

A novel management method for disseminated intravascular coagulation like syndrome after a sting of *Hemiscorpius lepturus*: A case series

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Received 4 December 2010; received in revised form 17 April 2011; accepted 29 April 2011

Abstract. In this case series report we aim to report a Disseminated Intravascular Coagulation (DIC)-like syndrome associated with *Hemiscorpius lepturus* sting in 4 individuals and a novel management protocol for this life-threatening condition that comprised partial exchange transfusion in severe scorpionism.

INTRODUCTION

Scorpion sting is considered to be an important public health problem in Khuzestan province, in southwest of Iran. *Hemiscorpius lepturus* (Hemiscorpiidae) occurs along the Iranian border, especially adjacent to Khuzestan in the south-west where it is responsible for 67% of scorpion sting fatalities (Radmanesh, 1990a). This type of scorpion which is an inhabitant of this part of Iran, especially in northern parts of the province is the most lethal scorpion in Iran (Radmanesh, 1990b). Although most victims develop local symptoms after being stung such as pain and swelling, approximately 30% of them further develop systemic symptoms as hyperthermia, sweating, flushing, vomiting, restlessness, neurological symptoms and hematological disturbances (Radmanesh 1990a, Pipelzadeh *et al.*, 2007). In more severe cases neurological symptoms are predominant (Radmanesh, 1990b, 1998). Intravascular hemolysis is one of the most common hematological complications after being stung by *H. lepturus* and in more severe forms; the victims develop hemoglobinuria (Pipelzadeh *et al.*, 2007). Some of them

develop coagulation disorders leading to prolongation of Prothrombine Time (PT), Partial Thromboplastine Time (PTT) and bleeding diathesis (Pipelzadeh *et al.*, 2007) & Disseminated Intravascular Coagulation (DIC) (Afzali & Pezeshki, 1998).

Despite Antivenome injection & transfusion of blood products such as packed Red Blood Cells (RBCs) & Fresh Frozen Plasma FFP, patients' conditions deteriorate. They develop bleeding at venipuncture sites, cutaneous ecchymosis & then pulmonary, gastrointestinal and Central Nervous System (CNS) hemorrhage. These symptoms are followed by respiratory failure and vasopressor-unresponsive hemodynamic instability leading to death. The scenario begins clinically with paroxysms of intravascular hemolysis and dark color urine consequently leading to a clinical syndrome resembling DIC. At present there is no established effective management for this severe DIC-like syndrome and all other supportive modalities don't change the outcome (Afzali & Pezeshki, 1998, Pipelzadeh *et al.*, 2007). However, prolonged Activated Partial thromboplastine time (APTT) was associated with moderate to severe form of

scorpionism, didn't change the outcome of children in south east Turkey (Bosnak, 2009). A clinical syndrome similar to DIC-like syndromes following scorpion sting has been described in some reports in which the patients developed renal dysfunction and thrombocytopenia but had normal coagulation profile which resembled Hemolytic Uremic Syndrome (HUS) (Mocan *et al.*, 1998, Valavi & Ansari, 2008). They were treated by supportive care. A few case reports of death due to this DIC like condition are being reported annually (Radmanesh, 1990a, Afzali & Pezeshki, 1998; Shahbazzadeh *et al.*, 2009). Uncontrollable bleeding tendency & then spontaneous hemorrhage are rare complications of scorpion stings. Absence of appropriate management leads to death (Shahbazzadeh *et al.*, 2009). Mild forms of this condition lead to coagulation disturbances which can be treated by supportive care and blood products transfusion in addition to antivenom. Severe forms are associated with gastrointestinal, pulmonary and CNS bleeding resembling DIC usually leads to multiple organ failure and eventually death. We performed partial exchange transfusion (PET) in 4 cases in manual manner by transfusion of 4 units of packed RBC's, FFP & normal saline & phlebotomy sequentially in each session in Razi hospital (Ahvaz, Khuzestan, Iran), a referral center for scorpion sting for adults in Khuzestan province and report their hospital course briefly.

