Complex Regional Pain Syndrome

Shakya S,[1] Amatya S,[2] Thapa S,[2] Thapa P,[3] Pokharel S[4]

[1]Department of Anesthesiology and Critical Care, Dhulikhel Hospital, Kathmandu University Hospital, Kathmandu University School of Medical Sciences, Dhulikhel, Kavre, Nepal.

[2]Nepal Pain Care and Research Center, Kathmandu, Nepal.

[3]Nepal Army Institute of Health Sciences, Kathmandu, Nepal.

[4]BP Koirala Memorial Cancer Hospital, Chitwan, Nepal.

Corresponding Author

Samir Shakya

Department of Anesthesiology and Critical Care, Dhulikhel Hospital, Kathmandu University Hospital, Kathmandu University School of Medical Sciences, Dhulikhel, Kavre, Nepal.

E-mail: reemas4765@gmail.com

Citation

Shakya S, Amatya S, Thapa S, Thapa P, Pokharel S. Complex Regional Pain Syndrome. *Kathmandu Univ Med J.* 2024;85(1):123-6.

ABSTRACT

Complex regional pain syndrome is chronic pain condition involving hyperalgesia and allodynia of extremities. The pathophysiology of CRPS is thought to be combination of different factors that take place at the time of initial injury. Sixty two years female presented to us with severe leg pain after intravenous cannulation during her spine surgery and associated with hyperalgesia and allodynia. On examination, there was shinny skin and nail changes on right leg and significant surface temperature difference between two legs. Patients were managed conservatively with patient education, physical therapy, pharmacological management, and psychological therapy with diagnosis of complex regional pain syndrome. Diagnosis is a clinical finding based on the Budapest diagnostic criteria. Early treatment with multidisciplinary approach to pain management is necessary to achieve complete recovery and prevent damage. Complex regional pain syndrome is life altering condition but understanding the etiological factors helps us to an early diagnosis and a better implementation of treatment.

KEY WORDS

Allodynia, Budapest criteria, Complex reginal pain syndrome, Hyperalgesia

INTRODUCTION

Clinicians frequently face the challenging and maladaptive condition of chronic neuropathic pain like complex regional pain syndrome (CRPS), a painful and disabling disorder often involving hyperalgesia and allodynia of extremities with vasomotor, sudomotor, inflammatory, trophic, and motor changes in affected extremity.[1] CRPS type I has no demonstrable nerve lesion and Type II has demonstrable nerve injury. Worldwide, the incidence and prevalence of CRPS ranges from 5.46 to 26.2 per 100,000 persons year, more frequent in women (2-3:1), age(50-70) years, and predominantly in arms with risk factors like: Caucasian race, depression, drug abuse, prolong immobilization, menopause, osteoporosis, asthma, rheumatoid arthritis, headache, smoking, and angiotensin-converting-enzyme inhibitor treatment.[2-4] Lack of a clear definition of CRPS led to underreporting of incidence of CRPS. Historically, it was known as ''reflex sympathetic dystrophy'', ''causalgia'', ''algoneurodystrophy'', or ''Sudeck atrophy'.[5-7] IASP gave first set of diagnostic criteria and later came Budapest Criteria and CRPS severity score.[7,8] Despite being studied for over two decades, exact pathogenesis of CRPS is still incompletely understood.[9,10] Clinical course is believed to begin with acute, or warm phase followed by chronic, or cold phase.[9,10] Early initiation of therapy is integral to patient prognosis, with goals of restoring limb functionality, decreasing pain, and improving quality of life.[11,12]

CASE REPORT

A 62-year-old female presented to us on 24th February, 2024 to rule out the possible cause of her right leg pain for 3.5 months which was sudden onset, severe, continuous, deep, burning, sharp throbbing in nature with NRS of (7-9) after intravenous cannulation in dorsum of foot during her second spine surgery.[7-9] Pain was radiating from the dorsum of foot to anterior lateral aspect of leg and was associated with hyperalgesia and allodynia. Pain was aggravated with touch, pressure on the affected area, walking or any movement of right leg whereas partially relieved on rest and medication like:- Pregabalin, NSAIDs, opioids. She also complained of swelling of right leg which subsides later as

