ACUTE RENAL FAILURE ASSOCIATED WITH MASSIVE HAEMORRHAGE IN A HAEMOPHILIAC

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Acute renal failure has recently been discussed by Milne (1957), and the clinical features have been described by Bull, Joekes, and Lowe (1955, 1956, 1957). One of the principal causes is renal ischaemia, which may result from acute renal circulatory insufficiency in conditions involving haemorrhage and shock. Acute renal failure might therefore be expected to occur in haemophiliacs after massive haemorrhage. This has not, to our knowledge, been recorded, although Macfarlane *et al.* (1957, Case 10) have described a case of acute tubular necrosis caused by hypotension occurring in a haemophiliac during a lengthy and extensive operation. This was performed under cover of parenterally administered beef antihæmophilic globulin (A.H.G.), and was not associated with much bleeding. The following case is therefore worth reporting.

Case Record

A man aged 44 had suffered from repeated episodes of haemorrhage all his life. His elbow-, knee-, and ankle-joints were deformed, and showed radiological changes consistent with those due to hæmophilia. A brother had died in infancy after circumcision.

On May 13, 1956, he developed a severe pain in the abdomen during a bout of coughing. A hæmatoma then appeared in the epigastrium. During the next few days the pain ceased and the blood started tracking downwards. On waking on May 19 the pain had returned, and he was unable to pass water. In the course of the day his abdomen became distended, the pain increased in intensity, and he started vomiting small quantities of altered blood. He managed to pass only a very small quantity of blood-stained urine. By the afternoon he was found to be in a state of shock, with a blood pressure of 90/60 and a pulse rate of 140 a minute, and was admitted to a local hospital. A blood transfusion was given that evening, after which his blood pressure rose to 130/98. He was then transferred to Addenbrooke's Hospital.

On admission his lower abdomen was discoloured, tense, and tender, and measured 44 in. (112 cm.) in circumference. His girth was normally about 38 in. (96.5 cm.). His blood pressure was 135/85 and pulse rate 140. Catheterization produced only 60 ml. of grossly blood-stained urine. He remained anuric for the rest of the day.

Laboratory Findings.—Haemoglobin, 10.8 g./100 ml.; leucocyte count, 6,700/c.mm.; platelets, 430,000/c.mm.; blood urea, 60 mg./100 ml. Thromboplastin generation test—method of Biggs and Douglas (1953) as modified by Bell and Alton (1954): A.H.G., 15% of normal activity. Christmas factor, normal activity.

The diagnosis of classical hæmophilia (A) was therefore confirmed; the patient had obviously had a large hæmorrhage into the abdominal wall, and it was thought that he had also developed acute renal failure. A prophylactic transfusion of fresh plasma and blood (1 litre of each) was given, fluids were restricted, and glucose (20%) and appropriate amounts of saline were administered intravenously.

He remained oliguric during his first two days in hospital, passing less than 75 ml. of urine in 24 hours. Diuresis started on the third day after admission. The urine was no longer blood-stained, but bleeding into his abdominal wall occurred again on the third and fourth days in hospital, the hæmatoma becoming more tense and painful, his girth increasing to 45 in. (114 cm.), and his hæmoglobin level falling to 5.2 g./100 ml. A further transfusion of 2 litres of fresh blood was therefore given. His blood pressure did not fall below 120/80 at any time, and his diuresis was not interrupted, although his blood urea rose progressively to a level of 380 mg./100 ml. on the fifth day after admission. Thereafter his general condition improved, and his hæmatoma regressed. In view of the falling level of serum potassium noted at that time, he was given 8 g. of potassium citrate daily by mouth. After the 10th day in hospital the serum potassium level started to rise.

On the sixteenth day after admission it was noticed that his hæmoglobin level had dropped to 7.3 g./100 ml. There were no accompanying symptoms or signs until the eighteenth day, when a large melaena stool was passed. Blood and plasma transfusions were started again, and 3 litres of plasma and 4.5 litres of blood were given over a period of three days. His blood pressure did not fall below 100/60 during this episode, and his urinary output was maintained satisfactorily. However, his blood urea rose from 130 to 170 mg./100 ml., and his serum potassium fell once more. At this stage it was thought necessary to treat him with potassium intravenously as well as by mouth. For the sake of convenience, potassium citrate was added to the blood which was being transfused at the time, the dose given amounting to 2.78 g./litre, or 25 mEq of potassium per litre. Whenever the rate of the transfusion with added potassium was increased above 50 drops a minute (3 ml. a minute) the patient developed a severe pain along the course of the vein into which the blood was running. When the rate of infusion was decreased the pain was relieved within a few minutes. Blood, plasma, or glucose-saline without added potassium did not on any occasion produce a similar pain.

After this incident the patient's recovery was uninterrupted. Forty days after admission his blood urea had fallen to 20 mg./100 ml.; the specific gravity of his urine varied between 1004 and 1016, and it contained no protein. On readmission four months later his urine was still protein-free, and its specific gravity varied between 1004 and 1028.

The urine volume, blood urea, hæmoglobin, and serum electrolyte changes during his illness are recorded in the Chart.

