TOPICAL REVIEW

Complex Regional Pain Syndrome in the Head and Neck: A Review of the Literature

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This article reviews the features of complex regional pain syndrome (CRPS), including its pathophysiology, diagnosis, and treatment. CRPS is a pathology that has been described as occurring almost always in a limb, but this review provides a focus on the literature reporting cases in which the face, head, and neck were affected. Very few cases were found that seemed to meet the International Association for the Study of Pain criteria for the disease. The clinical characteristics were similar to those of CRPS elsewhere in the body, with the main features being burning pain, hyperalgesia, and hyperesthesia starting after a trauma to the craniofacial region. Physical signs were reported less frequently. The treatment of choice was seen to be a series of stellate ganglion anesthetic blocks, which resulted in a good outcome in all the cases reviewed.

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The term *causalgia,* now called complex regional pain syndrome (CRPS) type II, was first described by Mitchell et al[1,2] in 1867 when they reported cases that occurred during the American Civil War. Soldiers who had sustained nerve injuries presented with intense burning pain and hypersensitivity to light mechanical stimulation, and the skin on the area of the lesion was red, hot, and shiny. Soldiers who had undergone surgical limb amputation reported similar symptoms at the stump end.[2,3] Cases occurring during World War II were reported later by Leriche.[4,5] He described some pain relief obtained in these patients after stripping the sympathetic plexus from major arteries. The term *reflex sympathetic dystrophy* (RSD), now called CRPS type I, was proposed by Evans[6] in 1946. This term implied an autonomic component affecting pain severity and trophic changes in the soft tissues.

Most of the cases of CRPS reported in the literature refer to limb injury, and very few cases are described occurring in the head and neck region. Accordingly, this review will focus on CRPS from an orofacial pain point of view, citing and discussing all the cases reported to date in the literature.

Taxonomy

A new classification of chronic pain by the International Association for the Study of Pain (IASP)[7] had the purpose of sim-

plifying diagnosis of traumatic neuralgias—to overcome the confusion created by the previously used terms *reflex sympathetic dystrophy* and *causalgia*—and of recognizing the fact that the influence of the autonomic nervous system on the disease is far from clear. The new name created is *complex regional pain syndrome*. Two types of CRPS have been proposed: CRPS type I (RSD) and CRPS type II (causalgia). Both terms refer to a syndrome characterized by spontaneous pain or allodynia and hyperalgesia, not limited to the territory of a single peripheral nerve, and associated with edema, abnormal skin blood flow, or abnormal sudomotor activity. The difference between the 2 types resides in the fact that in CRPS type II (causalgia), a lesion of a major nerve is reported, while an unspecified noxious event precedes CRPS type I (RSD).[8,9]

The influence of the autonomic nervous system on the pain is considered separately from the type of CRPS. Response to a sympatholytic procedure such as a stellate ganglion anesthetic block is used to differentiate between sympathetically maintained pain (SMP) and sympathetically independent pain (SIP); this is in addition to and independent of the diagnosis of CRPS type I or II.[9,10]

Pathophysiology

The mechanism by which pain and the other physical abnormalities develop in CRPS is not fully understood. Trauma seems to be the precipitating factor, causing damage to a peripheral nerve and inducing neurobiologic changes in both peripheral and central components of the nervous system. This is considered to reflect a deafferentation mechanism that produces abnormal afferent input into the central nervous system (CNS), which causes a painful sensation independent of or not proportional to any actual noxious stimuli applied to the nociceptors.[9,11,12]

The following modifications in the neural tissue have been observed and studied to try to understand the mechanisms through which pain is perceived:

1. Sensitization of nociceptive fibers[9,13,14]
2. Cross-activation between injured afferent fibers (ephaptic crosstalk)[12,15,16]
3. Sprouting of somatic afferent fibers from adjacent intact nerves[12,13]
4. Activation of afferent fibers by sympathetic efferents[12,13,17–22]
5. Neuroma formation[12,15,23]
6. Changes induced in the CNS[12,13,15,23–29]

