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Digital Clubbing in a Patient with the Complex Regional Pain Syndrome

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ABSTRACT

The complex regional pain syndrome (CRPS) is a chronic pain condition characterized by peripheral and central nervous system dysregulation with consequent persistent cutaneous hyperalgesia and allodynia. Although usually involving an extremity following injury or surgery, the condition has been described in persons with herpes zoster, migraine headaches, thalamic strokes, and trigeminal and glossopharyngeal neuralgias. Many post-traumatic and post-surgery cases resolve within the first year with a smaller subset progressing to a chronic form in which the inflammatory response ("warm complex regional pain syndrome") is eventually superceded by autonomic nervous system abnormalities ("cold complex regional pain syndrome").

Objective: To report a case of the complex regional pain syndrome with the added feature of digital clubbing.

Keywords

Complex regional pain syndrome, Clubbing, Dysautonomia, Reflex sympathetic dystrophy, Sudeck atrophy.

Case Report

The patient is a 77-year-old man who injured his thumb in a table saw accident at the age of 57. The wound was closed by primary intention and subsequently became infected with *Pseudomonas aeruginosa* and *fusobacterium necrophorum*. Although the infection responded to two weeks of outpatient treatment with intravenous imipenem, the thumb remained warm, tender, and swollen for approximately 6 months after which it became cold, cyanotic, and exquisitely hypersensitive and tender to touch. Over the ensuing 20 years the injured thumb became atrophic and the fingernails on the affected side developed early signs of clubbing (Figure 1).

Discussion

The complex regional pain syndrome (CRPS) is a chronic pain condition characterized by peripheral and central nervous system dysregulation with consequent persistent cutaneous hyperalgesia and allodynia. Although usually involving an extremity following injury or surgery, the condition has been described in persons with herpes zoster, migraine headaches, thalamic strokes, and trigeminal and glossopharyngeal neuralgias. Many post-traumatic and post-surgery cases resolve within the first year with a smaller subset progressing to a chronic form in which the inflammatory response ("warm complex regional pain syndrome") is eventually superceded by autonomic nervous system abnormalities ("cold complex regional pain syndrome") [1-3].

Using a murine model of cutaneous mechanical hypersensitivity and allodynia, Cao and associates have shown that the normal conduction of pain signals by dorsal horn parvalbumin-positive (PV+) interneurons onto primary afferent terminals and excitatory interneurons is mediated by the retinoic acid alpha receptor (RARα). Deletion of RARα in PV+ interneurons or the use of a RARα antagonist in the spinal cord prevented the development of mechanical hypersensitivity and allodynia in their murine model, supporting the importance of central nervous system (CNS) sensitization in CRPS and raising the prospect that medications that inhibit RARα may prove useful in the treatment of this disorder [4].

Other studies have emphasized the roles that Schwann cells, satellite cells in the dorsal root ganglia, spinal microglia and

astrocytes, neuropeptides, the sympathetic nervous system, and proinflammatory components of the immune system play in the generation of neuropathic pain including that associated with CRPS [5-16].

As in the presented case, the affected limb in patients with CRPS may become dystrophic with signs of sympathetic nervous system hyperactivity. These findings were previously described in patients with reflex sympathetic dystrophy (RSD), an acronym now considered synonymous with type I CRPS (i.e., symptoms and signs are not limited to the distribution of a single peripheral nerve). A variety of clinical features have been described in patients with RSD/type I CRPS including those seen in the presented case's thumb – cold and cyanotic skin, muscle wasting, tremor, and brittle and clubbed nails [17-19] (Table 1).

