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Symptomatic Improvement of Post-Vaccination Complex Regional Pain Syndrome After Surgical Treatment for Underlying Carpal Tunnel Syndrome in an Adolescent Boy

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Abstract

A 15-year-old adolescent boy developed severe, treatment-refractory upper limb complex regional pain syndrome (CRPS) after a COVID-19 vaccination, characterized by initial hand paresthesia that progressed to widespread severe pain, allodynia, marked range-of-motion limitations, trophic changes, and insomnia. Although nerve conduction studies (NCS) were reported as normal, severe allodynia prevented distal evaluation. We devised a stepwise diagnostic block, which isolated the primary pain generator to the carpal tunnel. A meticulous re-evaluation of the NCS data also revealed findings consistent with minimal carpal tunnel syndrome (Padua class 2). Surgical intervention, including median nerve neurolysis, tenosynovectomy, and release of the ulnar artery, based on these findings, resulted in remarkable and sustained improvement in pain, insomnia, and upper limb function over a two-year follow-up. This case highlights that underlying peripheral pathology, identifiable by innovative diagnostic blocks and careful NCS re-evaluation, can be a treatable primary driver of severe post-vaccination CRPS.

Categories: Neurology, Pain Management, Orthopedics
Keywords: carpal tunnel syndrome, complex regional pain syndrome, covid-19 vaccines, nerve conduction study, pain management, stepwise diagnostic block

Introduction

Complex regional pain syndrome (CRPS) is a challenging condition characterized by severe pain that is disproportionate to any inciting event [1]. Because CRPS is a clinical diagnosis of exclusion based on non-specific signs and symptoms, with no confirmatory test or validated diagnostic biomarker, establishing an accurate diagnosis remains inherently difficult [1,2]. It is reported that CRPS can be triggered not only by major trauma but also by minor needle-stick injuries, such as vaccinations, blood sampling, or blood donations [3-5]. While localized vaccine-related upper limb and shoulder conditions, including shoulder injury related to vaccine administration (SIRVA), are recognized clinical entities [6], vaccination can also rarely be followed by widespread neuropathic pain across the entire extremity. In younger patients, the involvement of psychological problems is sometimes suggested due to the dramatic nature of the symptoms [7]. However, a systematic review found no consistent association between psychological factors and the development of CRPS [8].

Recently, the possibility that treatable peripheral nerve disorders may underlie the widespread symptoms of CRPS has been pointed out [9]. Based on our clinical findings demonstrating that distal compressive neuropathies can cause proximal shoulder pain and dysfunction, we have proposed two new concepts to explain this pathophysiology: retrograde neuropathic pain (RNP) and parallel crush syndrome (PCS) [10]. RNP is a phenomenon in which pain from a distal nerve disorder, such as carpal tunnel syndrome (CTS), occurs retrogradely in a proximal region. PCS, on the other hand, refers to the interaction between parallel-running nerves. This phenomenon describes how damage to a major nerve trunk, such as in CTS or cubital tunnel syndrome, can lower the pain threshold in the territories of adjacent smaller nerves, like the radial or musculocutaneous nerves, making them symptomatic. Unlike double crush syndrome [11], this concept also includes the pathomechanism whereby concurrent damage to multiple parallel nerve trunks, even without a serial lesion, can cause extensive symptoms. Consistent with this concept, it has been reported that CTS can concurrently impair ulnar nerve conduction - particularly in the sensory fibers - at Guyon's canal [12], and that such ulnar nerve involvement can improve following carpal tunnel release alone [13].

We experienced a case of an adolescent boy who developed severe upper limb CRPS following a COVID-19 vaccination. The symptoms were refractory to treatment at a university hospital. We diagnosed him with underlying CTS and performed surgical treatment, resulting in remarkable symptomatic improvement. Here, we report this case and discuss the involvement of peripheral nerve disorders in the pathophysiology of CRPS from the perspective of RNP and PCS.

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Case Presentation

Patient characteristics

A 15-year-old adolescent boy presented with a chief complaint of pain, paresthesia, and motor dysfunction of the entire left upper limb.