After nerve injury, primary afferent neurons undergo biologic changes that lead to abnormal sensitization and spontaneous ectopic discharge[9,30]; in fact, spontaneous firing of nociceptive C-fibers and mechanoceptive Aß-fibers has been described.[14] These observations would explain some of the clinical symptoms reported by CRPS patients.[31]

The presence of ephapses between nerve fibers has been reported.[16] This abnormal connection allows transfer of stimuli from one nerve fiber to another with cross-activation of neural pathways. Such coupling would tend to amplify both ectopically and naturally generated impulse activity[15] and might be responsible for increased pain perception (allodynia, hyperalgesia, hyperpathia) in CRPS patients.

Gregg[12] observed nerve collaterals in association with zones of previous trigeminal nerve injury; these collaterals derived either from the proximal trunk of the same injured nerve or, in other cases, from adjacent nerves. Woolf et al[32] also described sprouting of A-fibers into lamina II of the dorsal horn of the spinal cord. What might happen is that, after this neural rewiring, lamina II, which usually receives only nociceptive inputs, will receive also non-nociceptive inputs that may be misinterpreted as noxious[13] and thereby cause pain even when light touch or pressure is applied to the skin (allodynia). In other cases, activation of the second-order neurons in the dorsal horn might be due to release of substance P and calcitonin gene-related peptide from normally non-nociceptive A-fibers after a phenotypic switch in these fibers following nerve injury.[13,33,34]

In 1944, Granit et al[17] suggested that a short-circuiting phenomenon develops where collateral sympathetic efferents synapse with afferent sensory fibers at the site of injury.[22] After partial nerve injury, sensory axons begin to express ß-receptors on their membrane and become sensitive to circulating catecholamines, and the same modification has been seen in the dorsal root ganglion neurons.[9,13,22,35] Moreover, nerve injury induces sprouting of sympathetic efferents around the cell bodies of sensory neurons in the dorsal root ganglion.[9,20–22] The influence of sympathetic activity on peripheral afferents may also occur indirectly when the release of norepinephrine stimulates the release from postganglionic sympathetic terminals of prostaglandins that sensitize sensory affer-

ents.[22,36] All these phenomena would lead to excitation of pain fibers by outgoing sympathetic impulses,[18,19] a mechanism that is thought to occur in SMP.

After nerve injury, if the nerve sheath has been damaged or displaced, the sprouting neurons will likely grow with a chaotic organization, which is called a neuroma. It is not a true neoplasm, but a disorganized structure that includes axoplasmic elements, myelin, Schwann cells, and connective tissue elements.[11,15,37] Neuromas are extremely sensitive to norepinephrine released by sympathetic efferents in the area of the lesion[38] and can produce spontaneous continuous pain as well as episodic pain triggered or aggravated by pressure or tension.[11] Axons that have been demyelinated may also become hyperexcitable and show spontaneous impulse discharge, mechanosensitivity, and rhythmic after-discharge in response to mechanical and electrical stimuli.[39–41] Their discharge pattern is very similar to the pattern of axons associated with neuromas, but the latter are usually more hyperexcitable.[15]

The possibility that central changes in neuronal excitability occur after damage in the periphery makes plausible the hypothesis that the CNS is involved in the origin of the continuous pain.[42] After nerve injury the trigeminal ganglion undergoes a certain degree of cell loss[43,44] involving massive degenerative responses in the central fiber projections to the trigeminal spinal nuclei[45,46]; this deafferentation process has been reported to initiate secondary changes in the receptive zones of the brain stem where neurons become tonically hyperactive,[28] but it is unclear whether these changes occur to a significant degree in trigeminal brain stem nociceptive neurons.[47–49] On the other hand, sensory cells located in the dorsal root ganglia and in the cranial nerve ganglia are normally intrinsically rhythmogenic,[50,51] but the magnitude of discharge is augmented significantly by chronic nerve injury.[47–52]

Other changes may occur at other sites in the CNS. Livingston[27] suggested that a constant source of pain would trigger a reverberating pattern of firing in the internuncial pool in the dorsal horn of the spinal cord, so that the neuronal activity would then become self-perpetuating and cause the pain to persist.[26,53] Recent studies[54–59] suggest that neuroimmunologic mechanisms may be involved in the development and maintenance of neuropathic pain, particularly those involving the role of interleukins and tumor necrosis factor.

