Severe Complications of Reflex Sympathetic Dystrophy: Infection, Ulcers, Chronic Edema, Dystonia, and Myoclonus

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Objective: To determine the prevalence, type of complication, predisposing factors, and treatment for severe complications in a population of reflex sympathetic dystrophy (RSD) patients.

Design: Retrospective analysis of the data from RSD patients collected over a 12-year period, to investigate the involvement of predisposing factors in an RSD population without severe complications compared with an RSD population with severe complications.

Setting: Outpatient clinic of a department of surgery at an academic university hospital.

Patients: A total of 1,006 patients with the diagnosis of RSD established according to prospectively defined criteria.

Main Outcome Measures: The signs and symptoms of every RSD patient who visited the department were prospectively documented in the medical history; these data were retrospectively analyzed with special regard to RSD with severe complications—infection, ulcers, chronic edema, dystonia, and/or myoclonus—for prevalence, type of complication, and treatment.

Results: Seventy-four RSD patients who were mostly young and female developed severe complications. More than one complication occurred in 91% of the affected extremities. Severe complications developed more frequently in the lower extremity (65%). In patients in whom the acute RSD started with a decreased skin temperature of the affected extremity, severe complications developed significantly more often than in acute RSD patients with a warm skin temperature of the extremity from the onset of the disease (p < .001).

Conclusions: It is important to recognize “cold” RSD immediately at the onset of the disease because this group of RSD patients has a higher risk of developing a severe complication, mostly followed by a severe disability that is resistant to therapy.

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REFLEX SYMPATHETIC dystrophy (RSD) is a syndrome generally occurring after trauma or after an operation on an extremity. In some cases, it may appear spontaneously.1 The injury initiating RSD may be a contusion, dislocation, or a fracture of an extremity. In prospective studies,2,3 the incidence of RSD after Colles fracture varied from 7% to 37%. Carpal tunnel release, tumor resection, arthroscopy, or nail extraction are examples of operations on extremities that can induce RSD.4,5

At present, there is no consensus about the pathophysiology of RSD. As its name indicates, one theory is that the illness is induced by an abnormal reflex of the orthosympathetic system. However, blockade of the orthosympathetic system is not always an effective treatment.6,7 For this reason, RSD was recently renamed Complex Regional Pain Syndrome (CRPS).8 Sudeck in 19429 introduced the hypothesis that RSD is based on an exaggerated inflammatory response to injury or operation. In a prospective study by Veldman et al.,1 it was shown that the acute phase of RSD is characterized by classical signs and symptoms of inflammation (edema, increased skin temperature, redness of the skin, limited range of motion, and pain). Histologic and scintigraphic studies support this theory,10,11 in which oxygen-derived free radicals and/or neuropeptides may play a role.11,12 RSD is difficult to treat, but the best results are obtained when it is diagnosed early and treated immediately.13,14,15

Only 20%-30% of RSD patients return full-time to their previous employment.17 In our experience, patients with a severe complication such as infection, ulcers, chronic edema, dystonia, or myoclonus of the affected extremity are very difficult to treat. Such complications generally lead to severe additional disability. For this reason, we retrospectively analyzed the extensively and prospectively documented data of a population of RSD patients with severe complications for prevalence, type of complication, and treatment. To investigate a possible involvement of predisposing factors, we compared the data (medical history and clinical signs and symptoms) from the RSD patients without a severe complication within this population to the data from the RSD patients with severe complications.

PATIENTS AND METHODS

All new patients presenting at the outpatient clinic of a university hospital department of surgery were examined for signs and symptoms of RSD. The following were the criteria for the diagnosis of RSD1:

1. At least four of the following: unexplained pain within the affected area; difference in skin color compared with the other extremity; edema of the affected area; difference in skin temperature compared with the other extremity; limited active range of motion.
2. The occurrence of, or increase in, the above signs and symptoms after the extremity was used.
3. Above signs and symptoms present in an area larger than the area of primary injury or operation, including the area distal to the primary injury.

These signs and symptoms present at the time of the first examination were noted in a fixed patient record file.1 During the period January 1, 1984 to January 31, 1996, 1,006 patients...
met the criteria for RSD. Almost 90% of these patients visited our department only once for a second opinion or for therapeutic advice. From this selected population, no conclusions could be drawn as to the prevalence of severe complications in RSD patients.