History of present illness

After receiving his third COVID-19 vaccination in his left upper arm, the patient developed paresthesia on the radial side of his left hand. As the symptoms progressively worsened - leading to severe pain and paresthesia in the entire upper limb distal to the elbow, erythema, swelling distal to the wrist, and insomnia - he was referred early to the neurology department of a university hospital. Nerve conduction studies (NCS), laboratory blood tests, and magnetic resonance imaging (MRI) of the left upper arm injection site, cervical spine, and brain revealed no obvious abnormalities. Because of the persistent pain, he underwent multidisciplinary evaluations and intensive treatment at the university hospital's pain clinic, including medications, more than five brachial plexus blocks, and two sessions of pulsed radiofrequency treatment. During this period, his condition was officially certified as a vaccine-related adverse event (residual disability) by the Japanese Ministry of Health, Labour and Welfare. As the symptoms failed to improve despite ongoing university hospital care, he was referred to our institution 11 months after symptom onset and underwent surgical intervention at one year post-onset.

Initial examination

Left shoulder flexion was limited to 30 degrees, and elbow flexion was limited to 45 degrees; the range of motion of the wrist and fingers was unmeasurable due to pain. The patient reported pain throughout the upper limb, but it was particularly severe distal to the elbow and more pronounced on the medial side than the lateral side. A strong Tinel sign was elicited by light tapping over the carpal tunnel. Allodynia was present in the median nerve territory of the fingertips, provoked even by a 2.83 Semmes-Weinstein monofilament. He met the Budapest criteria [1]. Objective findings included delayed nail growth on the affected fingers compared to the contralateral side (Figure *1*, Video *1*).

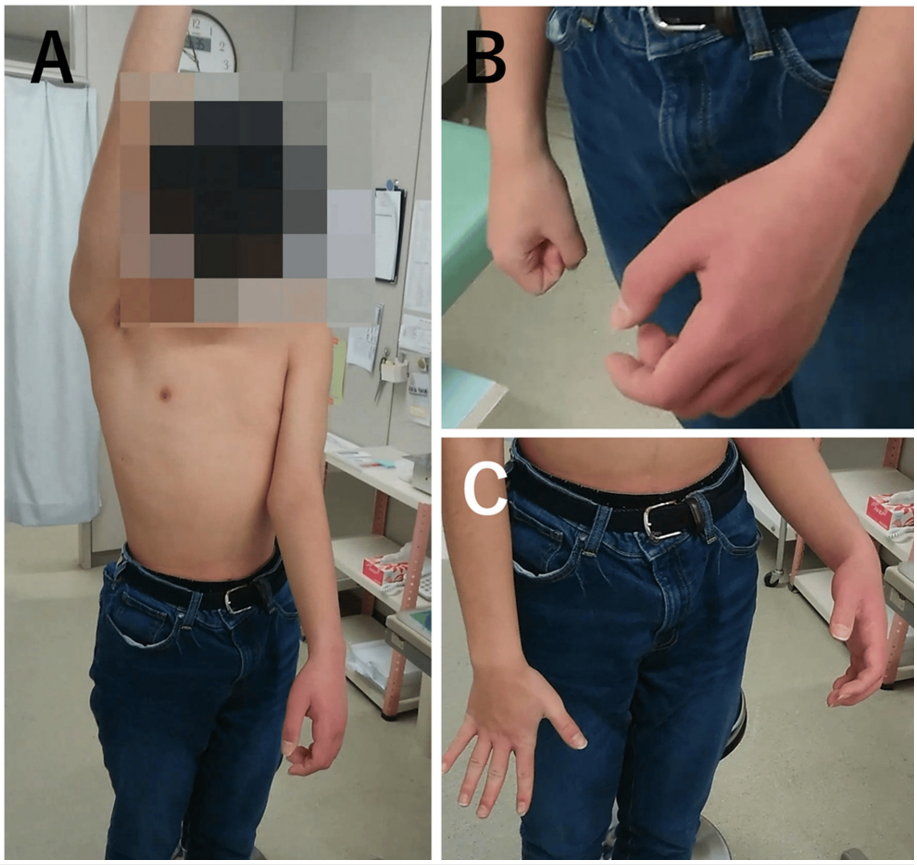


FIGURE 1: Clinical presentation at the initial examination showing restricted range of motion.

(A) Shoulder flexion, (B) finger flexion, and (C) finger extension were limited compared to the contralateral side.



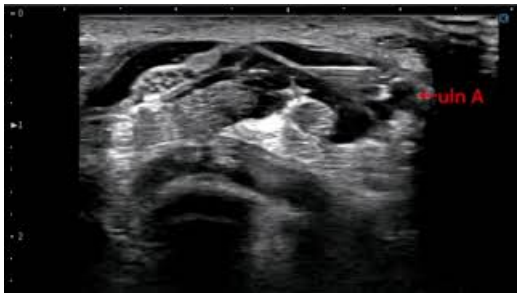
VIDEO 1: Clinical presentation at the initial examination showing restricted range of motion.

