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An Unusual Challenging Case of Complex Regional Pain Syndrome Involving all 4 Limbs: A Case Report

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Background: Complex regional pain syndrome (CRPS) is characterized by disproportionate pain along with autonomic signs and trophic changes. In rare instances, it can spread to other extremities.

Case Report: We report an unusual case of gradual progression of CRPS to all 4 extremities in a patient who developed CRPS following a traumatic event. Despite receiving adequate medical management, her pain pattern spread to her other extremities, causing significant functional impairment, and she eventually had to undergo minimally invasive procedures, namely stellate ganglion blocks (SGB) and spinal cord stimulators (SCS), for management of her symptoms.

Conclusions: SGB and SCS have been documented to relieve pain in patients with CRPS. However, they do not appear to prevent progression and spread of the disease. Our patient had a cumulative benefit from SGB. The authors would like to highlight an unusual pattern of evolution of CRPS and advocate research for management of treatment-resistant pain patterns.

Key words: Complex regional pain syndrome, CRPS, stellate ganglion blocks, spinal cord stimulators, Budapest criteria, case report

BACKGROUND

Complex regional pain syndrome (CRPS), also known as reflex sympathetic dystrophy, causalgia, or algodystrophy is a rare, chronic pain syndrome with an estimated global prevalence of 5-26 per 100,000 persons (1). It is characterized by hyperalgesia, allodynia, and autonomic and motor dysfunctions, which are usually limited to a single extremity and preceded by trauma affecting the involved extremity (2). CRPS is of 3 types: CRPS I, which often follows a minor injury, CRPS II, which follows a nerve injury, and a third recently identified but less diagnosed subtype, CRPS not otherwise specified, which includes patients that display some features of CRPS without completely satisfying diagnostic criteria and without another disease process that fully explains their symptoms (2,3). CRPS usually presents as distally localized, diffuse pain, which is associated with autonomic signs and trophic changes of the skin and nails. In some rare instances, it could spread to an ipsilateral limb (also known as hemisensory spread) or may spread to involve the opposite extremity (also known as mirror-image spread) (4).

The exact pathophysiological mechanisms underlying CRPS are yet to be identified, but a few open-ended hypotheses postulate autonomic disturbances and sympathetic overflow as the cause for development of CRPS (5,6). Historically, CRPS has been treated with medical management, which includes (but is not limited to) use of typical pain medications, such as nonsteroidal anti-inflammatory drugs, opioids, and anticonvulsants like gabapentin and pregabalin (7). In the last few

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decades, interventional pain modalities, namely stellate ganglion blocks (SGB), thoracic or lumbar sympathetic blocks, dorsal root ganglion (DRG) stimulators, and spinal cord stimulators (SCS), have gained popularity for the management of CRPS (4,6,7).

We report an unusual case where CRPS was initially diagnosed in one extremity, and despite appropriate medical management, it gradually progressed to involve all 4 extremities and caused significant functional limitation to the patient.

A written, informed consent was obtained from the patient for presentation of this case report.