RSD patients presenting at our outpatient clinic have been examined since 1984 according to an extensive standardized protocol, and the data entered into a computerized patient record file. One part of this file consists of data obtained by a questionnaire and includes age at the time of the visit to our outpatient clinic, age at the onset of the disease, gender, the initiating cause of the RSD (eg, trauma, surgery, spontaneous, others), the patient's description of the skin temperature of the affected extremity at the onset of the RSD, the presence of RSD in another extremity, and modes of treatment before the patient visited our outpatient clinic. The file also included data obtained by physical examination of the patient as described by Veldman et al. The pain of the affected area was scored by the Visual Analog Scale, while edema (present or absent) skin color (blue, red, normal) and skin temperature (cold, warm, normal) of the affected extremity were assessed clinically and documented in comparison to the unaffected contralateral limb. Limitation of the active range of motion was measured with a goniometer. Infection, ulcers, chronic edema, dystonia, and myoclonus of the RSD extremity were noted. From this documented population of RSD patients, we retrospectively studied the subgroup of RSD patients that developed (recurring) infection, ulcers, chronic edema, dystonia, and/or myoclonus of the affected extremity. According to the Dystonia Medical Research Foundation, dystonia is defined as a syndrome of sustained muscle contraction, frequently causing twisting and repetitive movements, or abnormal postures. The dystonia seen in our study consisted of severe focal dystonia with abnormal posture of the affected extremity such as a clenched fist or an inversion and equinus position of the foot. Myoclonus was defined as involuntary, brief, jerky movements, produced by muscle contraction. Dystonia and myoclonus belong to the movement disorders of RSD.

In this population of RSD patients with severe complications, we also analyzed cases suspected of auto-mutilation.

Statistical analysis was performed by Fischer's exact test, two-sided. For the age range only, the Kruskal-Wallis test, two-sided, was performed. The population of RSD patients without a severe complication was compared with the population who developed a severe complication in their RSD extremity. If an RSD patient was found to have complications in more than one extremity suffering from RSD, the data from the extremity first affected with RSD (primary RSD extremity) were used when describing the patient population. When describing the complications, the extremities affected with RSD were described. The level of significance was set at $p < .05$.

RESULTS

Within the documented population of 1,006 RSD patients, 74 patients (10 male and 64 female) developed a severe complication in the primarily affected extremity (table 1). In 5 patients, a complication developed in a second extremity with RSD, while in 2 patients complications occurred in all four extremities with RSD. In the RSD complication population, the age varied between 15 and 69 years (median 35 years). The severe complications were localized in the upper extremity in 26 patients and in the lower extremity in 48 patients. The skin temperature of the affected extremity noted by the patient at the onset of RSD (primary skin temperature) was cold in 46 patients and warm in 19 patients; in 9 patients no difference in skin temperature was observed or remembered at the time of RSD onset.

In 44 patients, RSD developed after injury (ie, contusion, dislocation or fracture); in 20, it after an operation (ie, carpal tunnel release, arthroscopy of the knee); in 3, after an inflammatory process (ie, paronychia, infected ulcer); and in 2 patients, RSD developed after an injection. In 5 patients, no precipitating factor was found.

RSD developed in a second extremity in 21 patients and was present in all four extremities in 6 of the 21. In 15 of these patients, the RSD developed in another limb without any precipitating factor, in 4 after injury, in 1 after an operation, and in 1 patient after an injection.

Most patients from this RSD complication population were referred to our outpatient clinic after intensive treatment elsewhere. The medical treatment of these patients in other hospitals most frequently consisted of intravenous regional sympathetic blockade and/or sympathetic blockade. Intravenous regional sympathetic blockades with guanethidine were performed in 28 of these 74 patients before they visited our outpatient clinic, with no improvement in 27 patients (96%) and with some decrease of complaints in 1 patient. In 32 of the 74 RSD patients who developed a severe complication, a sympathetic ganglion block (stellate ganglion blockade for the upper extremity, lumbar sympathetic block for the lower extremity) was performed in other hospitals. Only 2 patients showed some improvement, whereas in 30 cases (94%) the sympathetic block had no success.

In comparison with the data of our overall population ($n = 932$) of RSD patients without severe complications, the patients ($n = 74$) with complications in the primary extremity were younger ($p < .001$) and more often female ($p = .02$) (table 1). Also, the skin temperature at the onset of RSD was significantly colder in patients with complications ($p < .001$). Severe complications developed more frequently in a lower extremity affected by RSD than in an upper extremity ($p < .001$). Development of the RSD in another limb occurred more frequently in the complication group of patients ($p < .001$).

