Case Report

Orofacial complex regional pain syndrome

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Abstract: Complex regional pain syndrome (CRPS)—an extremely painful primary pain disorder related to trauma—is rare in the orofacial region. The authors describe a case of orofacial CRPS with a clinical phenotype that fits the Budapest diagnostic criteria. A 39-year-old female patient presented with left-side facial pain that had been untreated for 10 months. Symptoms included burning pain and allodynia accompanied by swelling and redness on exposure to cold or stress. The diagnosis was confirmed after stellate ganglion anesthetic block resulted in substantial improvement.

Keywords: complex regional pain syndrome, orofacial pain, stellate ganglion block

Introduction

Complex regional pain syndrome (CRPS) is a severe, disabling, chronic pain condition that generally affects the extremities and is posttraumatic in nature. It is rare in the orofacial region. CRPS is primarily caused by damage to or dysfunction of the peripheral nervous system or central nervous system (CNS) and is characterized by sensory, vasomotor, sudomotor, and motor clinical symptoms/signs and prolonged excessive pain [1]. CRPS was previously referred to as causalgia and reflex sympathetic dystrophy (RSD). Diagnosis of CRPS often relies on criteria comprising various clinical signs and symptoms [2]. In a 2003 workshop in Budapest, Hungary, experts in CRPS established new guidelines for CRPS diagnosis, which were published in a 2007 review. Sensitivity and specificity for a clinical diagnosis of CRPS were very good when 2 of 4 sign categories and 3 of 4 symptom categories were present. The clinical criteria include continuous pain disproportionate to the inciting event, at least 1 symptom in a minimum of 3 of the following 4 categories, at least 1 sign in a minimum of 2 categories mentioned below, and presence of signs and symptoms not explained by other diagnoses [1,2]. The diagnostic criteria for CRPS comprise 4 categories:

(1) Sensory changes such as allodynia (pain caused by non-painful stimuli) or mechanical hyperalgesia (increased response to a painful stimuli) [1].
(2) Vasomotor changes, including temperature asymmetry and skin color changes and color asymmetry [1].
(3) Sudomotor changes, including edema, perspiration changes and asymmetry, skin color changes (reddish or bluish), and bilateral skin temperature changes [1].
(4) Motor/trophic changes: In general, pain reduces muscle strength. Central motor symptoms include tremor and fixed dystonia–like postures (patients exhibit sustained muscle contractions causing repetitive and twisting movements). Trophic changes in hair, nail, and skin may also be present [1].

Starting in 1994, CRPS was classified as type I (patients without confirmed nerve injury; previously referred to as causalgia) [1]. About 15% of patients who received a diagnosis of CRPS were considered “without a diagnosis”. Hence, a third diagnostic subtype—CRPS not otherwise specified (CRPS-NOS)—was introduced to include these patients [1]. A 2003 population-based study of CRPS in the United States found it to be extremely rare (5.46 per 100,000 people per year for CRPS type I, and 0.8 per 100,000 people per year for CRPS type II). The male: female ratio was 4:1, median age at onset was 46 years, and more than 74% of patients recovered with little or no treatment [3].

The pathophysiology of CRPS is unclear and may involve several factors, which can change during the course of the condition. Currently, 3 pathophysiological mechanisms are considered important in CRPS pathogenesis: “neurogenic inflammation, autonomic dysfunction and CNS neuroplasticity” [4]. In addition, the roles of genetics and psychological factors are a matter of debate. CRPS of the face, head, and neck is rare, and very few such cases satisfy the disease diagnostic criteria. CRPS of the head and neck is characterized by burning pain, hyperalgesia, and hyperesthesia after craniofacial trauma or injury [4]. The preferred treatment is a series of stellate ganglion anesthetic blocks, which results in good outcomes for most patients with facial CRPS. This report describes diagnosis and treatment of a case of orofacial CRPS that began after traumatic injury to the trigeminal nerve.

Case Report

A 39-year-old female patient presented to the Center for Temporomandibular Disorders, Orofacial Pain and Dental Sleep Medicine, with pain on the left side of the face for 10 months. The pain began after an extraction of tooth number #12, in the maxillary left quadrant (maxillary left first premolar). The patient reported that the extraction was complicated and prolonged. She required 2 injections of local anesthetic during the procedure and reported that she felt pain despite these injections. Conventional analgesics did not relieve the pain after the extraction. Dental procedures, including treatment for dry socket, were performed with the hope of relieving the presumed odontogenic pain but instead resulted in worsening and spread of the pain. The patient was later advised to undergo root canal treatment for the adjacent tooth, #13 (maxillary left second premolar). The patient later underwent apicectomy for #13 and was then advised to have a bridge for #11 (maxillary left canine), #12, and #13. After the apicectomy for #13 did not relieve the pain, she consulted an orthonolaryngologist and a dentist. She was treated with various medications, including antibiotics, muscle relaxants, tricyclic antidepressants, flunarizine, prednisone 5 mg, tramadol, diclofenac, methylprednisolone, and vitamin B supplements. She then visited a pain physician who advised treatment with the anticonvulsant oxcarbazepine 150 mg and nortriptyline 25 mg. These medications resulted in a mild reduction in pain and swelling.

