NEPHROPATHY IN MARATHON RUNNERS*

C. P. DANCASTER, W. C. DUCKWORTH AND C. J. ROPER, *Grey's Hospital, Pietermaritzburg*

The Comrades Marathon is run annually between Pietermaritzburg and Durban—a distance of over 50 miles. It is considered one of the most gruelling long-distance races in the world. Entries have exceeded 600 in recent years and the course is completed by most starters in between 6 and 11 hours.

Competitors usually suffer no ill-effects, apart from blisters, muscle stiffness and cramps, but after the 1967 run down to Durban we saw one competitor with severe nephropathy, and there was a similar recurrence after the 1968 run up to Pietermaritzburg.

CASE REPORTS

Case 1

B.L., aged 38 years, ran approximately 450 miles in training during 4 months before the race and lost 30 lb. in weight. He did 3 or 4 runs of 30 miles without suffering any ill-effects, and, as is usual, did not do any strenuous running for 2 weeks before the race. During the race he felt very well until he approached the last few miles into Durban. He can remember nothing after the 45th cutting, which is about 4 miles from the finishing post. However, he ran on, but fell down unconscious about a mile further on when he was in the vicinity of Westridge Park. He was told that a doctor was unable to feel his pulse at that time and that his legs felt ice cold. He was unconscious for about one hour. During this time he had been put in a car and taken to a house. That night he had extreme diarrhoea and vomiting, and he had intermittent vomiting for a week afterwards.

He was first seen by us 13 days after the race. A story of anuria was then obtained for the first time and only on direct questioning about his urinary output. During the race he had passed a few drops of urine at approximately the 40-mile mark. For 48 hours after the race he had passed no urine and at the end of this time he had passed urine which had looked like strong tea. As far as he was aware his urinary output since then had been normal. He had returned to work as a motor-car salesman, but felt extremely tired and lethargic and had anorexia and nausea.

On examination a loud 4th heart sound was audible and his blood pressure was 200/130 mm.Hg. There were no other abnormal cardiovascular or respiratory signs and his fundi were normal. Blood urea was 186 mg./100 ml. The urine contained a moderate amount of albumin, but nothing was abnormal microscopically. The ECG was normal.

During the following 2 weeks his urinary output was in excess of 1,000 ml. daily, and his blood pressure slowly came down to 130/85 mm.Hg. His blood urea fell steadily, as did his quantitative albuminuria (Esbach's), and both were normal after 2 weeks.

He continued to feel well during the course of the next year. Assessment of renal function at the end of this time showed a blood urea concentration of 30 mg./100 ml. and creatinine clearance 115 ml./mm. His urine was normal biochemically and microscopically.

Case 2

A.D., aged 27 years, was an outstanding athlete and won the 1968 Gary Player trophy awarded to the person with the fastest combined time for the canoe and Comrades Marathon. He had previously run the Comrades Marathon in 1965 in 9 hours 41 minutes without any untoward effects. He had trained for 4 months, running an average of 8 miles per day and 25 - 35 miles on Saturday, that is an average of about 70 - 80 miles per week. In this race he ran well for 34 miles, but then felt ill and developed severe diarrhoea. He had to defaecate in the veld at least 3 or 4 times. He felt very ill, but despite this he finished the race in 8 hours 16 minutes. He felt very dizzy and weak at the finish. He continued to have diarrhoea for the rest of the day and also vomited a few times that evening.

He cannot remember passing any urine during the race. On the evening of the race he passed urine twice. The first specimen was a fairly large quantity, but the second was only a small amount and was dark-brown in colour.

During the 4 days following the race he passed a total of only 1½ glasses of concentrated urine. For 3 of the first 4 days he passed no urine at all.

He was admitted to hospital on the second day after the race. He was given 2 litres of Groote Schuur Hospital rehydration fluid and 1 litre of Ringer's lactate intravenously. Despite this intravenous fluid he passed no urine. An intravenous injection of Lasix, 40 mg., was given, but no urine flow was produced.

