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Clinical consequences of centipede bite: Is it neurotoxic?

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Abstract

The primary purpose of this article was to review the current literature regarding the clinical consequences of

centipede envenomation in humans, in order to determine whether the bite of these arthropods is neurotoxic to humans or not. A thorough search of the literature regarding the clinical consequences of centipede bites in humans was applied, with great respect to neurological symptoms potentially caused by such bites. Centipede bite commonly causes only local reactions, which usually resolve within a few days without sequelae. The patients in the majority of centipede envenomations describe a painful but benign syndrome. However, mild constitutional symptoms are relatively frequent. Remarkably, centipedes can rarely cause severe systematic reactions such as anaphylaxis or even hypotension and myocardial ischemia. Factors such as patient age, comorbidity, anatomic site of envenomation, and size/species of centipede should be considered when evaluating a centipede envenomation victim. According to the current literature, the centipede bite does not seem to be neurotoxic to humans. However, it commonly causes symptoms mediated by the nervous system. These include local and generalized symptoms, with the first dominated by sensory disturbances and the second by non-specific symptoms such as headache, anxiety and presyncope. Based on our results, the answer to our study's question is negative. The centipede bite is not neurotoxic to humans. However, it commonly causes symptoms mediated by the nervous system, which include primarily local pain and sensory disturbances, as well as generalized non-specific symptoms such as headache, anxiety and vagotonia.

Key words: Centipedes; Pain; Sensory disturbances; Envenomation; Scolopendra

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Core tip: Centipede bite commonly causes only local reactions, which usually resolve within a few days without sequelae. The patients in the majority of cases describe a painful but benign syndrome. Mild constitutional symptoms are relatively frequent, whereas severe systematic reactions, such as anaphylaxis, hypotension and even myocardial ischemia, are rare. According to the current literature, the

centipede bite does not seem to be neurotoxic to humans. However, it commonly causes symptoms mediated by the nervous system. These include local and generalized symptoms, with the first dominated by sensory disturbances and the second by non-specific symptoms such as headache, anxiety and vagotonia.

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INTRODUCTION

Centipedes

Taxonomy: Centipedes are invertebrate animals belonging to phylum Arthropoda, class Chilopoda and subphylum Myriapoda^[1,2]. Although over 8000 species are estimated to exist worldwide, only 3000 have been described, in habitats varying from deserts to the Arctic^[3]. There are four major orders (all venomous) of centipedes: Geophilomorpha (innocuous soil dwellers, small), Scolopendramorpha (giant or tropical centipede-known stingers), Scutigeraomorpha (fast but delicate house centipedes) and Lithobiomorpha (garden or rock centipedes-resemble small scolopendramorpha in appearance with many anecdotal reports of stings)^[2].

Morphology: Centipedes are distinguishable from insects by their many (from less than 20 to more than 300) legs (at least nine pairs) and by their largely uniform bodies (not divided into head, thorax and abdomen)^[4]. They are slender, multisegmented arthropods characterized by one pair of legs on each body trunk segment^[1,2] and one pair of antennae. Their coloration may range from bright yellow to brown-black (Figure 1). They have two sharp stinging structures connected to muscular venom glands and these structures constitute actually the modified first pair of centipede legs^[2]. These venomous fangs, their key characteristic, are their hunting and defensive equipment^[1].

Centipedes range in length between 0.05-30 cm^[2,4] and the common centipede is usually 2-3 cm long^[4]. The *Scolopendra* are the largest centipedes, probably the most venomous and therefore the most dangerous. They range between 8-15 cm in length (Figure 1), and *Scolopendra heros* (*S. heros*) can achieve lengths of more than 20 cm^[2]. Giant centipedes are found in a few places including Africa (*Scolopendra spp.*)^[4], New Guinea (*Scolopendra morsitans* and *subspinipes*)^[5] and Philippine Islands (*Scolopendra subspinipes*)^[6]. *Scolopendra* usually have a yellow-brown body with orange and blue cephalic/caudal parts^[2] (Figures 1 and 2).

Habitation: Centipedes have a worldwide distribution and are well represented in Europe and Africa^[2,4]. They are found

in wild habitats, warm temperate and tropical climates, but also in gardens^[2,4]. They are found mainly in soil (Figure 2) and litter and prefer dark damp environments, such as below rocks and logs^[1,2,7]. Common centipede hides by day in crevices, such as under loose bark, leaves or stones^[4]. Centipedes can sometimes be found inside sheds or even enter houses, especially in wet weather (rainy days)^[2,4], thus constituting common household arthropods^[8].