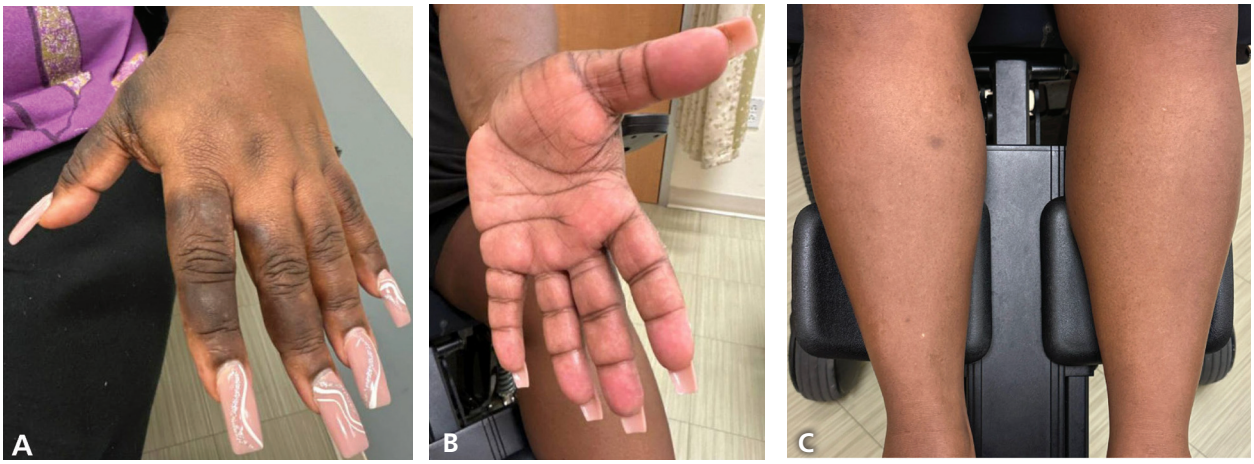
CASE PRESENTATION

We report the case of a 48-year-old, right-handed woman with a past medical history significant for diabetes mellitus type 2 and breast and ovarian cancer who developed CRPS after a work-related accident in which she sustained injury to her dominant right hand. Patient sustained trauma to her right upper extremity in 2009, when a bookshelf fell on her arm at school. Subsequently, she developed CRPS in her right upper extremity. She trialed opioids and pregabalin, along with desensitization techniques, but failed to receive adequate analgesia. Patient then underwent a right-sided SGB under ultrasound guidance and reported satisfactory pain relief with a change in the Visual Analog Scale (VAS) score from 10/10 (pre-SGB) to 5/10 (post-SGB). But this pain relief was transient, and the patient eventually received cervical SCS for management of her symptoms. However, over the next few years, she started noticing similar symptoms in her left upper extremity (LUE), with the inability to hold even a cup of water with her left hand and a constant feeling of "something crawling in her left hand." She denied the presence of any neck pain and always reported pain to be in her arms, which was associated with paresthesia and trophic changes in her skin and nails (Fig. 1). Subsequently, she was diagnosed with mirror-image spread of CRPS in her LUE (as per the Budapest criteria (Fig. 2). Since she had satisfactorily responded to an SGB in the past, a multimodal approach with a left-sided SGB under ultrasound guidance along with desensitization techniques and medical management was employed, to which she responded adequately with change in the VAS score from 7/10 (pre-SGB) to 3/10 (post-SGB).

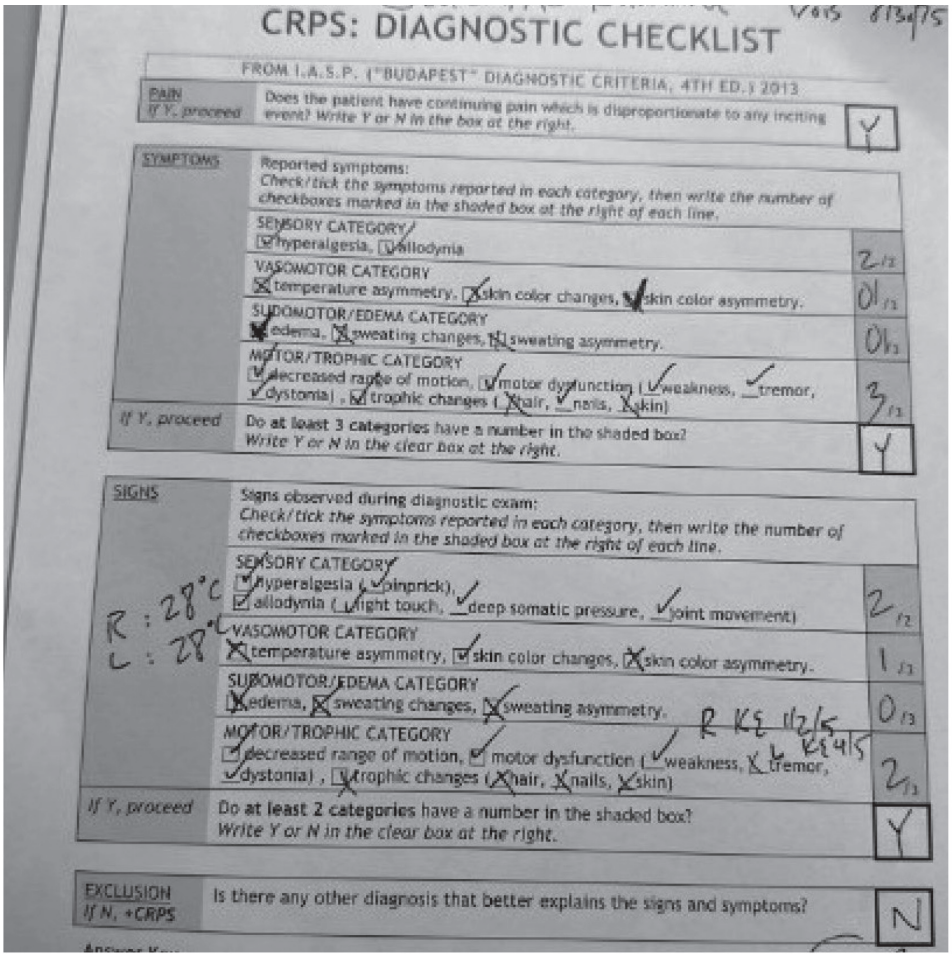
Over the next few months, she started noticing similar disproportionate pain in her bilateral lower extremities (BLE) (left > right), which adversely affected her functional mobility. She reported diffuse pain in her left lower leg, which was associated with intermittent numbness in the entire leg and excessive sweating (Fig. 1). Her pain was debilitating her to an extent that she needed a walker for home ambulation and a powered wheelchair for long-distance ambulation. After excluding differentials like lumbar radiculopathy, lumbar myelopathy, and deep vein thrombosis, she was diagnosed with CRPS in her BLE (as per the Budapest criteria). At this point, all 4 limbs of our patient were affected with CRPS. Our patient was not approved for a new cervical SCS by her work compensation, but she was eligible for a lumbar stimulator. Hence, we placed one lead in the cervical spine and one lead in the thoracic spine with an implantable pulse generator in the lumbar spine to help her with her chronic, widespread pain pattern (Fig. 3). Patient responded well to this approach and reported an improvement of 65% in her symptoms.