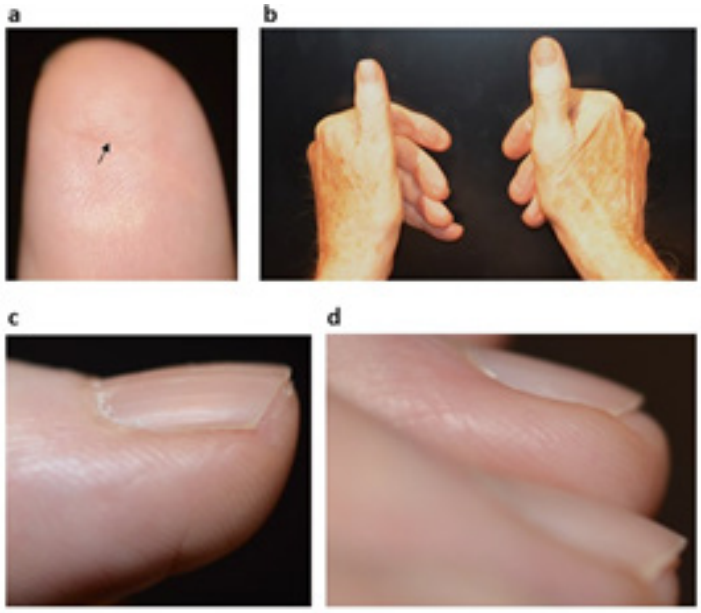

Figure 1: Photographs of the injured hand.
a. Site of injury (arrow). b. Atrophy of the left thumb and thenar eminence. c. Clubbing of the left thumbnail, d. Clubbing of the fingernails of digits 2 & 3. Note the convex curvature of the clubbed nails.

Table 1: The International Association for the Study of Pain diagnostic criteria for CRPS*.

Continuing pain which is disproportionate to any inciting event
Must report at least one symptom in three of the four following categories: Sensory: hyperalgesia and/or allodynia; Vasomotor: temperature asymmetry and/or skin color changes and/or color asymmetry; Sudomotor: edema and/or sweating changes and/or sweating asymmetry; Motor/trophic: decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia).
Must have at least one sign at the time of evaluation in two or more of the following categories: Sensory: hyperalgesia (to pinprick) and/or allodynia (to light touch or deep somatic pressure or joint movement); Vasomotor: temperature and/or skin color changes and/or asymmetry; Sudomotor: edema and/or sweating changes and/or sweating asymmetry; Motor/trophic: decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nails, skin).
There is no other diagnosis that better explains the signs and symptoms.

Table 2: Pathophysiology of CRPS*.

Nerve injury
Ischemic reperfusion injury or oxidative stress
Central sensitization
Peripheral sensitization
Altered central nervous system function or sympathoafferent coupling
Inflammatory and immune related factors
Brain changes
Genetic factors
Psychologic factors

There are two principal signs of clubbing of the fingers, both of which are the result of proliferation of the tissue between the nail plate and underlying bone: 1. The normal nail plate makes an angle of 20°or more dorsalward with the axis of the finger. Diminution in this angle is evidence of clubbing and may be associated with increased convexity of the nail; 2. The Floating Nail sign, which is demonstrated by showing a "sponginess" or rebound when the base of the nail is compressed against underlying bone [20].

CRPS management options include physical and occupational therapy, biphosphonates, calcitonin, subanesthetic intravenous ketamine, free radical scavengers, oral corticosteroids, and spinal cord stimulation (Table 3). Unfortunately, despite treatment, the majority of persons with CRPS experience a significant reduction in their quality of life.

Table 3: Treatments for CRPS*.

TREATMENT		Supporting randomized clinical trials
Physical & occupational therapy	Standard	Positive
Oral corticosteroids (for acute CRPS)	Standard	Positive
Anticonvulsants	Standard	Equivocal
Analgesic antidepressants	Standard	None
Transdermal lidocaine	Standard	None
Opioids	Standard	None
Sympathetic nervous system block	Standard	Negative
Spinal cord stimulation	Standard	Positive (< 5 year efficacy)
Pain focused psychological therapy	Standard	None
Graded motor imagery or mirror therapy	Uncommon	Positive
Calcitonin	Uncommon	Positive
Vitamin C (prevention after injury)	Uncommon	Positive
Topical dimethylsulfoxide (DMSO)	Uncommon	Positive (warm CRPS)
Oral N-acetylcysteine	Uncommon	Positive (cold CRPS)
Biphosphonates	Emerging	Positive
Subanesthetic intravenous ketamine	Emerging	Positive
Intravenous immunoglobulin	Emerging	Positive
Oral tadalafil	Emerging	Positive
Intrathecal baclofen (CRPS + dystonia)	Emerging	Positive
Low dose oral naltrexone	Emerging	None

*Derivation of table data: Birklein F, Ajit SK, Goebel A, Perez RSGM, Sommer C. Complex regional pain syndrome-phenotypic characteristics and potential biomarkers. Nat Rev Neurol. 2018;14(5):272–284.