well as skin discoloration, warmness, and nail changes in the affected leg. She was known case of DM under Metformin, Linagliptin and long-acting insulin but her blood sugar was not under control. She was under Pregabalin 150 mg twice a day for the neuropathic pain. Her history revealed that she underwent spine surgery thrice (April, 2022 = L5 Laminectomy for lumbar central canal stenosis with right L5 radiculopathy; November, 2023= Trans lumbar interbody fusion (TLIF) for spondylolisthesis L5/S1; January, 2024 = Revision surgery for spondylolisthesis). **Physical examination:** Gait was limping. **On inspection,** right leg was shinner in compared to left along with nail changes on right toes (Fig. 1). There was no swelling/redness or any color changes/ bruises or abnormal sweating or any type of injury to the leg. **On palpation,** the difference in the surface temperature between two legs were noted. Measured temperature on right leg was 96.4°*F*(i.e 35.7°*C*) and left leg was 91.2°*F*(i.e 32.9°*C*) (Fig. 2). **Sensory;** Patient complained of severe burning pain with light touch/ pressure/ gentle palpation of the affected limb. Hyperesthesia and Allodynia were present in anterolateral aspect of the leg and dorsum of foot. **Motor;** L4, L5, S1: - 4/5 whereas Reflex were not appreciated due to severe pain. The back and knee examination were normal. Provisional diagnosis was made to be "CRPS type I" based on Budapest criteria. Patient was conservatively managed with pregabalin 150 mg BD, amitriptyline 25 mg OD, analgesic (tramadol 37.5 mg + paracetamol 370 mg) SOS and antioxidants (Bioxy capsules 4 100 mg) (beta-carotene, vitamin A, C, E), as well as patients' education, mirror therapy, physiotherapy, and rehabilitation with the future plan of right lumbar sympathectomy and follow up in 2 months.

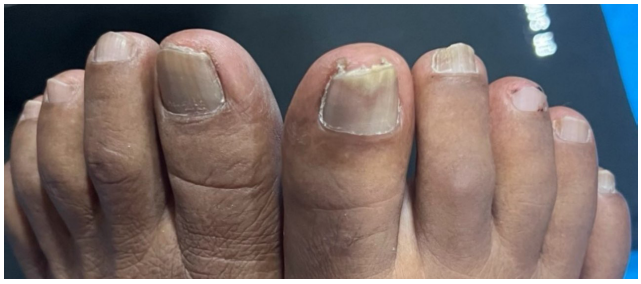

Figure 1. Trophic changes (shinny skin and Nail changes)

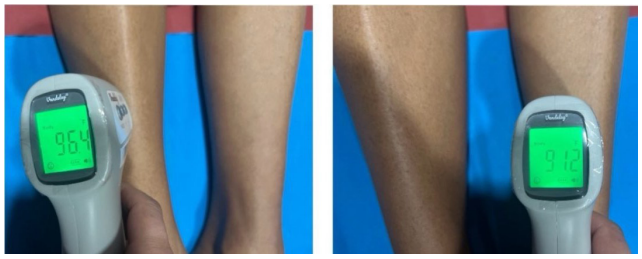

Figure 2. Difference in surface temperature between two legs

DISCUSSION

Budapest criteria has high sensitivity (0.99) and improved specificity (0.41-0.68) (Table. 1).[13,14] Diagnosis is essentially a clinical finding based on diagnostic criteria with additional tests to exclude other differential conditions. In this case also, the diagnosis was made based on the clinical findings and Budapest criteria. Thermography may be the most common and basic diagnostic method utilized, and temperature differences are component of the CSS.[15] There are roles of bone scintigraphy, radiography, 3-phase bone and QSART(20).[16-20] Skin fluximetry by laser doppler technique is most precise technique that is currently available for early diagnosis of CRPS I.[18]

Recent studies suggest existence of two different sources of inflammation: Acute, and neurogenic, that causes an increase in tissue permeability and vasodilation and hypothesized a dysregulation between normal neural-mast cell interaction leading to prolonged inflammation and delayed tissue repair.[18] Starting with inciting or traumatic events, leading to peripheral nervous system sensitization and decrease in depolarization threshold likely contributing to hyperalgesia in these patients. Coupling between sympathetic and peripheral nociceptive nervous systems may develop over time leading to

