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RHABDOMYOLYSIS AND MYOGLOBINURIA IN 19 PATIENTS WITH CHRONIC ALCOHOLISM

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Summary

We report on our experience with 19 cases of rhabdomyolysis in chronic alcoholic patients. The clinical spectrum of the disease was characterized by a wide variability in the extent of myolysis. Acute renal failure of variable degree was common and five patients required dialysis treatment. Other complications included irreversible shock, respiratory failure and hypercalcaemia. Early recognition of the disease is important, because the most frequent complication – myoglobinuric renal failure – can be avoided if proper treatment is instituted at the beginning of the disease.

Introduction

Rhabdomyolysis and its consequence, myoglobinuria, are frequent causes of acute renal failure, comprising five to 15 per cent of all episodes of acute renal failure. Among numerous other aetiologies [1] chronic alcoholism is of particular importance and represents the most frequent cause of myoglobinuria in our studies with large numbers of patients [2]. We report on our experience with 19 cases of rhabdomyolysis in chronic alcoholics observed during recent years among 103 patients with myoglobinuria.

Patients and methods

Nine chronic alcoholics (1 female, 18 males; 30–71 years old, mean 44.7 years), referred to our departments of Medicine and Neurology, were investigated. Among the reasons for admission acute renal failure, delirium tremens, and seizures were most frequent. No patient presented with a recent history of prolonged coma. During their hospital stay serum creatinine, creatine kinase (normal <70U/L) and myoglobin concentrations [3] in serum (normal <70μg/L) and urine (normal <50μg/L) were measured serially.

Results

Clinical picture

The clinical picture was characterized by a wide variability of symptoms. Some patients presented without severe clinical features, but in others the disease