Centipedes are nocturnal carnivores with a wide range of prey^[2,4,7]. Centipedes emerge at night to hunt primarily for insect larvae (crickets, cockroaches) and occasionally for slugs, worms, small snakes and even small mammals, catching them using their powerful venomous fangs^[2,4]. These fast-moving arthropods use their venom to paralyze prey prior to eating^[2]. Ants and termites are, among other animals, their natural predator^[7].

Purpose of the study

The purpose of this article is to review the current literature regarding the clinical consequences of centipede envenomation in humans, searching for neurological symptoms that could be potentially caused by centipede bites. Thus, with this review, we aimed to determine whether the bite of these arthropods is neurotoxic to humans or not. As "neurotoxins" we considered all venom components affecting the nervous system, not only those causing serious and lethal consequences (e.g., paralyzing agents) but also those having a milder and temporal effect (e.g., pain-inducing agents).

RESEARCH

A careful and thorough search of the English language literature, regarding all the clinical consequences of centipede bites in humans, was applied with great respect to neurological symptoms potentially caused by such bites. For a comprehensive review of existing data Pubmed was searched using the following terms: "centipede bite" and "symptoms". The available data are restricted and most relevant information is provided by articles reporting cases of centipede envenomation in humans and its management.

CENTIPEDE ENVENOMATION

Epidemiology

Centipedes may display aggressive behavior^[2]. Although their bites are not rare, few studies have evaluated the effects of centipede venom in humans and the literature over this issue is limited^[2]. The lack of basic knowledge on venomous arthropods and the usually benign clinical course contribute to the frequent care of centipede bite victims at home (instead of a treatment reference center), leading to underestimation of the number of cases^[9].

In a remarkable number of cases (63%) who seek medical care, victims bring the agent in for identification. The genera most frequently reported to bite humans

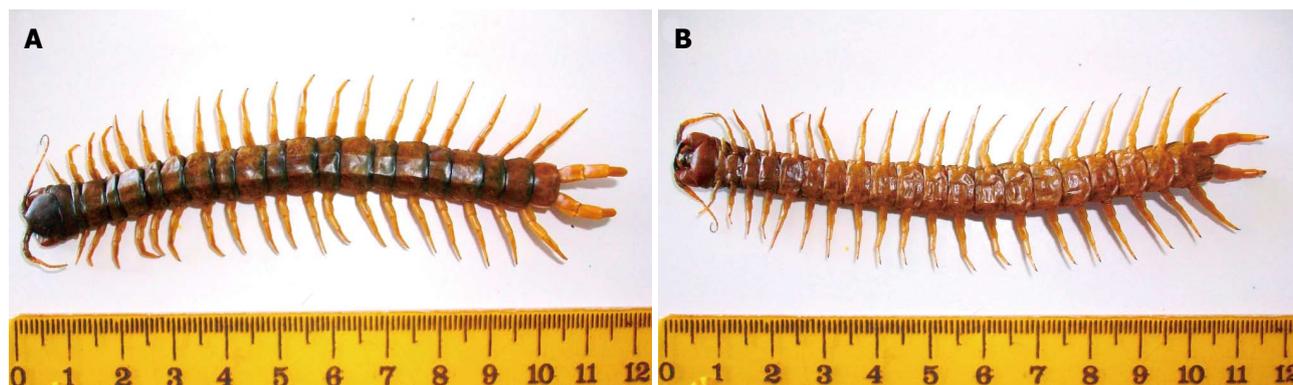


Figure 1 *Scolopendra singulata* is the most common scolopendromorph centipede species in the Mediterranean area. A: Superior surface; B: Inferior surface. Photograph by Ioannis N Mavridis, PhD.

