Scorpion Sting and Acute Kidney Injury: Case Series from Pakistan

Abstract:

Objectives: ~~we~~ We aim to report here a series of cases developing AKI after scorpion stings.

Patients and Methods: During a period of 25 years that is; from January 1990- December 2014 all the patients coming to Sindh Institute of Urology and Transplantation, with AKI after scorpion sting are included in study. AKI was defined according to RIFLE criteria and Scorpion sting was labeled on history of person stung by scorpion.

Results: During studied period 18 patients were brought with scorpion sting. Mean age of patients was 29.22±18.48 years, 7 were male and 11 females. Mean duration of insult was 8.94±4.12 days. Sixteen out of 18 patients were either oliguric or anuric on presentation. Uremia was advanced on arrival with mean urea of 324.38±116.82 and creatinine of 11.8±4.30 mg/dl. Hyponatremia was a common finding with mean sodium of 129.16±8.76 meq/l. Extensive tissue damage at site of sting observed in many patients and mean values for LDH and CK were 2349.71±3499.15 and 3116.23±5468.22 U/L respectively. Hemodialysis required in all patients. Complete renal recovery seen in 13 patients, 2 expired and 3 discharged from hospital in partial state of recovery and never turned for follow up.

Conclusion: Scorpion sting is major health problem in many parts of our country, in majority it takes a benign course but in some may affect multiple organs and result in death.

Key Words: AKI, RIFLE criteria, Scorpion Sting

Introduction:

There are about 2000 species of scorpion exist all over the world, most populated in warm and dry tropical regions. In most species the sting is painful, but not fatal to humans. Approximately 25-40 species has been reported having toxins dangerous to human (1). More dangerous species have been reported from Iran, Indian sub-continent, Turkey and Middle Eastern countries. *Mesobuthus tumulus*, an Indian red scorpion is the most lethal species in India (2).While *Hemiscorpious lepturus* most important from Iran, this species is endemic in Khuzestan and south of Iraq (3). A dangerous and fatal species reported from United States is *Centruroides exilicauda* or bark scorpion (1). The poison involved is mainly neurotoxin; but several components including hemolysins, agglutinins, hemorhagins,leucocytolysins, coagulins, lecithin and cholessterin has been reported (4). Toxicity of venom is contributed by its proteolytic content and phospholipases A_2, each venom contains 50-100 different polypeptides (5). The renal injury may be caused by pigment nephropathy (myoglobin or hemoglobin pigment), interstitial nephritis by direct toxin effect, rhabdomyolysis, intravascular hemolysis or vasculitis (5).

The scorpion venom has been described to delay the closing of neuronal sodium channels, resulting in "autonomic storm" this is because of sudden pouring of endogenous catecholamine into the circulation. Autonomic storm is characterized by transient parasympathetic and prolonged sympathetic stimulation (2).
~~Autonomic stimulation occurs after envenomation.~~ Animal studies have shown induction of both pro and anti inflammatory cytokines after exposure to venom (6). Reported renal pathologies are acute tubular necrosis, interstitial nephritis, mesangial proliferation and hemolytic uremic syndrome (5,7,8,9,10). We aim to report here a series of cases from our institution treated during last 25 years.

Patients and Methods:

This study is based on a series of 18 patients with AKI after scorpion sting from a retrospective chart review of all patients admitted to the Sindh institute of Urology and Transplantation, Karachi, Pakistan between January 1990 and December 2014. AKI was identified and staged according to RIFLE criteria (11). Patients with preexisting kidney disease were excluded. Diagnosis of scorpion sting was based on history of stung by scorpion, which was seen by patient or close relative. Renal scan was done in all patients; those with normal size non obstructed kidneys were included in study. Patients with other co-morbid were not included in study.
Renal biopsy performed in three cases, and evaluated with light microscopy (LM) and immune histochemistry. For LM, routinely 10 serial sections are cut and stained by hematoxylin and eosin (H&E), Masson's trichrome stain, periodic acid Schiff (PAS), and silver (Gomori's methenamine silver, GMS). While immune-histochemistry for myoglobin, tissue sections were immersed in peroxidase quenching solution and rinsed with PBS. Primary antibody (polyclonal rabbit anti human Myoglobin, Dako, Glostrup, Denmark) in dilution of 1:400 was applied for 30-60 minutes at room temperature followed by PBS rinsing. Secondary antibody (HRP: horse reddish peroxidase. Dako LSAB +/HRP kit, Dako, Glostrup, Denmark) was applied for 10 minutes at room temperature followed by PBS rinsing. Enzyme conjugate was applied for 10 minutes at room temperature followed by PBS rinsing. Chromogen substance (DAB, Dako, Glostrup, Denmark) was applied for 5-10 minutes followed by PBS rinsing and light counter stain with hematoxylin and mounting of slides.

