Gastrointestinal manifestations in severe scorpion envenomation

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SUMMARY

Objectives — To evaluate the type and incidence of gastrointestinal manifestations secondary to scorpion envenomation and their prognostic significance.

Patients and methods — All patients admitted to our ICU for scorpion envenomation were included in this retrospective chart review of a 13-year period (1990 – 2002).

Results — During the study period, 951 patients were admitted for scorpion envenomation and 72 (7.6%) died. Ages ranged from 0.5 to 90 years with a mean of 14.7 ± 17.4 years. Gastrointestinal symptoms were present in 700 patients (73.6%): nausea in 24 (2.5%), vomiting in 687 (72.2%) and diarrhea in 41 patients (4.3%). At univariate analysis, the presence of diarrhea was associated with a fatal outcome (P < 0.05). Diarrhea was also correlated with other indicators of severe envenomation and poor prognosis: respiratory failure (P = 0.01), neurological failure (P < 0.0001), liver failure (P < 0.0001) and low blood pressure requiring catecholamine support (P = 0.02). The multivariate analysis showed that young age (age less than 5 years), fever > 38.5 °C, neurological failure and pulmonary edema were independent factors of severity. Digestive disorders were more frequent in children and in this subgroup diarrhea appeared to be associated with poor outcome. In a subset of patients for whom data were available, fatal cases demonstrated significantly higher liver enzymes levels on admission.

Conclusion — In Tunisia, gastrointestinal symptoms are often observed in severe scorpion envenomations, especially in young patients. In children, diarrhea and elevated liver enzymes are associated with poor prognosis.

RÉSUMÉ

Manifestations gastro-intestinales secondaires à l’envenimation scorpionique

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Objectifs — Évaluer l’incidence, les caractéristiques cliniques et le pronostic des manifestations gastro-intestinales secondaires à l’envenimation scorpionique.


Résultats — Au total, 951 malades ont été admis pour envenimation scorpionique. L’âge moyen était de 14,7 ± 17,4 ans (0,5 à 90 ans). Des signes gastro-intestinaux ont été observés chez 700 malades (73,6 %) : nausées chez 24 malades (2,5 %), vomissements chez 687 malades (72,2 %) et des diarrhées chez 41 malades (4,3 %). La diarrhée était associée à un mauvais pronostic (P < 0,05) et significativement corrélée à la présence d’une détérioration respiratoire (P = 0,01), neurologique (P < 0,0001), hépatique (P < 0,0001) et l’utilisation de catécholamines (P = 0,02). En analyse multivariée, le jeune âge (âge < 5 ans), le coma, l’œdème pulmonaire, et la fièvre > 38,5 °C étaient des facteurs indépendants de sévérité. Les troubles digestifs étaient plus fréquents chez les sujets les plus jeunes. Dans ce sous-groupe, la diarrhée était un facteur de gravité. En outre le taux des transaminases était significativement plus élevé chez les malades dont l’évolution a été fatale.

Conclusion — Les manifestations gastro-intestinales sont souvent observées chez les malades piégés par scorpion, en particulier chez les sujets jeunes. Chez les enfants, la diarrhée et l’élévation des enzymes hépatiques représentent un facteur de gravité.

Introduction

Scorpion envenomation is common in tropical and subtropical regions. In Tunisia, almost 40,000-stung patients are recorded per year [1]. Around thousand of them have systemic manifestations requiring hospitalization and about 10 patients eventually die [1].

Cardiopulmonary manifestations, mainly cardiogenic shock and pulmonary edema, are the leading causes of death after scorpion envenomation [2, 3]. The severe forms of scorpion envenomation result usually from a sting from one of two species: Androctonus australus and Butus occitanus [1, 2]. However the dangerous form of scorpion envenomation (including heart failure) are more frequently observed with Androctonus australus species [1, 2].

Moreover, severe envenomation may be accompanied by gastrointestinal manifestations and metabolic acidosis [4]. The incidence of gastrointestinal manifestations following scorpion envenomation is variable according to the type of the scorpion and the age of the patient [5]. In fact these signs are relatively more frequent in children, than adult patients [6]. The aims of the present study were to determine the incidence, clinical manifestations, biological disturbances and the prognosis of gastrointestinal complications secondary to severe scorpion envenomation.