Table 1. Diagnostic criteria for CRPS (Budapest criteria) (A-D Must apply)*

A. The patient has continuing pain which is disproportionate to any inciting event.	☐
B. The patient has at least one sign in two or more of the categories.	☐
C. The patient reports at least one symptom in three of more of the categories.	☐
D. No other diagnosis can better explain the signs and symptoms.	☐

Category		Sign (You can see or feel a problem)	Symptom (the patient reports a problem)
1. Sensory	Allodynia (to touch and/or temperature sensation and/or deep somatic pressure) and/or hyperalgesia (to pinprick)	☐	Hyperesthesia does also qualify as symptom ☐
2. Vasomotor	Temperature asymmetry and/ or skin color changes and /or skin color asymmetry	If you notice temperature asymmetry: must be >1^{0}C ☐	☐
3. Sudomotor/ Edema	Edema and/or sweating changes and/or sweating asymmetry	☐	☐
4. Motor/ Trophic	Decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/ or trophic changes (hair/nail/skin)	☐	☐

*A third diagnostic subtype called CRPS-NOS (not otherwise specified) can be considered for patients who have abnormalities in fewer than three Budapest symptoms categories, including those who had more documented signs and symptoms in the past, if current "signs and symptoms" are still felt to be best explained by CRPS.

distinct symptomatology of CRPS.[7] Continuous peripheral sensitization increases efficacy of synaptic nociceptive firing in dorsal horn mediated by neuropeptides decreasing threshold for response to mechanical and thermal stimuli leading to hyperpathia and allodynia. NMDA receptors play an important role in central sensitization.[18] Chronically, structural changes in somatosensory cortex as disease continues leading to motor dysfunction and impaired recognition. During acute phase, increased expression adrenergic receptors and decrease in circulating norepinephrine potentially leading to vasodilation and over time this leads to increased peripheral catecholamine sensitivity, and subsequent excessive vasoconstriction and hyperhidrosis that develops, leads to the cold, clammy extremities seen chronic phase of disease.[7] HLA (DQ1, B62, and DQ8) are associated with CRPS with fixed dystonia.[19] Evidence suggests psychological stress link to CRPS disease development and progress.[7]

Physical/occupational/psychological therapy (graded motor imagery (GMI)/ mirror therapy) with a goal to improve functionality and range of motion of extremity and achieve reduction in pain and increased mobility.[21] Education and information/ Cognitive behavioral therapy is useful in these patients. Gabapentin, Tricyclic antidepressants, pregabalin, carbamazepine; evidence for their use in CRPS is limited.[7] NSAIDs, corticosteroids and free radical scavengers were used in early CRPS.[18] Oral corticosteroids having direct evidence from CRPS clinical trials, but longer courses are contraindicated.[22] Free radical scavengers (vitamin C, N-acetyl cysteine, Dimethyl sulfoxide) have shown some efficacy in prevention and treatment.[4] Bisphosphonates significantly relieve spontaneous pain and improve functional status of patients with an early disease. The recent use of ketamine and lignocaine cream are helpful in the management of CRPS.[18] National Institute for Health and Care Excellence 7 recommends spinal cord stimulation (SCS) for patients experiencing pain for 6 months or more despite adequate conventional management.[23] Sympathetic nerve block is a treatment option for patients who are refractory to pharmacological treatments, especially when performed early course of disease.[18]

CRPS is a life-altering condition. Due to unclear pathophysiology, treatment is driven by available evidence and clinician experience in a multidisciplinary fashion based on the 4 pillars of management. As research continues to reveal more about the involved mechanisms, future treatment will presumably shift to more novel mechanism-based treatments.

