Defibrination Syndrome due to Scorpion Venom Poisoning

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Summary: Disseminated intravascular coagulation occurred in dogs given scorpion venom subcutaneously in doses of 3 mg./kg. body weight. Treatment with heparin reversed the coagulation abnormality of the syndrome and 10 out of 12 dogs survived. Necropsy findings in human patients stung by scorpions suggest that this syndrome also occurs in man.

Introduction

This study was prompted by the finding that the sting of the scorpion often proved fatal in children and adults within 24 to 48 hours. Necropsy examinations carried out on four children and three adults who died of scorpion venom poisoning showed congestion in all the organs. Subendocardial haemorrhages were present in two, mural thrombosis of the heart in one, and massive haemorrhage of the adrenals in one and of the frontal lobe in another. There were pinpoint haemorrhages in the cerebral cortex. Histological examination showed occlusions of small blood vessels with thrombi in the heart, lungs, brain, kidneys, and adrenals, which indicated disseminated intravascular coagulation resulting in defibrination and consequent haemorrhages.

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Materials and Methods

The venom used was from a scorpion of the species *Buthus tamulus*, which is very common in Kurnool, a part of Rayalaseema from which this study is reported. Venom was extracted from the telson by means of a six-volt electric shock (Deoras, 1960). Drops of venom issuing from the sting were collected in a previously weighed glass test-tube. The contents of the tube were diluted with a known volume of distilled water. Fresh venom was used throughout the study. Clotting-time (Lee and White, 1913), prothrombin time (Quick, 1935), serial thrombin time (Brodsky *et al.*, 1968), euglobulin lysis time (Cash, 1966), platelet count (Dameshek, 1932), and fibrinogen levels (Devi and Naganna, 1969) were estimated.

Preliminary experiments carried out on six dogs showed that the venom in doses of 0·75 mg./kg. injected subcutaneously had no effect at all, doses of 2·5 mg./kg. had some effect, but doses of 3 mg./kg. had the maximum effect and invariably killed the dogs in two to four hours. Similarly, 25-mg. doses of heparin given intramuscularly to four dogs in a

preliminary experiment showed that the clotting-time of the blood was doubled in one hour. The level of heparin in the blood was maintained at two to three times the control level by repeated injections every four hours.

The effects of subcutaneous injections of 3 mg./kg. of venom were then noted on the first group of 12 dogs. A similar injection of venom preceded by 25 mg. of heparin intramuscularly was given to the second group of 12 dogs and the effects were noted. The second group was given a further dose of heparin every four hours for 24 hours, this was then tailed off over the next 12 hours. Wherever excessive salivation and vomiting were present dexamethasone 2 mg. intramuscularly was given after injection of venom.

Results

Of the 12 dogs given venom alone 10 died. All these had clinically excessive salivation, initial restlessness, dilated pupils, tachycardia, rapid respiration, and frequent urination and defaecation. All the dogs became very quiet half to one hour after the injection. Disturbances in heart rate and rhythm occurred in 10 of the dogs, distension in eight, and grossly bloody motions in four. Though necropsy examinations were carried out on all of the dogs that died, the results are confined to six in which complete coagulation studies were done.

Coagulation studies performed two hours after the injection of venom showed a prolonged serial thrombin time, hypofibrinogenaemia, thrombocytopenia, and a normal or slightly raised euglobulin lysis time compared with the control values before the injection of venom. In only one case was there a decrease in euglobulin lysis time (Table I). Prothrombin time was increased in all cases, the values being 52, 70, 56, 40, 80, and 75% of preinjection values in the six dogs.

Necropsy studies on these six dogs showed subendocardial haemorrhages in five, haemorrhages into kidney and lung in four, and haemorrhagic necrosis of intestines in four: congestion of all the organs was found in the six. On histological examination there were thrombi occluding the capillaries and haemorrhages in the heart, kidney, and lungs in five cases, the intestines in four, the spleen, liver, and adrenals in three, the pancreas in two, and the brain in one.

Of the 12 dogs given heparin and venom 10 survived. Clinically excessive salivation was present in 10 of the 12 dogs, which could be controlled by dexamethasone. All the dogs were less restless, but frequent urination and defaecation occurred in only two, of which one died. Coagulation studies showed that there was no fall in fibrinogen levels or platelet counts in the dogs treated with heparin, nor were the results of thrombin clotting-time affected to any great extent (Table II). This fact may have been due to sampling of blood four hours after injection of heparin.