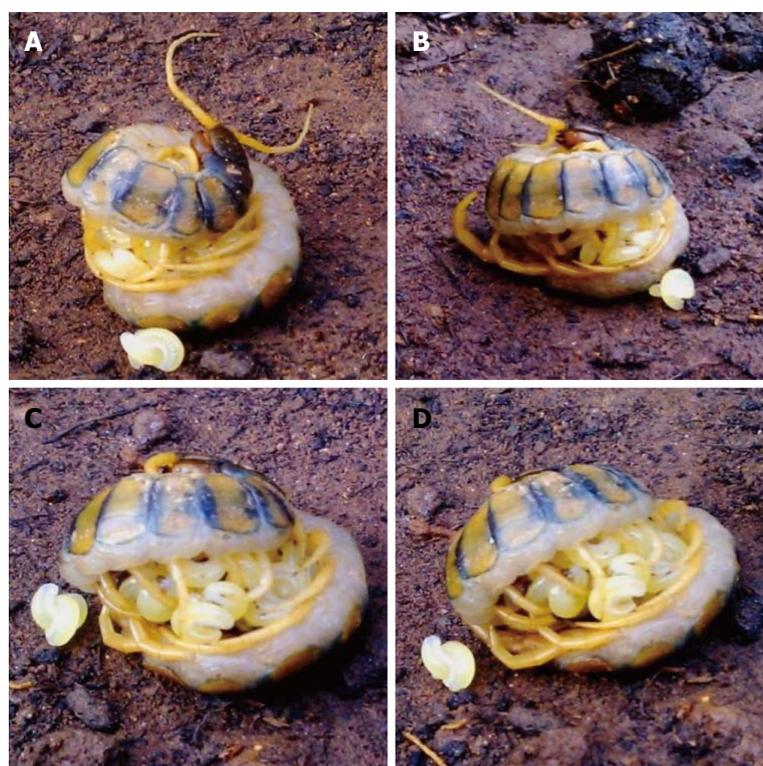


Figure 2 Female *Scolopendra singulata* wrapping around her babies to keep them safe in warm and wet environment (Mediterranean area). A-D: Different views. Photograph by Ioannis N Mavridis, PhD.

include *Cryptops* (58%), *Otostigmus* (33%) and *Scolopendra* (4%)^[9]. There is a predominance of accidents in the warm rainy season [reproductive period of the centipede (Figure 2), associated with their sinanthropic habits], in the morning hours and also among females^[9] and ages between 20-60 years^[9,10]. Centipede bites often occur as the victim is dressing or while in bed^[2]. Upper and lower extremities are the parts of the body most commonly affected^[9].

Centipede bite

A centipede bite is an injury resulting from the action of centipede's forcipules, pincer-like appendages that pierce the skin and inject venom into the wound, which is not actually a bite, as the forcipules are modified legs rather than true mouthparts^[11]. Despite some reports of tenacious attachments requiring removal with a noxious

agent (e.g., alcohol) or even surgery, centipedes tend to release from the skin immediately^[2].

Centipede venom

The complete mechanism of centipede venom toxicity is not yet completely understood^[12] and this venom, as well as the venom apparatus of centipedes, remains largely unexplored^[13,14]. It contains several different enzymes, but is different to most other arthropods in that metalloproteases appear to be important. Cardiotoxic, myotoxic and neurotoxic activities have been described, with the latter being unusual in the fact of involvement of G-protein coupled receptors, directly as neurotoxin-targets or indirectly by activation of endogenous agonists^[14]. Noteworthy, the contents of approximately 1000 venom glands are required for a fatal sting in an average adult^[2].

More specifically, the venom from *Scolopendra* species

is a lipid-toxin complex, similar to that of scorpion, which facilitates local cellular penetration and absorption^[2]. Its compounds include 5-hydroxytryptamine (serotonin), histamine and cardiodepressant Toxin-S, mediating significant cardiovascular effects, a smooth muscle contractile agent with muscarinic activity, proteinases and lipoproteins^[2,12]. *S. heros* contains also a cytolytic potentiating both its local and systemic effects.

The Chinese red-headed centipede (*Scolopendra subspinipes mutilans*) is a venomous centipede found in East Asia and Australasia^[15] and its venom contains 26 neurotoxin-like peptides^[13]. Several of these neurotoxins contain potential insecticidal abilities, and they act on voltage-gated Na⁺, K⁺, and Ca²⁺ channels^[13]. Among them, neurotoxin SsmTx-I blocks voltage-gated K⁺ channels in dorsal root ganglion neurons, but has no effect on voltage-gated Na⁺ channels^[15]. Moreover peptide μ -SLPTX-Ssm6a inhibits voltage-gated Na⁺ channels and is more potent analgesic than morphine in rodents^[16]. Finally, toxin RhTx induces pain and targets the heat activation machinery (potently activates the capsaicin receptor TRPV1) to produce excruciating pain^[17].