The pain level reported by the patient during the first appointment, as documented on a visual analogue scale (VAS), was 9/10. After the initial extraction, the pain was distributed in the left maxillary area (second division of the right trigeminal nerve CN-V2). During the next couple of months, the pain spread to the left temporomandibular joint and angle of the mandible (Figs. 1, 2). The patient reported that the pain worsened during periods of emotional stress and cold exposure. She also noticed changes in the color of the skin over the left maxilla, including redness of the maxilla and a darkened hue of the skin of the left maxilla. The patient reported that during periods of stress or exposure to cold there was an initial sensa-
tion of warmth followed by redness and swelling in the left maxilla and a feeling of heaviness. She also reported allodynia during activities such as face washing and applying cosmetics, especially on the nose and maxilla. Touching the gingiva adjacent to the extracted tooth during brushing or with fingers exacerbated the pain. During this period, pain quality changed from sharp or achy to burning, accompanied by swelling and a feeling of heaviness in the maxilla. The pain also started radiating to her left temporo-mandibular joint and the angle of the mandible. She also reported redness and tearing of the eye when pain was severe. She visited multiple health care providers, including dentists. All treatments administered, including dental procedures performed to relieve her pain, seemed to worsen the pain or improve it for only a few days.

Her medical, family, and psychosocial histories were noncontributory. Clinical examination revealed mild asymmetry in the left maxilla and diffuse swelling and redness in the left maxilla. The skin of the maxilla was somewhat dark, and skin pigmentation was darker than on the right side. Examination of the cranial nerve revealed allodynia and hyperalgesia to pin prick in the left maxilla of the left CN-V2 distribution. Temporomandibular joint examination showed no abnormalities. Trigger points in the left deep masseter and temporalis partially reproduced the aching pain. There was also hyperalgesia in the gingiva above #13.

Clinical examination revealed that intraoral and extraoral structures were within normal limits. An intraoral dental examination showed no dental pathology. Percussion and palpation of hard and soft tissues did not induce the patient’s chief complaints. A diagnostic anesthetic block (CN-V2 block and local infiltration) had no effect on the pain. Orthopantomography (OPG) and magnetic resonance imaging (MRI) showed no obvious maxillofacial or dental pathology. The clinical complaints, observations, negative radiographic findings, and International Association for the Study of Pain (IASP) diagnostic criteria indicated a provisional diagnosis of CRPS. Informed consent was obtained from the patient.

She was started on gabapentin 900 mg (Capsule Gabapentin, Sun Pharma Laboratories Ltd., Ranipool, India) in divided doses/day and nor-triptiline 25 mg (Tablet Primox, Sun Pharma Laboratories Ltd.) in divided doses/day. She reported a 50% decrease in pain. Owing to the partial relief, the medications were gradually tapered and stopped. Treatment with clonidine 0.1 mg/day (Tablet Arkamin, Unichem, Dehradun, India) was initiated, and the dose was gradually titrated to 1 mg in divided doses/day. The patient reported an 80% reduction in pain, but with no change in skin redness.

MRI scans of the brain and temporomandibular joint showed no abnormalities. CRPS patients respond well to sympathetic blockade; hence, the patient was referred to the Department of Anesthesiology and Pain Medicine for a left stellate (sympathetic) ganglion block. The patient underwent 2 consecutive ipsilateral stellate ganglion blocks (performed by an anesthesiologist under fluoroscopic guidance), separated by a 1-month interval, after which she reported a 90% reduction in facial pain and skin redness.

The clonidine dosage was gradually tapered to a maintenance dose of 0.6 mg in divided doses/day. Three months after the stellate ganglion blocks, the patient reported that pain was tolerable (1/10 on the VAS) and that episodes of facial redness were rare. She reported only 1 further episode of redness.

**Discussion**

CRPS rarely affects the orofacial region, perhaps, in part, because of the uniqueness of the trigeminal nerve. Neuropathic pain and CRPS after trauma to the head or dental procedures is rarer than CRPS caused by spinal injury or injury to the extremities, again because of differences in the trigeminal pain pathway. The nerve may be uniquely programmed for denervation of terminal branches, e.g., during shedding of deciduous teeth [4,5]. CRPS in the orofacial region usually starts after a traumatic event, like tooth extraction, or after trauma to the orofacial region, as in this case. It can begin immediately, or days, weeks, or even months, after an injury or inciting event. The present patient reported that the extraction was traumatic and complicated and that she could feel “pain” during extraction despite receiving 2 injections of local anesthetic. Preemptive analgesia is often recommended to prevent neuropathic pain. Extensive tissue damage and failure to obtain adequate analgesia during the procedure in this patient may have contributed to CRPS development.

