Reflex Sympathetic Dystrophy

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Introduction

Background

Reflex sympathetic dystrophy (RSD), also known as complex regional pain syndrome (CRPS), is an incompletely understood response of the body to an external stimulus, resulting in pain that usually is nonanatomic and disproportionate to the inciting event or expected healing response. As early as the 1930s and 1940s, a short circuit in the reflex arc between somatic afferent sensory fibers and autonomic sympathetic efferents was postulated to explain overall increased sympathetic stimulation. Currently, no specific pathologic, histologic, or biochemical markers of this condition exist.\(^1\,^2\,^3\)

Reflex sympathetic dystrophy of the hand. Delayed image palmar view reveals increased tracer diffusely involving the entire right wrist, metacarpals, and phalanges, with juxta-articular accentuation. Relatively less increased uptake is observed distally, but all areas are involved. The dot of increased activity distal to the third ray is a hot marker indicating the right side.
Reflex sympathetic dystrophy of the foot. Delayed image plantar view reveals increased tracer uptake diffusely involving the lowermost right leg, ankle, tarsals, metatarsals, and phalanges. Uptake is less distally than proximally, but all areas are involved. The dot of increased activity distal to fifth toe is a hot marker indicating the right side.

Although controversy continues regarding the term, definition, and process of diagnosis, the presence of sympathetically maintained pain is accepted as an etiology for, or at least as a significant component of, many regional pain problems.\[4,5\]

Recent studies

According to Andresen et al, outpatient CT-assisted temporary thoracic sympathetic nerve blockade is an effective adjunct therapy, with a low complication rate, for complex regional pain syndrome (CRPS). In their study, in addition to physiotherapy and pharmacotherapy with analgesics and calcitonin, sympathetic nerve blockade was performed 3 times, at 2-day intervals. The CT-assisted puncture was performed in the prone position at the level of the intervertebral space of the second and third thoracic vertebrae. All patients reported immediate pain relief. Color-coded duplex ultrasonography of the arteries of the affected limb was performed before and after puncture and showed increased peripheral blood flow.\[6\]

Sharma et al collected epidemiologic and other data regarding CRPS, via the Reflex Sympathetic Dystrophy Syndrome Association of America, to help elucidate the epidemiology, symptoms, progression, therapy, and psychosocial factors related to the disease.\[7\] Their findings included the following:

- It most often affects white women 25-55 years of age.
- It is often precipitated by trauma (surgical or nonsurgical) and commonly involves the lower extremities (approximately 56%) and upper extremities (approximately 38%).
- Pain is usually accompanied by edema, vasomotor, sudomotor, motor, and trophic changes.
- It commonly spreads to other areas of the body.
- Multiple pharmacologic and nonpharmacologic interventions usually fail.
- It frequently interferes with work (approximately 62% disability rate), sleep (approximately 96%), mobility (approximately 86%), and self-care (approximately 57%).
Both remission and relapse are common.

**Clinical guidelines**

The following are the clinical diagnostic criteria for CRPS[8]:

(1) Continuing pain, which is disproportionate to any inciting event

(2) Must report at least one symptom in 3 of the 4 following categories:

* **Sensory:** Reports of hyperesthesia and/or allodynia

* **Vasomotor:** Reports of temperature asymmetry and/or skin color changes and/or skin color asymmetry

* **Sudomotor/Edema:** Reports of edema and/or sweating changes and/or sweating asymmetry

* **Motor/Trophic:** Reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)

(3) Must display at least 1 sign at time of evaluation in 2 or more of the following categories:

* **Sensory:** Evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or deep somatic pressure and/or joint movement)

* **Vasomotor:** Evidence of temperature asymmetry and/or skin color changes and/or asymmetry

* **Sudomotor/Edema:** Evidence of edema and/or sweating changes and/or sweating asymmetry

* **Motor/Trophic:** Evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)

(4) There is no other diagnosis that better explains the signs and symptoms

**Presentation**

**Demographics**

Patients younger than 50 years predominate. In the upper extremity, orthopedic surgeons see children only rarely. Rheumatologists, who generally use less strict criteria for diagnosis, report a slightly higher frequency of involvement in children. Similarly, pediatricians report a moderate frequency of lower extremity neurovascular or neuroregulatory disease in children that has been termed reflex sympathetic dystrophy (RSD). In these children, a bone scan pattern often reveals marked decreased tracer uptake on delayed images compared to increased uptake in adults; therefore, this may represent a different condition, such as pseudodystrophy.

In the upper extremity, the author’s experience demonstrates a clear female preponderance, especially in patients presenting to the orthopedic surgeon.
The incidence of reflex sympathetic dystrophy (RSD) following trauma is difficult to estimate, since the literature is replete with studies in which clinical criteria for the diagnosis of RSD vary dramatically, with many often equating unexplained pain to RSD.\[9\] For example, upper extremity RSD, as understood and treated by hand surgeons, is described differently than lower extremity RSD diagnosed by rheumatologists or hip RSD described by obstetricians. Some authors suggest that 8-10% of patients with fracture develop RSD, but in this author's experience, the frequency is much lower.

