Reflex Sympathetic Dystrophy Syndrome Following Herpes Zoster

Ignacio Querol, MD, Tudela, Spain
Teresa Cisneros, MD, Tudela, Spain

Reflex sympathetic dystrophy syndrome (RSDS), or algodystrophy, is a poorly understood, painful syndrome that consists of multiple symptoms, including vasomotor instability, swelling, and chronic pain involving an extremity. Although RSDS following herpes zoster is classically recognized, only a few well-documented cases of this complication have been reported to date.

We present the case of a 63-year-old white woman with characteristic signs and symptoms of RSDS in the left upper limb that appeared 3 weeks after she had a typical herpes zona involving the left C5–C6 dermatomes. Early diagnosis and treatment with physiotherapy, intranasal salmon calcitonin, and oral calcium achieved a progressive improvement of the disease, which healed without sequelae in a brief time.

Reflex sympathetic dystrophy syndrome (RSDS), or algodystrophy, is a clinical syndrome characterized by pain, tenderness, dystrophic skin changes, swelling, stiffness, and vascular instability.[1] The pathogenesis of RSDS is poorly understood, and no single hypothesis proposed to date explains all features of this disorder. The classically accepted idea is of a sympathetic nervous cause; injury causes afferent painful stimuli to persist with abnormal activity in the internuncial pool of the spinal cord and, in turn, the stimuli increase efferent sympathetic activity.[2] An alternative inflammatory concept has been proposed in which RSDS is interpreted as a prolonged, regional chemical inflammatory state that affects all tissues from skin to bone.[3]

The cause of RSDS is unknown. Several predisposing factors have been identified, but in at least 20% of cases, no obvious predisposing factor was found. Trauma (including surgery, fracture, crush injury, and sprains) is the factor most frequently involved. Other conditions, such as hyperthyroidism, pregnancy, diabetes mellitus, hyperlipidemia, and psychogenic factors, increase susceptibility to the disorder.[1]

Although RSDS as a complication of herpes zoster was first described by Sudek[4] in 1901, only a few reports of well-documented cases of varicella-zoster virus infection as the precipitating factor in RSDS have been published.[5-10]

We present the case of a patient with characteristic signs and symptoms of RSDS in the left upper limb 3 weeks after she had a typical herpes zoster involving the left C5–C6 dermatomes.

Case Report

A 63-year-old white woman showed an erythematous rash with clear grouped vesicles involving the left C5–C6 dermatomes and accompanied by severe pain in the left arm. She visited her family doctor, who referred her to our hospital. On admission one week after the onset of symptoms, only a few grouped necrotic ulcers, hemorrhagic crusts, and umbilicated vesicles remained present in the left infraclavicular area (Figure 1) and external side of the left arm. She was diagnosed with herpes zoster; and oral acyclovir, 800 mg 5 times daily, was prescribed for 7 days. Although the vesicles healed without bacterial infection or severe scarring, she continued to complain of intense burning pain and hyperalgesia in the dermatomal distribution of the rash.

In the 3 weeks following resolution of skin lesions, the patient experienced pain, swelling, redness, and stiffness in the phalangeal, metacarpophalangeal, and wrist joints. The mobility of these joints also was limited, resulting in an inability to fulfill the complete active flexion (Figure 2) and extension. Movement of the shoulders was normal,

Drs. Querol and Cisneros are from the Departments of Dermatology and Rehabilitation, Hospital Reina Sofía de Tudela, Tudela, Spain.
Reprints: Ignacio Querol, MD, Unidad de Dermatología, Hospital Reina Sofía, Crtra. de Tarazona, Km. 3, 31500-Tudela (Navarra), Spain (e-mail: iqueroln@posta.unizar.es).

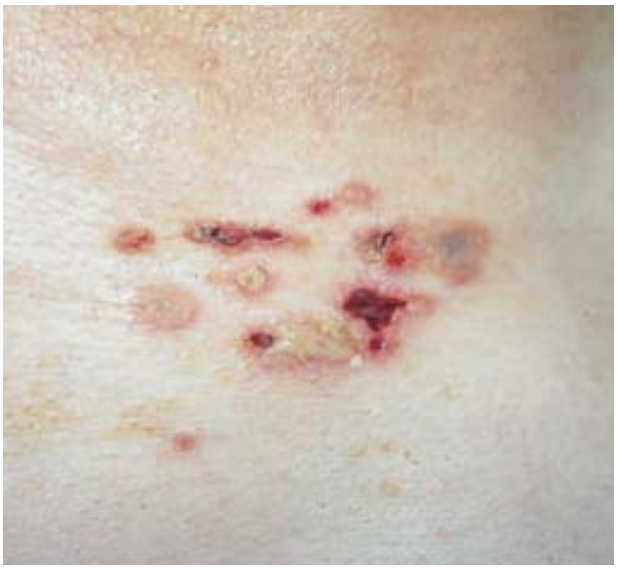

Figure 1. Clinical appearance of herpes zoster lesions: grouped necrotic ulcers, hemorrhagic crusts, and umbilicated vesicles in the left infraclavicular area.