CRPS initially presents as signs of “excessive post-traumatic inflammation”, which includes reddening, increased temperature, edema, pain during normal range of movement, and hyperalgesia, primarily caused by nociceptor sensitization. Unsuccessful treatment or failure to diagnose CRPS during the initial 3 to 6 months may result in CNS reorganization. The interval from initial injury to CRPS onset is variable. One hypothesis is that persistent peripheral stimulation with noxious stimuli leads to peripheral and central sensitization. These changes, coupled with impaired processing in the CNS, may lead to sympathetic hyperactivity and play a role in the pathogenesis of CRPS [6]. After severe trauma, the affected area may exhibit clinical features of CRPS, but the symptoms are usually self-limiting and resolve within 18 months. However, in the present patient, the initial traumatic extraction was followed by invasive procedures, including treatments for dry socket, apicoectomy, and crown cutting, that resulted in persistent peripheral stimulation, thereby contributing to widening of the receptive field and enhanced peripheral and central sensitization. Neuropeptides may partially explain sympathetic nervous system (SNS) hyperactivity resulting in acute symptoms, including asymmetry in skin color/temperature. Some evidence suggests the presence of central disturbance of the SNS and that inflammation and the SNS may be linked.

The present patient reported burning pain associated with hyperalgesia. Skin color changes could be interpreted as an orofacial analogue of CRPS of the extremities [4]. She also had clinical symptoms of CRPS, including pain deep in the affected area, autonomic symptoms, trophic changes, and

![Fig. 1 Frontal profile of patient with redness in the left maxillary and mandibular division of the trigeminal nerve](image1)

![Fig. 2 Lateral profile of patient with redness in the left maxillary and mandibular division of the trigeminal nerve](image2)
changes in perception, such as a foreign-body sensation and a feeling of increased size. The pain was exacerbated by movement, contact, temperature changes, and stress.

In this case study, the patient reported pain disproportionate to the initiating event. Her symptoms could be categorized as sensory (hyperalgesia and allodynia), vasomotor (changes and asymmetry in skin color), sudomotor/edema (edema), and clinical (sensory signs of allodynia to light touch and hyperalgesia to pin prick, obvious during sensory testing, vasomotor signs of skin color changes, and skin color asymmetry). These findings are consistent with the Budapest criteria for diagnosis of CRPS (3 of 4 symptom categories and 2 of 4 sign categories) [1].

Currently, there are no validated instruments that serve as gold standards for diagnosis. However, lab testing—including blood testing—plain radiography such as OPG, and advanced imaging techniques such as MRI are used to exclude diagnoses other than CRPS. A stellate ganglion block was used diagnostically and therapeutically to confirm the diagnosis in this case [1,4,6].

Prognosis is uncertain, but most patients with no comorbidities exhibit significant recovery. Incorrect or late diagnosis can result in chronic CRPS, which is associated with extensive disability and considerable socioeconomic burdens. Outcomes have not been studied in multicenter randomized controlled trials, and there is wide variation in reported primary outcomes from other studies. However, early therapeutic intervention is widely believed to prevent development of chronic disease. A treatment consensus has been developed and proposed as guidelines for the condition [1,7,8]. The guidelines focus on interdisciplinary management for functional restoration and suggest use of medications and blocks when a patient is unable to start a treatment regimen or fails to progress during treatment. The guidelines also suggest that selected patients should have immediate access to medications, blocks, and psychotherapy, if required. To begin the process of functional restoration, multiple modalities are often required at onset [1].

Patients with orofacial CRPS require rehabilitation and pain relief. Clonidine (α2 adrenergic agonist) is used to manage chronic pain, including CRPS. A recent systematic review suggested that epidural and intrathecal clonidine has a role in CRPS management [9], and a previous case study reported that oral clonidine was useful for a patient with sympathetically maintained pain [10].

Blockade of the somatic nerve or sympathetic ganglion is performed in more-complex cases of CRPS. Sympathetic nerve blocks (SNB) are the most common type of nerve blocks used. Although SNB have been used diagnostically and therapeutically in CRPS treatment, systematic reviews and randomized controlled trials have yielded little evidence of the effectiveness of such applications. At present, SNB are used empirically for management and have been found to be clinically effective, as they sometimes help to reduce pain and hasten rehabilitation [1]. The present patient reported that changes in facial color after exposure to cold and during stress interfered with her quality of life. Stellate ganglion block resulted in relief.

This is a detailed, comprehensive report of an unusual variant of a rare condition. Orofacial CRPS was successfully managed by clonidine 1 mg in divided doses/day and 2 consecutive ipsilateral stellate ganglion blocks. The clonidine dose was subsequently tapered to a maintenance dose of 0.6 mg in divided doses/day. The present findings highlight the importance of early referral, diagnosis, and multidisciplinary management for successful rehabilitation of patients with orofacial CRPS.

Conflict of interest
None.

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