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Complex Regional Pain Syndrome Caused By Snake Bite: A Case Report

Yılan Sokmasına Bağlı Kompleks Bölgesel Ağrı Sendromu: Bir Olgu Sunumu

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Summary

Complex regional pain syndrome (CRPS) is a painful and disabling disorder that can affect one or more extremities. The pathophysiology of CRPS is not clear but peripheral and central sensitization resulting in neurogenic inflammation has been held responsible. A 66- year-old male patient was admitted to our outpatient clinic with complaints of swelling, pain, warmth, and restriction in movements of the left upper extremity after a snake bite. Electromyographic evaluation was compatible with toxic neuropathy. A hand X-ray showed demineralization of the carpal bones. CRPS was diagnosed based on clinical and radiological findings. Medical and physical therapy were performed and symptomatic relief was obtained. This case is presented to emphasize snake bite as a rare cause of toxic neuropathy and CRPS. *Turk J Phys Med Rehab 2012;58:69-71.*

Key Words: Snake bite, envenomation, neuropathy, pain syndromes

Özet

Kompleks bölgesel ağrı sendromu (KBAS), bir veya birden çok ekstremiteyi etkileyebilen, ağrılı ve kısıtlayıcı bir tablodur. Patofizyolojisi aydınlatılamamıştır ancak nörojenik inflamasyon ile sonuçlanan periferik ve santral sensitizasyon sorumlu tutulmaktadır. Altmışaltı yaşında erkek hasta polikliniğimize yılan sokması sonrası sol kolda gelişen şişlik, ağrı, ısı artışı ve hareket kısıtlılığı ile başvurdu. Elektromyografik inceleme toksik nöropati ile uyumluydu. El grafisinde karpal kemiklerde demineralizasyon saptandı. Klinik ve radyolojik bulgularla KBAS tanısı kondu. Medikal ve fizik tedavi uygulandı ve semptomatik iyileşme sağlandı. Bu olgu, yılan sokması sonrasında nadir de olsa toksik nöropati ve KBAS gelişebileceğini vurgulamak amacıyla sunulmuştur. *Türk Fiz Tıp Rehab Derg 2012;58:69-71.*

Anahtar Kelimeler: Yılan sokması, zehirlenme, nöropati, ağrı sendromları

Introduction

Snake bite is an important health problem, especially in rural and farming areas. The principal effects of envenomation with snake toxins are related to neurotoxicity, nephrotoxicity, myotoxicity, cardiotoxicity, coagulopathy, vascular endothelial damage and local reactions (1,2). It is known that snake neurotoxin can affect the neuromuscular system in different ways. It has been demonstrated by various electrophysiologic studies that snake neurotoxins can result in impairment of presynaptic and postsynaptic neuromuscular conduction (1-3).

Complex regional pain syndrome (CRPS) is a painful and disabling disorder that can affect one or more extremities. Usually, its onset is precipitated by a physical injury, for example, a fracture, sprain, or surgery. Sometimes no particular cause can be found, therefore, it is defined as idiopathic (4).

An upregulation of peripheral axonal adrenoreceptors, an increased sensitivity to catecholamines due to sympathetic denervation, and release of neuropeptides resulting in neurogenic inflammation have been proposed as pathogenetic mechanisms (5,6).

A prototypic presentation of a patient with CRPS includes persistent "burning" dysesthetic pain in a limb with a region of

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intense allodynia, hyperalgesia, extreme guarding of the affected limb, diminished strength and range of motion (ROM), and objective evidence of local autonomic dysregulation and trophic changes in the skin, hair, and nail (5). The diagnosis is based on observation and measurement of clinical symptoms and signs. Modified International Association for the Study of Pain (IASP) diagnostic criteria can be used for the clinical diagnosis (7,8). Differentiated by the presence of a demonstrated nerve lesion, CRPS can be classified into type I and type II, of which type I, without a nerve lesion, is the most common (4).

