Complex regional pain syndrome type 1 in young adults

Yasin Demir,[1] Ümüt Güzelküçük,[1] Serdar Kesikburun,[1] Berke Aras,[2] Mehmet Ali Taşkaynatan,[1] Arif Kenan Tan[1]

(1) University of Health Sciences, Gülhane Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Ankara, Turkey

(2) Kastamonu Physical Medicine and Rehabilitation Center, Department of Physical Medicine and Rehabilitation, Kastamonu, Turkey

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Corresponding Author:
Yasin Demir
University of Health Sciences, Gülhane Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Ankara, Turkey,
yasin.demir3@saglik.gov.tr

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ABSTRACT

Aims: This study aimed to conduct a medical chart review of complex regional pain syndrome (CRPS) type 1 young male patients admitted to a rehabilitation center with the intention of developing a better understanding of the condition. **Methods:** We retrospectively reviewed the medical records of patients with CRPS type 1 aged between 18-25 years. Demographic and clinical charecteristics such as age, gender, initiating event, affected side, and the rate of recovery was noted for analysis. **Results:** The study included 61 patients with CRPS type 1 (mean age: 22.7±2.1 years). Fracture (39.3%) was the most common initiating factor. Unilateral CRPS type 1 was determined in 50 cases, 60.8% of the cases were on the right side, and 72.5% were on the upper extremity. The three-phase bone scintigraphy was consistent with a clinically diagnosed CRPS type 1 in 36 patients (59%). A full recovery of the disease was recorded in 31 (50.8%) cases. **Conclusions:** This study showed that the upper extremity was affected three times more than the lower extremity and fracture was the most common precipitating event. The rate of work return in younger adults was high.

Introduction

Complex regional pain syndrome (CRPS) is the current diagnostic label for the syndrome historically referred to as reflex sympathetic dystrophy, causalgia, and a variety of other terms (1). It is a clinical entity characterized by the presence of allodynia or hyperalgesia, edema, sweating changes, abnormal skin color and temperature, trophic changes of nails and hairs and often impairment of motor function in the affected extremity (2). It usually requires long-term, intensive medical therapy whereby many CRPS patients are no longer able to perform their usual (social) role in everyday life. As a result, CRPS has a major impact on quality of life (3).

The International Association for the Study of Pain (IASP) has recommended dividing CRPS into two types considering the presence of nerve lesion secondary to injury (4). CRPS Type 1, which has been referred to in the past as reflex sympathetic dystrophy, features no major nerve lesion. CRPS type II is associated with known nerve injury. The vast majority of patients diagnosed with CRPS have type 1.

Although there have been many published reports of CRPS type 1, it is still a poorly understood disorder in respect of pathophysiology, treatment and recovery. Previous studies investigating CRPS have included patients from all age groups (1,5-14). There might be clinical differences between age groups and it can be helpful to identify the clinical characteristics of young adults as they constitute a significant part of the work force and thereby, productivity. These injuries seen in young persons of productive age might lead to considerable economic losses.

The primary aim of the present study was to conduct a retrospective medical chart review of CRPS type 1 young patients referred to a rehabilitation center with the intention of developing a better understanding of the condition. Thus, it was aimed to be of benefit in indicating ways to prevent disease, and increase the recovery rates of this population group.

Methods

The study participants were consecutive admissions to the tertiary rehabilitation center from January 2010 to April 2017. A retrospective review was made of the medical records of patients aged between 18-25 years without a history of nerve

injury and who were diagnosed as CRPS type 1 according to IASP criteria (2). The IASP CRPS criteria include continuing pain disproportionate to any inciting event and four distinct diagnostic categories. The four categories are recognized as sensory findings including hyperesthesia, allodynia, hyperalgesia; vasomotor findings including temperature and/or skin color asymmetry; sudomotor findings including edema and/or sweating changes; motor/trophic findings including decreased range of motion, motor dysfunction (weakness, tremor, dystonia), trophic changes of hair, nail, skin. Clinical diagnostic decision rules are endorsed as the presence of signs observed by the physician on clinical examination in two or more of these categories and symptoms reported by the patient in at least three of four categories.

The study had the approval of local ethical committees. This study was conducted in accordance with the Helsinki Declaration 2008 principles. All charts were reviewed by one of the authors (BA). Data regarding demographic characteristics and clinical features including age, gender, time since injury, etiology, affected side, total rest time, frequency and duration of hospitalization, three phase bone scintigraphy (TPBS), treatment type and recovery were recorded and then analyzed.

Statistical Analysis

Statistical analysis was performed using SPSS v.21.0 for Windows (SPSS, Chicago, IL, USA). Continuous variables are presented as mean ± standard deviation (range) and categorical variables are shown as frequency and percentage. Categorical variables were compared between groups using the Chi-square test. For all statistical tests, a value of $p<0.05$ was considered statistically significant.