N-methyl-D-aspartate (NMDA) receptors on central nociceptive neurons seem to be responsible for some of the clinical characteristics of neuropathic pain. Activation of these receptors requires a prior activation of an amino-3-hydroxy-5-methylisoxazole-4-proprionic acid (AMPA) or metabotropic receptor that causes expulsion of magnesium ions from the NMDA receptor. After stimulation by glutamate, this allows opening of the calcium-ion channels that depolarize the neuron. Calcium also stimulates intracellular synthesis of nitric oxide, which diffuses out of the neuron and causes ongoing presynaptic excitation and release of more glutamate.[11,13,60] The phenomenon of central sensitization that follows is a reflection of so-called "neuroplasticity" and is associated with increased neuronal excitability, hyperalgesia, and allodynia.[15,47,48]

The different mechanisms listed above are not mutually exclusive, and more than one is likely to occur in the peripheral nervous system and CNS after partial or complete nerve lesion.

In addition to pain, other abnormalities are seen in CRPS, and some of them are believed to be related to an altered function of the sympathetic system. These are edema, which may be diminished after sympathetic block,[61] and abnormalities in sudomotor activity and skin blood flow. It is thought that the vasculature develops an increased sensitivity to local cold-temperature stimuli and catecholamines[9]; this has been shown experimentally by testing the thermoregulatory response to skin cooling and warming, and suggests that both an inhibition and an activation of sympathetic reflexes may be present.

Trophic changes such as abnormal nail growth, increased hair growth, palmar and plantar fibrosis, thin glossy skin, and hyperkeratosis have been hypothesized to have an inflammatory pathogenesis,[9] and scintigraphic investigations strongly support an inflammatory component in CRPS.[22,62]

Signs and Symptoms of CRPS

The clinical presentation of CRPS patients is very heterogeneous. Pain is the prevalent symptom, but its characteristics can vary substantially. It can be spontaneous as well as evoked by stimuli, continuous as well as episodic or paroxysmal. The quality can be burning, shooting, throbbing, pressing, and aching. The location of the pain is usually deep inside the distal part of the affected extremity, and

Table 1 Prevalence of Signs and Symptoms of Somatic CRPS Compared to CRPS in the Head and Neck

Signs/symptoms	Somatic CRPS[63]	CRPS in the head and neck
Pain	75%	100%
Hyperalgesia/hyperesthesia	70%–80%	54%
Allodynia	70%–80%	38%
Dysesthesia	70%	8%
Edema	50%	23%
Sweating abnormalities	50%	15%
Skin color changes	75%–98%	46%
Skin temperature changes	75%–98%	46%

the intensity is disproportionate to the inciting event and decreases when the extremity is elevated.

Other abnormal sensations related to pain that are found in CRPS patients include mechanical and thermal hyperalgesia, hyperesthesia, allodynia, hyperpathia, and dysesthesia. In addition to these, signs of inflammation are present together with a number of typical abnormalities that are probably related to autonomic dysfunction. These include edema, abnormality of sweating (either hypohidrosis or hyperhidrosis), and skin changes whereby the skin appears mottled, reddish, bluish, or pale. The skin of the affected side can be either warmer or colder compared to the other side. There also may be trophic changes such as abnormal nail growth, with the nails becoming coarse and rigid; increased hair growth, where the hair can become either thin and sparse or coarse and thick; thin, glossy skin; and hyperkeratosis. Additional signs are stiffness in the joints, movement restriction, and muscle weakness.[9,30] Stiffness of the joints might lead to splinting of the affected part to prevent further aggravation of the pain and fibrosis due to decreased joint movement.