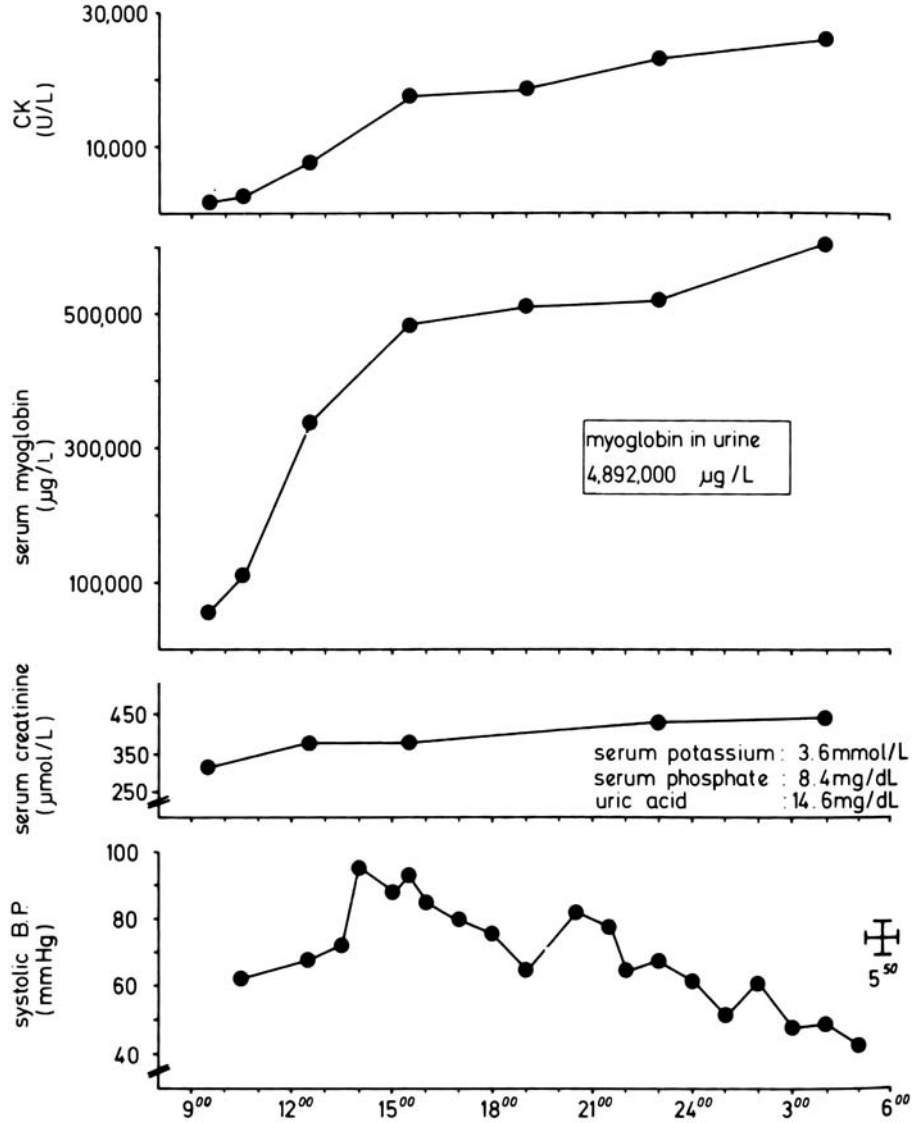

Figure 1. Clinical course and laboratory data of a patient with chronic alcoholism and rhabdomyolysis presenting with irreversible shock

followed a dramatic course with initial shock, respiratory insufficiency and kidney failure. Ten patients presented with delirium tremens, six had generalized seizures. Muscle tenderness or muscle swelling were found in only five patients and brown discolouration of urine in only four. Seven patients presented with initial respiratory failure (pO_2 <60mmHg), three of whom had to be treated by artificial ventilation. Four patients presented with shock. This seems to be the most severe complication of the syndrome, since two of these patients died in irreversible shock. In these patients no cause of the shock other than rhabdomyolysis could be found on post mortem examination. Figure 1 shows data of one of these patients: during his short hospital stay, this patient had a dramatic increase in creatine kinase activity and myoglobin concentrations in serum and in urine. Clinically, there was oligoanuria and shock resistant to all therapeutic measures. The patient died within 24 hours of admission.

Two other patients died from causes not related to myolysis.

Laboratory data

Table I shows laboratory data in our 19 patients. It may be seen that the extent of myolysis, as measured by creatine kinase activity and myoglobulin concentrations in serum and in urine was greatly variable. The fact that many patients

TABLE I. Laboratory data in 19 chronic alcoholics with rhabdomyolysis

Patient number	age/ male female	peak CK (U/L)	peak myoglobin (μg/L) serum	urine	peak creatinine (μmol/L)	initial serum K^+ (mmol/L)
1	41 M	2,920	11,559	1,016	336	4.6
2	31 M	96,800	64,293	716,352	159	3.1
3	30 M	2,516	1,115	1,509	292	3.0
4	53 M	8,064	5,398	3,998	88	4.3
5	43 M	8,681	389	11	133	3.0
6	42 M	3,394	2,240	11	80	4.2
7	37 M	4,828	3,310	13,629	141	3.9
8	41 M	14,370	3,560	42,050	97	2.7
9	35 M	2,827	1,737	69	106	3.8
10	50 M	25,754	600,995	4,892,000	424 (D*)	3.6
11	35 M	1,049	16,627	14,183	981 (D*)	6.5
12	44 M	2,292	517	883	133	4.2
13	49 M	561	1,390	21	583	2.9
14	45 F	2,878	–	–	1,132 (D*)	3.0
15	71 M	1,106	4,237	–	1,061	4.5
16	62 M	1,146	–	–	477	2.9
17	46 M	26,292	436,934	34,440	507 (D*)	5.5
18	50 M	2,775	35,635	–	1,344	2.9
19	45 M	29,600	37,012	627	1,070 (D*)	6.6

(D*) = dialysis treatment

could only be investigated after the maximum extent of their rhabdomyolysis may have contributed to this seemingly great variability. In the most severe cases the parameters of myolysis in serum (creatine kinase, serum myoglobin) were increased up to 10,000 times the upper normal limits. In urine, myoglobin was elevated up to 100,000 times the upper normal limits.

It may also be recognized from Table I that there was no correlation between the extent of myolysis and the impairment of kidney function, as measured by serum creatinine. The occurrence of renal failure was common, with only five patients exhibiting maximal serum creatinine concentrations below 130μmol/L.