Case Reports:

Case No. 1

A 23 year old lady was referred to our hospital with primary complaint of hemoptysis after being stung by *H. lepturus* 1 day prior to admission (PTA) date on her upper back side of the trunk. In a local hospital she received 5 ml of antivenom (according to health services recommendations) on the same day she was stung. About 6 hours PTA she developed hemoptysis and then she was transferred to our hospital. However, she presented later with dark color urine and prolonged PT. Several units of FFP and packed RBC's were transfused during her stay

in the hospital. On Physical examination at admission she was toxic with aubergine discoloration of skin. Pulse rate was 100/min, blood pressure (BP) 150/80 mmHg and temperature (Tem) 39.2°C with respiratory rate (RR) 20/min. Sclera was had a colour resembling egg plant surfaces aubergine coloured, lung and heart were normal in physical examination. Sting site was on the back trunk and it was erythematous with peripheral ecchymosis. Laboratory findings were as follows: Hb: 8.8 g/dL, Hct: 27.4%, WBC: 32,400/mm³, Neutrophil count percent: (PMN) 78%, Platelets: 238x10³/mm³, PT: 20 seconds, with International normalization Ratio (INR): 1.6, PTT: 50 sec (Control: 30 sec), Blood Urea Nitrogen (BUN): 17 mg/dl, Creatinine (Cr): 2.8 mg/dl and 4+ Hemoglobin on Urine examination urinalysis.

6 hours later 1st session of partial exchange transfusion was performed. Her general condition dramatically improved, but PT was yet prolonged. The 2nd and 3rd sessions of exchange transfusion were performed consecutively. Coagulation profile gradually improved, hemoglobiniuria decreased and she was discharged without any complications on the 20th admission day.

Case No. 2

A 17 year-old girl was referred to our center due to excessive hematuria one day after scorpion sting. She developed nausea, vomiting and then hematuria. She was brought to a local physician and subsequently her physician noted jaundice and referred her to our center. On physical examination, blood pressure was 190/110 mmHg and otherwise normal. She had yellowish discoloration of sclera and the site of scorpion sting was seen on the lateral side of the right thigh. Initial laboratory findings were work ups included: Hb: 7.3 mg/dl, WBC count: 31,900/mm³, PMN: 91%, Platelet count: 226,000/mm³, PT: 25 sec with INR: 2.1, Ptt: 55 sec (Control: 30 sec), Blood sugar: 280 mg/dl, BUN: 26 mg/dl, Cr: 1.2 mg/dl, 3+ Hemoglobine on urinalysis. Several hours later her level of consciousness decreased accompanied by hemoptysis, tachypnea and bilateral coarse crackling rales on lung examination. She was transferred to Intensive Care Unit (ICU) and

underwent artificial ventilation due to severe hypoxia and respiratory exhaustion (PaO₂: 33mmHg, PaCO₂: 46 mmHg, PH: 7.28, HCO₃: 21.3, on FIO₂: 21%).

During the next three days several transfusions of FFP and Packed RBC's were performed without clinical or laboratory response but with no clinical response. Partial Exchange Transfusion was then performed for 3 times and her general condition, coagulation profiles, hematologic and urinalysis findings gradually improved. She was then weaned off from ventilator in the 8th day of hospital admission. She was discharged from hospital in the 21st day after admission with a good condition.

Case No. 3

A 22 year-old man was admitted due to sting by *H. lepturus* since 14 hours PTA in his back trunk. He soon developed pain, nausea, vomiting and tea color urine. According to health service guidelines he was treated in a local hospital. At admission physical examination revealed BP: 110/70 mmHg, RR: 18/min, pulse rate: 80/min, Temperature: 39.8°C. Heart and lung examination was normal. Sting site in the back area was tender, warm and erythematous. Initial laboratory findings showed PT: 16 seconds with INR: 1.3, PTT: 51 sec, Hb: 11.6mg/dl, WBC: 12,700/mm³, PMN: 85%, BUN: 19 mg/dl, Cr: 0.9 mg/dl, U/A: 4+ Hemoglobine. In the 2nd day of admission and in spite of receiving FFP and packed RBC's he developed decreased level of consciousness and dilated pupils while reactive to light, aubergine color of skin and sclera. Lung on examination was clear and heart examination revealed tachycardia. His laboratory findings were BUN: 50 mg/dl, Cr: 3.3 mg/dl, Na: 116 meq/Lit, k: 4 meq/Lit, PT>50 seconds with INR> 3.75, PTT>80 seconds, Hb: 5 g/dl, Hct: 13.8%, 4+ Hemoglobine in urinalysis. At this time he underwent partial exchange transfusion. Coagulation profile derangement improved gradually after and then PET, especially at the 3rd was performed for 2 more sessions. PT and PTT were normalized and his general condition and level of consciousness completely improved. However, he developed his condition was complicated

with acute tubular necrosis (ATN) and then underwent hemodialysis. He was discharged in the 26th day after admission in recovery phase of ATN and in otherwise good condition.