All patients were followed up till death or complete renal recovery except 3 who lost follow up after first discharge from hospital.

Statistical methods: Statistical analysis was done on SPSS version 15.0. Quantitative variables reported as means ± SD and Qualitative as percentages.

Results:

A total of 18 cases with AKI secondary to scorpion sting were registered during the study period. There were 11 females and 7 males with mean age of 29.22±18.48 years. Patients were brought from different cities of Baluchistan province, distance was 323 – 585 km from Karachi in southwestern direction. Fourteen (78%) cases were stung during months of summer which extends from April to September in this region, and temperature ranges from 32 to ~~44^{0}C~~51^{0}C during these months.

Severe pain, tingling, numbness or burning sensation at site of sting was noticed in all of patients. The second most common symptom was decline in urine output, reported in 89% patients Table 1. Most frequent site was either foot in 6 cases, then thigh in 3, trunk 3, hand 2, neck 2, pectoral region and forehead one each. Laryngeal edema and airway obstruction, requiring mechanical ventilation, was noticed in one patient. Laboratory values of the day of reporting at this hospital are given in Table 2, blood urea, serum creatinine, CK, LDH, were increased several folds over the reference range, while AST and ALT were found mildly raised. Hyponatremia was common with mean sodium of 129.16±8.76 meq/l. Urinalysis was available in 14 patients, dipstick revealed 1-3+ protein in 9 patients, while 1 had 4+ protein. Microscopy revealed hematuria in 14 cases. Renal biopsy was performed in 3 patients; ~~it~~ revealed acute tubular necrosis in all ~~3~~ and pigment casts in 2; glomeruli were found to be normal. Two patients had cardiac arrhythmias, one recovered and other died. Three patients had disturbed sensorium on presentation with Glasgow coma scale 3-9.

Renal replacement therapy was required in all patients. Complete renal recovery occurred in 13(72.22%), while 2 died during acute phase of illness; the rest 3 lost for follow up after discharge from the hospital. Those who expired; one was 60 years male who started recovering renal functions, developed brady-arrhythmia and died of probably delayed cardiomyopathy. While other who was 75 years female brought unconscious and died on same day of reaching to this hospital. Photographs from necrotic lesion at site of sting, scorpion provided by one of patient and renal biopsy from one patient are given here Fig. 1, 2 and 3.

Discussion:

In literature reported health hazards from scorpions are mostly from Iran, mid eastern countries, Indian subcontinent, Mexico and North African Countries. Large epidemiology published from Iran reports majority cases stung during summer and female affected more than male (12). We have also noticed similarities in both, that is gender and season. *Hemiscorpius lepturus* is the commonly reported scorpion species from the region where our studied patients belong. Others reported are *Mesobuthus tumulus*, *Androctonus crassicanda*, and *M. eupeus* (16). Scorpion was provided by one patient of present study population shown in Fig.1.

Pancreatitis after scorpion sting has been reported as early as 1970 (13), effect of toxin studied on animal cardiac muscle reported in 1974 (14), then human studies on cardiac dysfunction and pulmonary edema in literature from Israel, states that cardiac injury persisted for prolonged duration (15). One of our patients who died after 15 days of scorpion sting while already

recovering from renal failure could be due to delayed cardiomyopathy as he developed brady arrhythmia and hypotension at this late stage. A series of cases developing renal injury first reported by Malhotra et al in 1978 (8), later isolated cases are found in literature, we have also reported one case from present cohort previously in 1998 (7). Renal injury in these patients may result from intravascular hemolysis, rhabdomyolysis after extensive tissue necrosis, both may cause pigment nephropathy. Then direct toxic effect of venom may cause interstitial nephritis, release of cytokines and vasodilatation may lead to ischemic tubular necrosis. Furthermore, "autonomic storm" may lead to shock and renal cortical necrosis. In present study we have found evident acute tubular necrosis and pigment nephropathy, while we are uncertain about interstitial nephritis and acute cortical necrosis as we have not performed renal biopsy in all and then 3 of our patients lost follow up and in them we are not sure whether they recovered or developed chronic kidney disease.