Nine patients had severe renal failure with maximal serum creatinine concentrations above 350μmol/L and five patients underwent dialysis treatment. All surviving patients recovered normal kidney function.

The incidence of hypokalaemia – even in patients with considerable renal impairment – was rather high, six patients presenting with serum potassium concentrations of 3.0mmol/L or less. Hypocalcaemia was also common in the acute phase of the disease, as it is in rhabdomyolysis of other origins. One patient (patient 19) developed hypercalcaemia (3.73mmol/L) during the polyuric phase of myoglobinuric renal failure. Five patients had mild (>60,000/mm^3) thrombocytopenia.

Discussion

The syndrome of rhabdomyolysis and myoglobinuria in chronic alcoholism, first described by Hed et al [4] in 1955 represents one of the major causes of sporadic paroxysmal myoglobinuria [1,2,5]. In studies with large patient series it represents up to 23 per cent of all cases of rhabdomyolysis [2]. In our own series of 103 patients with rhabdomyolysis, it accounts for 18.4 per cent of cases. As shown by the present series the mortality from the syndrome is considerable. Particularly, patients presenting with initial shock seem to be at high risk. The shock may be due to extravasation induced hypovolaemia and to vasoactive substances liberated by muscle necrosis.

The most frequent complication – as in other forms of rhabdomyolysis – is acute renal failure, often requiring dialysis treatment. In our series five of 19 patients had to undergo haemodialysis treatment. It is noteworthy that no correlation existed between the extent of myolysis and the degree of renal impairment. On the contrary, some of the patients with the most elevated myoglobin levels and creatine kinase activities retained completely normal serum creatinine values. This observation, however, should not be interpreted as evidence against a causal role of myoglobin in the aetiology of myoglobinuric renal failure. Urinary acidity and the diuresis at the beginning of rhabdomyolysis, precipitating factors such as electrolyte disturbances and pre-existing hypovolaemia, and the institution of early therapeutic measures (forced diuresis and alkalinization of urine) are prime determinants in the development of the myoglobinuric renal failure [1]. Patient 2 (Table I), for example, retained serum creatinine values near normal, in spite of massive myolysis with extremely elevated creatine kinase values and rather high myoglobin concentrations, both

in serum and in urine. In this patient diuretic therapy could be instituted shortly after the development of rhabdomyolysis.

In other patients, however, (for example patients 11, 14, 15, 18, 19) admission to hospital was delayed and renal function was already impaired, whereas actual measurements of creatine kinase were apparently suggestive of minor muscle damage. In these patients with established renal failure diuretic therapy is unsuccessful and potentially hazardous.

The pathogenesis of rhabdomyolysis in our patients is certainly multifactorial. Although patients with prolonged coma – a condition known to produce muscle compression myolysis – were excluded from our series, mechanical stress often seems to play an important role as a precipitating factor in the development of rhabdomyolysis in alcoholics. This is clearly demonstrated by the fact that many patients presented with agitation during delirium or with generalized seizures. Several lines of evidence, however, indicate that these factors are not the only mechanisms operative during rhabdomyolysis in chronic alcoholism. For example, creatine kinase elevation in patients with seizures of other origins are consistently lower than in alcoholics [7]. The frequent appearance of respiratory failure as an indicator of respiratory muscle involvement and evidence from radionuclide imaging [8] also indicates the existence of systemic and not only local factors. Hypokalaemia, present also in a considerable proportion of our patients, is considered to be one of these systemic factors precipitating rhabdomyolysis in alcoholics. Hypokalaemia is known to induce muscle damage, especially when combined with physical stress [9]. Other factors, such as hypophosphataemia and undefined nutritional deficiencies in alcoholics have been implicated in the pathogenesis of rhabdomyolysis in chronic alcoholism [10].

Whatever the pathogenetic factors may be, recognition of rhabdomyolysis in these patients is of great importance since a severe and most frequent complication – acute myoglobinuric renal failure – may be avoided, if proper treatment is instituted in time [6].

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