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On examination he appeared normally hydrated. He had bilateral subconjunctival and peri-orbital haemorrhages. His blood pressure was 160/90 mm.Hg. His heart rate was 60/min. There was some tenderness to pressure of his thigh muscles. The reflexes in the lower limbs were strikingly brisk. The remainder of the physical examination was normal. An electrocardiograph was normal.

On admission his blood urea was 176 mg./100 ml., serum chlorides 87·0 mEq./litre, serum sodium 119·5 mEq./litre and serum potassium 3·9 mEq./litre. His haemoglobin was 12·2 G/100 ml., packed cell volume 39%, and his white blood count 8,000/cu.mm., of which 77% were polymorphs, 1% eosinophils, 8% monocytes and 14% lymphocytes. The platelet count was 210,000/cu.mm. The erythrocyte sedimentation rate (Westergren) was 18 mm. in the first hour. His serum glutamic oxaloacetic transaminase (SGOT) was 135 Karmen units, the serum glutamic pyruvate transaminase (SGPT) 180 Reitman-Frankel units, lactic acid dehydrogenase (LDH) 1,500 Wroblewski units, serum aldolase 4·3 milliunits per ml. and serum alkaline phosphatase 6·1 King-Armstrong units. His total serum proteins were 6·0 G/100 ml., of which albumin was 3·4 G/100 ml. and globulin 2·6 G/100 ml. The total serum bilirubin was 0·76 mg./100 ml., of which conjugated bilirubin was 0·39 mg./100 ml. The zinc sulphate turbidity was 7·7 units and the thymol turbidity 2·7 units. His bleeding time was 2 minutes and clotting time 10 minutes. The prothrombin index was 70%.

Examination of the urine revealed albumin ++ and a specific gravity of 1·010. The sodium content of the urine was 23·6 mEq./litre and the urea content 0·5 G/100 ml. Microscopic examination revealed 40 red blood cells and 6 - 8 white blood cells per high-power field. Numerous granular casts were present. Spectroscopic examination of the urine for blood pigment and myoglobin was negative. The occult test for blood in the urine was positive.

He was treated conservatively by restriction of protein and fluids. For the first 2 days in hospital, i.e. the third and fourth postexertion days, he passed no urine at all. Thereafter his 24-hour urinary output began to increase and on successive days was 330 ml., 225 ml., 540 ml. and 980 ml. He then went into a diuretic phase and passed up to 4,000 ml. of urine daily. The blood urea remained high and on the 6th postexercise day was 176 mg./100 ml. Thereafter the blood urea slowly dropped and 2 weeks after the race it was normal. He was discharged from hospital, clinically well, 16 days after admission.

DISCUSSION

Acute renal failure following exercise is rare. Less than 30 documented cases have been reported, but the true incidence is probably higher.[1] In the reported cases hyperpyrexia has always been a striking feature, and the normal temperature in these two cases is unusual. Both in 1967 and in 1968 the race was run on a typical, cloudless, autumn day in May. The temperature was not unduly high on either day.

The factors likely to be implicated in the pathogenesis of renal failure in these patients were dehydration, aggravated by diarrhoea and rhabdomyolysis with pigmenturia.

Abnormal muscle metabolism, judged by raised serum aldolase and other enzymes, was present in all competitors tested in the 1965 Comrades Marathon.[2] There are certain circumstances which may predispose to severe muscle breakdown, and these include biochemical and structural abnormalities in the myoglobin, potassium depletion and haemolysis. McArdle described abnormal muscle metabolism due to an absence of muscle phosphorylase.[3] Myoglobinuria occurs in about half the reported cases of this disease.[4] A structural abnormality in myoglobin has also been suggested as a cause of severe rhabdomyolysis.[5] Potassium plays an important role in normal muscle function, and in dogs potassium depletion has produced muscle degeneration.[6] In man acute degeneration has developed following severe diarrhoea with low serum potassium.[7,8]

The haemolytic episodes causing march haemoglobinuria are not fully understood. Several studies have suggested traumatic damage to the red blood cells in the soles of the feet.[9,10] Ono[11] found that myoglobin and not haemoglobin was the pigment in the urine and suggested that many examples of march haemoglobinuria were really march myoglobinuria.

