ANTIVENIN THERAPY OF SPIDER BITE ENVENOMATION

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ABSTRACT:
Spider bites are major public health problem in many tropical countries. In many countries antivenom therapy is not fully developed. The purpose of this study is to examine the features of envenomation and treatment protocol provided to individuals having spider bites. The antivenom therapy and its effectiveness in the relief of symptoms were observed in patients admitted to King Fahad Hospital, Al-Baha, during 1994-1999. Victims of spider bite exhibits signs and symptoms included swelling and pain, necrosis, fever, pulmonary edema, respiratory distress hypertension and renal distress and death may occur due to cardio-pulmonary arrest. Treatment protocol was found very effective and it consists of symptomatic treatment in addition to antivenom of spider. Treatment was given according to severity of clinical manifestation and complications of envenomation. Clinicians should be aware of the clinical features of spider bite in order to treat other severe or minor cases. The results of our study have demonstrated the efficacy of antivenom in reducing circulating venom, symptoms and morbidity. It is hoped that the information contained within this article will be of help to medical practitioners dealing with spider bite. Antivenom therapy is more efficient when administered as earlier as possible after envenomation and with appropriate quantities of antivenom.

Keywords: Antivenom, antivenom therapy, spider bite, symptoms of spider bite.

INTRODUCTION
Spiders (black and brown) are common in the Al-Baha region of Saudi Arabia, but dangerous bites from them have not been well-documented. The mature black widow spider (Latrodectus mactans) has characteristics glossy black colour and hour-glass configuration on its ventral surface that distinguishes it from closely related species which are distributed throughout temperate and tropical latitudes (Bucur and Obasi, 1999). Black widow spiders (BWS) (Latrodectus sp.) are found worldwide. Envenomation in men usually occurs as the result of chance intrusion into the spider’s domain by the human (Rauber, 1984). These spiders are often found indoors in the corners of cupboards, under furniture and other dark, secluded places and in garden sheds. They are found world-wide and are endemic to most continents (Gunja, 2002). Brown spider venom is a colorless and crystalline liquid, and has a complex molecular composition with several different toxins. Through proteomic approaches, it was determined that the venom is composed of heterogeneous proteins varying in molecular mass, but with a predominance of toxins in the region of 3-40 kDa (daSilveira et al., 2002; Machado et al., 2005; deCastro et al., 2004). Accidents involving brown spiders (Loxosceles genus) have been associated with clinical manifestations characterized by dermonecrosis (Veiga et al., 2001) with gravitational spreading at and near the bite site, and to a lesser extent with systemic involvement (Ribeiro et al., 2007), such as acute renal failure, intravascular hemolysis, thrombocytopenia and disseminated intravascular coagulation. The spiders of the Loxosceles genus have a worldwide distribution, and accidents have been described on all continents (daSilva et al., 2004; Hogan et al., 2004; Swanson and Vetter, 2006).
Alpha-latrotoxin (α-ltx), a component of the venom of black widow-spiders (BWS), binds to higher vertebrates presynaptic nerve terminals, stimulating massive neurotransmitter release. This neurotoxic protein is responsible for most of the symptoms elicited in men by the bite of BWS, i.e. a neurological syndrome named latroderctism (Bugli et al., 2008). These spider bites can produce severe envenomation in humans. The only specific treatment is the early administration of antivenom (deRoodt, 2002).

In this study we are discussing the various treatment protocol provided to patients having spider bites (brown spider and BWS), admitted to Al-Baha hospital, Saudi Arabia.

METHODS

Patients who were hospitalized with the diagnosis of spider bite at the King Fahad hospital, Al-Baha, were included in this study. Their hospital records were analyzed.

RESULTS

Clinical symptoms of spider bite of 5 cases were given below:

Table 1
Symptoms of spider bite in few cases

<table>
<thead>
<tr>
<th>Case Title</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>Necrotic skin lesion, cellulites, bleeding, vomiting, fever, tachycardia, pulmonary edema</td>
</tr>
<tr>
<td>Case 2</td>
<td>Swelling, edema, burning sensation abdominal pain and rigidity, chest pain, renal distress</td>
</tr>
<tr>
<td>Case 3</td>
<td>Dermonecrosis, severe local and regional pain, fever, nausea, hypertension, headache, hemorrhages at the bite site</td>
</tr>
<tr>
<td>Case 4</td>
<td>Dermonecrosis, radiating pain and profuse sweating at the site of bite, cold and hot flushes, edema,</td>
</tr>
<tr>
<td>Case 5</td>
<td>Painful muscle spasm, hypertension, respiratory distress, abdominal cramping</td>
</tr>
</tbody>
</table>

DISCUSSION

The envenoming of the human caused by the spider is the major cause of serious clinical problems or death. It is one of the significant causes of mortality and morbidity in human all over the world. Appropriate treatment must be started as soon as possible after the bite because of rapid diffusion of toxin.

Patients were given IV furesemide, calcium gluconate, hydrocortisone, chlorpromazine and 40% oxygen by venture mask. 40% oxygen is administered because many patients were having short of breathing. These were symptomatic treatment but the effective therapy was the administration of spider antivenin (Antivenin, Latroderctus mantans, Merck Sharp Dome), which resulted in dramatic improvements of patient’s condition. In addition local xylocaine and IM injection of anti histamine, IV diazepam, pethidine and haloperidol were also administered. Bugli et al., in 2007 was reported the medical treatment for BWS bites, which include intravenous calcium for pain relief and muscle relaxation. The response to other muscle relaxants such as methocarbamol and diazepam is inconsistent. Acetaminophen and ibuprofen are used for pain relief in milder cases, though narcotic analgesics may be often necessary.