The severe complications of RSD were analyzed individually for each extremity affected (table 2). In total, 154 complications were seen in 85 extremities in 74 patients. A combination of

<p>| Table 1: Population of RSD Patients Without and With Severe Complications |
|--------------------------|--------------------------|--------------------------|--------------------------|</p>
<table>
<thead>
<tr>
<th></th>
<th>Without Complication</th>
<th>With Complication</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>932</td>
<td>74</td>
<td>.001</td>
</tr>
<tr>
<td>Age range (median)</td>
<td>10-84 (44)</td>
<td>15-69 (35)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>699 (75)</td>
<td>64 (87)</td>
<td>.02</td>
</tr>
<tr>
<td>Male</td>
<td>233 (25)</td>
<td>10 (13)</td>
<td></td>
</tr>
<tr>
<td>Extremity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper</td>
<td>578 (62)</td>
<td>26 (35)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Lower</td>
<td>354 (38)</td>
<td>48 (65)</td>
<td></td>
</tr>
<tr>
<td>Primarily cold skin</td>
<td>280 (30)</td>
<td>46 (62)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>temperature</td>
<td>280 (30)</td>
<td>46 (62)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Multiple RSD</td>
<td>120 (13)</td>
<td>21 (28)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Etiology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trauma</td>
<td>621 (66)</td>
<td>44 (59)</td>
<td>*</td>
</tr>
<tr>
<td>Surgery</td>
<td>182 (20)</td>
<td>20 (27)</td>
<td>*</td>
</tr>
<tr>
<td>Spontaneous</td>
<td>94 (10)</td>
<td>5 (7)</td>
<td>*</td>
</tr>
<tr>
<td>Other</td>
<td>35 (4)</td>
<td>5 (7)</td>
<td>*</td>
</tr>
</tbody>
</table>

*Not significant.
complications in one extremity was present in 78 of these 85 limbs (91%). Presentation of a single complication was seen in 7 extremities, including infection (n = 1), ulcers (n = 3), and chronic edema (n = 3).

Infection as a complication was seen in 30 extremities. Ulceration of the skin and/or chronic edema was frequently followed by infection of the affected limb (n = 24). In 13 of these cases, a subsequent amputation was necessary. The infection consisted in 9 cases of erysipelas due to Streptococcus haemolyticus group B, and in 4 cases the chronic edema was followed by cellulitis due to Staphylococcus aureus. In two cases, erysipelas was controlled successfully with intramuscular long-acting penicillin (on our advice, a dosage of 2 million units), whereas in one case penicillin was ineffective and amputation was necessary. In the 6 other cases, erysipelas was treated in our hospital with a combination of intravenous mannitol (100 grams per 24 hours) infusion and intravenous penicillin (6 million units per 24 hours), curing the infection in 5 cases, and failing in one case, in which there was a subsequent amputation.

In 5 patients, RSD developed in an area with a traumatic or surgical wound, contaminated with anaerobic bacteria. Appropriate antibiotic therapy performed in other hospitals, in combination with debridement, did not cure the infection. In one of these patients, who had a chronic ulcer after a superficial second-degree burn wound complicated by RSD of the hand, debridement, intravenous antibiotics, intravenous mannitol, and verapamil cured the ulcer and reduced the RSD complaints. In 4 patients, the ulcerating wound infected with anaerobic micro-organisms was resistant to the above therapy, but was cured by transplantation of a free revascularized myocutaneous flap performed in our hospital.

Ulcers were observed in 26 RSD extremities. Ulceration was followed in 73% by infection of the extremity with RSD.

Chronic edema as a complication of RSD was seen in 27 extremities (fig 1). In 18 RSD extremities (62%), chronic edema was followed by infection. Chronic edema progressed to mimic elephantiasis in 5 cases. Because of the coexistent hyperpathy, compressive stockings were tolerated in only 3 patients, reducing the edema in these cases. Elevation of the edematous extremity was the only alternative, and 55% of the patients with this problem in the lower limb used a wheelchair in the presenting position, for comfort and protection. Tenotomy or lengthening tenoplasty of the finger flexor tendons was only performed in our hospital when, because of the “clenched fist,” daily hygiene became impossible or pressure spots developed. Dystonia always persisted after this operation but was less severe and allowed for better care of the hand.

Myoclonus as a complication of RSD was found in 21 limbs, localized in 9 upper extremities and in 12 lower extremities. In the 6 other cases, myoclonus was cured by transplantation of a free revascularized myocutaneous flap performed in our hospital.

In 51 RSD patients, movement disorder (dystonia and/or myoclonus) developed in 62 extremities. These movement disorders were complicated by infection, ulcers, and/or chronic edema in 25 limbs (40%).