Patients and methods

Patients

We retrospectively included all patients admitted for scorpion envenomation over a period of thirteen years (1990 — 2002) to the intensive care unit (ICU) of Habib Bourguiba university hospital, Sfax, Tunisia. The diagnosis of scorpion envenomation was based on a history of scorpion sting.
Methods
The patients medical files were retrospectively reviewed, and the following data collected: age, gender, vital signs (heart rate, respiratory rate, systolic and diastolic blood pressure), body temperature in °C (Temp), Glasgow coma scale score (GCS), simplified acute physiology score (SAPS II) calculated within 24 hours after admission (for adults), Pediatric Risk of Mortality score calculated within 24 hours after admission (for children), use of mechanical ventilation, use of inotropic drugs, presence of shock defined as systolic blood pressure (SBP) less than 90 mmHg or decrease of SBP greater than 40 mmHg, cardiac arrest, fluid intake volume, and urinary output. Biochemical parameters measured on admission and during the ICU stay were arterial blood gases and acid base state, hemoglobin concentration, platelet counts, serum glucose and sodium levels, blood urea and values of plasma protein concentration, aspartate aminotransferase (ASAT), alanine aminotransferase (ALAT), direct and total bilirubin.

A medical committee of five physicians of our ICU examined retrospectively all the available data in order to classify patients according to the presence of pulmonary edema at admission. The diagnosis of pulmonary edema was based on the presence of clinical and radiological features of cardiogenic pulmonary edema and on the presence of arterial hypotension. The medical committee took particularly into account the presence of signs of respiratory distress (tachycardia, inspiratory retractions), the presence of intercostal spaces and the presence of lung crackles on auscultation of one or both lungs. In addition, the medical committee looked for signs of interstitial and/or alveolar pulmonary edema on the chest roentgenograms. In patients receiving mechanical ventilation, arterial hypotension was defined as a PaO2/FiO2 ratio < 300. The response to treatment of the clinical, radiological and gas exchange abnormalities was also taken into account for the diagnostic of pulmonary edema.

The gastrointestinal manifestations were searched at any time following scorpion envenomation such as the presence of nausea, vomiting, diarrhea, melena and hematemesis. For each patient we measured the duration of ICU stay and the mode of ICU discharge (at home or transfer to another medical unit). We stratified patients into two grades of severity at baseline, according to the presence or absence of systemic manifestations. Grade II included patients with systemic manifestations, grade III included patients with cardio-respiratory manifestations, mainly cardiogenic shock and pulmonary edema or severe neurological manifestations (coma and/or convulsion). This classification is currently recommended by the Tunisian health ministry and is used in clinical practice. In our institution, dobutamine was administered if pulmonary edema was suspected, since it was previously demonstrated that scorpion envenomation can result in pulmonary edema secondary to acute left ventricular failure [2] and that dobutamine was demonstrated to be efficient to improve cardiac function in this specific condition [1, 2].

Evidence of organ failure [7], such as neurological, cardiac, respiratory, hematological, renal, and liver failures were noted in each patient. Neurological failure was defined by a Glasgow coma scale score ≤ 6 (in the absence of sedation). Hepatic failure was defined as a total bilirubin level ≥ 51 μmol/L in the absence of hemolysis and/or a serum transaminase level higher than twice normal values and hepatic encephalopathy [7]. Finally, we tried to find a correlation between the presence of gastrointestinal manifestations and the outcome.

Statistics
The characteristics of patients in both groups with and without gastrointestinal manifestations were analyzed by the chi-square test. Continuous variables were expressed as mean (± SD) and subgroups evaluated by Student t-test. Risk factors were evaluated by univariate analysis and by multivariate analysis by a multiple logistic stepwise regression procedure. Odds ratios were estimated from the β coefficients obtained, with respective 95% confidence intervals (CI 95%). For comparable data a P value less than 0.05 was considered statistically significant.

Results
Nine hundred fifty one patients, admitted for a scorpion sting, were analyzed. There were 769 patients (80.8%) in the grade III group and 182 patients (19.2%) in the grade II group. Scorpion envenomation is more frequent during summer. Indeed 82.3% of our patients were admitted between June and September. The mean age was 14.7 ± 17.4 years, ranging from 0.5 to 90 years. Six hundred eighty five patients (72%) were less than 16 years old (figure 1). Fifty patients had a history of one or several diseases, mainly arterial hypertension observed in 22 patients (2.3%).

