

Case Report

Posttraumatic Complex Regional Pain Syndrome and Related Comorbidities

CRISTINA-ELENA GOFIȚĂ¹, ANCA EMANUELA MUȘETESCU¹,
PAULINA LUCIA CIUREA¹, MIHAIL-VIRGIL BOLDEANU²,
MAGDALENA RODICA TRĂISTARU³, ANA-MARIA BUMBEA³,
OTILIA-CONSTANTINA ROGOVEANU³

¹Department of Rheumatology, University of Medicine and Pharmacy of Craiova, Romania

²Department of Immunology, University of Medicine and Pharmacy of Craiova, Romania

³Department of Medical Rehabilitation, University of Medicine and Pharmacy of Craiova, Romania

ABSTRACT: The complex regional pain syndrome (CRPS) is a neuropathic disorder, often precipitated by a fracture, injury of the soft tissue or a surgical procedure followed by extended immobilization. Clinical signs and symptoms of this syndrome include abnormalities of pain processing (mechanical and thermal allodynia, hyperalgesia and hyperpathia), skin changes regarding local temperature and the presence of erythema, cyanosis or mottled appearance, neurogenic edema, motor and trophic disorders. The CRPS has three evolutionary stages-acute, dystrophic and atrophic, and it is divided into two types, reflecting the absence or presence of nerve damage. The patient presented in this study was a female with a history of metabolic syndrome, diagnosed with polyarticular chronic gout, which despite the specific drug treatment administered, had multiple predisposing factors for the development of CRPS consecutive to the fracture of both bones of the right forearm. It is evident that the recovery period after injury is slightly different in each individual and depends on the severity of the injury and patient factors such as age, general condition and the presence of other comorbidities. The delay between the onset of symptoms and her presentation to the physician, conferred a poor prognosis for the developing pathology, with important functional and motor impairment.

KEYWORDS: CRPS, metabolic syndrome, nerve lesion, neurovegetative dystonia

Introduction

The complex regional pain syndrome (CRPS) is a disease with multiple clinical manifestations of neurogenic inflammation translated through severe allodynia, as well as alterations in the blood flow serving the affected segment [1], swelling, abnormal skin coloration and maladaptive neuroplasticity [2].

Based on the existence of neural damage, there is a different terminology for CRPS. CRPS type I, where no nervous lesion is detected, previously called reflex sympathetic dystrophy or algoneurodystrophy, is a neuropathic chronic condition characterized by debilitating regional pain (spontaneous or provoked), increased sensitivity to tactile stimuli, swelling, vasomotor and sudomotor abnormalities (due to sympathetic dysfunction) [3], and the alteration of the motor function (muscular weakness, tremor and muscle spasms) [4,5].

The difference between CRPS type 2 and CRPS type 1 is that type 2 occurs after injury (section, contusion, avulsion) of a peripheral nerve or one of its branches or the trunk [6].

CRPS may be a consequence of a variety of trigger factors, of which the most frequently

incriminated is peripheral trauma (55-60%), specifically distal radius fracture [7,8].

CRPS has been reported more frequently in women compared to men (women to men ratio of 4:1), the average age of onset between 50-60 years.

Amongst CRPS predisposing factors we mention neurovegetative dystonia, hyperparathyroidism, use of certain drugs-angiotensin-converting enzyme (ACE) inhibitors, metabolic syndrome, alcohol abuse, smoking and psychological factors.

The use of adequate perioperative analgesia, minimal invasive surgical techniques, avoidance or reducing the immobilization period of the affected segment as well and early postoperative mobilization decrease the risk of CRPS, but their benefits remain unproven [9].

Case Report

We present the case of a 57-year-old patient, admitted on the Rheumatology Department of the Emergency County Hospital of Craiova.

The patient accused increased, constant burning pain, allodynia, and hyperpathia in the upper right limb.

Additionally, polyarticular pain was described in the left metacarpophalangeal joints (MCP) and proximal interphalangeal joints (PIP), left IIIrd, IVth and Vth metatarsophalangeal joints (MTP), ankles and both knees.

