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CAPTOPRIL IN HYPERTENSIVE EMERGENCIES*)

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ABSTRACT

A 4-year-old girl is presented suffering from severe hypertension due to hemolytic-uremic syndrome. Injection of reserpine and hydralazine was ineffective. Captopril, an oral angiotensin I-converting enzyme inhibitor, showed the dramatic hypotensive effect in our patient.

INTRODUCTION

Captopril (SQ 14, 225), an orally active angiotensin I-converting enzyme inhibitor, represents a new mode of treatment of hypertension. Many studies have shown that this agent is effective in lowering blood pressure in essential and renovascular hypertension as well as in hypertension associated with advanced renal disease in adults[1,2)]. However, there have been few reports on the effectiveness of captopril in children[3,4)]. In this paper we report the successful treatment of severe hypertension in a patient with uremia due to hemolytic-uremic syndrome (HUS).

CASE REPORT

A 4-year-old girl was referred to Hiroshima University Hospital because of acute renal failure. She was the product of a normal pregnancy and delivery. There was no family history of renal disease.

She had appeared to be in good health until 4 years of age when petechiae and purpura of the trunk were first noted. The patient was admitted to a local hospital where severe anemia with a hemoglobin level of 7.3 g/dl was found. The red blood cells showed the characteristic featares of fragmentation hemolysis, anisocytosis and fragmented, helmet-shaped, and burr cells. The platelet count was depressed to 49,000/cmm. There were no characteristic changes in the white blood cell counts or differential, but count of 10,000 to 15,000/cmm with a slight predominance of polymorphonuclear leukocytes were found. Serum heptoglobin level was less than 10 mg/dl (normal; 40-150 mg/dl). Serum LDH level was increased to 1625 U/1 (normal; 240-530 U/1). Total bilirubin was 2.4 mg/dl. Total hemolytic complement was within the normal range. Urinalysis showed marged proteinuria and mild hematuria. The blood pressure had been extremely high since the onset of symptoms (217 ± 17/163 ± 11 mmHg) and hypertensive encephalopathy developed. A diagnosis of HUS was made and the patient was

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treated with urokinase and dipyridamole. Blood urea notrogen (BUN), serum creatinine and potassium levels gradually increased during the 13 days prior to admission to our hospital.

On admission, blood pressure was 240/200 mmHg. She became in a stupor and convulsion of the extremities was noted. BUN and serum creatinine were 81.9 mg/dl and 5.1 mg/dl, respectively. Admission electrolyte values were: Na 134 mEq/1; K 6.2 mEq/1; Ca 5.1 mEq/1; P 5.9 mg/dl. The clinical course of the patient is summarized in Figure. The patient was treated with peritoneal dialysis and became anuric. Injection of high dose of reserpine intramuscularly and hydralazine intravenously was started, but they were ineffective. Peritoneal dialysis for 48 hr did not lower the hypertension. Plasma renin activity measered during treatment with reserpine and hydralazine was 7.1 ng/ml/h (normal; 0.1–2.0 ng/ml h). The level of plasma angiotensin I and II was 1745 pg/ml (normal; less than 200 pg/ml) and 217 pg/ml (normal; less than 110 pg/ml), respectively. The prothrombin time, partial thromroplastin time and fibrinogen levels were all within normal limits, and the platelet count was 110,000/cmm. However, plasma fibrin degradation products (FDP) were increased to 320 μg/ml, and urinary excretion of FDP was also increased (40 μg/ml, normal; less than 0.1 μg/ml). Plasma antithromrin III was 113% (normal; 75–125%) and heparin therapy was begun. Ten days after admission, the platelet count was 260,000/cmm. However, recovery from renal failure was not made.

For the treatmint of hypertension, captopril administration was started with a dose of 4.1 mg (0.3 mg/Kg/dose). One hour after the first administration, blood pressure was depressed to a level of 160/110 mmHg. Repeated administration every six hours was effective, but the effect was transient and not enough to normalize the blood pressure. Captopril 6.25 mg (0.45-mg/Kg/dose) every six hours was very effective, and the blood pressure became normal. After the blood pressure had been reduced to the normal level, the administration of captopril 4.1 mg once a day was enough to maintain the blood pressure within the normal range.