No local inflammatory signs were observed in any patients. Indeed, the Tunisian scorpions do not cause local toxicity. The mean systolic blood pressure (measured in 576 patients) was 96.5 ± 28.3 mm Hg. Five hundred eighty five patients (61.5%) had a pulmonary edema, while 195 patients (20.5%) presented cardiogenic shock.

Mean body temperature (in °C) (measured in 941 patients) was 37.8 ± 1.1 °C, ranging from 35 to 42 °C.

Seven hundred patients (73.6%) had gastrointestinal symptoms. Nausea was observed in 24 patients (2.5%), vomiting in 687 (72.2%), and diarrhea in 41 (4.3%). The mortality was significantly higher in patients presenting diarrhea. However, neither vomiting nor nausea was correlated with a poor outcome (table I).

There were a good correlation between the presence of diarrhea and the young age (P = 0.02). Indeed, 88% of patients with diarrhea were aged less than 15 years. Moreover, the presence of diarrhea was associated with the presence of respiratory failure (P = 0.01), neurological failure (P < 0.0001), liver failure (P < 0.0001) and the use of catecholamines (P = 0.02). Finally, the mean systolic blood pressure was significantly lower in the group without diarrhea (table II).

The multivariate analysis showed that neurological failure, body temperature > 38.5 °C, pulmonary edema and age less than 5 years were independent factors of poor prognosis but not the presence of diarrhea (table III). Diarrhea was more frequent in children (age ≤ 15 years) than in adults (5.2% vs. 1.9% respectively; P = 0.022). In children (N = 685), the presence of diarrhea was associated with poor prognosis (P = 0.02) (table IV). Serum ASAT, ALAT, and bilirubin levels were measured at admission in 166 patients. Mean levels of ASAT and ALAT were significantly higher in patients with fatal outcome (table V). In addition high values of total bilirubin were associated with a poor outcome (table V). Liver failure was observed in 17 patients (1.8%), and was correlated with a poor prognosis (mortality at 41.1% in the liver failure group vs. 7.4%, P < 0.0001).

Discussion
We have confirmed in the present retrospective study that the presence of diarrhea in young patients with severe scorpion envenomation was associated with a fatal outcome. This finding...
may have important implications in clinical practice, as it appears to identify the severely envenomated patients at higher risk of death. Indeed, the presence of diarrhea was correlated with young age, respiratory failure and neurological failure. To our knowledge, our study is the first human study establishing a correlation between a gastrointestinal manifestations and a poor outcome in scorpion envenomation patients.

Cardiopulmonary manifestations, mainly cardiogenic shock and pulmonary edema, are the leading causes of death after scorpion envenomation [2, 3]. In our study, the species of scorpion was not available in our file. However, a sample of 132 scorpions collected in the Sfax area (South Tunisia) has shown 70% of Androctonus australus, the 30% remaining were shared between Butus occitanus and Scorpio maurus. Androctonus australus is always seldom encountered. In some other samples coming from different regions of the Tunisia, it was regularly collected but constituted 1 or 2% of the samples [8]. Nevertheless, in our country the severe forms of scorpion envenomation requiring hospital admission usually result from a sting by one of two species: Androctonus australus and Butus occitanus [8]. Moreover, the most dangerous form of scorpion envenomation were more frequently observed with Androctonus australus species [8].

Scorpion envenomation may cause severe cardio-respiratory and neurological failure in human and animals [4]. The precise pathogenesis of scorpion envenomations is not completely understood and has been debated in the past. However, severe envenomation may be accompanied by gastrointestinal manifestations and metabolic acidosis even in the absence of hypoxia [4]. The incidence of gastrointestinal manifestation varies from 11% to 100% [5, 6, 9, 10] according to the type of the scorpion and age of the patients. These signs represent systemic manifestations indicating a severe form of scorpion envenomation. They are relatively more frequent in children than in adult patients [6]. In our study, almost 74% of our patients have experienced gastrointestinal manifestations on admission, but the frequency of diarrhea may have been underestimated due to the retrospective design of the study. In the univariate analysis, the presence of diarrhea was associated with a poor prognosis. In addition the presence of diarrhea was associated with previously identified factors associated with poor outcome: young age, respiratory failure and neurological failure. However, the multivariate analysis showed that neurological failure, body temperature > 38.5°C, pulmonary edema and age less than 5 years were independent factors of poor prognosis but not the presence of diarrhea. Digestive disorders were more frequent in children and in this age subgroup diarrhea was associated with poor outcome. The association with other severity factors suggests that diarrhea is not an independent factor but the presence of diarrhea may predict a dangerous form of scorpion envenomation with cardio-respiratory and/or neurological failure.