Routine laboratory tests are unchanged in CRPS. Plain radiography demonstrates visible demineralization with patchy, subchondral or sub-periosteal osteoporosis, metaphyseal banding and profound bone loss. Bone scanning in early CRPS reveals increased uptake and may return to normal later. MRI is not diagnostic, but can be helpful to exclude other pathologies and in CRPS may demonstrate early bone and soft tissue edema, joint effusions and late atrophy with fibrosis (5).

A patient with a history of snake bite, who developed CRPS, has been described to emphasize the neurological manifestations following envenomation and to alert the physicians of the rare possibility of its progression into CRPS and the importance of a correct diagnosis in the planning and instruction of treatment strategies.

Case Description

A 66-year-old male patient presented to the outpatient clinic of Physical Medicine and Rehabilitation Department with pain, swelling, and limitation of movement in the left hand. The patient was bitten by a snake through the thumb of the left hand while cutting wood four months ago. Following the bite, the upper left extremity began to swell and was painful. The patient received treatment in an emergency unit but antisnake venom was not given and the offending snake was not identified. He attended to our hospital when desquamation in the skin and limitation of movement in the extremity became obvious. The patient had a medical history of diabetes mellitus and hypertension. Physical examination revealed mild edema, warmth, skin color change and sweating in the left hand. Contractures were present in the dorsiflexion (10 degrees) and palmar flexion (40 degrees) of the left wrist, and metacarpofalangeal and distal interfalangeal flexion (45 degrees) of the fingers of the left hand. Neurologic examination revealed hypoesthesia and hypoalgesia in the forearm and decrease in muscle strength of dorsiflexion of the wrist and flexion of the fingers. Deep tendon reflexes were normal. Laboratory tests were normative except an increase in C-reactive protein (CRP) which was found to be 14.1 mg/L. X-rays of the hands demonstrated patchy osteoporosis which was a sign of demineralization (Figure 1). The diagnosis of CRPS was made according to the modified criteria of IASP. An electromyography (EMG) was performed and prominent neurogenic motor unit potential changes were observed which indicated a toxic neuropathy involving the motor and sensory branches of the radial, median, and ulnar nerves. Neuropathic pain was verified in the patient according to the Leeds assessment of neuropathic symptoms and signs (LANSS pain scale) (9). Pregabalin was prescribed with a daily dose of 300 mg. Steroid therapy was not started because the patient was diabetic. Physical modalities including contrast baths, transcutaneous electrical nerve stimulation (TENS) , and ultrasound (US) were applied daily for 20 days along with active-assisted ROM and stretching exercises. The patient's complaints decreased at the end of his hospital stay, but no significant improvement was achieved in his joint ROMs and the finding of demineralization in the X-rays persisted.

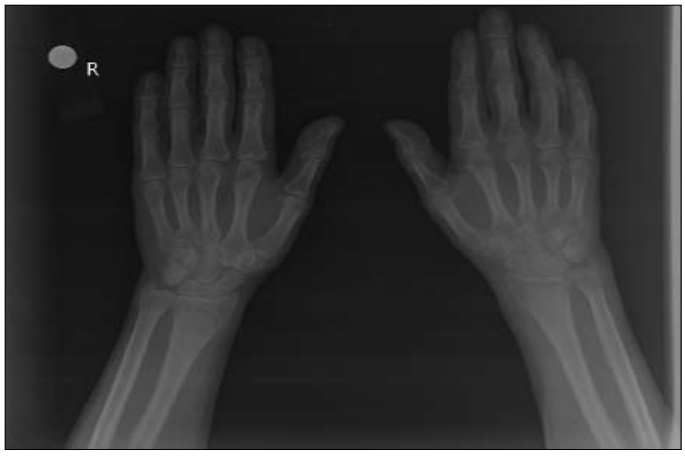

Figure 1. Patchy osteoporosis in the left hand of the patient.