Stung on trunk and neck allow more venom to reach the blood and thus cause more morbidity half of our patients had stunged in these regions. Pain at site of sting, numbness and tingling sensations are commonly described symptoms (1,2,7,8) and reported by all of our patients. Similarly decline in urine output from oliguria to absolute anuria is also well reported entity (5,7,8) and found in 89 % of present study population. Local manifestation vary from no sign other that mild edema to ecchymosis, extensive cellulites and necrosis (16,17), in our studied population 61% patients had these findings, tissue necrosis was extensive ~~enough~~ in 3 patients, ~~to~~and required skin grafting in later ~~on~~ stage(Fig.2). Area involved around site ranged from 50-2000mm in these patients, available photograph is from patient who had medium size necrotic area. High levels of muscle enzymes i.e; LDH, CK and AST can be explained with extensive tissue damage at site of sting. Hyponatremia has been reported in one case by Chadah et al (17) and hypernatremia one case by Derakhshan et al (10) in past studies, in our study average patients had low serum sodium levels. We could not measure fractional excretion of sodium (FeNa) in our patients, 4 patients had absolute anuria, and some reached late to this hospital. Thus we are not in position to comment on renal handling of sodium in these cases from our own experience.

Malhotra et al in their case series performed renal biopsy in 4 patients and reported mesangial proliferation, variable degree of tubular damage and mild interstitial inflammation. We have done renal biopsy in 3 and find acute tubular necrosis in all with presence of pigment casts in tubular lumina in one case. Pigment was myoglobin as proved by immune histochemistry (Fig.3).

Limitations: FeNa was not available in our studied population and majority patients had low serum sodium but we cannot comment on renal handling of sodium in these patients.

Conclusion: Scorpion sting is important issue to address in parts of country where poisonous species inhabitants. Fatal complications may occur at early as well as late after sting.

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Table1: Clinical Parameters of Patients (N=18)

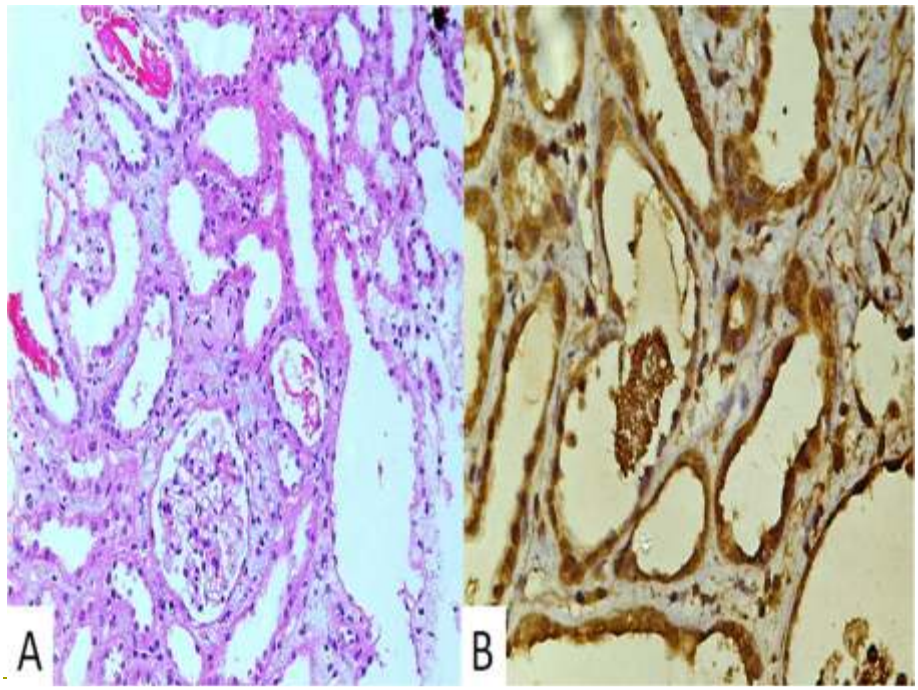
Parameter	**numbers**	**%**
Local pain, numbness, tingling	18	100
Oligo-anuria	16	88.88
Local ecchymosis, cellulites, necrosis	11	61.11
Hematuria/ hemetamesis	10	55.55
Drowsiness/ altered sensorium	4	22.22

Table 2: Laboratory Parameters of Patients (N=18)

Parameters	**mean±SD**
Hb (g/dl)	7.6±3.04
Urea (mg/dl)	324.38±116.82
Serum Creatinine (mg/dl)	11.8+4.30
Serum Sodium	129.16+8.76
Serum Potassium (meq/l)	4.9+1.24
LDH (U/L)	2349.71+3499.15
CK (U/L)	3116.23+5468.22
AST (U/L)	91.56+158.75
ALT (U/L)	65.93+79.79
Proteinuria on dipstick (%)	55.55
Micrpscopic hematuria (%)	77.77

Fig. 1: Scorpion provided by one patient included in cohort.