REFERENCES

1. Borchers AT, Gershwin ME. The clinical relevance of complex regional pain syndrome type I: The Emperor's New Clothes. *Autoimmun Rev.* 2017;16(1):22-33.
2. Sandroni P, Benrud-Larson LM, McClelland RL, Low PA. Complex regional pain syndrome type I: incidence and prevalence in Olmsted county, a population-based study. *Pain.* 2003;103(1-2):199-207.
3. de Mos M, de Bruijn AGJ, Huygen FJPM, Dieleman JP, Stricker BHC, Sturkenboom MCJM. The incidence of complex regional pain syndrome: A population-based study. *Pain.* 2007;129(1-2):12-20.
4. Márquez Martínez E, Ribera Canudas MV, Mesas Idáñez Á, Medel Rebollo J, Martínez Ripol P, Candela Custardoy A, et al. Síndrome de dolor regional complejo. *Semin la Fund Esp Reumatol*. 2012;13(1):31-6.
5. Goh EL, Chidambaram S, Ma D. Complex regional pain syndrome: A recent update. *Burn Trauma*. 2017;5(1):1-11.
6. Eldufani J, Elahmer N, Blaise G. A medical mystery of complex regional pain syndrome. *Heliyon*. 2020;6(2):e03329.
7. Shim H, Rose J, Halle S, Shekane P. Complex regional pain syndrome: a narrative review for the practising clinician. *Br J Anaesth*. 2019;123(2):e424-33.
8. Harden RN. Complex regional pain syndrome R. Br J Anesth. 2001;87(1):99-106.
9. Misidou C, Papagoras C. Complex regional pain syndrome: An update. *Mediterr J Rheumatol*. 2019;30(1):16-25.
10. Baronio M, Sadia H, Paolacci S, Prestamburgo D, Miotti D, Guardamagna VA, et al. A medical mystery of complex regional pain syndrome. *Autoimmun Rev.* 2020;6(1):28-35.
11. Baygutalp F, Kul A. Effect of early orthopedic rehabilitation on development of complex regional pain syndrome type 1. *Eurasian J Med*. 2020;52(2):110-4.
12. Lewis JS, Kellett S, McCullough R, Tapper A, Tyler C, Viner M, et al. Body Perception Disturbance and Pain Reduction in Longstanding Complex Regional Pain Syndrome following a Multidisciplinary Rehabilitation Program. *Pain Med (United States).* 2019;20(11):2213-9.
13. Urits I, Shen AH, Jones MR, Viswanath O, Kaye AD. Complex Regional Pain Syndrome, Current Concepts and Treatment Options. *Curr Pain Headache Rep*. 2018;22(2).
14. Harden RN, Bruehl S, Perez RSGM, Birklein F, Marinus J, Maihofner C, et al. Validation of proposed diagnostic criteria (the "budapest Criteria") for Complex Regional Pain Syndrome. *Pain.* 2010;150(2):268-74.
15. Harden RN, Bruehl S, Perez RSGM, Birklein F, Marinus J, Maihofner C, et al. Development of a severity score for CRPS. *Pain.* 2010;151(3):870–6.
16. Wertli MM, Brunner F, Steurer J, Held U. Usefulness of bone scintigraphy for the diagnosis of Complex Regional Pain Syndrome 1: A systematic review and Bayesian meta-analysis. *PLoS One.* 2017;12(3):1-18.
17. Ringer R, Wertli M, Bachmann LM, Buck FM, Brunner F. Concordance of qualitative bone scintigraphy results with presence of clinical complex regional pain syndrome 1: Meta-analysis of test accuracy studies. *Eur J Pain (United Kingdom).* 2012;16(10):1347-56.
18. Castillo-Guzmán S, Nava-Obregón TA, Palacios-Ríos D, Estrada-Cortinas JÁ, González-García MC, Mendez-Guerra JF, et al. Complex regional pain syndrome (CRPS), a review. *Med Univ.* 2015;17(67):114-21.

19. Ganty P, Chawla R. Complex regional pain syndrome: Recent updates. *Contin Educ Anaesthesia, Crit Care Pain.* 2014;14(2):79–84.

20. Lee HJ, Kim SE, Moon JY, Shin JY, Kim YC. Analysis of quantitative sudomotor axon reflex test patterns in patients with complex regional pain syndrome diagnosed using the Budapest criteria. *Reg Anesth Pain Med*. 2019 Sep 8:rapm-2019-100415.

21. Smart KM, Wand BM, O'Connell NE. Physiotherapy for pain and disability in adults with complex regional pain syndrome (CRPS) types I and II. *Cochrane Database Syst Rev.* 2016 Feb 24;2(2):CD010853.

22. Harden RN, Oaklander AL, Burton AW, Perez RS, Richardson K, Swan M, et al. Complex regional pain syndrome: practical diagnostic and treatment guidelines, 4th ed. *Pain Med*. 2013 Feb;14(2):180-229. doi: 10.1111/pme.12033. Epub 2013 Jan 17. PMID: 23331950.

23. NICE. Neuropathic pain in adults: pharmacological management in non-specialist settings. NICE Guidel. 2013;updated 20(April 2018):1-36.