Table 1 shows the percentage of the prevalence of CRPS symptoms based on the values reported by Boas[63] and compared to the prevalence of symptoms of CRPS in the head and neck extrapolated from the cases in the literature (see below, and Table 2). It is evident that pain is the main feature of the disease when it occurs in the face, followed by hyperalgesia and/or hyperesthesia. The other signs or symptoms are much less frequent in comparison to CRPS elsewhere in the body.

Diagnostic Criteria

No standardized criteria for the diagnosis of CRPS are in common use. Bonica[30] introduced the idea of stages (grade 1, grade 2, and grade 3) related to the severity of the symptoms (severe, moderate, and mild, respectively). An RSD score system for diagnosis of CRPS was proposed by Gibbons and Wilson[64] based on the presence of the following in the patient's clinical presentation: allodynia/hyperpathia, burning pain, edema, color/hair growth changes, sweating changes, temperature changes, radiographic changes, quantitative measurements of vasomotor/sudomotor disturbances, bone scan with RSD, and response to sympathetic block. The patient was assigned 1 point for positive, a half point for equivocal, and no points if the criterion was negative or not mentioned. The condition was scored as follows: total RSD score less than 3 = patient considered not to have RSD; total RSD score between 3 and 4.5 = patient may have RSD; total RSD score 5 or more = patient probably has RSD. However, because of the lack of agreement on the definition and diagnostic criteria for CRPS (causalgia/RSD), in 1993 a special consensus workshop of the IASP examined and revised the IASP taxonomy for this disorder.[7,8] The names CRPS type I (RSD) and CRPS type II (causalgia) were suggested, and diagnostic criteria were listed (Fig 1). Associated signs and symptoms were also listed, but not used for the diagnosis of CRPS.[7] These include atrophy of the hair, nails, and other soft tissues; alterations in hair growth; loss of joint mobility; impairment of motor function, including weakness, tremor, and dystonia; and the presence of sympathetically maintained pain. To differentiate between SMP and SIP, a sympatholytic procedure is used without playing a role in the differential diagnosis of CRPS types I or II.

The criteria stated for the diagnosis of CRPS have yet to be validated in empirical studies. As one step in the validation process, Galer[65] proposed that the CRPS criteria should be able to distinguish CRPS patients from patients with other neuropathic pain syndromes of distinct and known etiology. In his study he compared CRPS patients to patients with painful diabetic neuropathy and concluded that the IASP diagnostic criteria may lack specificity, since 37% of diabetic subjects met the criteria listed for CRPS (Fig 1).

A further evaluation of IASP diagnostic criteria was performed by Bruehl et al.[66] Their survey showed that although sensitivity was quite high (0.98), specificity was low (0.36); they therefore proposed modifications to the criteria. Other

Criteria for CRPS type I (reflex sympathetic dystrophy)	Criteria for CRPS type II (causalgia)
•Condition develops after an initiating noxious event.	•Condition develops after a nerve injury.
•Spontaneous pain or allodynia/hyperalgesia occurs, is not limited to the territory of a single peripheral nerve, and is disproportionate to the inciting event.	•Spontaneous pain or allodynia/hyperalgesia occurs and is not necessarily limited to the territory of the injured nerve.
•There is or has been evidence of edema, skin blood flow abnormality, or abnormal sudomotor activity in the region of the pain since the inciting event.	•There is or has been evidence of edema, skin blood flow abnormality, or abnormal sudomotor activity in the region of the pain since the inciting event.
•The diagnosis is excluded by the existence of conditions that otherwise would account for the degree of pain and dysfunction.	•The diagnosis is excluded by the existence of conditions that otherwise would account for the degree of pain and dysfunction.

Fig 1 CRPS criteria.[7,8]

changes were also suggested by Harden et al[67]: separate the signs and symptoms into 2 different categories, and require the presence of signs and symptoms in each of 4 categories (sensory, vasomotor, sudomotor/edema, and motor/trophic).