DISCUSSION

CRPS is a chronic neuropathic pain syndrome whose definition and diagnostic criteria have evolved over time. In the 1870s, Silas Weir Mitchell, an American Civil War physician, first coined the term "causalgia" for development of pain in the distal extremity following a traumatic partial nerve injury. A few decades later, physician Paul Sudeck noted similar symptoms in a patient with a distal bone fracture without any nerve injury and named it "Sudeck's syndrome." Then in the 1940s, Dr. James Evans observed that patients with "causalgia" or "Sudeck's syndrome" demonstrated adequate analgesic relief with a sympathetic block, and he coined the term "reflex sympathetic dystrophy" for the same pain syndrome (2,25). In 1993, diagnostic criteria (8) for reflex sympathetic dystrophy were first identified using the Veldman criteria. In 1994, the International Association for the Study of Pain published the first diagnostic criteria for CRPS, known as the Orlando criteria, which were revised in 2019, and the revised criteria are now known as the Budapest criteria (3,9,10). The Budapest criteria categorize symptoms into 4 broad categories, which are: sensory, vasomotor, sudomotor/edema, and motor/trophic (Table 1). It requires that the patient report at least one symptom in 3 or more of the categories, display at least one sign in 2 or more of the categories, and must have continuing pain, which is disproportionate to any inciting event with no other diagnosis explaining the signs and symptoms (3). The



Figs. A and B) Demonstration of the trophic changes (skin pigmentation, alteration in skin texture) in patient's LUE. LUE, left upper extremity. C) Demonstration of the trophic changes in patient's BLE. BLE, bilateral lower extremities.



CRPS: DIAGNOSTIC CHECKLIST

FROM I.A.S.P. ("BUDAPEST" DIAGNOSTIC CRITERIA, 4TH ED.) 2013

PAIN *If Y, proceed*	Does the patient have continuing pain which is disproportionate to any inciting event? *Write Y or N in the box at the right.*	Y
SYMPTOMS	Reported symptoms: *Check/tick the symptoms reported in each category, then write the number of checkboxes marked in the shaded box at the right of each line.*	
	SENSORY CATEGORY ☑ hyperalgesia, ☐ allodynia	2/2
	VASOMOTOR CATEGORY ☒ temperature asymmetry, ☒ skin color changes, ☑ skin color asymmetry.	01/3
	SUDOMOTOR/EDEMA CATEGORY ☑ edema, ☒ sweating changes, ☒ sweating asymmetry.	01/3
	MOTOR/TROPHIC CATEGORY ☑ decreased range of motion, ☑ motor dysfunction (☑ weakness, ☑ tremor, ☑ dystonia), ☑ trophic changes (☒ hair, ☐ nails, ☒ skin)	3/5
If Y, proceed	Do **at least 3 categories** have a number in the shaded box? *Write Y or N in the clear box at the right.*	Y
SIGNS	Signs observed during diagnostic exam: *Check/tick the symptoms reported in each category, then write the number of checkboxes marked in the shaded box at the right of each line.*	
	SENSORY CATEGORY ☑ hyperalgesia (☑ pinprick), ☑ allodynia (☑ light touch, ☑ deep somatic pressure, ☑ joint movement)	2/2
	VASOMOTOR CATEGORY ☒ temperature asymmetry, ☑ skin color changes, ☒ skin color asymmetry.	1/3
	SUDOMOTOR/EDEMA CATEGORY ☒ edema, ☒ sweating changes, ☒ sweating asymmetry.	0/3
	MOTOR/TROPHIC CATEGORY ☑ decreased range of motion, ☑ motor dysfunction (☑ weakness, ☒ tremor, ☑ dystonia), ☒ trophic changes (☒ hair, ☒ nails, ☒ skin)	2/5
If Y, proceed	Do **at least 2 categories** have a number in the shaded box? *Write Y or N in the clear box at the right.*	Y
EXCLUSION *If N, +CRPS*	Is there any other diagnosis that better explains the signs and symptoms?	N