Discussion

Snake venoms consist of pharmacologically active components including enzymes, such as acetylcholinesterases, L-amino acid oxidases, serine proteinases, metalloproteinases, and phospholipases, and nonenzymatic proteins used for immobilization and digestion of prey. Snake envenomation can cause tissue necrosis locally and hemostatic disturbances, shock, myocardial damage, rhabdomyolysis, paralysis, and acute renal failure systemically (10). Snake venom poisoning is considered among disorders of the neuromuscular junction, such as myasthenia gravis (11). Snake venoms cause muscle weakness by binding to the neuromuscular junction both pre- and post-synaptically. Seneviratne et al. (2) have demonstrated that in a group of 56 patients, who developed neurologic signs after snake bite, ptosis was seen in 85.7%, ophthalmoplegia in 75%, limb weakness in 26%, respiratory failure in 17.9%, palatal weakness in 10.7%, neck muscle weakness in 7.1%, and peripheral neuropathy in 1.8%. Studies on patients with snake envenomation have revealed a decrease in compound muscle action potential (CMAP) amplitudes and presynaptic blockage (11,3). Singh et al. (3), based on electrophysiological assessment in patients with Bungarus caeruleus bite, postulated that both presynaptic and postsynaptic blockade at neuromuscular junction are responsible for the neuromuscular manifestations. The EMG in our patient revealed a decrease in CMAP amplitudes and electrophysiological changes compatible with toxic neuropathy of the median and ulnar nerves.

Snake venom phospholipases A2 (PLA2) show myotoxic activity and also evoke inflammatory and nociceptive responses (12). Subcutaneous injection of PLA2s isolated from Bothrops asper venom was shown to induce hyperalgesia in rats and administration around healthy sciatic nerve was found to produce mechanical allodynia ipsilateral to the injection (13). During inflammatory states,

various immune cells produce and release PLA2s which indicate that the data derived from these experimental studies may have general implications for the understanding of inflammatory pain (13). A snakebite may trigger inflammatory responses by PLA2s in the snake venom and hypoxia due to fear of movement caused by pain may contribute to inflammation through accumulation of inflammatory mediators and free radicals. Continuous nociceptive input by hypoxia, inflammation, or sympathetic stimulation may lead to sensitization which results in CRPS (4).

The development of CRPS following snake bite, however, is extremely rare. Only one case report has been found in the literature which describes a patient who developed CRPS type-1 following a mountain pit viper bite (14) As far as we know, ours is the second case report. Envenomation with marine species, such as stonefish, jellyfish, stingrays and Trachinus draco that results in severe pain, edema, erythema, local inflammation and cardiac symptoms have been described in the literature, but no case of CRPS exists (15-18). The clinical findings of our patient indicated a diagnosis of CRPS which was also supported by the patchy osteoporosis found in his X-rays. The differential diagnosis of CRPS includes inflammatory arthritis, cellulitis, osteomyelitis, deep venous thrombosis, chronic vascular disorders, diabetic neuropathy, entrapment neuropathies, and malignancy (5). The clinical history, blood tests, EMG and radiologic findings of our patient were not indicative of these diseases. Our patient had gone through an immobilization period due to pain, edema and inflammation which might have triggered the chain of events leading to CRPS. Snake envenomation had also caused neuropathy of the median and ulnar nerves that contributed to the development of CRPS. Our patient was categorized as CRPS I because there was no actual nerve injury.

Different treatment approaches are available for CRPS which can be divided into physical/occupational therapy, pharmacologic, interventional, and psychological techniques. Elevation of the extremity, lymphatic massage, use of compression garments, contrast baths, desensitization training, fluidotherapy, TENS, ultrasound, heat or ice packs, and paraffin baths may be used to achieve edema control and elimination of pain (19,7). Splinting and active ROM exercises may be useful to prevent stiffness and development of contractures (19).

Our patient was treated with a physical therapy program consisting of active-assisted ROM and stretching exercises for the limitations of ROM in his hand joints and contrast baths, TENS and US were performed to help alleviate the pain and edema. Nonsteroidal antiinflamatory drugs had been ineffective and although among pharmacologic agents the strongest evidence exists for the steroids, they could not be used because he was diabetic. We prescribed pregabalin with an initial dose of 150 mg daily which was increased to 300 mg daily a week after. Since CRPS presents with pain of neuropathic character it seems reasonable to extrapolate some data from studies of neuropathic pain management and apply these results to CRPS (20). The efficacy of pregabalin in CRPS has not been proven but our patient reported a significant decrease in his pain. However, this decrease may not be solely due to the use of pregabalin because other interventions were also performed along with medical treatment.