Diagnostic Tests

The diagnosis of CRPS is mainly clinical; on the other hand, the following objective diagnostic procedures have been reported in the literature to confirm the diagnostic impression of autonomic, sensory, and motor dysfunction.

- Quantitative sensory tests. These tests measure subjective responses to superficial stimulation and provide information regarding peripheral nerve function of myelinated and unmyelinated afferent fibers responding to tactile, pressure, thermal, and noxious stimuli.[9]
- Laser doppler flowmetry. This procedure measures the skin blood flow in the tested area, which can be compared to that in the contralateral side.[9,68]
- Infrared thermography. Infrared thermography records the distribution of skin temperature. Each area of the skin is then compared with the identical contralateral area.[9,69,70]
- Quantitative sudometer axon reflex test. This test measures evoked sweat response and gives information on the function of the sudomotor reflex loops. It is a valuable test, but because it examines axon reflex, it cannot be used to test the effect of sympatholysis.[9,69,70]
- Bone scintigraphy. Bone scintigraphy gives information about changes occurring in bone vascularity. It tells only of significant changes that occur during the subacute period.[71,72] A 3-phase bone scan can give a more discriminative scintigraphic description of the disease.[73,74]
- Plain radiographs. Radiographic images can show the status of mineralization in the bones of the affected side in comparison to the contralateral side. Positive findings can be observed in chronic stages but can also be related to disuse atrophy.[75]
- Sympathetic nerve blocks. This method is a diagnostic and therapeutic treatment at the level of the sympathetic ganglia, where a local anesthetic, intravenous phentolamine, or regional intravenous blocks with an adrenergic blocking agent can be used. The side effects of such invasive procedures include miosis, ptosis, and enophthalmos (Horner's syndrome); recurrent laryngeal nerve injury leading to hoarseness; and occasional shortness of breath (from phrenic nerve block). Sympathetic nerve blocks can also result in hemidiaphragm paralysis. Loss of consciousness, seizures, and severe arterial hypotension may occur if the vertebral artery is injected. Air embolism and pneumothorax may occur.[76]

Treatment

There is no specific protocol designed for the treatment of either CRPS type I or type II, but several procedures and pharmacologic interventions have been tried. Not all treatments are effective in every patient; this is the reason why different treatments are often tried, starting with the least invasive techniques and evaluating the result and the patient's satisfaction with the treatment. The purpose of the therapy is to relieve pain and improve function. For pain control, some efficacy and very few and mild side effects have been seen with the use of transcutaneous electrical nerve stimulation[9,77] or peripheral nerve stimulation. The use of biofeedback has also been suggested to enable the patient to alter sympathetic activity and increase or decrease blood flow to the affected area.[78]

Many medications have been tried from among those used in the treatment of other types of neuropathic pain. Nonsteroidal anti-inflammatory drugs have been helpful in some cases,[9,10,15,79] as well as corticosteroids,[9,10,15,80,81] to address the peripheral component of the pain; opioids have also been useful in some patients.[9,10,13,82] Membrane stabilizers acting on sodium channels, such as phenytoin, carbamazepine,[10,13,15,83] mexiletine,[9,10,13,15,84] and local anesthetics,[9,10,13,15,85] have been suggested with the purpose of reducing the normal and ectopic firing of neurons. Good results have been reported with tricyclic antidepressants, with amitriptyline being the most frequently used.[9,10,82] Other kinds of antidepressants do not have the same effect on neuropathic pain,[10,86] but venlafaxine, a serotonin and norepinephrine reuptake inhibitor, has been suggested.[13,65] Gabapentin is a relatively new drug that is being used in trigeminal neuralgia and has been suggested for the treatment of other kinds of neuropathic pain[9,10,13]; it has also been used for the treatment of CRPS with encouraging results.[87] The use of topical capsaicin has been suggested to reduce peripheral inputs,[10,13] and another medication, N-acetylcysteine, has also been tried.[88]

Other methods that have been used are administration of scavengers of oxygen free radicals,[88,89] deep brain stimulation in the sensory thalamus and the medial lemniscus,[9,77] and epidural spinal cord stimulation.[9,77,90] With this last technique it was reported that CRPS patients had more satisfactory results than other chronic pain patients.[90]