View video here: https://www.youtube.com/watch?v=4pU8o6f1SYo

Diagnostic blockade

First, to circumvent the difficulty in the evaluation caused by severe allodynia, an ultrasound-guided brachial plexus block using an axillary approach was performed using 1% lidocaine. Thirty minutes post-block, the limb could be temporarily touched. However, active range of motion distal to the elbow remained unchanged, and despite the sensory numbness, the patient reported persistent subjective pain.

Next, to identify the primary pain generator, an ultrasound-guided median nerve block was performed at the proximal carpal tunnel using 0.75% ropivacaine. This was performed concurrently with hydrodissection of the flexor tendons and the ulnar artery. On ultrasound, strong adhesions were suspected between the median nerve and the flexor digitorum tendon to the middle finger. An increase in arterial pulsation was also confirmed following hydrodissection around the ulnar artery (Video *2*).



VIDEO 2: Ultrasound-guided median nerve block (diagnostic block) at the proximal carpal tunnel.

Using an in-plane approach, a 23-gauge catheter needle was inserted from the radial side. Hydrodissection was performed sequentially, targeting the dorsal aspect of the median nerve, followed by the flexor tendons, the palmar aspect of the nerve, the synovial adhesions observed between the nerve and tendons, and finally, the tissue surrounding the ulnar artery.

View video here: https://youtu.be/GEx67tQGi_U

One hour after the proximal block, at a time point when the lidocaine effect had dissipated and only the distal ropivacaine block was active, the patient was re-evaluated. This revealed a near-complete recovery of range of motion for the entire upper limb, including the shoulder, and a complete resolution of allodynia. The effects of the nerve block and hydrodissection lasted for two days but relapsed on the third day (Figure *2*, Video *3*).

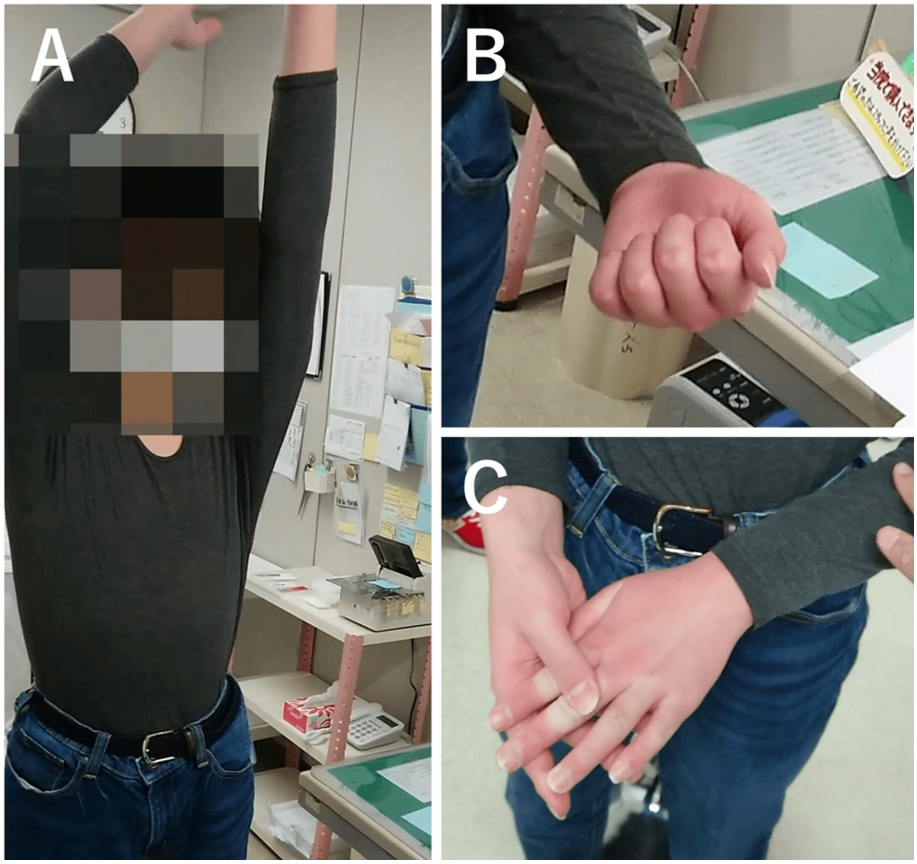


FIGURE 2: Temporary improvement after the stepwise diagnostic block.