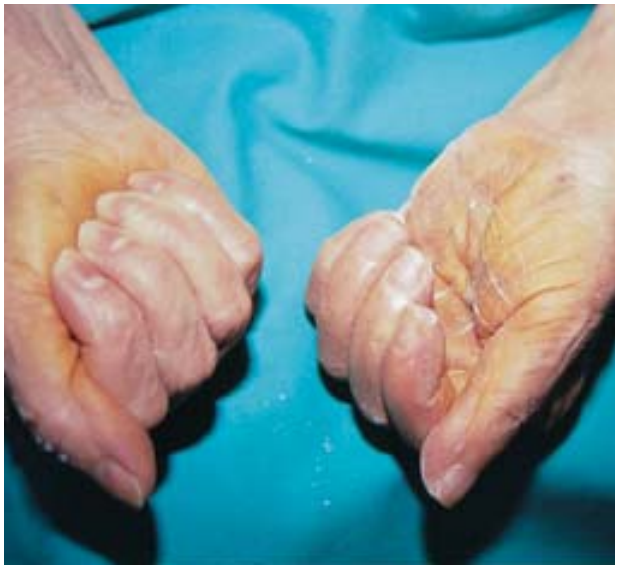

Figure 2. Mobility of the phalangeal and metacarpophalangeal joints of the left hand was limited, with inability to fulfill complete active flexion.

and there were no other articular abnormalities. The skin of the left fingers and hand was edematous, cold, moist, cyanotic, and smooth. The patient noted excessive sweating in the involved cutaneous areas, and paroxysmal hyperhidrosis was precipitated by triggers such as emotions or physical efforts (eg, active flexion of the joints of the left hand). This was demonstrated by results of an iodine-starch reaction test. (Figure 3).

Radiographs of the left hand revealed patchy osteoporosis of the carpal and metacarpal bones, consistent with the diagnosis of RSDS. Results of routine biochemical and hematologic tests were normal.

The patient was referred to the Department of Rehabilitation for treatment. Intranasal salmon calcitonin (100 IU daily) and calcium (600 mg/d orally) were administered for 30 days. Intensive physiotherapy (including hydrotherapy with ice baths alternating with hot water baths, therapeutic currents of low frequency, massage to increase circulation, and active and active-assisted physical exercises) also was undertaken.

Within days, the pain decreased, and the patient's hand function slowly improved. At the completion of physical therapy, her hand function returned to 90% of normal capacity, and she was discharged and given a regular exercise program to follow. Four months after the condition first occurred, the patient was completely free of symptoms, with complete mobility of the involved joints and no notable cutaneous changes.

Comment

It is well known that varicella-zoster infections may result in an array of neurologic disorders.[11,12] The most common neurologic complication of herpes zoster is postherpetic neuralgia, followed in decreasing incidence by a variety of other syndromes including peripheral motor neuropathy, cranial nerve palsies, myelitis, encephalitis, thrombotic cerebral vasculopathy, acute ascending polyradiculitis, and aseptic meningitis. However, RSDS is a very uncommon complication of herpes zoster, and only a few reports have been noted in the literature.[5-10]

Several pathways can explain the role of herpes zoster in triggering RSDS. First, herpes zoster produces an intense pain, derived from herpetic and postherpetic neuralgia. Researchers believe that an initial nociceptive afferent stimulation can sensitize a wide range of multireceptive neurons in the spinal internuncial neuron pool that are at the center of an abnormal reflex, resulting in excessive sympathetic outflow.[1,2]

Second, varicella-zoster infection produces an injury in the peripheral nerve fiber. Some hypotheses invoke the formation of ephapses (abnormal synapses), usually between efferent sympathetic nerves and afferent sensory nerves or sensitized peripheral nerves that may discharge spontaneously.[1]

A final hypothesis involves the provocation of local tissue inflammation secondary to the cytopathic changes induced by the varicella-zoster infection, which determines the production of