DISCUSSION

Hypertension is a common finding in acute renal failure. The pathogenesis of hypertension varies according to the type of renal lesion. In patients with acute renal failure due to HUS, the hypertension is associated with high plasma re-

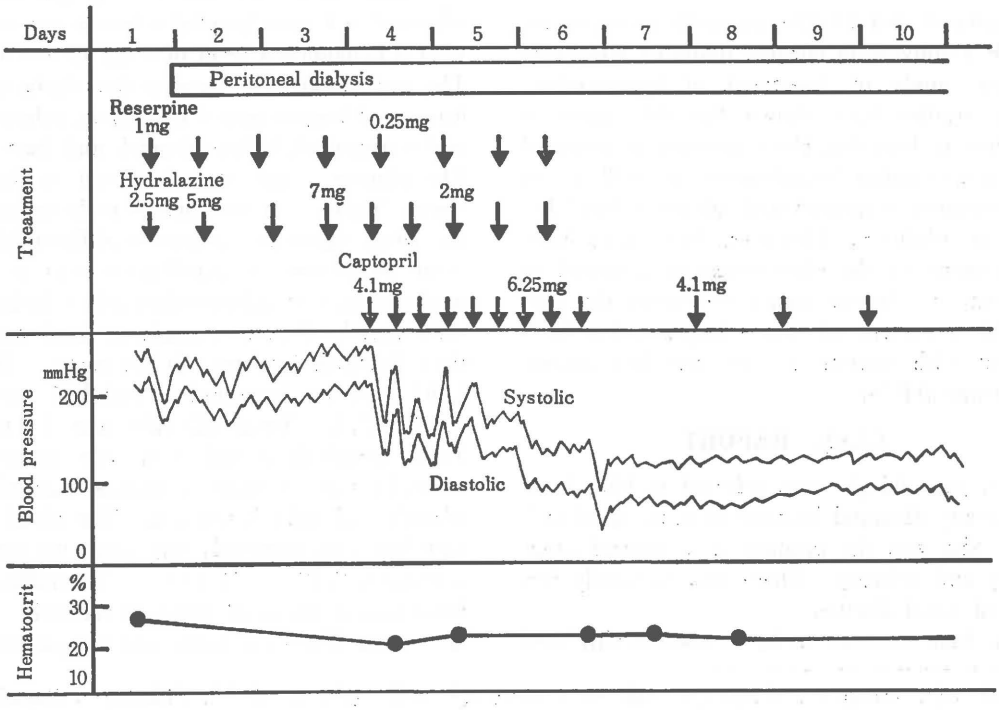

Fig. Clinical course of the patient

nin activity as well as salt and fluid overload[5].

We have reported here the successful treatment of a child with severe hypertension with captopril in whom parenteral antihypertensive therapy with available drugs had proved ineffective. Captopril inhibits the enzyme that converts angiotensin I to angiotensin II[6,7]. Enzyme activity was inhibited by 56% 30 minutes after captopril was given and by 92% after 120 minutes[7]. This drug has been shown to lower blood pressure successfully in patient with different types of hypertension[1-4]. There is a significant, although not very close, correlation between baseline plasma renin activity and blood pressure reduciton[2]. The plasma renin activity and the levels of angiotensin I and II were high in our patient. The possibility that hydralazine resulted in high renin activity could not be excluded. However, the dramatic hypotensive effect of captopril, as well as the high plasma renin activity before administration of this drug, indicates that the hypertension in our patient was in part due to an excess of angiotensin II.

Because converting enzyme has been shown to be identical with kininase II, blockade of this enzyme may also lead to accumulation of circulating bradykinin, a potentially vasodilating hormone. It is not clear particulary in patients with normal or low plasma renin activity, whether captopril lowers blood pressure by eliminating the vasoconstrictor angiotensin II or by allowing the vasodilator bradykinin to accumulate. Man in't Veld et al[7]. reported that captopril's effect on blood pressure in an anephric patient depended on the state of sodium balance and that an extrarenal kallikrein-kinin sytem was important. Although no changes in blood bradykinin concentration has been demonstrated, it is possible that the hypotensive effect is mediated by changes in local concentrations of bradykinin and angiotensin in the kidniys or blood vessels[8].

In our patient, small doses given infrequently could be used after normalization of blood pressure. The prolonged hypotensive effect may be due to hypovolemia caused by peritoneal dialysis. However, hematocrit value did not increase.

Blood pressure reduction was rapid and the maximal antihypertensive effect could be achieved mostly within the first 2 houst of treatment. Increasing the dose of captopril does not enhance the amplitude of the hypotensive effect but increases its duration[2]. Side effects including rashes, fever, transient loss of taste and agranulocytosis have been reported[1,2,9]. No side effect was observed in our patient. The rapid reduction in blood pressure, prolonged duration of action and low toxicity makes this drug suitable for the treatment of hypertensive emergencies. The possible pathophysiologic effect chronic hyperreninemia and chronic elevation of angiotensin I as well as suppression of aldosterone remains unanswered.

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