Case No. 4

A 17 year-old boy was admitted after being stung by *H. lepturus* in the left thigh since 20 hours before admission. He was initially administered anti-scorpion venom (Anti-venom immunoglobulin) and analgesics. Then because of dark color urine and hematemesis he was referred to our center. Physical findings on admission were, BP: 110/60 mmHg, PR: 110/min, RR: 24/min, Tem: 37.2°C, Sclera was faint aubergine color, heart and lung examinations were normal, on the left thigh a 1.5 cm² black necrotic tender area was noted. Laboratory findings on admission were, Hb: 3.6 g/dl, Hct: 10%, Platelet count: 183,000/mm³, WBC count: 7200/mm³, PT: 38 seconds with INR: 3.1, PTT: 82 seconds, BUN: 19 mg/dl, Cr: 1.6 mg/dl, Na: 137 meq/Lit, K: 4 meq/Lit, 4+ hemoglobine in urinalysis. During the hospital course he developed gum bleeding and hematemesis for 3 episodes in spite of transfusion of several units of Packed RBC's and FFP. His condition deteriorated and he developed tachypnea (RR: 40/min) and hypoxia (Pao: 55 mmHg, O₂ saturation was variable (on room air). He was then transferred to ICU and was managed by nasal prong without ventilatory support. Then PET was performed every other day for 3 times. Hypoxia, tachypnea, hematuria and coagulopathy gradually improved following PET. He was transferred to ward and was later discharged on the 10th day of hospital admission (Figures 1 and 2).

DISCUSSION

Up to now there isn't effective management for patients with DIC like syndrome due to sting by *H. lepturus*. Exchange transfusion is a procedure in which considerable amount of circulating blood is replaced by FFP & packed RBC's. We carried out this procedure for the first time in these patients and all of our patients had dramatic response and

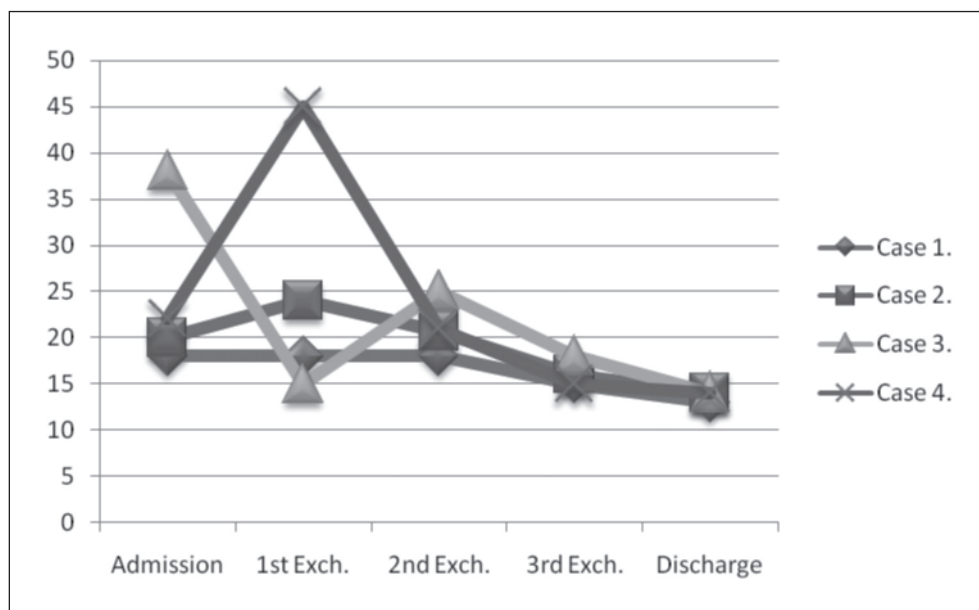


Figure 1. Changes in Prothrombine time (PT) during the hospital course in the 4 cases