COMMON CLINICAL FINDINGS

Local

Centipede bite commonly causes only local reactions^[8], which usually resolve within a few days without sequelae (excluding local skin necrosis)^[2]. Skin reactions at the bite site are the commonest symptom after a centipede attack on humans^[18]. Clinically, the wound is viewed as a cutaneous lesion characterized by two hemorrhagic marks forming a chevron shape caused by the large paired forcipules of the centipede^[11]. Local reactions include intense worsening local pain^[2,4,9,10,18-23] of sudden onset or even lingering "dull" pain at the sting site^[2], edema^[2,4,9,10,18,21-24] (severe edema is mostly observed in cases of bites by *Otostigmus spp.*^[19]), erythema^[2,9,18,19,21-24], transient hemorrhagic oozing from the puncture site^[9,25], itchiness^[22], burning sensation^[9,25], induration^[2], numbness and tingling, extraordinary tenderness (on physical examination), throbbing^[2,25] and paresthesias^[20,25], lymphangitis/lymphadenitis, local infection^[25] or necrosis^[2,25] and development of a red streak at the skin^[2]. Hemorrhagic vesicles and blisters formation is described less often^[12,18,26,27]. Limited range of motion or even weakness, reduction of flexibility and severe "sprained" sensation at the affected limb have been also reported^[2].

Severe skin reactions are rare^[28]. Abscess formation^[20] and late development (within days or even weeks) of local necrotic area or recurrence of swelling with intense local itching (pruritus) may occur at the site of envenomation^[2]. Cases of severe local toxicity and bacterial infection (usually from Gram positive cocci) have been also described^[28]. Some cases even lead to cellulitis and necrotic fasciitis of the bite region^[28], usually a limb that if left untreated could lead to amputation.

Generalized

Common effects of centipede bites may include mild

constitutional symptoms which usually resolve without sequelae^[2]. These include headache^[9,12], anxiety, (low) fever, dizziness, chest discomfort or pain, near syncope, palpitations, nausea, vomiting, general feeling of unwellness, flushing, writhing, sharp pain at various body areas and restlessness secondary to the pain^[2,12]. Constitutional upset occurs in a small minority^[25].

UNCOMMON AND RARE CLINICAL FINDINGS

It is known that centipedes, among other insects, can cause not only local but also systematic clinical effects such as anaphylaxis or even hypotension and myocardial ischemia (from vasospasm and myocardial toxic effects of the venom)^[29]. The toxins released with envenomation cause vagal activity which could result in circulatory symptoms. Histamine and Toxin S are considered as mediators for myocardial injury^[30]. Cases of acute myocardial ischemia have been described following a centipede bite, either as presenting manifestation^[25] or following local symptoms^[29,31].

Furthermore, sensitivity reactions are not uncommon, although late hypersensitivity reaction is described less often^[12]. Immediate type allergic reaction against centipede venom has been reported, with dyspnea, general fatigue and urticaria and positive prick test. Some relationship between centipede allergy and bee allergy has been supported^[32]. An immune complex deposition syndrome (type III hypersensitivity reaction) manifesting as recurrence of swelling associated with pruritus at the sting sites, has been further suggested^[2].

Proteinuria, usually in the context of nephritic syndrome^[33], as well as extensive myonecrosis with subsequent compartment syndrome, rhabdomyolysis and acute renal failure may rarely occur due to centipede bite^[2,34].

Other very rare clinical consequences following centipede bite include psychological disturbances and Korsakoff syndrome (Japanese *Scolopendra* species)^[2], Wells' syndrome (eosinophilic cellulitis)^[35] and pericoronitis^[36]. The patient may rarely feel fine (almost "euphoric") a few hours after the bite^[2]. Irritability and uncontrollable cry (beside local symptoms) have been reported in neonates^[37] and systemic side effects (due to systemic absorption of the venom) in infants, requiring, though, no active intervention^[8]. Remarkably, a fatality has been reported following a sting by a large specimen of *S. subspinipes* to the head of a small Filipino child^[2]. Finally, there is also a report of postmortem injury (subcutaneous cavity on the victim's forearm) caused by a centipede^[38].

DIFFERENTIAL DIAGNOSIS

Differential diagnosis from snake (especially viper) bites is essential in regard to treatment strategy. The length of the biting animal (2-30 cm for centipedes), the bite mark characteristics (pointed in shape for centipedes), the presence of hemorrhagic vesicles, the progression of

Table 1 The commonest neurological symptoms caused by centipede bite in humans

Local
Pain (sharp, dull)
Paresthesias (numbness, tingling, burning sensation)
Weakness
Generalized
Headache
Anxiety
Presyncope (vago-tonia)
Sharp pain at various body areas
Flushing

local reactions (usually remaining localized to a 10 cm × 10 cm area of involvement), as well as the wound size, are useful in the differentiation between centipede and viper bites in clinical practice^[39].

