■ CASE STUDY

Reversal of Acute Complex Regional Pain Syndrome Using the Practical Application of Neurodiagnostic Evaluation Process: A Case Study

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Abstract

In 2005, a patient in my practice developed complex regional pain syndrome type 1 (CRPS 1) after bunion surgery. The condition was properly diagnosed within 4 weeks with a diagnostic technique that I routinely use to diagnose chronic musculoskeletal pain, and it was successfully treated. The tests, which are based on primitive and postural reflexes in infants, were adapted to reflect normal and abnormal motor behaviors in adults after provocation of reflexes of the autonomic nervous system (afferent C fibers in peripheral nerves). Approximately 60 days after my patient's operation, the tests indicated a positive reflex at the posterior tibial nerve in the operated foot. Surgery to remove an accessory ossicle from the talus adjacent to this nerve resolved the CRPS 1 within 2 weeks. Since CRPS 1 is a dysfunctional state of the autonomic regulatory control of pain, it was postulated that a test based on autonomic nerve function could isolate the source of CRPS 1. The Practical Application of Neurodiagnostic Evaluation process was shown to be diagnostic for the cause of acute CRPS 1 and to allow its reversal. Further evaluation of the test for diagnosis and treatment of CRPS is needed.

Introduction

The Practical Application of Neurodiagnostic Evaluation (PANE) process was described in the *Journal of Practical Pain Management* over several issues between August 2008 and May 2009.[1-4] Beck presented a theory and technical description of a diagnostic technique to evaluate chronic musculoskeletal pain.

Briefly, the PANE process applies to adults the postural reflex tests usually used with infants and young children. The tests were adapted to reflect normal and abnormal motor behaviors in adults when reflexes of the autonomic nervous system are provoked. The objective is to locate a subclinical nerve entrapment among peripheral nerves.[1-3] The theory was that if the small unmyelinated fibers in peripheral nerves are among the most vulnerable in entrapment conditions, then nociceptor afferent C fibers might be damaged early in the process.[1,5] Normal input from C fibers contributes to homeostasis of the organism by sending signals to the brain regarding secondary pain, temperature, and proprioception (via mechanoreceptors).[6-8] They

are also vulnerable to sensitization from local trauma.[5] Peripheral nerve sensitization may result in two very specific outcomes:

1. Chronic pain syndromes may result from excessive firing of the nerve via decreased excitation thresholds to noxious stimuli. Disruption in the signals from peripheral nerves can create central nervous system sensitization, which is a known mechanism for development of chronic allodynic pain and neuropathic pain.[9]

2. Chronic firing of a peripheral nerve from a subclinical entrapment syndrome could ultimately alter a protective postural reflex, such as the flexor/withdrawal reflex. If so, this may be measurable by testing motor reflexes.[1-4,10]

Damage to these unmyelinated fibers, or even the smallest myelinated sensory (Aδ) fibers, is not necessarily measurable on standard nerve conduction velocity studies. Their diameter is too small. Individual fibers in a peripheral nerve vary greatly in diameter, myelination, and afferent or efferent direction. Nerve conduction velocity studies assess the fastest 20% of these fibers.[11]

However, these small fibers do function as afferents in motor reflexes, including fight-or-flight, withdrawal reflexes, and postural reflexes.[10] Therefore, injuries in a peripheral nerve might be identified during detection of motor reflexes that fail. Faulty motor reflexes, it is theorized, compromise normal posture and balance. This causes muscle inhibition, weakness, and asymmetric muscle function, which create musculoskeletal pain. So the developers of the PANE process adapted existing motor reflex tests used in assessing the neurologic development of children to develop postural reflex tests for adults. One fairly visible reflex is the withdrawal reflex in newborns. From birth until the age of 1 year, a child will withdraw from a scratching sensation. After age 1 year and in a neurologically intact adult, there is no withdrawal to the sensation of (non-noxious) scratching of the skin. In the PANE process, this withdrawal reflex is elicited by either applying pressure or scratching along a peripheral nerve in the extremities or scratching a patient along the dermatome of a spinal nerve root.[1-4] The former is similar in principle to Phalen's test for carpal tunnel syndrome, where compression of the nerve (by wrist flexion) creates paresthesia, confirming the presence of carpal tunnel syndrome. The latter is similar in principle to pediatric postural reflexes, such as the placing reflex, where allowing a baby's anterior ankle to graze the edge of a platform causes the baby to step up and plant his foot on the platform; the Galant reflex, where stroking along the trunk produces a side-bending reflex in a neurologically intact infant; and the aforementioned withdrawal reflex. Video of the withdrawal and parachute reflexes can be seen at http://podiatrysandiego.com/html/skin_reflex.html[a,12] and http://podiatrysandiego.com/html/parachute_reflex.html.[a,13] The skin reflex particularly is