Results

The study comprised 61 patients with CRPS type 1. All of them were male with the mean age 22.7±2.1 years (Table 1). Patients reported having CRPS type 1 symptoms for a mean duration of 35.0±27.9 weeks. An antecedent event was reported by 82% of the cases with fracture was in 39.3%, soft tissue injury in 32.8% and tendon injury in 8.2%. In 18% of patients (11 cases), no precipitating event was reported or patients could not remember a specific injury (Figure 1).

An extremity was affected in all of the cases with upper extremities at the rate of 73.8% and lower extremities at 26.2%. Symptoms developed on the right side in 59% of patients and on the left side in 39% of the patients. Bilateral symptoms were determined in 1.6% of the cases. There was no significant difference between upper and lower extremities with right or left side involvement (Table 2).

Three phase bone scintigraphy was applied to all of the patients with mean time of 12.4±2.5 weeks. Findings were reported as 'consistent with CRPS' in 59% of the cases while reported as 'not consistent with the diagnosis of CRPS' in 41% of the cases.

The number of hospitalization was once in 21.3%, two times in 29.5%, three times in 29.5% and four or more times in 19.7% of the cases. The mean duration of hospitalization was 61.8±39 days and the mean duration of total rest was 98.4±79.4 days.

Treatment modalities were as follows: medical treatment, non- pharmacological therapies and invasive management. Medical treatment included non-steroid anti-inflammatory drugs, antidepressants and antiepileptic drugs. Non-steroid anti-inflammatory drugs were used in 52.5% of the patients, antidepressants were used by 19.7% and antiepileptic drugs were used by 18% of the patients. Non-pharmacological therapies included physical therapy, occupational therapy and mirror therapy. All of the patients were applied physical and occupational therapy. Mirror therapy was used in 6.5% of cases with CRPS type 1. Sympathetic ganglion block was applied in one case (1.6%).

Recovery rates were 48.9% in upper extremity and 56.3% in lower extremity and there was no significant difference between upper and lower extremity recovery rates (Table 2). Recovery rates were also compared according to different treatment methods and there were no significant differences between groups (Table 3).

Table 1. Demographic and clinical features of the patients

	Patients
Age (years)	22.7±2.1
Gender	
Male	61 (100)
Female	0 (0)
Symptom duration (weeks)	35.0±27.9
Initiating event	
Fracture	24 (39)
Soft tissue injury	20 (33)
Tendon injury	6 (10)
No initiating event	11 (18)
Side	
Upper	45(74)
Lower	16(26)
Length of hospitalization (days)	61.8±39.0
Total resting period (days)	98.4±79.4

Data are expressed as mean ± standart deviation for continuous variables,
number (percentage) for categorical variables.

Table 2. Comparison of upper and lower extremity involvement

	Upper Extremity	Lower Extremity	Total	P
Localization, n (%)				0.811
Right	26 (57.8)	10 (62.5)	36	
Left	18 (40)	6 (37.5)	24	
Bilateral	1 (2.2)	-	1	
Recovery				0.613
Yes	22 (48.9)	9 (56.3)	31	
No	23 (51.1)	7 (43.8)	30	

Discussion

Fractures and soft tissue injuries were found to be the most common initiating etiological factors resulting in CRPS type 1

Table 3. Recovery rates according to treatment methods

Treatment Methods	Recovery		P
	Yes	No	
Medical treatment			0.530
Yes, n (%)	20 (54.1)	17 (45.9)	
No n (%)	11 (45.8)	13 (54.2)	
Non-pharmacological therapies			N/A
Yes n (%)	31 (50.8)	30 (49.2)	
No n (%)	-	-	
Invasive management			N/A
Yes n (%)	-	1 (100)	
No n (%)	-	-	

N/A: not applicable

in young adults and the upper extremities were affected more often than the lower extremities. In addition, the TPBS was reported as negative for CRPS 1 in nearly half the patients. The impact of the disease on the ability to work was high as half the patients had become officially disabled despite several treatment methods. The present study also presents epidemiologic data on CRPS type 1 patients in young adults who were treated on an inpatient basis at our hospital, which is a tertiary rehabilitation center.

CRPS is a chronic neuropathic pain disorder with accompanying autonomic features. The pathogenesis of CRPS is not well defined, rendering this syndrome a global challenge in both diagnosis and treatment. Proposed mechanisms include exaggerated inflammation, altered sympathetic and catecholaminergic function, changed cutaneous innervation, central and peripheral sensitization, genetic and psychological factors (15,16).

Incidence of the CRPS type 1 changes between 5.5 and 26.2 cases per 100,000 people per year (5). The results of epidemiologic studies in the general population show that the number of new cases of CRPS type 1 is 50,000 per year in the United States (5,8,17). It is more common in women. Previously published ratios range from 2.3:1 to 4:1 (5,8). In general, white women between the ages of 35 and 55 years outnumbered any other sub-group. Previous evidence of sex differences in inflammatory markers showed that females often present greater levels of pro-inflammatory markers following immune challenge (18). Unlike the results of previous studies, all of the patients were male in the current study. The male dominancy of CRPS type 1 in the present study was probably due to the fact that our hospital primarily serves veterans.