If there is evidence of a sympathetic component of the pain (ie, SMP), other techniques or medications can be helpful. Since the activity of the sympathetic system aggravates the pain, inhibiting or reducing its tone should provide pain relief. One of the procedures that can be performed and has given good results in many studies[23,42,53,80,88,91-95] is a repetition of stellate ganglion blocks until the pain is significantly reduced, according to the patient's satisfaction. Different solutions have been injected, such as bupivacaine,[23,53,89,93,96] phenol,[91] morphine,[42] alcohol,[87] and unspecified local anesthetic.[42]

Another approach is through sympatholytic drugs that act on norepinephrine receptors. Guanethidine has been suggested,[13] because it decreases the presynaptic release of norepinephrine at the neuron site,[97-99] as has phentolamine,[13,15] which reduces the action of norepinephrine on the receptors by blocking both β_1 and β_2 receptors peripherally.[100-103] Probably the most widely used medication in this family is clonidine[9,10,13,15,104,105] because of its milder side effects. It acts centrally on presynaptic β_2 receptors as an agonist, and in doing so it decreases the release of norepinephrine from the presynaptic neuron.[98,99,101,102]

A more aggressive intervention, surgical cervical sympathectomy, has been described, with positive results.[15,106]

All the treatments designed to address the pain are meant to be accompanied by physical therapy to restore the patient's capacity to function.[9,78,79] The exercises to be performed need to be suited to the patient's state of the disease, starting with immobilization during the acute phase, proceeding to passive and active isometric exercises with stress-loading activities (scrubbing, walking, carrying weights), and finishing with isotonic training.[9,10] In the early stages, a process of gentle controlled stimulation via heat, massage, pressure, cold, vibration, and movement can help restore normal sensory processing.[10]

Appropriate counseling to manage psychologic issues such as depression, anxiety, anger, and personality disorders is indicated in some cases. Also, the cognitive-behavioral approach is often helpful to overcome pain avoidance, overprotection, movement phobia, and bracing.[10]

CRPS in the Head and Neck

A MEDLINE search for the cases of CRPS in the head and neck reported in the literature was performed. An account of the patients who did meet most of the IASP criteria, according to what was reported by the authors[23,42,53,81,88,91,93,104,106,107] in the original articles, is summarized in Table 2.