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helpful in understanding how the PANE process works.

The second facet of the theory supporting the PANE process is "loss of hierarchical control of the autonomic nervous system."[1-4,14] This allows re-appearance of primitive reflexes, such that an adult would demonstrate a withdrawal reflex if a scratch test were performed in the path of an injured peripheral nerve.[1-4] This loss of central organization is actually the progression from a *single* perceived noxious stimulus to a peripheral nerve sensitivity from *chronic* subthreshold stimulation (by mechanical entrapment of the nerve). This loss of control can ultimately put patients at risk for developing complex regional pain syndrome type 1 (CRPS 1).[1-4]

Chronic subclinical inflammation of a peripheral nerve creates neuritis. This produces the following sequence of events[1-5,15]:

1. lowering of the threshold of a peripheral nerve, such that non-noxious stimuli cause excitation of nociceptive C fibers;
2. activation of the hypothalamic-pituitary-adrenal axis over and over in response to the afferent overfiring (C fibers stimulating a fight-or-flight reflex);
3. depletion of synaptic neurotransmitters and excitation of adrenergic receptors;
4. chemical alteration of the descending antinociceptor pathways (sensitization) of the central nervous system:
   a. loss of regulation of homeostasis within the autonomic nervous system;
   b. re-appearance of autonomic (withdrawal) reflexes as a result of the loss of hierarchical control of the autonomic nervous system; and
   c. in late stages, neuropathic pain (starting with allodynia) and CRPS 1.

The sequence of tests to elicit withdrawal reflexes in adults allows the examiner to locate the source of the chronic neuritis and relieve it. This, in turn, allows the replenishment of neurotransmitters and a return to normal pain regulation. This can also resolve musculoskeletal pain for two reasons: first, the sympathetic control of muscle spindle activity and vasodilation/vasoconstriction to the painful muscle is restored; and second, because the patient is no longer employing compensatory gait strategies to off-load an injured nerve (neuritis).

The PANE process was also studied as the "scratch collapse test" by Patterson-Mackinnon et al.[16,17] They demonstrated the reliability of this technique compared with Tinel's sign, nerve conduction velocity, and neural tension tests, not only in accurately diagnosing or ruling out carpal tunnel syndrome,[16,17] but also in locating the anatomical level of entrapment.[18]

In the following case, we used the PANE process to identify the source of postoperative CRPS 1. It is important to note that the test was applied shortly after the symptoms developed. This test is not typically employed in long-standing cases of CRPS.

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A 38-year-old woman was seen in 2005 for right-foot pain. After a physical examination and X-rays, the pain was attributed to a bunion deformity and Morton's neuroma of the right foot. Ibuprofen, over-the-counter arch supports, and modifications to wider shoes failed to relieve the pain. Her preoperative symptoms included joint pain during range of motion and palpation of the right first metatarsophalangeal joint. She had no numbness, weakness, or radiating pain in either foot. She complained of an occasional burning pain plantar to the third and fourth metatarsal heads. She denied cramping pain in either foot. She was active and on her feet several hours a day during her work as a computer specialist at a casino. The surgical plan included a chevron osteotomy to correct the bunion and release of the Morton's neuroma.

X-rays illustrated an intermetatarsal angle between the first and second metatarsals of 12°, consistent with a moderate bunion deformity. Also present was an os trigonum (nonunited accessory ossicle) of the posterior process of the talus. Normal bone density was noted. No other bony abnormalities were noted. Preoperative laboratory test results were unremarkable.

Surgery to correct the bunion was performed first: chevron osteotomy with screw fixation, right first metatarsal. The procedure was without incident or complication.

