

# Association of Food Allergy from Dried Fish and Complex Regional Pain Syndrome-A Rare Case Presentation

Prakash R Deshmukh<sup>1\*</sup>, Helee Khetan<sup>2</sup>, Manjiri Ranade<sup>3</sup>, Kailash Kothari<sup>4</sup>

<sup>1</sup>FIPP, FIAPM, D. Anaesthesiology, Spine and Pain Management Centre, Kalyan West Pain Clinic of India, Mumbai, Maharashtra, India

<sup>2</sup>MD, Anaesthesiology, FPCI, Khetan Pain and Spine Clinic, Gorakhpur, India

<sup>3</sup>FIAPM, D. Anaesthesiology, Pain Clinic of India

<sup>4</sup>FIAPM, MD Anaesthesiology, Pain Clinic of India

**\*Address for Correspondence:** Dr. Prakash R Deshmukh, FIPP, FIAPM, D. Anaesthesiology, Spine and Pain Management Centre, Kalyan West Pain Clinic of India, Mumbai, Maharashtra, India

**E-mail:** [prakash\\_doc@yahoo.com](mailto:prakash_doc@yahoo.com)

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## ABSTRACT

Complex Regional Pain syndrome is a chronic condition that is most seen after trauma or other forms of injury to a body part. The role of inflammatory modulators is well-known in the development of CRPS, which is a chronic pain condition with uncertain etiology, often arising post-injury and characterized by severe, disproportionate limb pain. We report a unique case of CRPS following food allergy, a novel association not extensively explored in literature. A 36-year-old female developed debilitating wrist pain and swelling after consuming dried fish, along with her husband and a friend who experienced similar symptoms. Despite conventional therapies yielding minimal relief, a multidisciplinary approach, including Iguratimod and a stellate ganglion block, resulted in complete resolution within a month. The case challenges the conventional trauma-centric view of CRPS, suggesting a potential link between food allergy and its development. While CRPS is recognized for sympathetic nervous system involvement and neuroinflammation, this case introduces the concept of mast cell activation from food allergy as an underlying mechanism. Further exploration of this novel association may contribute to a broader understanding of CRPS pathogenesis, emphasizing the importance of considering diverse triggers beyond physical trauma in the evaluation and management of this complex pain syndrome.

**Key-words:** Complex Regional Pain Syndrome (CRPS), Allergy, Mast cells, IgE

## INTRODUCTION

Complex Regional Pain Syndrome (CRPS) is a chronic pain condition characterized by severe and disproportionate pain, often affecting limbs <sup>[1-3]</sup>. The exact cause is uncertain but typically arises after an injury or trauma. The pathogenesis involves abnormal responses in the peripheral and central nervous systems, leading to sustained pain signals.

Inflammatory processes and sympathetic nervous system dysfunction contribute to the complex nature of CRPS <sup>[4-6]</sup>. Clinical features include persistent, intense pain, often described as burning or throbbing, accompanied by skin temperature, color, and texture changes. Swelling, joint stiffness, and impaired motor function are standard. CRPS progresses through stages, with early symptoms such as excessive pain persisting beyond the expected healing period <sup>[7-9]</sup>. Timely diagnosis and a multidisciplinary approach, encompassing pain management, physical therapy, and psychological support, are crucial for effective treatment. Despite advancements, CRPS poses challenges, and comprehensive research is ongoing to unravel its intricacies and optimize therapeutic strategies <sup>[10]</sup>.

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It is a constellation of symptoms and signs that affect an individual, leading to a chronic pain condition that is unresponsive to routine therapy. It has not been found to have an underlying cause. However, various theories regarding the hypersensitization of neurons, misfiring of the sympathetic nerves and establishment of pain cycles are associated with it <sup>[11-13]</sup>. Cases of CRPS following trauma have been well-recorded and studied over the years. Here, we describe a uniquely presenting case of CRPS following food allergy.

### Case History

A 36-year-old female presented to the clinic with a history of pain and swelling in her right wrist for one month (Fig. 1). It was associated with stiffness throughout the day. It had not responded to any therapy and the patient had been having trouble with her routine life and work around the house. She had an episode of fever with body aches that lasted for one day, followed by swelling and pain in her right wrist and left ankle. There was no history of trauma to either of the joints.