Table 2 Summary of CRPS Cases in the Head and Neck

Author	Age, sex	Etiology	Symptoms	Exacerbating factors	Physical findings	Treatment	Final outcome
Bingham 1947[106]	28, M	Penetrating shell fragment in the right cheek	Continuous burning pain in the V 1–3 distribution	Warmth (when in the sun or a very hot day), jaw movements (eating, much talking)	Marked hyperalgesia in the V 1–3 distribution	Cervical sympathectomy	Pain-free at 3 months follow-up
Bingham 1947[106]	23, M	Mortar wounds on the left cheek	Mild to moderate continuous burning pain in the V2 distribution	Heat, jaw movements, emotional upset	Hyperesthesia in the cheek	Cervical sympathectomy	Symptoms resolved, no follow-up
Behrman 1949[101]	Not reported	Extraction of second lower molar, followed by extraction of the first molar	Intense mandibular pain extending to the temple, inability to eat	Menstrual periods, alcohol, heat; also when patient becomes annoyed	None reported	SG blocks; sympathectomy was suggested	Not reported
Hanowell and Kennedy 1979[23]	59, M	Carcinoma of the tongue, total laryngectomy, total glossectomy, left radical neck dissection, segmental mandibulectomy	Continued perception of cancerous tongue; continuous burning pain, phantom tongue, intermittent stabbing pain left mandibular area, bilateral aching, and burning pain in the cheeks and temporal region	Hot and cold stimuli	Induration, hyperemia left side of the face and submaxillary area, hyperesthesia left lower face not associated with paresthesia or numbness, trigger point demonstrated medially on the remaining left side of the mandible, pressure precipitated stabbing left-sided facial pain	SG block with bupivacaine, 50 mg amitriptyline at night	After third block, was complete pain relief that continued beyond 3 months; phantom tongue sensation continued intermittently, though no pain
Khoury et al 1980[53]	60, M	Left maxillectomy for carcinoma	Severe burning pain left upper eyelid, nose, face, and upper lip	Light touch, cold air or water, mastication	Skin erythema and edema, hypersensitivity of the skin supra/infraorbital nerve distribution, coolness in the left side of the face (left side of face was 2 degrees colder than the right)	SG block with bupivacaine	75% to 85% improvement after last injection, some sensitivity over the upper lip
Teeple et al 1981[93]	38, M	Trauma to the left side of the face and shoulder by a sail boom	Left upper extremity and and shoulder pain	None reported	Left pupil was larger than the right. Left palpebral fissure was larger than right. Left side of the face was pale and cool	Aspirin, SG blocks (LA not specified)	Pain-free at 6 months follow-up; resolution of pupillary condition
Jaeger et al 1986[42]	33, M	Left maxillary molar extraction	Intense left-sided constant burning facial pain radiating from the preauricular area to the orbit, zygoma, and mandible; constant "pinching" sensation over the left eyebrow and mandible; photophobia left eye	Cold air/liquids chewing, smiling, light touch over certain area of face	Slight facial swelling, slight increase in temperature (0.65° C), trismus (33 mm opening), cheek hyperesthesia	SG block (LA unspecified)	Pain-free at 15-month follow-up

Table 2 (continued) Summary of CRPS Cases in the Head and Neck

Author	Age, sex	Etiology	Symptoms	Exacerbating factors	Physical findings	Treatment	Final outcome
Jaeger et al 1986[42]	31, M	Subtotal resection of frontal sinus osteoma, second operation to treat the burning pain by obliterating the frontal sinus, followed by postoperative infection and another operation to reopen the sinus	Constant burning across the forehead radiating to orbits and maxilla	None reported	Tender suprabrow scar, marked hyperesthesia in forehead, mild loss of pinprick/ light-touch sensation	Bilateral morphine sulfate SG blocks	66% improvement of facial pain, persistent dysesthetic scar pain
Veldman and Jacobs 1994[88]	47, M	MVA with zygomatic arch impaction and orbital floor fractures	Heavy dull pain at the right side of the head and face	Sound and facial animation	Hyperesthesia right side of the face, mild facial paresis, slight swelling, erythema, warmth, hyperhidrosis	N-acetylcysteine 600 mg, 3 times daily	Partial decrease in facial pain; decreased redness, swelling, and warm areas
Saxen and Campbell 1995[104]	32, F	Left maxillary molar extraction	Constant burning pain on the left infraorbital area	Hot and cold stimuli	2 x 2-cm erythematous infraorbital patch, hyperesthesia on the cheek	SG bupivacaine block, clonidine 0.1 mg, 2 times daily	Pain relief for 24 hours, responded well to clonidine, follow-up not specified
Arden et al 1998[91]	69, M	Right external carotid to distal vertebral artery transposition	Diffuse sharp pain on the right cheek, jaw, and tongue; excessive salivation	Hot and cold liquids, light touch, citric substances	Hyperesthesia on the lower part of the face, mild loss of light-touch sensation	SG block with bupivacaine/ phenol	80% to 85% relief at 3-year follow-up with minimal pain attacks
Arden et al 1998[91]	69, M	Right external carotid to distal vertebral artery transposition	Intense burning pain right cheek and jaw; excessive salivation, mild tongue claudication	Mastication, cold stimuli, citric substances	Hyperesthesia in the lower face	SG block with bupivacaine	50% to 70% reduction in pain at 2½-year follow-up
Figuerola et al 2000[81]	37, M	MVA leading to head and neck injury	Constant burning pain, hyperpathia (left side of face)	Chewing, smiling, any light touch to certain areas of face	Increased skin temperature and pallor over the left side of face, allodynia	Methyl-prednisolone 60 mg/kg/d	Complete relief of all symptoms after 6 days; no follow-up

SG = stellate ganglion; MVA = motor vehicle accident; LA = local anesthetic.