With only the long-acting ropivacaine block at the proximal carpal tunnel active, the affected side showed improved (A) shoulder flexion range of motion (ROM), (B) finger flexion ROM, and (C) finger extension ROM, and the patient became able to touch the affected hand with the contralateral hand.



VIDEO 3: Temporary improvement after the stepwise diagnostic block

View video here: https://www.youtube.com/watch?v=CC3SLzDTSp0

Nerve conduction study

The NCS performed at the previous hospital was reported as within normal limits for both the median and ulnar nerves. However, our detailed re-evaluation of this data revealed that the distal motor latency of the left median nerve, stimulated to the abductor pollicis brevis at 7 cm, was 3.3 ms. In contrast, the distal motor latency of the left ulnar nerve, stimulated to the abductor digiti minimi at 7 cm, was 2.5 ms. This demonstrated a 0.8 ms distal motor latency delay for the median nerve compared to the ulnar nerve over an identical distance. Furthermore, the affected median nerve distal motor latency was mildly delayed compared to the contralateral median nerve distal motor latency of 3.0 ms (Table *1*, Figure *3*).

Nerve/Side	Stimulation Site	Latency (ms)	Duration (ms)	Amplitude (mV)	Area (mV·ms)	Segment	Distance (mm)	Interval (ms)	NCV (m/s)
Median/Left	Wrist	3.3	5.3	12.9	40.3	Wrist	70.0	3.3	-
Median/Left	Elbow	7.1	5.4	12.4	38.9	Wrist-Elbow	220.0	3.8	57.3
Ulnar/Left	Wrist	2.5	6.5	8.2	26.7	Wrist	70.0	2.5	-
Ulnar/Left	Below Elbow	5.9	6.7	7.6	27.4	Wrist-B.Elbow	215.0	3.4	62.9
Ulnar/Left	Above Elbow	7.6	6.7	7.5	27.7	B.Elbow-A.Elbow	100.0	1.7	57.5
Median/Right	Wrist	3.0	4.9	14.7	43.3	Wrist	70.0	3.0	-

TABLE 1: Nerve conduction study findings from the previous hospital.

B.Elbow: below elbow; A.Elbow: above elbow; NCV: nerve conduction velocity.