**Fig. 1:** Pre-procedure swelling in right hand

She had no history of similar complaints in the past. However, her husband and a family friend had also experienced similar symptoms. They had a history of fever and body aches for one day, followed by swelling in their ankles. Their condition was also unresponsive to routine treatment.

On further questioning, it was found that all three of them had consumed dried fish at a house party on the day before they developed the symptoms, while the rest of the guests had not. The fish had been procured from a vendor they routinely purchased it from but was cooked

differently this time. It was concluded that there was an allergic reaction to the fish they consumed.

Upon examination, she had pain in her right wrist, exacerbated by any movement. There was wrist oedema (Fig. 2), and the skin appeared stretched and thin over the joint. She had allodynia as well. Her pincer grasp was positive in the right hand. Her investigations were within normal limits, and she was diagnosed with CRPS (according to Budapest criteria) of the upper limb.



**Fig. 2:** Post procedure reduction in edema

She had minimal relief with pregabalin and underwent a stellate ganglion block (Fig. 3) on the right side (drug given Ropivacaine plus lidocaine at C7 vertebra base of uncinate process under fluroscopic guidance with monitored anesthesia care). The patient, her husband, and their friend were given Iguratimod 50 mg twice daily for one month as an immunomodulator. All three were completely asymptomatic after one month.



**Fig. 3:** Ptsosis after stellate ganglion block

## DISCUSSION

CRPS is a well-known condition with various symptoms and signs unexplained by any single diagnosis. The earliest case of CRPS that was reported was in 1812 when a soldier with a bullet injury to his upper arm presented with chronic burning pain <sup>[12-15]</sup>. CRPS following trauma and burns has been explored in literature.

While the exact mechanism behind CRPS is yet to be defined, the role of the sympathetic nervous system in the development of CRPS is well known. Thoracic sympathectomy is a definitive treatment for upper limb CRPS <sup>[16-18]</sup>. Over the years, studies have explored the role of inflammatory mediators that result in sensitization of nociceptive neurons and neuroinflammation, leading to the development of CRPS. In 2001, Weber *et al.* used transcutaneous electrical stimulation to provoke neuroinflammation in healthy subjects. They concluded that neurogenic inflammation is facilitated in CRPS, hypothesizing that there is neuropeptide release from primary afferents <sup>[19]</sup>. A study published by Huygen *et al.* in 2004 demonstrated that mast cells are involved in the inflammatory reactions seen in CRPS <sup>[5]</sup>. They also confirmed that the levels of interleukin-6 (IL-6) and tumour necrosis factor alpha (TNF $\alpha$ ), and mast cell markers like tryptase are significantly higher in the affected extremity <sup>[20-22]</sup>. In 2006, a study was published that measured the levels of several proinflammatory cytokines in blister fluids from CRPS patients using multiplex bead array assay and confirmed that elevated levels of IL-6, IL-8, TNF $\alpha$  and other cytokines can be used in an investigative panel for the diagnosis of CRPS <sup>[6]</sup>. These studies indicate mast cell activation in patients of CRPS with an inherent role played by inflammatory cytokines released from the degranulation of mast cells in CRPS <sup>[22]</sup>.

Mast cell activation is essential for releasing cytokines and histamines that regulate the immune response in allergic reactions. It is well known that mast cells are activated via immunoglobulin G (IgG) and IgE in patients who develop food allergies <sup>[23-26]</sup>. While an earlier study from the Netherlands published in 2009 found that IgE-mediated hypersensitivity is not more common in CRPS patients compared to the general population, a subsequent study conducted in Orthopaedic patients concluded that a positive history of allergy is a predisposing factor for CRPS <sup>[27]</sup>.

This suggests that allergic reactions predispose a person to the development of CRPS. A recent case report described a patient who developed CRPS following bilateral total knee arthroplasty and was diagnosed with metal hypersensitivity <sup>[9]</sup>. However, no significant studies have explored a link between food allergy and the development of CRPS <sup>[28]</sup>.

In the case we presented, we could diagnose her CRPS based on her presenting features according to the Budapest criteria. Her pincer grasp sign was also positive. This sign has been observed in other patients with CRPS, which we have published in a separate case series <sup>[29]</sup>. The only predisposing event in this patient's case was the development of food allergy following fish consumption, which immediately preceded the CRPS. Thus, it may be safe to say that in this patient, food allergy was the underlying cause of her CRPS <sup>[30]</sup>.

