—that is, an increase in creatinine clearance from 8 to 24.5 ml./min. over 15 months. However, in Case 3 the renal function, having been re-established, then deteriorated. The marked hypertension which occurred in this patient was possibly the cause of her deteriorating renal function. If prolonged dialysis therapy had been used in the treatment of the two postpartum non-survivors, with adequate management of the hypertension which occurred, ultimate recovery of sufficient renal function might have been achieved.

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