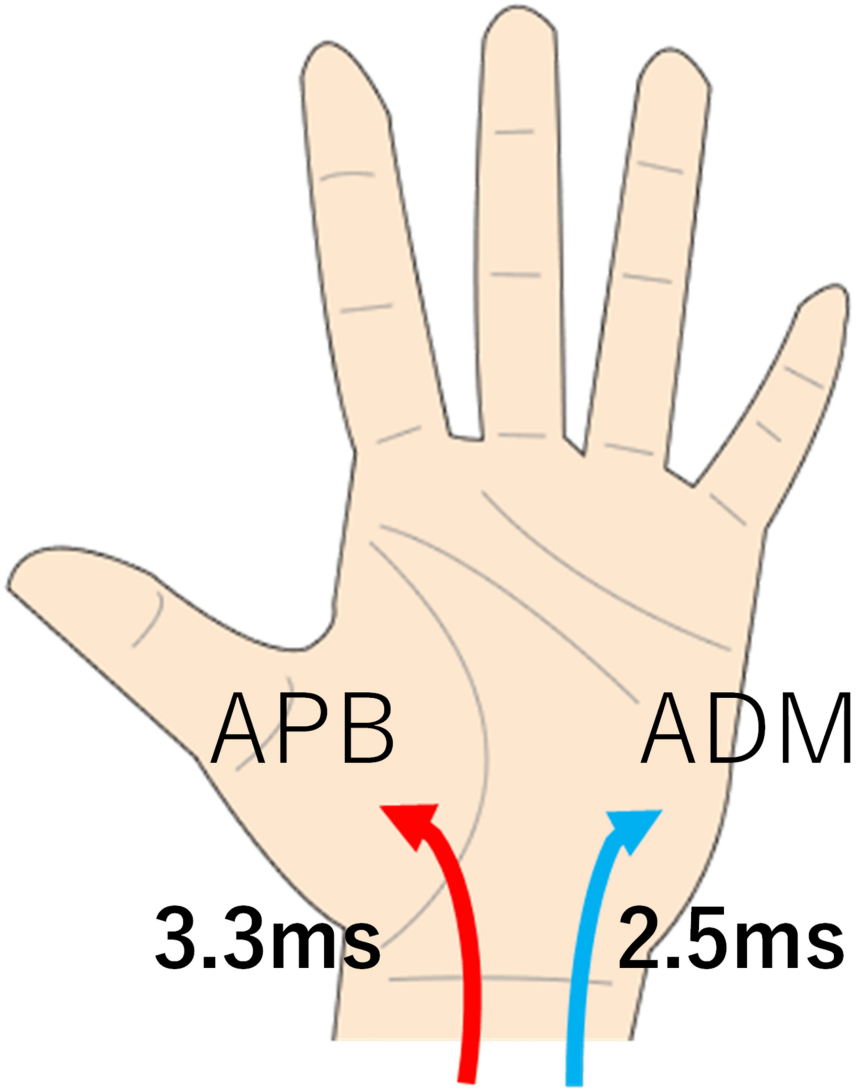


FIGURE 3: Schematic illustration of the nerve conduction study findings from the previous hospital.

The distal motor latency of the affected (left) median nerve recorded at the abductor pollicis brevis (APB) was 3.3 ms, showing a 0.8 ms delay compared to the ulnar nerve distal motor latency (2.5 ms) recorded at the abductor digiti minimi (ADM) over the same 70 mm stimulation distance.

Image credit: This illustration was created by the authors using Microsoft PowerPoint (Microsoft, Redmond, WA).

Surgical and intraoperative findings

Based on the diagnostic block results, the primary etiology of the pain was determined to be a pathology centered on CTS, and surgery was performed in accordance with our previously reported procedure [10]. First, Guyon's canal was released, and the ulnar nerve and vascular bundle were dissected. Next, upon transecting the transverse carpal ligament, strong adhesions were found between the median nerve and the underlying tissues. Cessation of blood flow in the vasa nervorum on the nerve surface was also confirmed in this area. Following external neurolysis of the median nerve, reperfusion was observed. Tenosynovial proliferation was noted around the flexor tendons, and this synovium was also strongly adhered to the median nerve. We dissected the median nerve from the flexor tendons and synovium, and performed a tenosynovectomy of the flexor tendons to the thumb, index, and middle fingers. After these procedures, the resistance to passive dorsiflexion of the fingers and wrist was markedly reduced. The median nerve demonstrated a pseudoneuroma-like swelling proximal to the site of compression. Finally, a fasciotomy of the constricted forearm fascia and lumbrical muscle fascia was performed (Figure *4*).

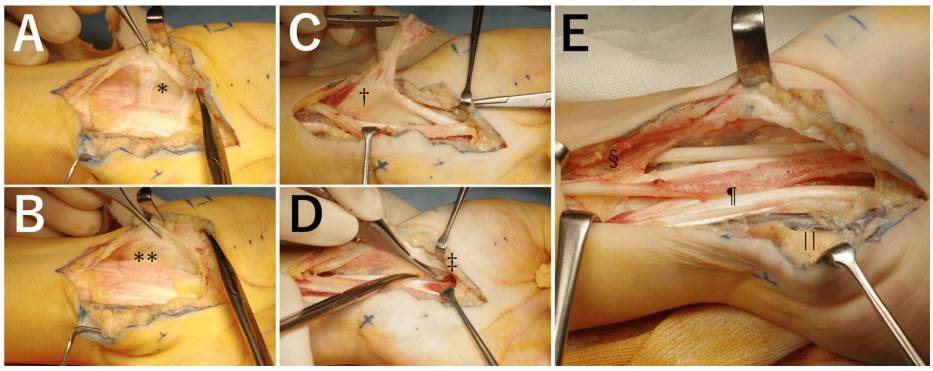


FIGURE 4: Intraoperative findings of the median nerve and surrounding structures.

(A) Adhesions between the median nerve and the dorsal side of the transverse carpal ligament were observed, along with cessation of blood flow in the vasa nervorum (*). (B) Reperfusion was confirmed following external neurolysis (**). (C) After dissecting the median nerve from the flexor tendons, tenosynovectomy of the flexor tendons (primarily of the thumb, index, and middle fingers) was performed (D) from the level of the flexor digitorum superficialis (FDS) insertion (†) to the lumbrical muscle origins (‡). (E) The median nerve exhibited pseudoneuroma-like swelling (¶) proximal to the compression site under the transverse carpal ligament, compared to the proximal palmar cutaneous branch level (§). The ulnar artery, vein, and nerve, which were released from Guyon's canal at the beginning of the procedure, are visible on the ulnar side (||).