Auto-Mutilation

In this population of RSD patients with severe complications, auto-mutilation was regularly suspected. In these cases, it
proved difficult to establish or exclude auto-mutilation as a cause of the complication. Nine patients with severe complications were suspected of auto-mutilation by other specialists. We could confirm auto-mutilation in 5 patients and disclaim this diagnosis in 3 patients. In 1 patient, the concerned extremity was amputated before the patient was seen by us.

All 3 RSD patients, inappropriately suspected of auto-mutilation had a chronic therapy-resistant ulcer with infection. These ulcers all healed after a split-skin transplantation or covering with a free revascularized myocutaneous flap.

In 5 RSD patients, we confirmed auto-mutilation. In 4 of these patients, edema was recognizable in an area distal to a sharply delineated skin grooving, induced by pinching off a limb. The extremity affected by auto-mutilation was not the primary extremity suffering from RSD.

One patient who was cured from RSD in a hand that was complicated by infection and ulcers had a recurrence of RSD after a coin-sized burn on the dorsal side of the same hand.

DISCUSSION

In a population of 1,006 RSD patients, 74 patients (7%) developed one or more severe complications in the affected extremity because of infection, ulcers, chronic edema, dystonia, or myoclonus. As far as we could determine, except for case reports, no single study has addressed the prevalence of such complications in a large population of RSD patients. Severe complications occurred more frequently in younger and female patients. The initiating factor for the development of RSD was similar in RSD patients with or without complications. RSD patients with one severe complication are at risk to develop subsequent complications in the affected extremity. Progression of RSD to another extremity was seen frequently in patients who had complications, compared with RSD patients without complications.

Classically, RSD develops in three phases, based on the alterations in skin temperature. During the beginning period (2 to 3 months), the skin is warm, followed by a phase of vasomotor instability lasting several months, and ending with a cold phase.\(^5\) In a previous report,\(^6\) 13% of the patients who had RSD started with a cold skin temperature, while others remained in the first “warm” stage for more than 10 years. Forty-six of the 74 RSD patients (62%) who developed a complication in the affected extremity had a cold skin temperature from the onset.\(^7\) In our view, the subdivision of RSD into primarily cold and primarily warm is clinically relevant because of the worse functional outcome of the primarily cold RSD\(^8\) and because of a higher incidence of recurrence or development of RSD in a second extremity\(^9\) and the development of severe complications.
Because it has been demonstrated that in "cold" RSD blood flow to the affected extremity is significantly decreased, while in "warm" RSD it is increased, and because there is evidence that in both "cold" and "warm" RSD the oxygen extraction is decreased, we hypothesize that the worse outcome of primarily "cold" RSD results from severe tissue hypoxia. Accordingly, in treating RSD patients since 1984, primarily "cold" RSD is treated early and vigorously with vasodilators such as verapamil retard (240 mg/24 h), ketanserin, or sympathetic blockade to optimize perfusion of the affected extremity.

In RSD extremities complicated by recurrent infections, treatment with only antibiotics was frequently not effective, and in 13 of the 30 infected RSD extremities a subsequent amputation was necessary. In our opinion, infected RSD extremities are frequently resistant to conventional therapy because of impaired oxygen consumption in the RSD extremity. RSD patients with chronic ulcers were often suspected of auto-mutilation because of the failure of conventional therapy. By curing the infected ulcer with a split-skin transplantation or a free revascularized myocutaneous flap, the suspicion of auto-mutilation could be disclaimed.

In our population of RSD patients, skin lesions consisted only of ulcers. We never noticed purpuric-like inflammatory dermatitis or bullae as described by Webster and colleagues. An RSD extremity with ulcers and or chronic edema is at risk of developing severe infection. In such cases, amputation eventually may be necessary.

In 1984, the movement disorder described in 4 RSD patients was interpreted as a distinct clinical syndrome of RSD. Schott introduced the theory that causalgia induces involuntary movements. Schwartzman and Kerrigan reported 15 RSD patients with severe dystonia in a population of 43 RSD patients with movement disorders in a total of 200 RSD patients. Dystonia associated with RSD was reported in 9 RSD patients by Jankovic and van der Linden. Bhatia described 18 RSD patients with movement disorders in a total of 200 RSD patients. The disability resulting from severe dystonia and from chronic edema is immense. In our experience, further efforts at curative therapy in these cases are ineffective and should be stopped in favor of an approach that accepts the situation and looks for solutions for the resulting disability.

Cooperation with a rehabilitation specialist is required for adaptation of the home situation. In addition, the RSD extremity should be supported with an orthosis, a wheelchair, or adaption of their home situation, as appropriate.

**References**