TABLE I.—*Effect of Scorpion Venom on Coagulation studies*

Dog No.	Hours after Injection	Serial Thrombin Time in Seconds at Incubation of							Fibrinogen (mg. 100 ml.s	Platelets · 10^3 cu. mm)	E.L.T.* (minutes)
		0 min.	10 min.	20 min.	30 min.	40 min.	50 min.	60 min.			
1	0	5·0	6·0	8·0	10·5	16·0	16·0	20·0	318	121	160
	2	8·0	12·0	28·0	31·5	35·5	48·0	67·0	164	59	176
2	0	3·5	4·0	4·5	6·0	8·0	12·0	18·0	400	288	148
	2	10·5	15·0	22·0	48·5	63·0	84·5	108·0	120	128	156
3	0	6·0	8·0	10·5	13·5	15·0	20·0	22·0	265	148	210
	2	12·0	14·5	25·0	50·5	70·5	85·0	110·5	188	79	125
4	0	3·0	5·0	7·5	8·5	10·5	12·5	15·0	380	119	125
	2	5·5	9·0	10·5	11·5	15·5	27·5	42·0	114	79	130
5	0	3·5	4·5	4·5	5·0	6·5	8·0	13·5	379	318	170
	2	5·5	6·5	9·5	11·0	16·0	42·5	61·5	146	141	180
6	0	3·5	5·0	8·5	12·5	16·5	22·0	25·5	418	261	178
	2	6·5	6·5	10·0	18·5	30·5	55·0	110·0	212	141	184

*Euglobulin lysis time.

TABLE II.—*Effect of Therapy on Coagulation studies*

Dog No.	Hours of therapy	Serial Thrombin Time in Seconds at Incubation of							Fibrinogen (mg./100ml.)	Platelet count $\times 10^3$/cu.mm.	E.L.T.	Therapy
		0 min.	10 min.	20 min.	30 min.	40 min.	50 min.	60 min.				
A	0	5	10·5	13	15·0	16·5	20·0	22·0	422	150	155	Heparin
	4	5	12·0	14·5	16·5	17·0	23·0	25·0	418	141	210	and
	24	—	—	—	—	—	—	—	432	155	160	cortisone
B	0	5	6·0	8·5	10·5	11·0	13·0	15·5	318	102	125	
	4	6·5	12·0	19·0	19·0	20·0	25·0	30·0	298	98	120	Heparin
	24	—	—	—	—	—	—	—	324	106	116	
C	0	3·0	4·0	6·5	8·5	10·0	12·0	18·5	511	82	125	Heparin
	4	3·5	4·0	7·5	8·5	11·5	13·0	22·5	540	82	115	and
	24	—	—	—	—	—	—	—	524	83	130	cortisone
D	0	7·0	8·5	12·5	14·0	16·0	20·5	22·0	438	72	115	Heparin
	4	7·0	8·0	13·0	16·5	18·5	21·0	25·0	432	71	130	and
	24	—	—	—	—	—	—	—	416	78	125	cortisone
E	0	3·5	6·5	8·0	9·5	16·5	22·5	28·0	398	109	176	
	4	4·5	7·5	8·5	12·5	16·0	23·5	30·0	378	108	186	Heparin
	24	—	—	—	—	—	—	—	380	110	168	
F	0	3·5	4·5	6·0	8·5	12·0	16·5	23·5	266	121	168	Heparin
	4	4·0	5·0	7·5	9·0	14·0	21·0	38·5	232	120	174	and
	24	—	—	—	—	—	—	—	284	124	180	cortisone

The data against zero hours of therapy indicate the baseline control values before injection of the venom or heparin and that against four hours indicate the values four hours after heparin and three hours after venom injections.

Discussion

Disseminated intravascular coagulation or defibrination syndrome is known to be concerned in the pathogenesis of various diseases (Hardaway and McKay, 1963). Heparin therapy is often effective in controlling the bleeding diathesis associated with this disorder (Bernstock and Hirson, 1960; Merskey *et al.*, 1967; Brodsky *et al.*, 1968). It is important, however, to distinguish between the syndromes of disseminated intravascular coagulation and primary fibrinolysis, since the treatment is different. In our study four tests were important in making the diagnosis: platelet count; serial thrombin time; euglobulin lysis time; and plasma fibrinogen levels, which can be used to distinguish between fibrinolysis and defibrination (Brodsky *et al.*, 1968). On the basis of these tests the coagulation studies carried out on the dogs given scorpion venom showed that the defibrination syndrome had occurred (Table I). Necropsy and histological examination confirmed this supposition.

The abnormal coagulation profile was reversed with heparin therapy and the dogs survived (Table II). The bites of some snakes cause intravascular coagulation (Best and Taylor, 1961) similar to that occurring after intravascular injection of thrombin (Hardaway *et al.*, 1960); however, such a syndrome due to a scorpion sting has not yet been described. Myocarditis (Poon-King, 1963), neurotoxicity (Brown, 1959; Manson-Bahr, 1961), and acute pancreatitis (Poon-King, 1963) have been stated to be the cause of death in patients poisoned with scorpion venom.

In cases of defibrination syndrome adequate doses of heparin by continuous intravenous drip produced dramatic effects (Brodsky *et al.*, 1968). Since it is difficult to give heparin by continuous intravenous drip to a conscious dog, and since given intramuscularly it takes about an hour to double the coagulation time, heparin was administered to the dogs one hour before injection of the venom. The aim of this study was mainly to determine whether heparin in adequate doses could prevent the defibrination syndrome occurring as a result of injections of scorpion venom. Similar coagulation studies need to be carried out in man, and the effect of giving heparin after venom injection in animals must be noted before the effect of heparin in similar cases in man is studied.

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