Most reflex sympathetic dystrophy patients recover completely over time.\[10\] Uncommonly, the syndrome progresses to the point of incapacitation and a "claw hand" is observed.

**Presentation and natural history**

Reflex sympathetic dystrophy (RSD) involving the hand, wrist, shoulder, ankle, and foot has been established, with diffuse involvement of adjacent carpals or tarsals, metacarpals or metatarsals, phalanges, and, frequently, the distal forearm or leg.\[7,11\] Rarely, segmental involvement of 1, 2, or 3 rays of the hand is observed. Involvement of the knee, although described, is less well documented and, along with focal pain conditions in the hip (often interchangeably termed reflex sympathetic dystrophy or transient osteoporosis), may be a different process.\[12,13\]

Radiologists and orthopedic surgeons usually agree to define reflex sympathetic dystrophy (RSD) (as stated by Schutzer\[14\]) as an "excessive or exaggerated response to an injury of an extremity, manifested by four somewhat constant characteristics: (1) intense or unduly prolonged pain, (2) vasomotor disturbances, (3) delayed functional recovery, and (4) various associated trophic changes."

The key feature is pain, which often is the initial presenting symptom. Various clinical schemas have been proposed that relate stages of disease to signs and symptoms and the time elapsed since the inciting event.\[15\] One example of staging by Rosenthal and Wortmann\[16\] is as follows:

- **Stage 1** has a duration of weeks to months. The limb has nonfocal pain, swelling with associated joint stiffness and decreased range of motion, and increased skin temperature.

- **Stage 2** has a duration of 3-6 months. Pain continues but decreases over time. Swelling evolves into thickening of the dermis and fascia. Early signs of atrophy and osteoporosis become evident, and the extremity becomes cooler.

- **Stage 3** is the atrophic stage. Pain continues and atrophy is exacerbated by continued decreased range of motion and increased joint stiffness. The extremity is cooler with decreased vascularity.

Symptomatically, reflex sympathetic dystrophy (RSD) is a condition of the extremities. Reflex sympathetic dystrophy is known and accepted best when it affects the upper extremity, predominantly in a regional distribution involving the distal forearm, wrist, hand, and, occasionally, the arm and shoulder. No pathophysiologic mechanism has been established. Efferent sympathetic nervous system overactivity and/or abnormal activity involving spinal internuncial neurons, peripheral nociceptors, and/or mechanoreceptors have been postulated.\[17,18\]

Many biomechanical factors have been considered, beginning with tissue injury as an initial inciting event, with substance P, histamine, and prostaglandins all possibly involved. Other possible etiologies include vasodilatation, shunting, and regional hypoxia associated with nociceptor stimulation,\[19\] as well as the role of alpha-adrenergic receptors in maintaining and controlling thermoregulatory modulation. Segmental involvement of 1, 2, or 3 rays in the hand has been reported infrequently, according to Kline and Holder,\[20\] and bilateral involvement is rare to nonexistent.

In the lower extremity (most often foot and ankle), a less well-defined clinical pattern also is associated with a similar spectrum of pathophysiologic speculations.\[21\] In the knee, potentially sympathetically related postoperative and posttraumatic signs and symptoms have been ascribed to RSD or other neuroregulatory processes but with less accepted clinical or diagnostic standards of reference. More recently, the term complex regional pain syndrome (CRPS)
has been introduced to encompass a variety of chronic pain syndromes, with RSD labeled as type I. All sympathetically maintained pain syndromes (SMPS) may not be RSD.

Preferred Examination

Radiologic examination

Radionuclide bone imaging (RNBI) is the only generally accepted imaging technique to provide objective and relatively specific evidence of reflex sympathetic dystrophy (RSD) in the upper and lower extremities, predominantly the hands and feet. Delayed bone imaging has been reported to be up to 100% sensitive for the variant of sympathetically maintained pain termed RSD by hand and foot surgeons.

Plain radiography is only 60% sensitive and not specific; when positive, radiographs often show only osteoporosis, occasionally in combination with soft tissue swelling or diffuse soft tissue atrophy.

No consistent findings have been found in the occasional study done with other imaging modalities, and none are suggested for diagnosis.

Nonimaging diagnostic testing

Pain in response to mild cooling stimuli: A drop of acetone or ethyl chloride spray provoking severe pain suggests SMPS rather than a sympathetically independent pain syndrome (SIPS).

Phentolamine test: The blocking of alpha-adrenergic receptors by intravenous phentolamine compared to a placebo helps classify patients as SMPS versus SIPS.

Limitations of Techniques

Patients are observed who present with acute or subacute pain and vasomotor or neuroregulatory signs or symptoms and who do not demonstrate the classic diffuse increased uptake on delayed RNBI. The relationship of these patients to those with abnormal RNBI remains unexplained.