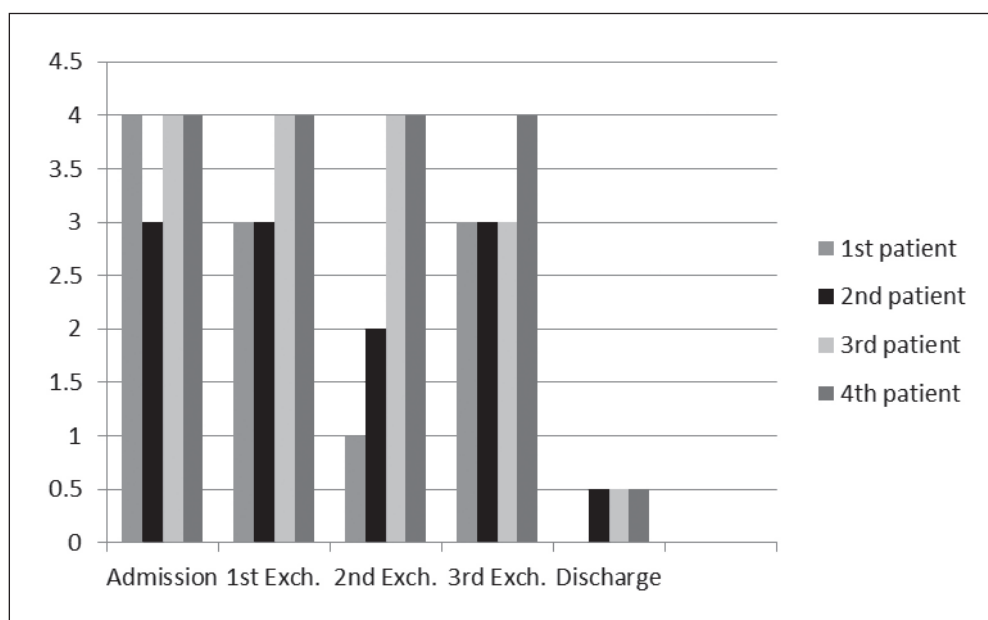


Figure 2. Comparison of level of hemoglobulinuria in 4 cases during the course of hospitalization

improved without any adverse events. Exchange transfusion is considered as an appropriate choice of treatment in different medical conditions. The well known of which is neonatal exchange transfusion following severe neonatal jaundice.

Besides this, there have been some reports in the literature introducing exchange transfusion as the mainstay of treatment in some serious conditions. In one report, a case of babesiosis presenting with significant pulmonary, renal and hepatic compromise

due to severe parasitemia (more than 10%) and release of cytokines was managed by lifesaving exchange transfusion (Jacoby *et al.*, 1980, Setty *et al.*, 2003; Soman *et al.*, 2003). Exchange transfusion also resulted in dramatic improvement as an adjunctive therapy in severe forms of *Plasmodium falciparum* malaria infection (Riddle *et al.*, 2002; Brownell *et al.*, 2011), by reducing parasitized red blood cells (RBCs) and removing cytokines (Powell & Grima, 2002). In previous study pulmonary edema, bilateral mydriasis, coma, leukocytosis & BUN increment were associated with high mortality (Bouaziz *et al.*, 2008). Our patients had some of these symptoms in addition to intravascular hemolysis & bleeding diathesis. In our experiment we encountered beneficial effects of PET in management of DIC like syndrome of scorpionism. All of our patients gradually improved clinically following PET and they all were discharged in a good general condition. In addition none of the patients develop other catastrophic conditions such as intracerebral hemorrhage & pulmonary or gastrointestinal bleedings improvement may be due to partial exchange transfusion by interruption of the pathophysiologic background of the DIC like syndrome. The effectiveness of PET in DIC like syndrome due to *H. lepturus* sting needs to be thoroughly investigated in blinded randomized controlled trials to provide proper evidences. Although our patients were discharged in good condition and the main complications of PET related to massive transfusion were prevented by supportive care, some late complications may develop several months later including hepatitis which was not evaluated in our study. Another limitation of our study is absence of coagulation factors measurement for discovering pathogenesis of this event that restrict proper management or prevention of this critical situation. Discovering possible new toxins or function which activate the coagulation factors and induce massive hemolysis will efficiently change the management of these patients.

Severe forms of *H. lepturus* sting syndrome presenting with hematuria and DIC like syndrome which didn't respond to

supportive care may respond well to PET which may be a life saving intervention and needs to be evaluated in randomized trials.

Acknowledgment. The authors thank Mr. Fazel Ghalabor and Mrs. Akram Taheri from Ahvaz Blood Transfusion Center for their cooperation in performing PET & Ahvaz Blood transfusion center for their support.

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