Postoperative course

Three days postoperatively, the pain intensity decreased to six out of 10 on a zero-to-10 pain scale. Postoperative therapy was initiated early, including gauze protection between the digits for edema prevention and active touching of the affected limb with the contralateral hand. To restore intrinsic muscle function, exercises such as the lumbrical grip, opposition, and middle finger radial and ulnar abduction were instructed [14]. Contrast baths were also used for autonomic symptoms. By three weeks postoperatively, range of motion had improved significantly. At six months, the nail growth disturbance had recovered to the same level as the contralateral side, except for the index finger. At the two-year follow-up, although some symptoms remained, the patient's insomnia had completely resolved; the Japanese Society for Surgery of the Hand version of the Quick Disabilities of the Arm, Shoulder, and Hand questionnaire (QuickDASH-JSSH) score (0-100 scale, where higher scores indicate greater disability) improved from 84 to 45 [15], and the Carroll test score (0-96 scale for the non-dominant hand, where higher scores indicate better function) improved from zero to 26 [16]. The affected hand was functional as an assistive hand. No recurrence of CRPS symptoms has been observed (Figures *5*, *6*, Video *4*). Written informed consent for the publication of this case report, including all clinical photographs and videos, was obtained from both the patient (who was a minor at initial presentation and has since reached adulthood) and his parents.

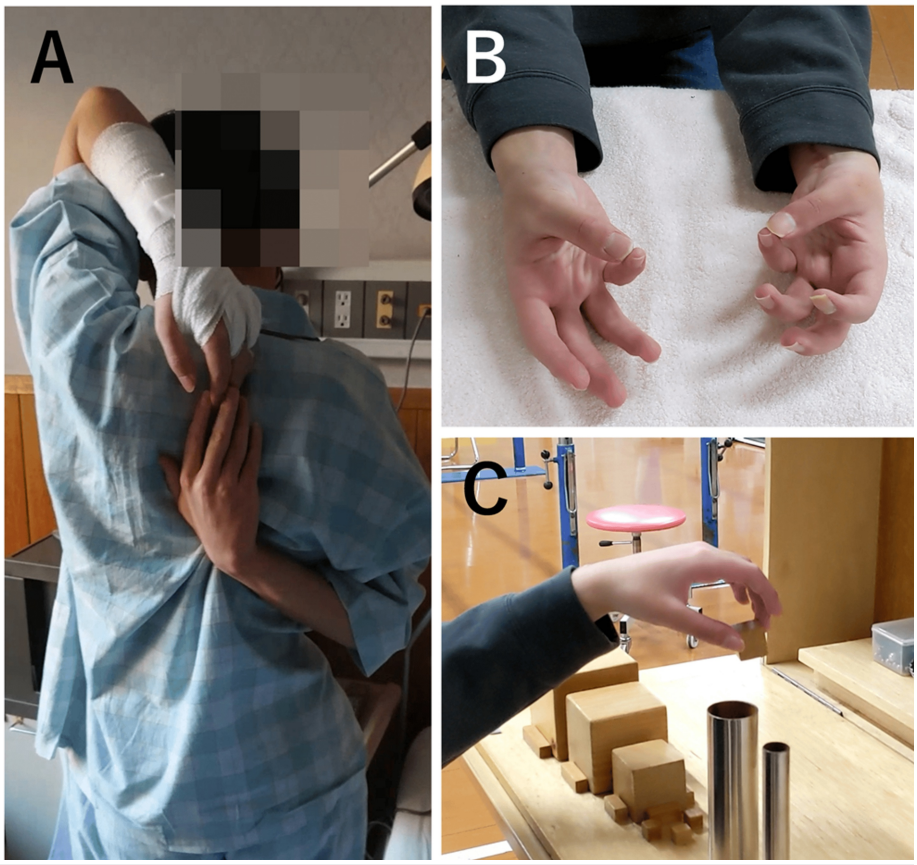
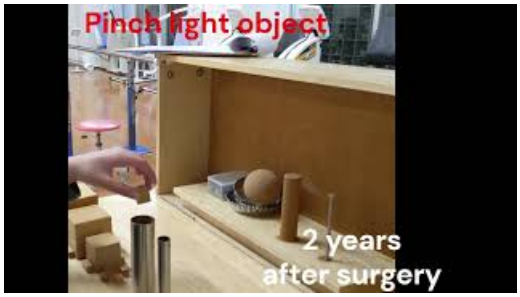


FIGURE 5: Postoperative improvement in range of motion and hand function.

(A) By three weeks post-operation, shoulder range of motion (ROM) was nearly full. (B) Thumb opposition became possible after six months, and at the two-year follow-up, this opposition was maintained, and (C) the patient became able to pinch light objects.