## CONCLUSIONS

The patient, along with her husband and a friend, developed CRPS symptoms, including severe pain and swelling, after consuming the fish at a social event. The case challenges the conventional understanding of CRPS solely in the context of trauma, suggesting a potential link between food allergy and the development of this complex pain syndrome. The identification of a possible link between food allergy and CRPS opens avenues for further research. Investigating the role of mast cell activation and inflammatory mediators in CRPS development, particularly in the context of allergic reactions, could provide valuable insights into the pathogenesis of this condition.

Future studies should explore the prevalence of food allergies in CRPS patients and assess the effectiveness of targeted interventions, such as immunomodulators, in managing CRPS symptoms triggered by allergic responses. The link between food allergy and CRPS needs to be explored further, considering the similar underlying mechanisms between the two conditions.

## CONTRIBUTION OF AUTHORS

**Research concept-** Prakash R Deshmukh, Helee Khetan, Manjiri Ranade, Kailash Kothari

**Research design-** Prakash R Deshmukh, Kailash Kothari

**Supervision-** Prakash R Deshmukh

**Materials-** Prakash R Deshmukh, Helee Khetan, Manjiri Ranade

**Data collection-** Prakash R Deshmukh, Helee Khetan, Manjiri Ranade

**Data analysis and Interpretation-** Prakash R Deshmukh, Helee Khetan, Manjiri Ranade, Kailash Kothari

**Literature search-** Helee Khetan, Manjiri Ranade

**Writing article-** Prakash R Deshmukh

**Critical review-** Prakash R Deshmukh

**Article editing-** Prakash R Deshmukh

**Final approval-** Prakash R Deshmukh

## REFERENCES

- [1] Iolascon G, de Sire A, Moretti A, Gimigliano F. Complex regional pain syndrome (CRPS) type I: historical perspective and critical issues. *Clin Cases Miner Bone Metab.*, 2015; 12: 4-10.
- [2] Park J, Lee YJ, Kim ED. Clinical effects of pulsed radiofrequency to the thoracic sympathetic ganglion versus the cervical sympathetic chain in patients with upper-extremity complex regional pain syndrome. *Med.*, 2019; 98: 1-12.
- [3] Kim ED. A Prospective, Randomized Cross-Over Trial of T2 Paravertebral Block as a Sympathetic Block in Complex Regional Pain Syndrome. *Pain Phys.*, 2019; 5: 12-20.
- [4] Weber M, Birklein F, Neundo EB, Schmelz M. Facilitated neurogenic inflammation in complex regional pain syndrome. *Pain*, 2001; 91(3): 251-57. doi: 10.1016/S0304-3959(00)00445-0.
- [5] Huygen FJPM, Ramdhani N, van Toorenenbergen A, et al. Mast cells are involved in inflammatory reactions during Complex Regional Pain Syndrome type 1. *Immunol Lett.*, 2004; 91: 147-54.
- [6] Heijmans-Antonissen C, Wesseldijk F, Munnikes RJ, Huygen FJ, et al. Multiplex Bead Array Assay for Detection of 25 Soluble Cytokines in Blister Fluid of Patients with Complex Regional Pain Syndrome Type 1. *Mediators Inflamm.*, 2006; 12: 10-20.
- [7] Kanagaratham C, El Ansari YS, Lewis OL, et al. IgE and IgG Antibodies as Regulators of Mast Cell and Basophil Functions in Food Allergy. *Front Immunol.*, 2020; 11: 30-38.
- [8] Li X, Kenter K, Newman A, O'Brien Stephen. Allergy/Hypersensitivity Reactions as a Predisposing Factor to Complex Regional Pain Syndrome I in Orthopedic Patients. *Orthoped.*, 2014; 37: 86-91.
- [9] Sagoo NS, Sharma R, Alaraj S, Sharma IK, Bruntz AJ, Bajaj GS. Metal Hypersensitivity and Complex Regional Pain Syndrome After Bilateral Total Knee Arthroplasty: A Case Report. *JBJS Case Connect*, 2021; 11: 12-20.
- [10] Deshmukh P, Khetan H, Ranade M, et al. Pincer Grasp Pain- A New Sign in CRPS-1: A Case Series. *Acta Sci Orthop.*, 2021; 4: 19-25.
- [11] Walton KD, Dubois M, Llinas RR. Abnormal thalamocortical activity in patients with Complex Regional Pain Syndrome (CRPS) type I. *Pain*, 2010; 150(1): 41-51.
- [12] Smart KM, Ferraro MC, Wand BM, et al. Physiotherapy for pain and disability in adults with complex regional pain syndrome (CRPS) types I and II. *Cochrane Database of Systematic Reviews*, 2022; 12(5): 12-18.
- [13] Birklein F. Complex regional pain syndrome. *J Neurol.*, 2005; 252: 131-38.
- [14] Argoff CE. A focused review on the use of botulinum toxins for neuropathic pain. *Clin J Pain*, 2002; 12(2): 20-30.
- [15] Siongco PRL, Rosales RL, Moore AP, et al. Botulinum neurotoxin injections for muscle-based (dystonia and spasticity) and non-muscle-based (neuropathic pain) pain disorders: a meta-analytic study. *J Neural Transm*, 2020; 127(6): 935-51.
- [16] Birthi P, Sloan P, Salles S. Subcutaneous botulinum toxin A for the treatment of refractory complex regional pain syndrome. *PMR*, 2012; 4(6): 446-49.
- [17] Safarpour D, Jabbari B. Botulinum toxin A (BOTOX) for treatment of proximal myofascial pain in complex regional pain syndrome: two cases. *Pain Med.*, 2010; 11(9): 1415-18.
- [18] Lessard L, Bartow MJ, Lee J, Diaz-Abel J, et al. Botulinum toxin A. *Plast Reconstr Surg Glob Open*, 2018; 6(10): 18-47.
- [19] Alexander GM, Aradillas E, Schwartzman RJ, Grothusen JR, Goebel A. Retrospective study plasma exchange therapy in patients with complex regional pain syndrome. *Pain Phys.*, 2015; 18: 383-94.
- [20] Hill KP. Medical marijuana for treatment of chronic pain and other medical and psychiatric problems: a clinical review. *JAMA J Am Med Assoc.*, 2015; 313(24): 2474-83.
- [21] Andrae MH, Carter GM, Shaparin N, et al. Inhaled cannabis for chronic neuropathic pain: a meta-analysis of individual patient data. *J Pain*, 2015; 16(12): 1221-32.