R : 28°C
L : 28°C

R KE 1/2/5
KE 4/5

Fig. 2. CRPS diagnostic checklist of the patient as per the Budapest criteria. CRPS, complex regional pain syndrome.

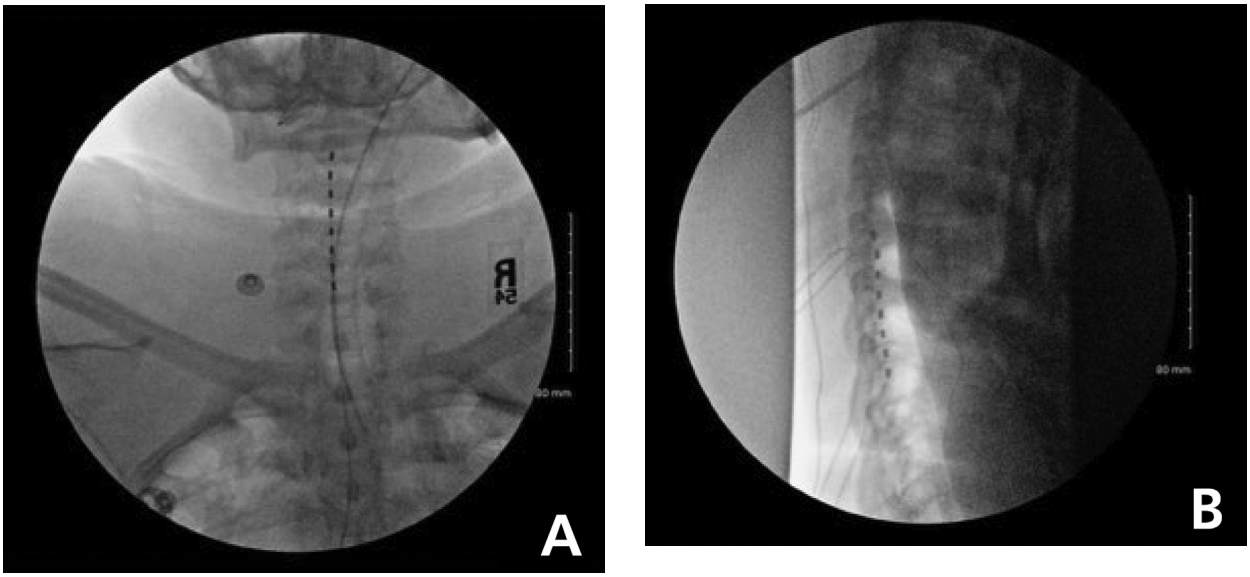


Fig. 3. A. Fluoroscopic image of SCS lead at C2 level. SCS, spinal cord stimulator. B. Fluoroscopic image of SCS lead at T7 level. SCS, spinal cord stimulator.

Table 1. Budapest criteria.

Harden-Bruehl criteria/Budapest criteria
General definition of the syndrome: CRPS describes an array of painful conditions that are characterized by continuing (spontaneous and/or evoked) regional pain that is seemingly disproportionate in time or degree to the usual course of any known trauma or other lesion. The pain is regional (not in a specific nerve territory or dermatome) and usually has a distal predominance of abnormal sensory, motor, sudomotor, vasomotor, and/or trophic findings. The syndrome shows variable progression over time.
- Establishing the clinical diagnosis requires the following criteria to be met:
1. Continuing pain, which is disproportionate to any inciting event.
2. Presence of at least one symptom in 3 of the 4 following categories:
a. Sensory: hyperesthesia and/or allodynia.
b. Vasomotor: temperature asymmetry, skin-color changes, and/or skin-color asymmetry.
c. Sudomotor/edema: edema, sweating changes, and/or sweating asymmetry.
d. Motor/trophic: decreased range of motion, motor dysfunction (weakness, tremor, or dystonia), and/or trophic changes (in hair, nail, or skin).
3. Presence of at least one sign at the time of evaluation in 2 of the following 4 categories:
a. Sensory: hyperalgesia (to pinprick), and/or allodynia (to light touch), and/or temperature sensation, and/or deep somatic pressure, and/or joint movement.
b. Vasomotor: temperature asymmetry (> 1°C), skin-color changes, and/or symmetry.
c. Sudomotor/edema: edema, sweating changes, and/or sweating asymmetry.
d. Motor/trophic: decreased range of motion, motor dysfunction (weakness, tremor, or dystonia), and/or trophic changes (in hair, nail, or skin).
4. No other diagnosis that better explains the signs and symptoms.