The patient is known with paralysis of the median and radian nerve consecutive to the fracture of both bones of the right forearm (Frykman II) at the age of 49 years, operated and viciously consolidated.

Postoperative the patient experienced pain, swelling and limited finger movement that persisted for up to three weeks without any signs of improvement.

In spite of physical and medical treatment, two years after the trigger event, the patient's complaints were not resolved, moreover sudomotor and vasomotor changes on the right forearm were observed, with a subsequent diagnosis of CRPS type 2 (Budapest criteria 2010) [10].

In addition, the patient is known with stage 2 essential hypertension on ACE inhibitors with aortic atheromatosis and hypertensive angiopathy.

Also, 10 years ago, the patient was diagnosed with type 2 diabetes with difficult-to-control glycemic values.

Clinical examination revealed multiple postfracture scars with normal appearance on the

right forearm, also with vasomotor skin disorder, manifested through low temperature, reduced elasticity and hydration of the affected limb.

In addition, allodynia and hyperalgesia were emphasized during the palpation of the right forearm.

Mobilization of the right elbow exhibited articular and tendinous stiffness, fixed in semiflexion.

The patient also presented muscular atrophies of the right arm and forearm, and the absence of the bicipital, tricipital and brachioradialis reflexes.

The right limb muscle strength was quantified as follows: flexion, extension and abduction of the shoulder were 3/5, while the flexion and extension of the elbow, as well as the flexion and extension of the wrist were 2/5.

The typical aspect of radial nerve palsy ("wrist drop") was observed, with the IVth and Vth fingers fixed in flexion, bilateral Heberden nodes in IInd to Vth fingers, discretely swollen right wrist and IInd and IIIrd MCP joints (Fig.1,2).

Left upper and both lower limbs had normal strength, sensitivity and reflexes.

Hair growth on the upper right limb was reduced with brittle nails which had a slow growth rate.



Fig.1. Multiple post fracture scars with normal appearance atrophies of the right arm and forearm



Fig.2. Radial nerve palsy (“wrist drop”)

Laboratory investigations revealed a slightly non-specific inflammatory biological syndrome (ESR, fibrinogen, CRP above the upper limit),

mixed dyslipidemia (elevated total cholesterol and triglycerides), hyperglycemia and hyperuricemia (Table 1).

Table 1. Blood test results accompanied by their recorded and normal values

Biological tests	Recorded value	Normal values
Erythrocyte sedimentation rate (ESR)	32mm/h	2-12mm/h
C-reactive protein	7.9mg/dL	0-5mg/L
Fibrinogen	426mg/dL	200-390mg/dL
Uricemia	7.2mg/dL	2.6-6mg/dL
Glycemia	125mg/dL	60-100mg/dL
Total cholesterol	279mg/dL	<200mg/dL
Triglycerides	190mg/dL	<150mg/dL

A forearm X-ray was performed showing diffuse osteoporosis in the bones of the forearm with discontinuity and significant bone resorption of the ulna, marked narrowing of the radiocarpal joint and elbow ankylosis (Fig.3). Hand X-ray was also performed displaying the

ankylosis in flexion of the IInd and IIIrd MCP, patchy osteoporosis and narrowing of the articular spaces with osteophytic proliferation on the distal interphalangeal joints (DIP) of the left hand. Left wrist X-ray was without pathological changes.



Fig.3. Right forearm X-Ray

The steadily elevated values of uric acid as well as the polyarthralgia at the knee level and small joints of the hands and feet have led to the musculoskeletal ultrasound evaluation of the incriminated joints.

Thus, ultrasound revealed the double contour sign in the femoral trochlear cartilage as well as at the ankle tibiotalar cartilage.

Furthermore, the feet ultrasound revealed tophaceous deposits with monosodium urate crystals as aggregates and hyperechoic spots on the Ist and IInd left MTP joints as well as grade 2 proliferative synovitis and microcrystalline deposits, double contour sign on bilateral IVth MTP joints (Fig.4,5).