The procedure for the Morton's neuroma was a decompression instead of excision. At the time of the operation, the nerve displayed no clinically evident pathologic appearance. There was considerable

fibrosis of the surrounding soft tissue, but no visible attenuation of the body of the nerve and no fusiform swelling consistent with a classic Morton's neuroma.

She had a normal postoperative course for the first 10 days. Her pain then began to escalate. There was no sign of infection. She had worsening edema over the course of the 10th through 30th days, at which time hyperesthesia, edema, and stiffness of her foot were evident. At that time, CRPS 1 was considered very likely. Her pain was concentrated at the surgical sites but extended to all toes and proximally to the ankle. A nerve block with 0.5% bupivacaine, 2% Xylocaine, and 0.5 cc of betamethasone acetate at the third intermetatarsal space provided considerable relief to the whole foot for
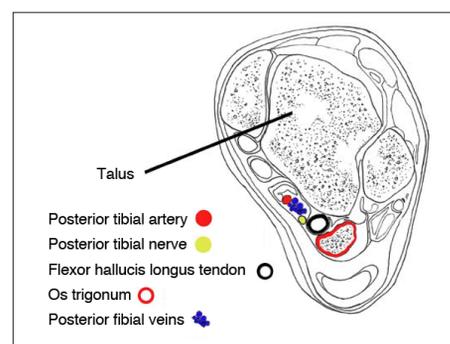

Figure 1. Posterior tibial nerve cross-section. This illustrates the relationship of the os trigonum off the posterior process of the talus and the contents of the tarsal tunnel at the level just above the subtalar joint. The nerve is just medial to the flexor hallucis longus tendon.

Posterior tibial artery ●
Posterior tibial nerve ●
Flexor hallucis longus tendon ○
Os trigonum ○
Posterior fibial veins

Posterior tibial nerve ●
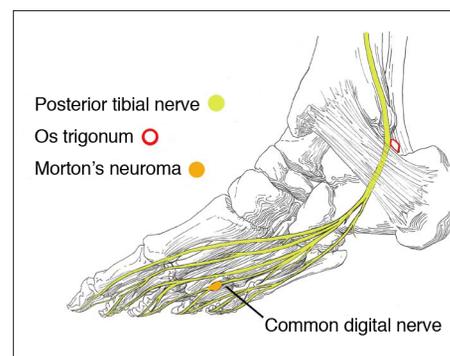Os trigonum ○
Morton's neuroma ●

Figure 2. Posterior tibial nerve side view. This illustrates the relationship of the os trigonum to the posterior tibial nerve in the tarsal tunnel, as well as the continuation of that nerve into the foot. One of the terminations is the common digital nerve, from which a Morton's neuroma arises.

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1 week. She attended physical therapy and received 1 more cortisone injection at the 3rd interspace over the next 30 days. Nonetheless, she could not bear weight on her right foot without the cast boot on. She complained of her ankle feeling "weak" and persistent foot pain. By the 60th postoperative day, she had had no further improvements. She was using a wheelchair at work and crutches elsewhere. She occasionally walked in the cast boot, which she found painful. Her right foot remained cooler than her left and was often "clammy." There was no mottling of the skin. X-rays of her right foot did not show disuse osteopenia, other than what would be expected 2 months after operation.

CRPS 1 is a dysfunctional state of the autonomic nervous system. The PANE process is a diagnostic examination of postural reflexes with a strong autonomic component (neural sensitization with loss of homeostasis). Therefore, it was postulated that the test could indicate the source of the developing autonomic dystrophy. Two months after operation, the PANE process revealed possible tarsal tunnel syndrome of the right ankle. This was accomplished by directly provoking the tarsal tunnel, then performing the resistance test. This condition was not observed during preoperative examinations. She specifically lacked the characteristic sharp, burning pain of the heel and arch or stiffness in the ankle. The only symptom may have been a burning sensation at the plantar forefoot, which was originally attributed to the suspected neuroma. The intermetatarsal (common plantar digital) nerve is one of the terminations of the posterior tibial nerve, which is the nerve compressed in tarsal tunnel syndrome (Figures 1 and 2).