Budapest criteria provide improved diagnostic specificity while maintaining good sensitivity (1,3,11,12).

Despite the advances in medicine, the exact pathophysiologic mechanisms responsible for the development of CRPS are yet to be ascertained (1,7). However, a unanimous consensus about a multifactorial interaction between the central nervous system, peripheral nervous system, sympathetic nervous system, immune system,

genetics, and mental health has been accepted (13,14). CRPS is often precipitated by insult to the peripheral nervous system, which causes an increase in the release of glutamate, inflammatory factors like substance P, tumor necrosis factor-alpha, and prostaglandin E2, along with degeneration of large somatomotor Aα fibers with sparing of Aδ fibers (14-16). Additionally, imaging studies (14,17) have documented that patients with CRPS undergo a decrease in gray matter volume in the dorsal insula, left orbitofrontal cortex, and cingulate cortex, coupled with an increase in gray matter volume in the bilateral dorsal putamen and right hypothalamus. Further, prolonged duration of pain has been associated with decreased gray matter in the left dorsolateral prefrontal cortex, while pain intensity has been positively correlated with volume in the left posterior hippocampus, left amygdala, and negatively correlated with volume in the bilateral dorsolateral prefrontal cortices (14,17).

It has commonly been observed that CRPS tends to involve the affected extremity, but, in some rare instances, it can spread to involve the ipsilateral limb (also known as hemisensory spread) or may spread to involve the opposite extremity (also known as mirror-image spread) (4,18,19). Although the mechanism illustrating the spontaneous spread of CRPS to other limbs is yet to be ascertained, the dominant pattern of spread of CRPS has been hypothesized to be due to its spread via spinal or cortically mediated mechanisms (19). Involvement of all 4 extremities without any new trauma is rarely seen. In this case report, we describe a rarely seen case of severe CRPS involving all 4 extremities, with mirror-image spread preceding hemisensory spread.

Use of sympathetic blocks like the SGB has been noted to provide relief in the symptoms of CRPS and decrease the dependence on oral pain medications while also increasing the patient's tolerance for physical therapy (14,20-22). In patients with CRPS, SGBs have been documented to regulate the response of the nervous system, cause vasodilation, and improve range of motion of the affected extremity, along with concurrent reduction of inflammation and pain (6,7). Stude et al (23) documented reversal of cortical shrinkage on functional magnetic resonance imaging and increased blood oxygenation levels along with reduction of pain scales one hour following SGB in patients with CRPS. It was interesting to note that our patient also demonstrated a cumulative benefit from SGBs.

Recently, SCS has emerged as a promising treatment for symptom relief in severe CRPS, which is resistant to pharmacological management and other modalities (4). The UK Royal College of Physicians also advocates the use of invasive neuromodulation interventions, such as SCS and DRG stimulation, for patients who have not responded to appropriate integrated management (24). It has been hypothesized that in CRPS, SCS provides relief by way of the gate control theory and causes preferential neurostimulation of faster A-beta fibers, which, in turn, leads to diminished propagation of painful stimuli from slower C-fibers (14,25). Kriek et al (26) postulated that SCS may even reverse the maladaptive cortical neuroplastic changes seen in CRPS and could even demonstrate immunomodulatory properties via the mediation of T cell activation. Although SCS has not been shown to change the overall CRPS disease course, it has been associated with decreased oral medication consumption, enhanced quality of life, and improved physical function (11,14,27).

CONCLUSIONS

Over the last few decades, many important advances have been made for the diagnosis and management of CRPS. Although CRPS is a relatively less common chronic pain syndrome, it is believed that many areas of uncertainty can be addressed with improved collection and sharing of observational data. Minimally invasive procedures like SGB and SCS could be considered as slightly high-risk procedures, but are worth trying for pain relief in patients with CRPS involving multiple limbs or in patients with CRPS which is resistant to pharmacological management. Through this case report, the we would like to present an unusual pattern of evolution of CRPS while also advocating for more research for the management of treatment-resistant pain patterns.

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