VIDEO 4: Postoperative improvement in range of motion and hand function.

View video here: https://youtu.be/Na7fl373YKI

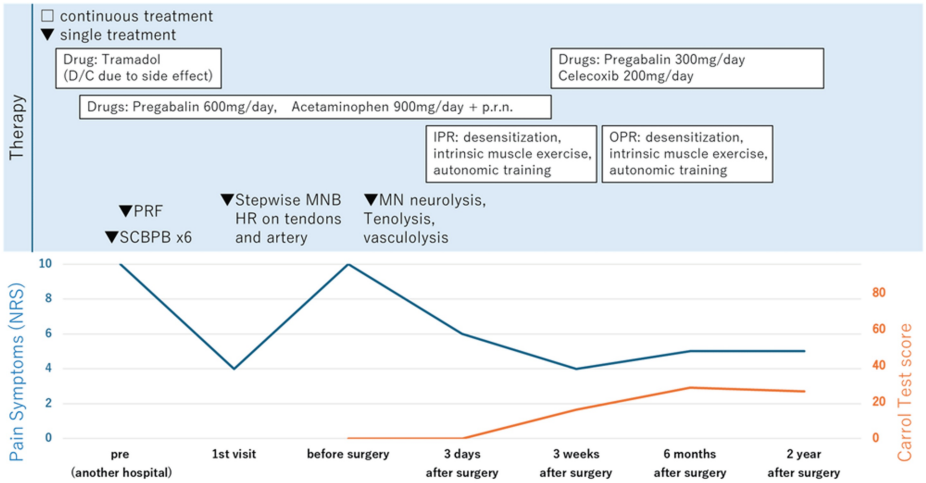


FIGURE 6: Timeline of interventions, pain score, and functional outcome.

This timeline summarizes the interventions (including medications, nerve blocks, and surgery) and the corresponding changes in the pain intensity (0-10 scale) and the Carroll test score at baseline (preoperative), 3 weeks, 6 months, and 2 years post-operation.

SCBPB: Supraclavicular brachial plexus block; PRF: pulsed radiofrequency; MNB: median nerve block; HR: hydro-release; MN: median nerve; IPR: inpatient rehabilitation; OPR: outpatient rehabilitation.

Discussion

This case is highly instructive as it describes a young patient who developed severe CRPS following vaccination, whose symptoms were refractory to standard treatments, and whose underlying etiology was identified as occult CTS.

A differential diagnosis includes functional neurological disorder [7,9]; however, several findings in this case are difficult to explain by this diagnosis alone. First, the objective trophic changes, such as nail growth disturbance, and their improvement following surgical intervention strongly suggest an organic etiology. Second, the consistent and positive response to a detailed diagnostic block points to specific peripheral nerve involvement. Third, the logical therapeutic pathway, wherein ultrasound findings of adhesions were confirmed intraoperatively and symptoms were reproduced and subsequently relieved by surgery, further supports an organic cause. Moreover, while localized post-vaccination conditions such as SIRVA have been reported [6], the absence of MRI abnormalities at the upper arm injection site and the extensive symptom distribution involving the hand, wrist, and autonomic/trophic changes clearly distinguished this presentation from a localized injection-site injury.

Diagnostically, this case was challenging because severe allodynia prevented physical evaluation of the distal limb, the primary site of pain. We therefore devised a stepwise diagnostic block. This technique involved first administering a brachial plexus block proximally to create a window for physical examination, followed by a block of the suspected primary pain generator in the carpal tunnel distally. This method allowed us to accurately isolate the extensive pain generator as being centered on the CTS. Although combining the local anesthetic block with perineural and perivascular hydrodissection to address the complex carpal tunnel pathology limits the ability to isolate the effect of the anesthetic alone, the prompt recurrence of symptoms after two days - once the local anesthetic effect had worn off - indicates that the anesthetic blockade of the median nerve was the primary factor driving this temporary relief.

A significant barrier to ancillary diagnosis was the report from the previous hospital stating the nerve conduction study was normal. However, upon our detailed re-evaluation, the distal motor latency of the affected median nerve showed a clear 0.8 ms delay compared to the ulnar nerve distal motor latency over the same distance, and was also delayed by 0.3 ms compared to the contralateral median nerve distal motor latency. Although absolute latency values fell within standard limits, this comparative latency difference over an identical distance indicates that minimal CTS - corresponding to Padua class 2 on the six-grade scale (where class 1 represents negative findings) - was electrophysiologically present [17].