We believe that our results may have important implications particularly outside of hospital settings, since the presence of diarrhea may help to identify dangerous forms of scorpion...
envenomation and to decide the transfer of these patients to a reference center for scorpion envenomation.

The most observed clinical manifestations are vomiting [6], diarrhea, hypersalivation, gastric distension [11] and dysphagia [11]. Hematemesis and a melena are rarely observed [12]. More rarely, scorpion envenomation can lead to acute pancreatitis [13, 14]. In our study, pancreatic damage was not assessed. In fact the venom of Tunisian species of scorpion can provoke a muscularin synodrome with lachrymal, nasal, salivary secretion and diarrhea but not a pancreatic damage [8], previously described with Leiurus quinquestriatus [13] and Tityus serrulatus species [14] but not with Androctonus Australus and Butus Occitanus species. In our study, no patient manifested melena or hematemesis and gastric distention was not assessed. These clinical manifestations can be explained by two mechanisms. The first is the neurovegetative action of the venom that leads to a hypersalivation by stimulation of adrenergic and cholinergic salivary gland receptors [12, 15]. In fact, gastrointestinal manifestations are the consequence of a massive liberation of neurotransmitters by the neuromuscular junctions of the venom and do not constitute a secondary event after envenomation. Indeed in established that scorpion envenomation leads to a hypersecretion of acid and peptic [12, 16], and a modification of gastrointestinal peristalsis [12, 17]. This leads to emesis, nausea and diarrhea. On the other hand, gastrointestinal manifestations may be related to gastrointestinal ischemia. This hypothesis was suggested by clinical and experimental studies [4, 18-21]. In an experimental study, Sofer et al. [4] found that gastrointestinal manifestations were associated with a decrease in calculated mucosal pH, an increase in gastric mucosal PCO₂ and an increase in the gradient between mucosal PCO₂ and PaCO₂ and an increase in blood lactates concentration, 30 minutes after the injection of scorpion venom in pigs. The evidence of gut mucosal ischemia seen in the post envenomation period may explain these findings.

This gastrointestinal ischemia may result either from the effects of catecholamines (epinephrine and norepinephrine) on the gastrointestinal perfusion or of the vasoconstriction reflex in the splanchnic territory secondary to the shock [4]. In our study, the finding that the mean systolic blood pressure was significantly lower in patients with diarrhea than those without diarrhea is compatible with this hypothesis. In addition, diarrhea occurred in patients with other markers of cardiovascular failure as well as more pronounced evidence of liver injury (ASAT, ALAT, and total bilirubin), suggesting severe cases with shock leading to gastrointestinal ischemia as well as hypoxic liver injury.

On the other hand, while massive sympathoadrenal output associated with shock may explain some of these findings, a direct action of the venom or one of its components on gastrointestinal organs cannot be ruled out. Further studies are needed to understand the mechanisms of gastrointestinal pathology following scorpion envenomation.

In conclusion, this retrospective study of 951 patients showed that, in Tunisia, gastrointestinal symptoms are often observed in severe scorpion envenomations, especially in young patients. In children, diarrhea and/or elevated liver enzymes are associated with poor prognosis.

REFERENCES


| Table V. – Biological parameters on admission in both groups (Fatal outcome and survivors). |
|-----------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| **Parameters**                    | **Outcome**     | **Patients [N]** | **Mean value (±SD)** | **P**            |
|-----------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| ASAT (UI/L)                       | Survivors       | 149             | 60.2 ± 43.4     | < 0.001         |
|                                   | Fatal outcome   | 17              | 190.9 ± 274.2   |                 |
| ALAT (UI/L)                       | Survivors       | 149             | 33.2 ± 23.9     | < 0.001         |
|                                   | Fatal outcome   | 17              | 79.1 ± 89.3     |                 |
| Total Bilirubin (μmol/L)          | Survivors       | 108             | 13.6 ± 12.8     | < 0.05          |
|                                   | Fatal outcome   | 10              | 26.2 ± 36.3     |                 |
| Direct Bilirubin (μmol/L)         | Survivors       | 108             | 0.6 ± 3.0       | > 0.05          |
|                                   | Fatal outcome   | 10              | 2.6 ± 6.9       |                 |