PROGNOSIS

The majority of centipede envenomation victims describe a painful but benign syndrome^[2]. The clinical course following most centipede stings appears self-limited (resolving within hours to few days^[2,10]) and rarely associated with any serious consequences^[2]. Even though prognosis of centipede bites is usually benign, presence of underlying disease could complicate the course of therapy^[40]. For example, underlying diabetes mellitus could complicate the course of the disease with more severe skin reactions and infections^[12]. In the interesting case described by Rouvin *et al.*^[40], the patient, an heterozygous for sickle cell disease female, suffered a prolonged and severe course of disease after a centipede sting.

PRINCIPLES OF TREATMENT

Despite the striking appearance of the offender and the significant pain associated with its sting^[2], the benign evolution of the clinical picture makes often therapeutic treatment unnecessary^[9]. Supportive treatment is usually enough for the symptoms of centipede bite victims to resolve within hours to few days and without any sequelae^[2,10]. This includes pain control, wound care and tetanus immunization^[2]. Pain-relief is the cornerstone of treatment^[25] and analgesics (such as paracetamol) are usually administered^[18]. Additionally, local anesthetics, systemic (such as prednisone^[18]) and/or topical corticosteroids, antihistamines and administration of a biscodaurin alkaloid may be considered, as needed according to the severity of the lesions^[9,24]. Factors such as patient age and comorbid conditions, anatomic site of envenomation, and size/species of centipede should be considered when evaluating a patient with a centipede envenomation^[2]. Noteworthy, therapeutic treatment is a rule for the victims of *Scolopendra* and *Otostigmus*^[9].

NEUROLOGICAL SYMPTOMS

Although the centipedes' venom contains neurotrans-

mitters (serotonin, histamine) and agents affecting the autonomic nervous system (smooth muscle contractile agent with muscarinic activity)^[2,12], its clinical effects are not primarily of neurological nature. Despite this observation there are some common symptoms mediated by the nervous system. Local neurological symptoms are mainly sensory disturbances and include acute pain^[2,4,9,10,18,19-23], lingering "dull" pain^[2], paresthesias^[20,25] such as burning sensation^[9,25], numbness and tingling (with extraordinary tenderness on clinical examination)^[2,25], and severe "sprained" sensation at the affected limb^[2]. Weakness has been reported but it seems to be probably due to the reduction of flexibility and limited range of motion of the affected limb^[2]. Generalized neurological symptoms include headache^[9,12], anxiety, dizziness and presyncope (vago-tonia^[30]), flushing, sharp pain at various body areas and restlessness secondary to the pain^[2,12]. Unusual neuropsychiatric symptoms may also occur in centipede bite victims and include nearly "euphoric" feeling (a few hours following the bite), psychological disturbances and Korsakoff syndrome^[2]. Table 1 summarizes the commonest neurological symptoms caused by centipede bite in humans.

So, is the centipede bite neurotoxic?

Given that, to the best of our knowledge, the centipede venom does not cause damage to nervous tissue and that the above-mentioned neurological symptoms are transient, the answer to our study's question is negative. The centipede bite is not neurotoxic to humans. However, it commonly causes symptoms mediated by the nervous system. These include local and generalized, with the first dominated by sensory disturbances and the second by non-specific symptoms such as headache, anxiety and presyncope. In rare cases, severe neuropsychiatric conditions such as Korsakoff syndrome can be observed.

CONCLUSION

Centipede bite commonly causes only local reactions, which usually resolve within a few days without sequelae. The patients in the majority of centipede envenomation cases describe a painful but benign syndrome. However, mild constitutional symptoms are relatively frequent and severe systematic clinical effects such as anaphylaxis and myocardial ischemia may rarely be observed. Factors such as patient age and comorbid conditions, anatomic site of envenomation, and size/species of centipede should always be considered when evaluating a patient with a centipede envenomation. According to the current literature, the centipede bite does not seem to be neurotoxic to humans. However, it commonly causes symptoms mediated by the nervous system. These include primarily local pain and sensory disturbances, as well as generalized non-specific symptoms such as headache, anxiety and vago-tonia.

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