Fig. 2- Site of Scorpion Sting, local necrosis.



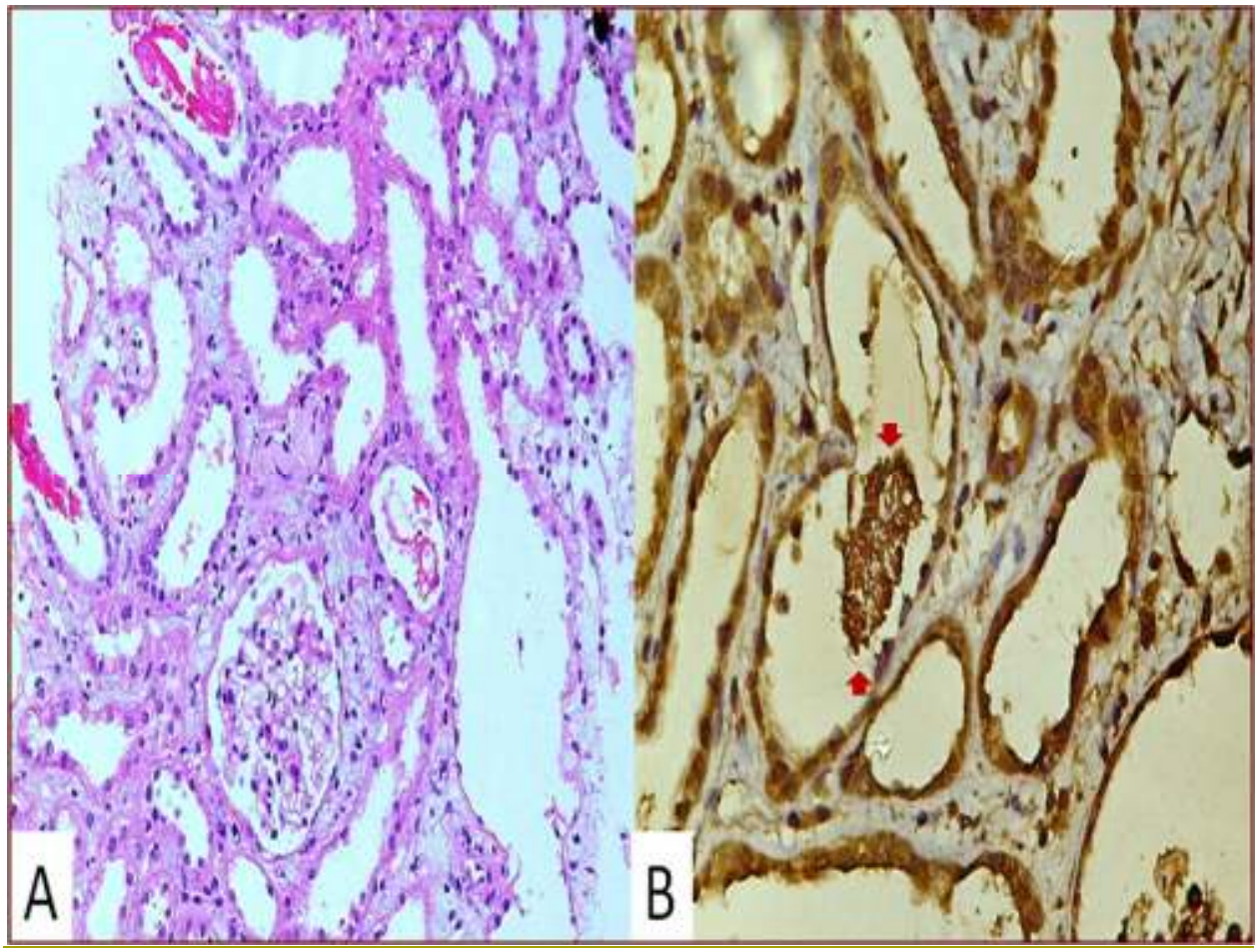


Fig 3: A- Light Microscopy. H and E stain, showing ATN and pigment casts in some lumina. B. Immune histochemistry, positive staining of pigment cast for myoglobin, tubules show non specific staining..