This discrepancy between severe clinical symptoms and minimal nerve conduction study findings is a critical point in discussing the association between CRPS and CTS. This gap can be attributed, first, to the physiological limitation that standard nerve conduction studies cannot evaluate abnormalities in the small-diameter A-delta and C fibers that transmit pain [18]. In fact, it has been reported that increased pain

sensitivity and central sensitization in CTS patients do not correlate with electrodiagnostic severity [19]. Furthermore, Del Piñal reported that more than half of the CRPS patients he operated on had normal nerve conduction study findings [9].

Although contemporary practice often focuses on symptoms distal to a nerve compression site, the phenomenon in which a distal entrapment neuropathy produces proximal pain - which we term RNP [10] - has deep historical roots. The nocturnal upper-limb pain and paresthesia termed "Akroparästhesie" (acroparesthesia) by Schultze in 1893 [20], long misattributed to thoracic outlet lesions, was eventually unified into CTS once median nerve compression at the wrist was identified as its true cause [21]. Brain et al. (1947) demonstrated that CTS causes pain radiating proximally to the forearm and shoulder that resolves after surgical release [22], and Kendall (1960) emphasized that this proximal arm and shoulder pain frequently led to misdiagnoses such as "costo-clavicular syndrome" or cervical spondylosis [21]. Even earlier, Cotugno (1764) recorded his clinical observation (vidi) that ulnar nerve pain at the elbow can ascend to the shoulder (ad humerum ascendere) [23], and Valleix (1841) described such proximal propagation toward the shoulder and neck, noting that neuralgia propagating toward the nerve trunk was termed "ascending neuralgia" (névralgie ascendante) [24].

It has been reported that some patients diagnosed with upper limb CRPS type 1 can achieve significant clinical improvement following median nerve release at the carpal tunnel [9]. Similarly, persistent neurological symptoms triggered by venipuncture during blood donation have been reported to involve the summation of underlying peripheral nerve factors, requiring targeted hospital treatment [25]. Furthermore, cases of neuropathy and CTS developing after various vaccinations, including rubella, influenza, and COVID-19 vaccines, have been reported [26-28]. We theorize the pathophysiology in this case as follows. The vaccination or needle-stick injury triggered the onset or manifestation of a pre-existing or subclinical CTS. An alternative explanation is that the CTS was pre-existing and unrelated to the vaccination, with the injection triggering CRPS in a limb already vulnerable to spreading pain, or that post-vaccination regional inflammation secondarily exacerbated the median nerve compression; this single case cannot definitively distinguish among these possibilities. Nevertheless, in any of these scenarios, the persistent afferent barrage from the peripheral lesion induced central sensitization and extraterritorial symptom spread [19,29], which, mediated by the RNP and PCS mechanisms based on our previous clinical findings [10], resulted in extensive pain distribution up to the shoulder. We were able to confirm this peripheral organic etiology using our stepwise diagnostic block. Therefore, rather than addressing the central sensitization itself, we chose to intervene on the primary pain generator - the peripheral pathology - with surgical intervention and subsequent postoperative therapy, thereby achieving symptomatic improvement.

Conclusions

Severe complex regional pain syndrome developing in an adolescent after vaccination should not be prematurely dismissed as psychogenic; the possibility of an underlying peripheral nerve disorder, such as carpal tunnel syndrome, must be thoroughly considered as the primary pain generator. When severe allodynia prevents evaluation of the distal limb, a stepwise diagnostic block - combining a proximal short-acting block with a distal long-acting block - is a highly effective strategy for identifying the true origin of the widespread pain.

Furthermore, a discrepancy between severe clinical symptoms, such as intense pain and proximal spread, and minimal nerve conduction study findings is not uncommon in such presentations. This discrepancy suggests the involvement of small-fiber abnormalities or central sensitization rather than the absence of a peripheral lesion. Ultimately, precise localization of the lesion using innovative stepwise diagnostic blocks, combined with a meticulous re-evaluation of electrophysiological data, can successfully identify a treatable peripheral nerve compression, offering a definitive surgical pathway for seemingly refractory post-vaccination CRPS.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Yusuke Hagiwara, Ryu Yoshida

Acquisition, analysis, or interpretation of data: Yusuke Hagiwara, Tomomi Wagatsuma

Drafting of the manuscript: Yusuke Hagiwara

Critical review of the manuscript for important intellectual content: Yusuke Hagiwara, Tomomi Wagatsuma, Ryu Yoshida

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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