CRPS type 1 is a painful condition that generally arises from a traumatic initiating event. The most common reported triggers are fracture, soft tissue injury, sprain and surgery (1,4,5). There is conflicting results regarding association between the severity of the traumatic injury and developing CRPS type 1. Jellad et al reported that CRPS type 1 occurs equally after minor and severe injuries (19). On the other hand, Ortiz-Romero et al stated that when compared to low-impact injuries, high-impact injuries have been considered significant risk for developing CRPS type 1 (14). In the current study, fracture and soft tissue injury were found to be the leading etiological factors contributing to CRPS type 1 in accordance with existing literature. In addition to these frequently encountered initiating events, central pathologies such as stroke and spinal cord injury may also lead to CRPS type 1 (1,6). More rarely, there have been published case reports of herpes zoster, burn scarring and angioplasty causing CRPS type 1 (20-22). Although some researchers have reported that all patients included in a study have claimed that their disease was associated with a traumatic event, some have shown the absence of an initiating event in approximately 10% of cases (4-8,23). In the current study, 18% of cases had no precipitating event or could not remember a specific injury.

CRPS type 1 mostly involves upper and lower extremities, although there have been rare reports of other sites such as the face, abdomen and pelvis (7,8). In the current study, the upper extremities were affected at three times the rate of lower extremities, but there was no significant difference between the right and left side of the body. It is fortunate that lower extremities are affected less frequently than upper extremities as lower limb lesions have been shown to be related to a lower rate of return to work than upper limb lesions (9).

There are informative tests and procedures that are not specific for the diagnosis of CRPS such as infrared thermography, quantitative sensory testing, sudomotor tests, TPBS and x-ray (spotty osteoporosis) (1,5,24-26). TPBS has been widely used to diagnose CRPS. It has been reported that 53-85% of the TPBS in these cases have shown a pattern consistent with CRPS (1,5). Imperfect reference tests may lead to under-estimation of the diagnostic accuracy of TPBS. In addition, biased results can occur when a dependency between the reference tests and TPBS exists (27). Shorter disease duration has been associated with a higher likely hood of a positive TPBS (28). It may be hypothesized that the higher rate of positive bone scans within the first year is related to the neurogenic inflammation which also may affect bone metabolism. It can be concluded that, the presence of positive scintigraphy findings may help in a CRPS diagnosis, but clinicians should persist with a diagnosis in cases of negative TPBS in the light of clinical findings. In consistent with literature, nearly half of the clinically diagnosed patients' bone scan was negative for CRPS type 1 diagnosis in the current study.

CRPS is one of the more challenging chronic pain conditions to treat successfully since the pathogenesis is not well identified. Most important part of the CRPS type 1 management is prevention. It is has been showed that oral administration of 500 mg of vitamin C per day for 50 days from the date of the injury reduces the incidence of CRPS-I in patients with wrist fractures (29).

Early detection and treatment is essential to prevent long-standing or permanent disability (30). Primary goal of the treatment in CRPS is functional restoration. The treatment consists of physical and occupational therapy, pharmacological treatment, sympathetic ganglion block, neuromodulation and behavioral therapy including patient education. Physical and occupational therapy includes physiotherapy, functional activities, transcutaneous electrical nerve stimulation, relaxation techniques, hydrotherapy and edema control strategies. Those therapy modalities applied in CRPS-I have been showed beneficial impact on the CRPS type 1 (30,31). Commonly preferred oral agents are: nonsteroidal anti-inflammatory drugs (ibuprofen, naproxen), anticonvulsants (gabapentin, pregabalin), tricyclic antidepressants (amitriptilin), bisphosphonates (pamidronate, alendronate) and calcium-channel blockers. Especially,

bisphosphonates and calcium-channel blockers have showed efficacy for restoring function in CRPS type 1 cases (32,33).

Response to treatment and resolution rates have been investigated by some authors. It has been shown that CRPS tends to continue, and only a minority of patients have full recovery (7,11-14). Regarding the prognosis, Bean et al reported in a longitudinal study that within the first year, 70% improved, especially in the function of the extremity and the visible symptoms (34). In the current study, half of the patients could return to work. The main reason for the high recovery rate might be related to the population age as the study only included young, active people who had to work.

As with all retrospective research, the data obtained were limited. First, the data were not collected prospectively in a standardized fashion. Second, other relevant characteristics, such as the effect of psychological factors, were not studied. Third, After PT, we assessed patients according to CRPS diagnostic criteria after physical therapy and we did not note any need medication for pain. Finally, there is a lack of long-term follow-up outcomes of the patients, which might be useful in better understanding this condition.

In conclusion, the data obtained in this study showed that the upper extremity was affected three times more frequently than the lower extremity and a fracture was the most common precipitating event. The return to work rates was higher than general population.

Acknowledgment

YD was responsible for writing. ÜG was responsible for acquisition of data. SK was responsible for analysis and interpretation of data. BA was responsible for acquisition of data. MAT was responsible for study conception and design. AKT was responsible for critical revision.

Conflict of interest

The authors do not have anything to disclose regarding conflict of interest with respect to this manuscript.

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