In fact, other current treatment strategies of CRPS similarly lack evidence as to their efficacy which may partially be due to the fact that complex mechanisms are involved in the pathogenesis of this disorder and not one single therapeutic modality is sufficient to attenuate all ongoing processes together. Increased insight in etiological and predisposing factors for CRPS may facilitate early diagnosis and improve the chance of good outcome.

It is of high importance to remember that envenomation with snake toxins may, although rarely, be complicated with CRPS and early recognition of its symptoms may render better management of this painful and disabling condition possible.

Conflict of Interest:

Authors reported no conflicts of interest.

References

1. Connolly S, Trevett AJ, Nwokolo NC, Lalloo DG, Naragi S, Mantle D, et al. Neuromuscular effects of Papuan taipan snake venom. Ann Neurol 1995;38:916-20.
2. Seneviratne U, Dissanayake S. Neurological manifestations of snake bite in Sri Lanka. J Postgrad Med 2002;48:275-8.
3. Singh G, Pannu HS, Chawla PS, Malhotra S. Neuromuscular transmission failure due to common krait (Bungarus caeruleus) envenomation. Muscle Nerve 1999;22:1637-43.
4. de Mos M, Sturkenboom MC, Huygen FJ. Current understandings on complex regional pain syndrome. Pain Pract 2009;9:86-99.
5. Mc Bride A, Atkins R. Complex regional pain syndrome. Curr Orthop 2005;19:155-65.
6. Wilson JG, Serpell MG. Complex regional pain syndrome. Continuing education in Anaesthesia. Critical Care & Pain 2007;7:51-4.
7. Chung OY, Bruehi S. Complex regional pain syndrome. Curr Treat Options Neurol 2003;5:499-511.
8. Harden RN, Bruehl S, Stanton-Hicks M, Wilson PR. Proposed new diagnostic criteria for complex regional pain syndrome. Pain Med 2007;8:326-31.
9. Bennett M. The LANSS Pain Scale: The Leeds assessment of neuropathic symptoms and signs. Pain 2001;92:147-57.
10. Hodgson WC, Wickramaratna JC. In vitro neuromuscular activity of snake venoms. Clin Exp Pharmacol Physiol 2002;29:807-14.
11. Sanmuganathan PS. Myasthenic syndrome of snake envenomation: a clinical and neurophysiological study. Postgrad Med J 1998;74:596-9.
12. Teixeira CF, Landucci EC, Antunes E, Chacur M, Cury Y. Inflammatory effects of snake venom myotoxic phospholipases A2. Toxicon 2003;42:947-62.
13. Chacur M, Milligan ED, Sloan EM, Wieseler-Frank J, Barrientos RM, Martin D, et al. Snake venom phospholipase A2s (Asp49 and Lys49) induce mechanical allodynia upon perisciatic administration: involvement of spinal cord glia, proinflammatory cytokines and nitric oxide. Pain 2004;108:180-91.
14. Bhattarai B, Shrestha BP, Rahman TR, Sharma SK, Tripathi M. Complex regional pain syndrome (CRPS) type-1 following snake bite: a case report. Nepal Med Coll J 2008;10:278-80.
15. Yamamoto R, Suzuki M, Hori S, Aikawa N. Stonefish "Okoze" envenomation during food preparation. Keio J Med 2010;59:19-22.
16. Winkel KD, Mirtschin P, Pearn J. Twentieth century toxinology and antivenom development in Australia. Toxicon 2006;48:738-54.
17. Clark RF, Girard RH, Rao D, Ly BT, Davis DP. Stingray envenomation: a retrospective review of clinical presentation and treatment in 119 cases. J Emerg Med 2007;33:33-7.
18. Halpern P, Sorkine P, Raskin Y. Envenomation by Trachinus draco in the eastern Mediterranean. Eur J Emerg Med 2002;9:274-7.
19. Bengtston K. Physical modalities for complex regional pain syndrome. Hand Clin 1997;13:443-5.
20. Stacey BR, Campbell P. Pregabalin and gabapentin for neuropathic pain and CRPS. www.rsds.org.