Differential Diagnoses

[Reiter Syndrome, Musculoskeletal]
Abdominal Aortic Aneurysm, Diagnosis
Osteoarthritis, Primary
Osteomyelitis, Acute Pyogenic
Osteomyelitis, Chronic
Rheumatoid Arthritis, Hands

Other Problems to Be Considered

Algodynia
Algodystrophy
Diffuse cellulitis
Diffuse local trauma
Neuroregulatory abnormalities
Pseudodystrophy
Phlebitis
Regional migratory osteoporosis
Scleroderma of the hands
Sudeck atrophy
Transient bone marrow edema
Transient osteoporosis
Transplant osteoporosis of the hip
Transplant regional osteoporosis
Vascular injuries

**Radiography**

**Findings**
Osteoporosis, although found in as many as 60% of patients with upper extremity reflex sympathetic dystrophy (RSD), is not specific, often representing changes of disuse secondary to the pain associated with RSD. Occasionally, soft tissue swelling or diffuse soft tissue atrophy may be seen; these are nonspecific findings.

**Magnetic Resonance Imaging**

**Findings**
MRI changes in established reflex sympathetic dystrophy (RSD) rarely have been evaluated, and as with studies using other modalities, the definition of RSD has varied considerably. In one study by Schweitzer et al.[28] involving the lower extremity (n=35), soft tissue thickening with and without contrast enhancement (n=31) was demonstrated without any marrow changes, while in another study of the upper extremity (n = 17) by Koch et al.[29] no marrow changes and only inconsistent soft tissue or muscle signal changes were seen.

In the hand, Sintzoff et al.[30] used MRI to detect what was believed to be bone marrow edema and then equated bone marrow edema to RSD. MRI thus is not an established technique in the imaging evaluation of RSD.

**Ultrasonography**

**Findings**
A single-power Doppler study by Nazarian et al.[31] involving the lower extremities suggested increased flow without side-to-side asymmetry in patients with reflex sympathetic dystrophy (RSD). Ultrasound thus is not an established technique in the imaging evaluation of RSD.

**Nuclear Imaging**

**Findings**
Three-phase radionuclide bone imaging (RNBI) is performed primarily because the differential diagnosis often includes infection or other lesions for which information about the perfusion to the extremity (phase I) or relative vascularity of the extremity (phase II) is helpful.

For regional reflex sympathetic dystrophy (RSD) of the hand or foot, the hallmark on the radionuclide angiogram (RNA; phase I) is diffuse increased perfusion to the entire extremity, including the distal forearm or leg and, occasionally, reaching the shoulder or hip, even when the inciting lesion is distal.

Similar diffuse increased vascularity, manifested by diffuse increased tracer accumulation on blood pool or tissue-phase images (phase II) is seen. On these images, juxta-articular accentuation may be seen. RNA findings are abnormal in approximately 40% of patients and blood pool findings in approximately 50%, most often in clinical stage I or II of the disease.

Delayed images demonstrate diffuse increased tracer throughout the hand or foot, including the wrist or ankle, with juxta-articular accentuation and, often, proximal uptake involving the forearm or leg and, occasionally, the shoulder and arm or hip and femur. Activity in the hands or feet usually is more prominent proximally than distally, but the amount of abnormal tracer uptake has not been correlated with clinical severity. Quantification occasionally has been helpful but is not used routinely.
Degree of Confidence

When radionuclide bone imaging (RNBI), especially in the upper extremity, demonstrates classic diffuse findings, reflex sympathetic dystrophy (RSD) is certain (specificity). When RNBI does not demonstrate that pattern, the most common variant of sympathetically maintained pain syndrome (SMPS) or complex regional pain syndrome (CRPS) type 1 is excluded (sensitivity).

In the lower extremity, patients with severe infection, especially if underlying diabetes mellitus is present, may demonstrate diffuse increased delayed image tracer uptake on RNBI performed to diagnose osteomyelitis. This is not usually a diagnostic issue clinically.

Multimedia

Media file 1: Reflex sympathetic dystrophy of the hand. Delayed image palmar view reveals increased tracer diffusely involving the entire right wrist, metacarpals, and phalanges, with juxta-articular accentuation. Relatively less increased uptake is observed distally, but all areas are involved. The dot of increased activity distal to the third ray is a hot marker indicating the right side.
Media file 2: Reflex sympathetic dystrophy of the foot. Delayed image plantar view reveals increased tracer uptake diffusely involving the lowermost right leg, ankle, tarsals, metatarsals, and phalanges. Uptake is less distally than proximally, but all areas are involved. The dot of increased activity distal to fifth toe is a hot marker indicating the right side.

References


**Keywords**

reflex sympathetic dystrophy, complex regional pain syndrome type I, CRPS-I, sympathetically mediated pain syndrome, SMPS, causalgia, algodystrophy, algodynia, Sudek's atrophy, Sudek atrophy, shoulder-hand syndrome, RSD

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