Among the several toxins described in the venom of spider, the dermonecrotic toxin is capable of stimulating dermonecrosis, hemolysis, platelet aggregation, renal disturbance, increase in vascular permeability, and dysregulated inflammatory response (daSilva et al., 2004; Chaim et al., 2006). Collagenase is said to be a major factor in the necrosis induced by bites of Loxosceles spiders. The black widow spider (Latroderctus mactans) introduces highly neurotoxic venom through its strong fangs. The venom targets mainly the presynaptic motor end plate, resulting in Ca$^{2+}$ influx and excessive release of noradrenaline and acetylcholine into synapses, causing severe muscle cramps, followed by fatigue of motor end plates and
muscle, rigors, sweating, vomiting, priapism, abdominal pain and rigidity, raised blood pressure and tachycardia (Ashton et al., 2001; Grasso et al., 1980). The neuro toxin of BWS is 120 kDa protein binds to two distinct receptors (latrophilin 1 and neurexin) (Lang et al., 1998; Lajus et al., 2006; Nicholson and Graudins, 2002), and can induce neurotransmitter release via both Ca^{2+}-dependent and -independent mechanisms.

Patient’s record showed that they have bitten by two types of spiders, black widow spider and brown spider. But the frequency of BWS bites was higher than brown ones. This reveals that BWS are more widespread as compare to brown spiders which are probably belonged to Loxosceles species. Most common clinical manifestations were radiating pain, tissue necrosis, abdominal cramps and rigidity, hot and cold flashes, pulmonary edema, tachycardia and transient rise in blood pressure. While abnormal finding were include leucocytosis, abnormal ECG and abnormal echocardiogram. One important thing is that lactrodectism must be differentiated with scorpion sting and acute abdominal emergencies.

Deaths after black widow spider bites were reported in 2001 and 2003 in Spain (Gonzalez et al., 2001) and Greece (Pneumatikos et al., 2003). The literature reveals regional disparities in the incidence and outcome of Latrodectus spider's bites, perhaps reflecting (differences in toxicity and behavior among endemic Latrodectus spp. Envenomation by Loxosceles spiders causes two main clinical manifestations: cutaneous and systemic loxoscelism (deOliveira et al., 2005). Several cytotoxic activities triggered by brown spider venom seem to be dependent on dermonecrotic toxins. The toxin has a hemolytic effect against erythrocytes (Futrell, 1992).

The difference in the severity of clinical manifestations in patients, may be related to a difference in volume or potency of venoms introduced at each bite. Cardiac manifestations are major causes, of morbidity and mortality in scorpion sting envenomation (Handel et al., 1994; Kumar et al., 1992; Soomro et al., 1998), are less commonly reported in spider bite envenomation especially with black widow spider bite (Gueron et al., 2000), may be related to a difference in the potency of their venoms (Yaron et al., 1974). Karcioğlu et al. (2001) reported the case of 59-years man with acute oliguric renal failure due to a combination of pre-renal and renal causes after being bitten by a black Latrodectus spider. However, the patient recovered within a week (Karcioğlu et al., 2001).

Fig. 1. Black widow spider with large abdomen and short reddish broad line.

All bites should be thoroughly cleansed and tetanus status updated as needed. Patients who develop systemic symptoms require hospitalization. Surgical excision of skin lesions is indicated only for lesions that have stabilized and are no longer enlarging. If latrodectism is considered to be the underlying origin for these symptoms, appropriate treatment should be administered. In cases of pregnancy, treatment should include L. mactans antivenin if believed to be clinically indicated. There is no current evidence that this antivenin is contraindicated in pregnancy (Sherman et al., 2000).

In this investigation patients were bitten by brown spider as well. Clinical symptoms of brown spider bites were resembled to those who had bitten by black widow spider. Figure 3 is a brown spider which is commonly found
Care must be provided because antivenin has its own effect, so anti-venin is suggested in life threatening cases or with severe systemic manifestation. But the effect produced by antivenin was striking even after a day of bite. The most common adverse reaction associated with antivenin administration is “serum sickness”, a type III hypersensitivity reaction that results from the injection of foreign proteins. Serum sickness develops within 2 weeks after serum injection and is caused by the deposition of immune complexes at certain tissue sites (Suntomtham et al., 1994). In the United States, the antivenin is given intravenously, is usually reserved for very severe cases, and the rate of allergic reaction is high (from 9% up to 80% in those skin testing positive). Deaths have been recorded after antivenin (Jelinek, 1997). The adverse effects encountered when using antivenoms are primarily allergic in nature. Anaphylaxis, which may be life threatening, is a major concern. Preparations to treat anaphylaxis must be made before initiating anti venom therapy (Heard et al., 1999). In the US, approximately 2500 BWS bites were reported to the American Association of Poison Control Centres (AAPCC) in 2001; in Australia about 250 cases per year require antivenom administration, with a majority of unreported cases not requiring hospitalization (Bugli et
Ahmed and Bushra (2008). In England, an adult female, bitten on the shoulder by a female Steatoda nobilis, developed intense radiating pain and local sweating at the bite site with gradual diminution of symptoms without specific therapy (Warrell et al., 1991).

CONCLUSION

The black widow spider and brown spider venoms contain most potent biological neurotoxin activities, which cause a local and acute inflammatory reaction that may evolve to dermonecrosis (a hallmark of envenomation) and hemorrhages at the bite site, besides systemic manifestations which may lead even to death. The apparent rarity of reported cases may be due to lack of awareness of above mentioned signs and symptoms as compared to scorpion stings, which are very well known in this region. We strongly recommend very early administration of antivenin in the medical management of spider envenomation. The advance in supportive care and anti venom efficacy has markedly improved the outcome of patients with spider envenomation.

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REFERENCES