The association between myoglobinuria and oliguric renal failure was dramatically illustrated in the 'crush' syndrome in British air-raid victims during World War II.[12] Approximately 25% of the reported cases of idiopathic recurrent rhabdomyolysis with myoglobinuria have died in renal failure.[13]

Case 2 had markedly elevated SGOT, SGPT and LDH levels 5 days after the race, and in the absence of any abnormality in liver function they were probably due to muscle damage. No myoglobinuria or haemoglobinuria was seen in our cases, but it was only looked for some time after the race. In neither case was there any evidence of haemolysis which might have contributed to anuria.

One other possible explanation for the renal damage is renal ischaemia. With severe exertion renal blood flow may be reduced with diversion of some of the blood to the contracting skeletal muscles.[14] It would, however, seem unlikely that this reduction would be large enough to cause renal damage. If, in addition, severe dehydration were to occur it is possible that renal ischaemia might be produced. We have no direct evidence to support this hypothesis. Renal ischaemia may have been a causative factor in case 1, who collapsed during the race, and no pulse could be felt by a doctor who examined him at that time. In case 2, however, there was strong evidence of muscle damage which would appear to have been a more probable cause of the renal pathology.

Hypertension was particularly pronounced in case 1. Both patients had abnormalities in cerebral function. Cerebral congestion and focal haemorrhages have been reported in this condition.

Other extrarenal manifestations include disturbances in liver function and abnormalities of blood coagulation with thrombocytopenia and purpura. Case 2 had bilateral conjunctival haemorrhages and haemorrhages in the eyelids, but his bleeding and clotting time were normal and he had a normal number of platelets in the peripheral blood. All liver-function tests were normal apart from a prothrombin index of 70%.

An interesting characteristic of the acute renal failure following exercise and heat stress is the severity and long duration of the oliguria. Five of the 8 cases described by Schrier *et al.*[1] had daily urine volumes of less than 75 ml. for 7 - 32 days. Case 2 passed no urine at all for 3 of the first 4 days following the race. Such severe oliguria or anuria may suggest acute necrotizing glomerulonephritis, acute renal vascular catastrophies or excretory obstructive disease. Since the last two entities may be remedied by surgical procedures, further diagnostic studies may be suggested. However, when marked oliguria is associated with renal failure secondary to heat stress and exercise it would seem advisable to be more conservative in pursuing potentially dangerous diagnostic procedures.

Eight out of 19 American army recruits who developed anuria following heat stress and exercise died.[1,15] In the survivors renal function returned to normal.

Tests of renal function done one year after the event in case 1 revealed normal creatinine clearance and blood urea, and renal function also returned to normal in case 2. Renal biopsy was not undertaken. In 6 surviving South African goldminers suffering from heat stroke and acute renal failure, renal histology returned to normal in 4, apart from slight interstitial fibrosis. In a fifth, interstitial fibrosis was more marked, and there was marked deterioration in renal structure over a period of 15 months in the sixth.[16]

A disturbing feature is that both these competitors were young and had done an average amount of training for this race. They felt fit before the race and had few danger signs during the event. It would appear to be wise for competitors to retire should any complications occur which might lead to further dehydration, particularly diarrhoea or vomiting, and any mental confusion should also be regarded as a danger signal. So keen is the desire to finish in most competitors that few would heed this advice. The amount of urine passed during the race is no guide, as many competitors do not pass any. Adequate hydration during the race is, of course, essential, but both these competitors had experienced helpers and had an average amount of fluid by mouth.

SUMMARY

Two cases of anuria following the Comrades Marathon are described. Both patients were young and had trained diligently. Neither had any warning symptoms until late in the race. Diarrhoea was severe in both patients. Eventual recovery of renal function was complete.

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