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References

1. Taylor S-Su, Noor N, Urits I, et.al. Complex regional pain syndrome: a comprehensive review. Pain Ther. 2021; 10: 875-892.
2. Ott S, Maihöfner C. Signs and symptoms in 1,043 patients with complex regional pain syndrome. J Pain. 2018; 19: 599-611.
3. Marinus J, Moseley GL, Birklein F, et al. Clinical features and pathophysiology of complex regional pain syndrome. Lancet Neurol. 2011; 10: 637-648.
4. Cao B, Scherrer G, Chen L. Spinal cord retinoic acid receptor signaling gates mechanical hypersensitivity in neuropathic pain. Neuron. 2022; 110: 4108-4124.
5. Scholz J, Woolf CJ. The neuropathic pain triad: neurons, immune cells and glia. Nat Neurosci. 2007; 10: 1361-1368.
6. Schlereth T, Drummond PD, Birklein F. Inflammation in CRPS: role of the sympathetic supply. Auton Neurosci. 2014; 182: 102-107.
7. Clark JD, Tawfik VL, Tajerian M, et al. Autoinflammatory and autoimmune contributions to complex regional pain syndrome. Molecular Pain. 2018; 14: 1-13.
8. Baronio M, Sadia H, Paolacci S, et al. Molecular aspects of regional pain syndrome. Pain Res Manag. 2020; 2020: 7697214.
9. Birklein F, Ajit SK, Goebel A, et al. Complex regional pain syndrome- phenotypic characteristics and potential biomarkers. Nat Rev Neurol. 2018; 14: 272-284.
10. Dirckx M, Stronks DL, Van Bodegraven-Hoff EAM, et al. Inflammation in cold complex regional pain syndrome. Acta Anaesthesiol Scand. 2015; 59: 733-739.
11. Sommer C, Leinders M, Üçeyler N. Inflammation in the pathophysiology of neuropathic pain. Pain. 2018; 159: 595-602.
12. Birklein F, Drummond PD, Li W, et al. Activation of cutaneous immune responses in complex regional pain syndrome. J Pain. 2014; 15: 485-495.
13. Knudsen LF, Terkelsen AJ, Drummond PD, et al. Complex regional pain syndrome: a focus on the autonomic nervous system. Clin Auton Res. 2019; 29: 457-467.
14. Kortekaas MC, Niehof SP, Stolker RJ, et al. Pathophysiological mechanisms involved in vasomotor disturbances in complex regional pain syndrome and implications for therapy: a review. Pain Pract. 2016; 16: 905-914.
15. David Clark J, Tawfik VL, Tajerian M, et al. Autoinflammatory and autoimmune contributions to complex regional pain syndrome. Mol Pain. 2018; 14: 1744806918799127.
16. Kohr D, Singh P, Tschernatsch M, et al. Autoimmunity against the β2 adrenergic receptor and muscarinic-2 receptor in complex regional pain syndrome. Pain. 2011; 152: 2690-2700.
17. Stanton-Hicks M. Complex regional pain syndrome (type 1 RSD; type II, causalgia): controversies. Clin J Pain. 2000; 16: S33-S40.
18. Żyluk A, Puchalski P. Effectiveness of complex regional pain syndrome treatment: a systematic review. Neurol Neurochir Pol. 2018; 52: 326-333.
19. Urits I, Shen AH, Jones MR, et al. Complex regional pain syndrome, current concepts and treatment options. Curr Pain Headache Rep. 2018; 22: 10.
20. DeGowin RL, DeGowin ed, DeGowin amp, et al. Diagnostic Examination. 6th Edition. New York. McGraw-Hill. 1994; 664-667.