A rather large os trigonum was observed when the X-rays were reviewed. It has been theorized that this nonunited portion of the posterior process of the talus may irritate the nearby posterior tibial nerve.[19] A diagnostic local anesthetic block into and just posterior to the right subtalar joint (the posterior tibial nerve is just external to the subtalar joint), supplemented with 0.5 cc of betamethasone acetate in suspension (4 mg/mL), provided considerable relief of symptoms and resolved the postural reflex for tarsal tunnel. The following week she reported

Figure 3. Practical application of neurodiagnostic evaluation 1 (the basic test). The examiner applies gradually increasing pressure to the patient's hands. The patient resists by externally rotating shoulders and abducting hands against the examiner's hands. The examiner stops when the patient returns consistent pressure.

Photo by Boyd Harris Photography.

Figure 4. Practical application of neurodiagnostic evaluation 2. Modest pressure is applied to the nerve being tested (in this case at the tarsal tunnel) for 1 or 2 seconds.

Photo by Boyd Harris Photography.

that for the duration of the steroid effect (approximately 1 week), the range of motion of her first metatarsal-phalangeal joint improved in physical therapy and her overall pain was reduced. By the 10th postinjection day, her pain had returned. Thereafter, diazepam 10 mg nightly and hydrocodone 30 mg – 40 mg daily in divided (5 mg) doses were the only medications that provided symptom relief, though incomplete.

The patient returned to the operating room for removal of the os trigonum. The anesthesiologist confirmed the presence of CRPS 1, noting the hyperesthesia and cold, clammy foot. The patient was administered both a spinal anesthetic to preoperatively numb the surgical site as well as a general anesthetic.

The os trigonum was easily identified and removed. No portion of the body of the talus or subtalar joint surface was disturbed. A separate surgical decompression of the tarsal tunnel did not appear to be indicated, because preoperatively she had obtained considerable temporary relief from a local anesthetic block, primarily of the posterior subtalar joint.

Results

The patient's initial postoperative course was unremarkable. She had considerable pain, which was controlled with hydrocodone. On postoperative day 3, she still had hyperalgesia to touch and a palpable temperature difference, with the surgical foot being cooler. By the 14th postoperative day, she had very little pain, requiring
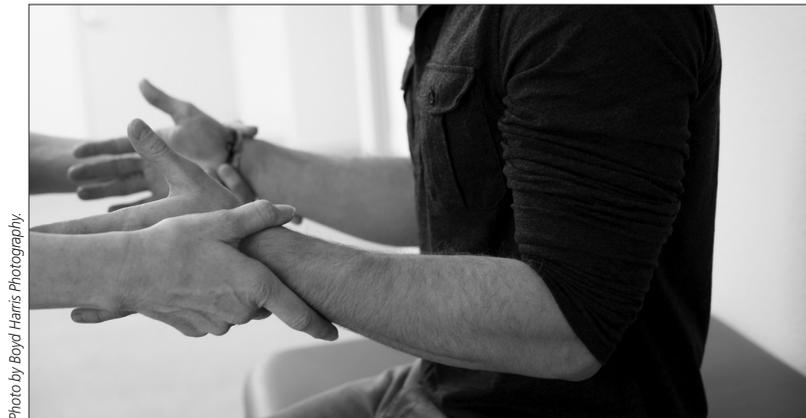
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Photo by Boyd Harris Photography.

Figure 5. Practical application of neurodiagnostic evaluation 3. The examiner repeats the basic test. If the nerve being tested is inflamed, the patient fails to resist the force applied and demonstrates a withdrawal reflex.
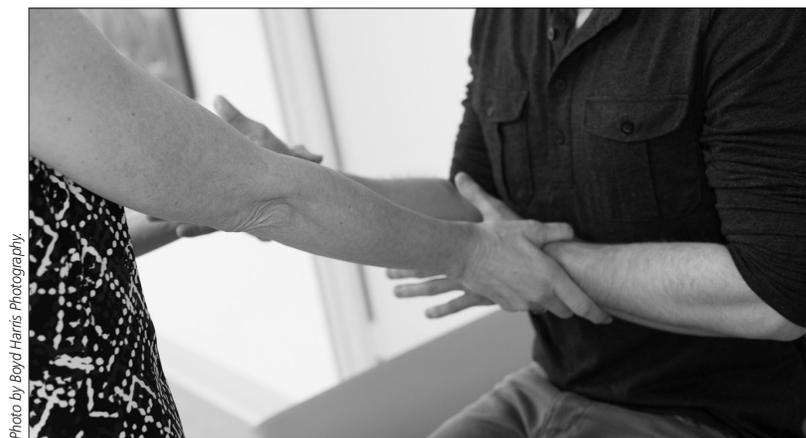

Photo by Boyd Harris Photography.