- [22]Whiting PF, Wolff RF, Deshpande S, et al. Cannabinoids for medical use: a systematic review and meta-analysis. *JAMA J Am Med Assoc.*, 2015; 313(24): 2456-73.
- [23]Meng H, Johnston B, Englesakis M, Moulin DE et al. Selective cannabinoids for chronic neuropathic pain: a systematic review and meta-analysis. *Anesth Analg.*, 2017; 125(5): 1638-52.
- [24]Stockings E, Campbell G, Hall WD, et al. Cannabis and cannabinoids for the treatment of people with chronic noncancer pain conditions: a systematic review and meta-analysis of controlled and observational studies. *Pain*, 2018; 159(10): 1932-54. doi: 10.1097/j.pain.0000000000001293.
- [25]Almog S, Aharon-Peretz J, Vulfsons S, et al. The pharmacokinetics, efficacy, and safety of a novel selective-dose cannabis inhaler in patients with chronic pain: a randomized, double-blinded, placebo-controlled trial. *Eur J Pain*, 2020; 24(8): 1505-16.
- [26]Zernikow B, Wager J, Brehmer H, Hirschfeld G, et al. Invasive treatments for complex regional pain syndrome in children and adolescents: a scoping review. *Anesthesiol.*, 2015; 122(3): 699-707. doi: 10.1097/ALN.0000000000000573.
- [27]Cheng J, Salmasi V, You J, et al. Outcomes of sympathetic blocks in the management of complex regional pain syndrome: a retrospective cohort study. *Anesthesiol.*, 2019; 131(4): 883-93.
- [28]O'Connell NE, Wand BM, Gibson W, Carr DB, Birklein F, et al. Local anaesthetic sympathetic blockade for complex regional pain syndrome. *Cochrane Database Syst Rev.*, 2016; 2016(7): 1-57.
- [29]Yang S, Chang MC. Effect of repetitive transcranial magnetic stimulation on pain management: a systematic narrative review. *Front Neurol.*, 2020; 11: 1-14.
- [30]Isagulyan E, Slavin K, Konovalov N, et al. Spinal cord stimulation in chronic pain: technical advances. *Korean J Pain*, 2020; 33(2): 99-107.

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