As with CRPS in other parts of the body, the signs and symptoms of CRPS in the face always start after a traumatic event, eg, a penetrating lesion on the skin of the face, tooth extraction, or surgical trauma to the craniofacial region (Table 2). Pain is always present, almost always of burning quality, and associated with hyperalgesia or hyperesthesia. Less frequently, skin color and temperature changes, numbness, and hypoesthesia were reported; rarely, edema and trophic changes involving the skin and hair were described, making the diagnosis of CRPS uncertain according to the IASP diagnostic criteria (Fig 1).

Rarely, diagnostic tests other than sympathetic blocks were performed (Table 2). This confirms that the diagnosis of CRPS is basically clinical; diagnostic procedures are used to confirm the diagnosis but are meaningless by themselves.

The treatment performed in almost all the patients (Table 2) was a series of injections in the stellate ganglion of local anesthetics—bupivacaine alone in most of the subjects, plus morphine or phenol in 1 patient each. The blocks were always preceded by a diagnostic trial to determine whether or not the sympathetic system had a role in maintaining the pain. The outcome was very

successful in all the patients and ranged from 50% to 100% pain relief. In 1 patient, the sympathetic blocks were associated with administration of 30 mg amitriptyline at nighttime.

Other sympatholytic modalities have been reported as alternatives to stellate ganglion blockade. In 1 patient, intravenous guanethidine was used in conjunction with physical therapy and produced partial improvement; in another, 0.1 mg clonidine was administered twice a day and resulted in substantial improvement of the pain. Two patients were treated with a more invasive procedure, cervical sympathectomy. The outcome was the complete resolution of symptoms. Pharmacologic treatment with methylprednisolone was used in a patient who refused the sympathetic block, and the result was excellent. N-acetylcysteine 600 mg 3 times a day was tried in another subject with moderately good results: the inflammation decreased, but the pain subsided only partially.

It is debatable whether the comparison between cases of CRPS in the head and neck with CRPS in other parts of the body may be valid because of the small number of reported cases of CRPS in the head and neck (Table 1). In addition, the case descriptions in the articles are brief, and authors may not have mentioned all of the symptoms.

Conclusions

In light of what the literature reviewed, CRPS in the head and neck seems to be a very rare condition, with only 13 cases clearly described since 1947. It may be that CRPS might be an atypical presentation of a more common disorder such as myofascial pain that not infrequently presents with different types of pain and abnormalities involving the autonomic system. Also, misinterpretation of patients' symptoms might have a role, together with the inflammation of the soft tissues that can cause some of the skin changes.

Another possibility is that the orofacial region may respond differently to trauma than would other locations, and this has been observed in animals.[108,109] Another possibility is that CRPS does occur, but it is very rare in the head and neck region.

Another important feature we found is that, although involvement of the sympathetic system is not required for the diagnosis of CRPS, the sympathetic system has a major role in the perpetuation of pain. In fact, sympatholytic procedures seem to be the treatment of choice, starting with a stellate ganglion block (with local anesthetic) that is repeated several times until the patient achieves a satisfactory result. Because relief from the pain and the other symptoms occurs after this treatment procedure, we do not find the recommendation of cervical sympathectomy justified, even though the reported results have been excellent.

Since only a few of the procedures suggested for the treatment of CRPS have been performed for the treatment of CRPS in the head and neck, it is impossible for us to conclude that the same approach works equally well in both situations. However, a series of sympathetic blocks with local anesthetics seems to be an effective procedure, regardless of the location of the symptoms.

The lack of controlled trials for the treatment of the cases reported does not allow us to reach definitive conclusions. Double-blind and controlled studies are necessary to evaluate the outcome of the treatments, but unfortunately the very small number of cases presented with this syndrome makes research difficult.

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