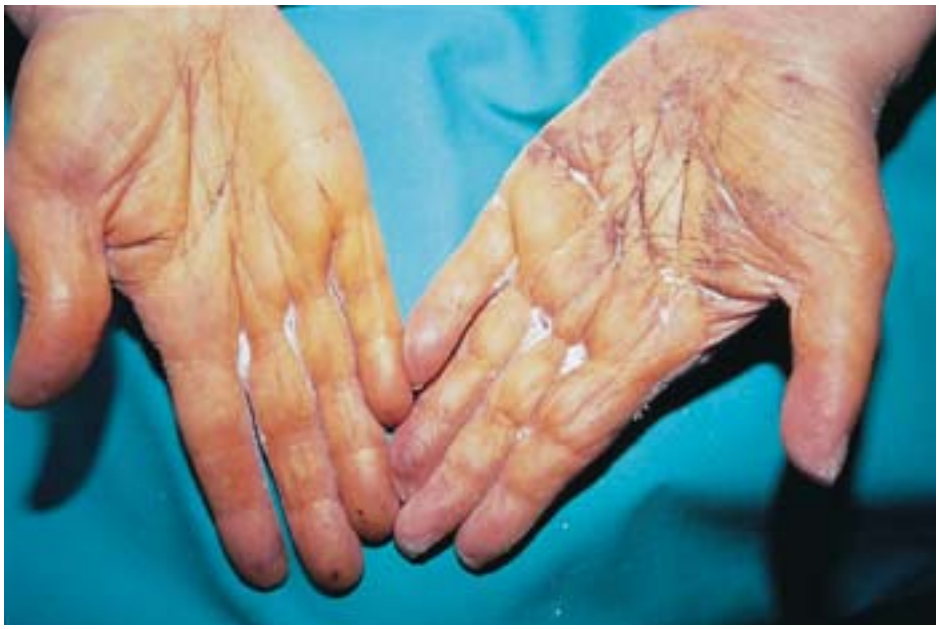

Figure 3. Excessive sweating was precipitated by active flexion of the joints of the left hand (demonstrated by an iodine-starch reaction test).

vesicles that may progress to ulcer formation with secondary infection. This local trauma has recently been proposed as being important in the pathogenesis of RSDS, by which a series of vicious circles is established in which vasodilatation, low flow, and persistent stimulation of nociceptors all play a part.[3]

RSDS is a dynamic process that may progress insidiously through 3 stages over several months.[13-15] The clinical features of stage I in the upper extremity are pain (which can be exacerbated by exposure to cold), swelling, and stiffness of the joints in the fingers and wrist. The skin may be pale or red and is usually moist due to hyperhidrosis.

Stage II is characterized by persistent burning pain in the hand associated with marked stiffness of the wrist and fingers. Atrophy of the muscles produces weakness of the hand and, eventually, flexion deformities of the fingers. The skin usually is pale, cold, and dry.

Stage III is a combination of all aspects of the earlier stages, in which inflammatory and atrophic changes are most prominent.[15] Many other skin changes have been described in association with RSDS[15-20]: xerosis, anhidrosis, cutaneous atrophy, recurrent ulcerating papules, reticulated hyperpigmentation, geometrically marginated erythema, pseudo-Kaposi sarcoma, hypertrichosis, and altered nail growth. RSDS also can complicate other cutaneous diseases, such as unilateral acrodermatitis continua,[21] epithelioid hemangioendothelioma,[22] chronic venous leg ulcers,[23] or systemic lupus erythematosus.[24]

The diagnosis of RSDS is based mainly on clinical data (eg, the patient's history and results of the physical examination), and no procedure or laboratory test can determine the diagnosis.[25] The International Association for the Study of Pain established criteria for the diagnosis of RSDS, all 4 of which must be satisfied: an initiating noxious event or a cause of immobilization; continuing pain, allodynia (pain in response to nonnoxious stimulation), or hyperalgesia (exaggerated pain in response to noxious stimulation) in which the pain is disproportionate to the inciting event; prior evidence of edema, changes in blood flow, or abnormal sudomotor activity in the region of the pain (ie, change in skin temperature, skin color, sweating); and the existence of conditions that would otherwise account for the degree of pain.[26]

Management of RSDS must be aimed at the restoration of movement and function. Physical therapy and mobilization are the cornerstones of treatment.[27] To be most effective, an active rehabilitation program is used in combination with other drugs (including analgesics, nonsteroidal anti-inflammatory agents, nifedipine, propranolol, phenoxybenzamine, corticosteroids, salmon calcitonin, and topical capsaicin) or techniques (such as transcutaneous electric nerve stimulation, ultrasonography, nerve blocks, stellate ganglion or paralumbar blockade, and surgical sympathectomy). Parenteral or intranasal salmon calcitonin is very useful if osteoporosis is present, especially in patients with early ankle and foot disease.

Although the condition is often self-limiting, many cases persist for years and may become permanent. Effective therapy necessitates early diagnosis because treatment within one year of onset is most successful.[28] In our patient's case, early recognition and management with physiotherapy, intranasal salmon calcitonin, and oral calcium achieved a progressive improvement of the disease, which healed without sequelae in a brief time.