Discussion

The patient had been severely oliguric for 72 hours, and had undoubtedly developed acute renal failure, although absorption of blood from the hæmatoma and to some extent from the gut had contributed to the level of his blood urea. The pattern of change of the serum electrolytes, together with the progressive increase of blood urea during the oliguric phase of his illness and its continued rise after the onset of diuresis, suggests that the failure was due to acute tubular necrosis. This was most probably caused by hypotension resulting from the acute blood loss on the day before his admission to Addenbrooke's Hospital. This concept is supported by the absence of any marked exacerbation of renal failure during subsequent episodes of hæmorrhage on the third and particularly the eighteenth day in hospital, when the patient's blood pressure had been adequately maintained by prompt transfusion.

Obstruction of the ureters by external pressure from the hæmatoma can be excluded as a cause of the uraemia, because further bleeding into the hæmatoma occurred on the third and fourth days in hospital without affecting the diuresis, which had then just started.

During the oliguric phase of his illness large volumes of plasma and blood were necessary to stop further bleeding and also to raise the hæmoglobin level. In view of the necessity for fluid restriction and a high carbohydrate intake, a 20% solution of glucose was given intravenously for

several days, and it was interesting to note that venous thromboses did not occur at the sites of infusion.

Pain along the course of a vein into which potassium is being infused has been reported (Semler, 1925; Pudenz *et al.*, 1938; Nadler *et al.*, 1950). The majority of instances occurred after the use of concentrated solutions of potas-

sodium citrate, which removes ionized calcium and increases the ratio of potassium to calcium ions acting on the nerve fibre (Katz, 1936; Brink and Bronk, 1937; Lehmann, 1937). Presumably the non-medullated nerve fibrils which subserve pain respond in a similar manner.

In our case the blood being transfused contained 2 g. (1%) of disodium citrate as an anticoagulant, as well as 1.5 g. (0.278%) of added potassium citrate. It is probable, therefore, that the lowering of the pain threshold was due to potentiation of the potassium effect by the citrate.

Summary

Acute renal failure, with complete recovery, is reported in a haemophiliac after massive haemorrhage into the abdominal wall.

Treatment included transfusion with large volumes of fresh plasma and blood.

Potassium citrate was given intravenously for a time, and was found to produce local pain when a threshold concentration was exceeded.

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REFERENCES

- Bell, W. N., and Alton, H. G. (1954). *Nature (Lond.)*, **174**, 880.
Biggs, R., and Douglas, A. S. (1953). *J. clin. Path.*, **6**, 23.
Brink, F., and Bronk, D. W. (1937). *Proc. Soc. exp. Biol. (N.Y.)*, **37**, 94.
Brown, G. L., and MacIntosh, F. C. (1939). *J. Physiol. (Lond.)*, **96**, 10P.
Bull, G. M., Joekes, A. M., and Lowe, K. G. (1955). *Lancet*, **2**, 1152.
— (1956). *Ibid.*, **1**, 186.
— (1957). *Ibid.*, **2**, 114.
Katz, B. (1936). *J. Physiol. (Lond.)*, **88**, 239.
Lehmann, J. E. (1937). *Amer. J. Physiol.*, **118**, 613.
Macfarlane, R. G., *et al.* (1957). *Lancet*, **2**, 251.
Milne, M. D. (1957). *Proc. roy. Soc. Med.*, **50**, 493.
Nadler, C. S., Bellet, S., Gazes, P. C., and Steiger, W. A. (1950). *J. Lab. clin. Med.*, **35**, 842.
Pudenz, R. H., McIntosh, J. F., and McEachern, D. (1938). *J. Amer. med. Ass.*, **111**, 2253.
Semler, R. (1925). *Klin. Wschr.*, **4**, 697.

SALT RETENTION AND URAEMIA IN BRAIN INJURY

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Cerebral disorders of various kinds may be followed by biochemical disturbance in which abnormally high levels of sodium and chloride in the blood are associated with extremely low levels of these ions in the urine. The term "salt-hoarding syndrome" has been suggested for this condition (de Wardener, 1956), and the term seems to be a satisfactory one so long as it is appreciated that uraemia appears to be an invariable concomitant of the hypernatraemia and hyperchlor-
aemia.

This syndrome was first reported by Allott (1939), who observed it in association with cerebral haemorrhage, adenoma of the choroid plexus, and tuberos scleroses. It has since been observed following a large variety of cerebral lesions. These include brain damage following head injuries (Higgins *et al.*, 1954), bulbar poliomyelitis (Allott, 1957), bilateral ligation of the anterior cerebral arteries (MacCarty and Cooper, 1951), operations on the pituitary (Cooper and MacCarty, 1951), leucotomy (McLardy, 1950), subarachnoid

Chart showing serum electrolyte changes, haemoglobin, blood urea, and volume of urine during patient's stay in hospital.

sium chloride (2–10%), given within a matter of minutes. A few were observed after a 1.14% solution of potassium chloride (155 mEq of potassium per litre) had been given at the rate of 3–5 ml. a minute. However, during the treatment of diabetic ketosis, once diuresis has started, solutions containing up to 30 mEq of potassium per litre are frequently given at a rate of 3 ml. a minute without causing pain. In our case pain was caused by an infusion containing practically the same concentration of potassium (25 mEq/l. as potassium citrate plus 5–7 mEq/l. in the plasma of the blood), given at the same rate, suggesting that a low threshold of excitability was present in the pain receptors in the vein wall.

It is known that spontaneous activity may be induced experimentally in nerve fibres by exposing them to potassium, which lowers the threshold of excitability (Brown and MacIntosh 1939). The same effect may be produced by