Figure 6. Practical application of neurodiagnostic evaluation 4. Complete withdrawal reflex is where the patient fails to resist the force applied. This is a positive test result for the nerve being tested.

results in a positive withdrawal reflex when a perturbing force that the patient must resist is applied (Figures 3-6).

Video of the complete PANE Process may be seen at http://podiatrysandiego.com/html/patient_demo.html.[a,23] It was performed on a volunteer patient who was not familiar with the test.

In the case illustrated, the PANE process (Figures 3-6) was applied soon enough after initial recognition of possible CRPS 1 and early empiric treatment. Her symptoms did not immediately resolve after the spinal anesthesia (without cortisone) wore off following the second operation. They resolved as she continued to heal from the operation.

It should be noted that this patient did not require any of the traditional treatments for CRPS 1—stellate ganglion blocks, ketamine infusions, gabapentin, antidepressants, or a dorsal column stimulator. The symptoms were managed and the CRPS 1 process slowed with anxiolytics, low-dose narcotics, physical therapy, and the local blocks just described. Because the peripheral nerve and joint blocks effected such significant pain relief and temporarily improved function, the patient was considered a good candidate for corrective surgery based on having located the source of the CRPS 1. Because this theory proved to be true, the disease never progressed to require traditional therapies. Although they might have relieved her pain, they were not necessary with the effectively placed anesthetic/cortisone blocks and the other medical treatment provided.

The clinical success of this simple diagnostic tool over the past 25 years may intersect with emerging research of the pathophysiology of both CRPS 1 and central nervous system sensitization. Although it was designed to diagnose and treat chronic musculoskeletal pain, routine utilization for diagnosing the source of CRPS 1 may be possible.

To date, we have evidence of reversing autonomic dystrophy (as opposed to true CRPS 1) in a handful of patients. Their symptoms, ranging from edema and vascular changes without pain to digital weakness after bunion surgery, all resolved with use of this technique. Further research specifically applying the PANE process to patients with acute CRPS 1 is needed. ❖

fewer than 6 hydrocodone per 24 hours. By that time, all signs of CRPS 1 had resolved. She no longer demonstrated the postural reflex at the right tarsal tunnel. She was walking in a cast boot by the 15th postoperative day and healed uneventfully over the next 60 days. She returned to work full time, full duty, and had no complaints of pain. Six months later, we removed the screws from the first metatarsal at her request. Before that operation, all her PANE test results for new or residual nerve entrapments were normal. CRPS 1 did not recur.

Discussion

CRPS 1 can be categorized as dysfunction of the sympathetic nervous system.[20] Several terms are used to describe the accompanying pain, including hyperalgesia, allodynia, and sympathetically mediated pain.[20] The normal regulatory process for dampening, or even correctly localizing, pain is absent. Its pathophysiology is the same as that used to describe both peripheral and central nervous system sensitization caused by chronic peripheral nerve stimulation.[5,21,22] These chronic precursors may include but are not limited to subclinical carpal tunnel, tarsal tunnel (as in the present case), nerve entrapment of the radial or deep peroneal nerves, and subclinical Morton's neuroma.

The nervous system will respond to manual provocation of that entrapped nerve with a withdrawal reflex. PANE testing on a nerve under compression or tension (whereby neuritis has developed)

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[a] The three videos illustrate two important aspects of the testing that resolved this patient's condition. First, the withdrawal reflex is seen when a baby younger than one year is scratched. Then, one of the primitive reflexes adapted for use in the PANE process, the parachute reflex, is demonstrated. Finally, the entire PANE process is demonstrated with a volunteer patient who was not familiar with it.

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

Acknowledgment

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