REFERENCES

1. Kozin F. Reflex sympathetic dystrophy syndrome: a review. *Clin Exp Rheumatol*. 1992;10:401-409.
2. Roberts WJ. A hypothesis on the physiological basis for causalgia and related pains. *Pain*. 1986;24:297-311.
3. Ecker A. Pathogenesis of reflex sympathetic dystrophy. *Arch Neurol*. 1989;46:482.
4. Sudek P. Uber die akute (reflecktorische) knochenatrophie nach entzundungen und verletzungen an den extremitaten und ihre klinischen erscheinungen. *Fortschr Geb Rontgenstr Nuklearmed Erganzungs*. 1901;5:277-293.
5. Ketz E, Schliack H. Zoster in C5-C6 mit Sudeckscher Krankheit. *Nervenarzt*. 1968;39:180-181.
6. Visitsunthorn U, Prete P. Reflex sympathetic dystrophy of the lower extremity: a complication of herpes zoster with dramatic response to propranolol. *West J Med*. 1981;135:62-66.
7. Grosslight KR, Rowlingson JC, Boaden RW. Herpes zoster and reflex sympathetic dystrophy. *Anesth Analg*. 1986;65:309-311.
8. Foster O, Askaria A, Lanham J, et al. Algoneurodystrophy following herpes zoster. *Postgrad Med J*. 1989;65:478-480.
9. Chester MH. Segmental reflex sympathetic dystrophy involving the thumb: a rare complication of varicella-zoster infection. *Anesthesiology*. 1992;77:1223-1225.
10. Kishimoto N, Kato J, Suzuki T, et al. A case of RSD with complete disappearance of symptoms following intravenous ketamine infusion combined with stellate ganglion block and continuous epidural block. *Masui*. 1995;44:1680-1684.
11. Polo JM. Trastornos neurológicos tras una infección por virus varicela-zoster. *Med Clin* (Barc). 1990;95:774-776.
12. Elliot KJ. Other neurological complications of herpes zoster and their management. *Ann Neurol*. 1994;35:S57-S61.
13. Veldman PHJM, Reynen HM, Arntz IE, et al. Signs and symptoms of reflex sympathetic dystrophy: prospective study of 829 patients. *Lancet*. 1993;342:1012-1016.
14. Dhar S, Klenerman L. Reflex sympathetic dystrophy (algodystrophy). *Br J Rheumatol*. 1993;32:2-3.
15. Webster GF, Schwartzman RJ, Jacoby RA, et al. Reflex sympathetic dystrophy: occurrence of inflammatory skin lesions in patients with stages II and III disease. *Arch Dermatol*. 1991;127:1541-1544.
16. Shelton RM, Lewis CW. Reflex sympathetic dystrophy: a review. *J Am Acad Dermatol*. 1990;22:513-520.
17. Webster GF, Iozzo RV, Schwartzman RJ, et al. Reflex sympathetic dystrophy: occurrence of chronic edema and nonimmune bullous skin lesions. *J Am Acad Dermatol*. 1993;28:29-32.
18. O'Toole EA, Gormally S, Drumm B, et al. Unilateral Beau's lines in childhood reflex sympathetic dystrophy. *Pediatr Dermatol*. 1995;12:245-247.
19. Kavanagh GM, Hollingworth P, Kennedy CT. Hypertrichosis and algodystrophy: an hypothesis to explain this uncommon association. *Br J Dermatol*. 1994;30:777-779.
20. Tosti A, Baran R, Peluso AM, et al. Reflex sympathetic dystrophy with prominent involvement of the nail apparatus. *J Am Acad Dermatol*. 1993;29:865-868.
21. Stephens CJ, McGibbon DH. Algodystrophy (reflex sympathetic dystrophy) complicating unilateral acrodermatitis continua. *Clin Exp Dermatol*. 1989;14:445-447.
22. Malane SL, Sau P, Benson PM. Epithelioid hemangioendothelioma associated with reflex sympathetic dystrophy. *J Am Acad Dermatol*. 1992;26:325-328.
23. Nennhaus HP. Reflex sympathetic dystrophy: the other villain in chronic venous leg ulcers. *J Dermatol Surg Oncol*. 1994;20:672-674.
24. Ostrov BE, Eichenfield AH, Goldsmith DP, et al. Recurrent reflex sympathetic dystrophy as a manifestation of systemic lupus erythematosus. *J Rheumatol*. 1993;20:1774-1776.
25. Galer BS. Reflex sympathetic dystrophy syndrome. *Lancet*. 1994;344:691.
26. Stanton-Hicks M, Janig W, Hassenbusch S, et al. Reflex sympathetic dystrophy: changing concepts and taxonomy. *Pain*. 1995;63:127-133.
27. Chard MD. Diagnosis and management of algodystrophy. *Ann Rheum Dis*. 1991;50:727-730.
28. Geertzen JHB, de Bruijn H, de Bruijn-Kofman AT, et al. Reflex sympathetic dystrophy: early treatment and psychological aspects. *Arch Phys Med Rehabil*. 1994;75:442-446.