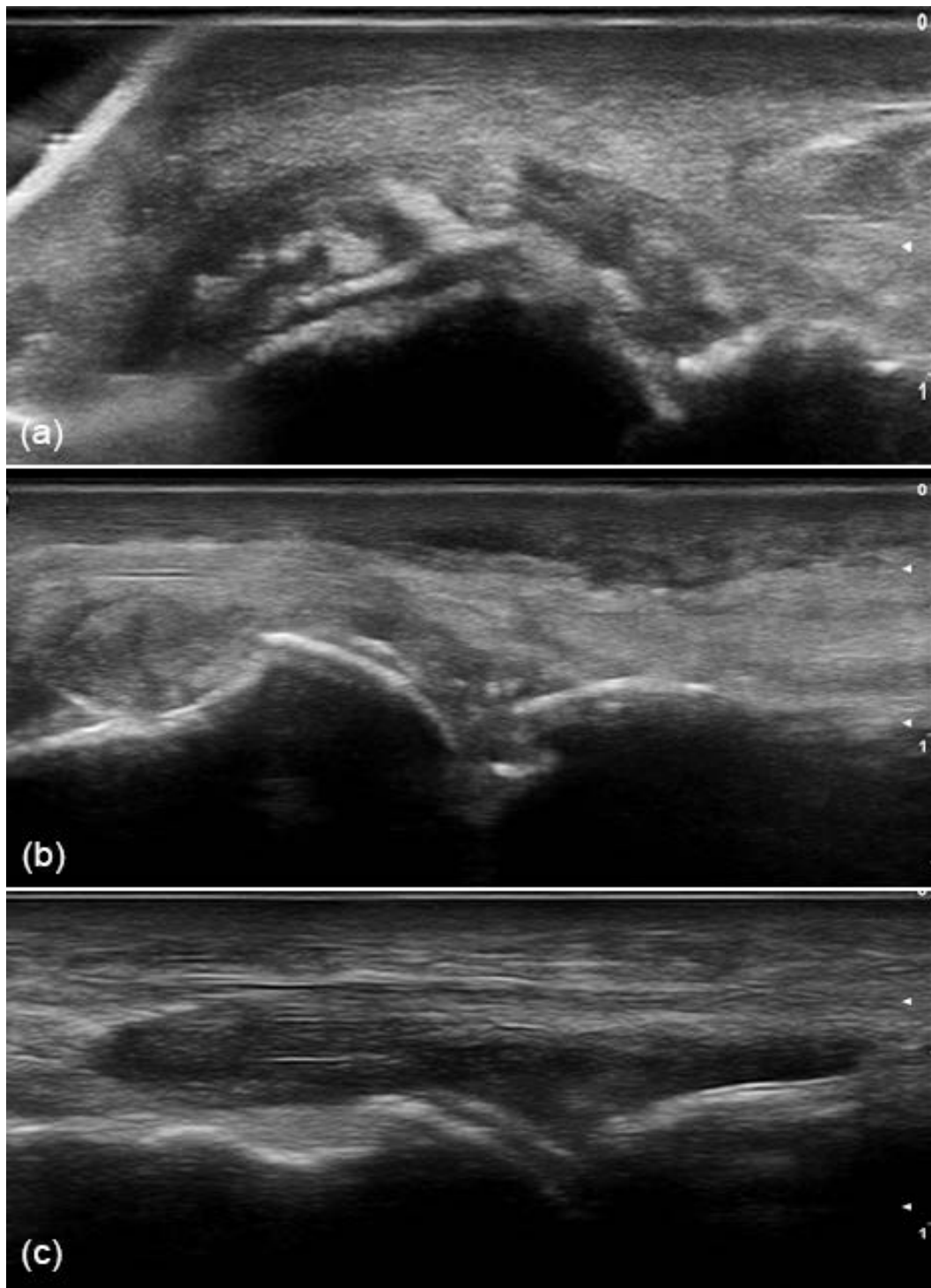


Fig.4. Longitudinal scan of first (a), second (b) and IV MTP joint with important distension of joint capsule due to aggregates of monosodium urate crystal deposition, hyperechoic spots (a, b) inside the joint and the double contour sign (a, b, c) with diffuse hyperechoic enhancement of the chondrosynovial interface, all characteristic imaging features of crystal-related arthropathy

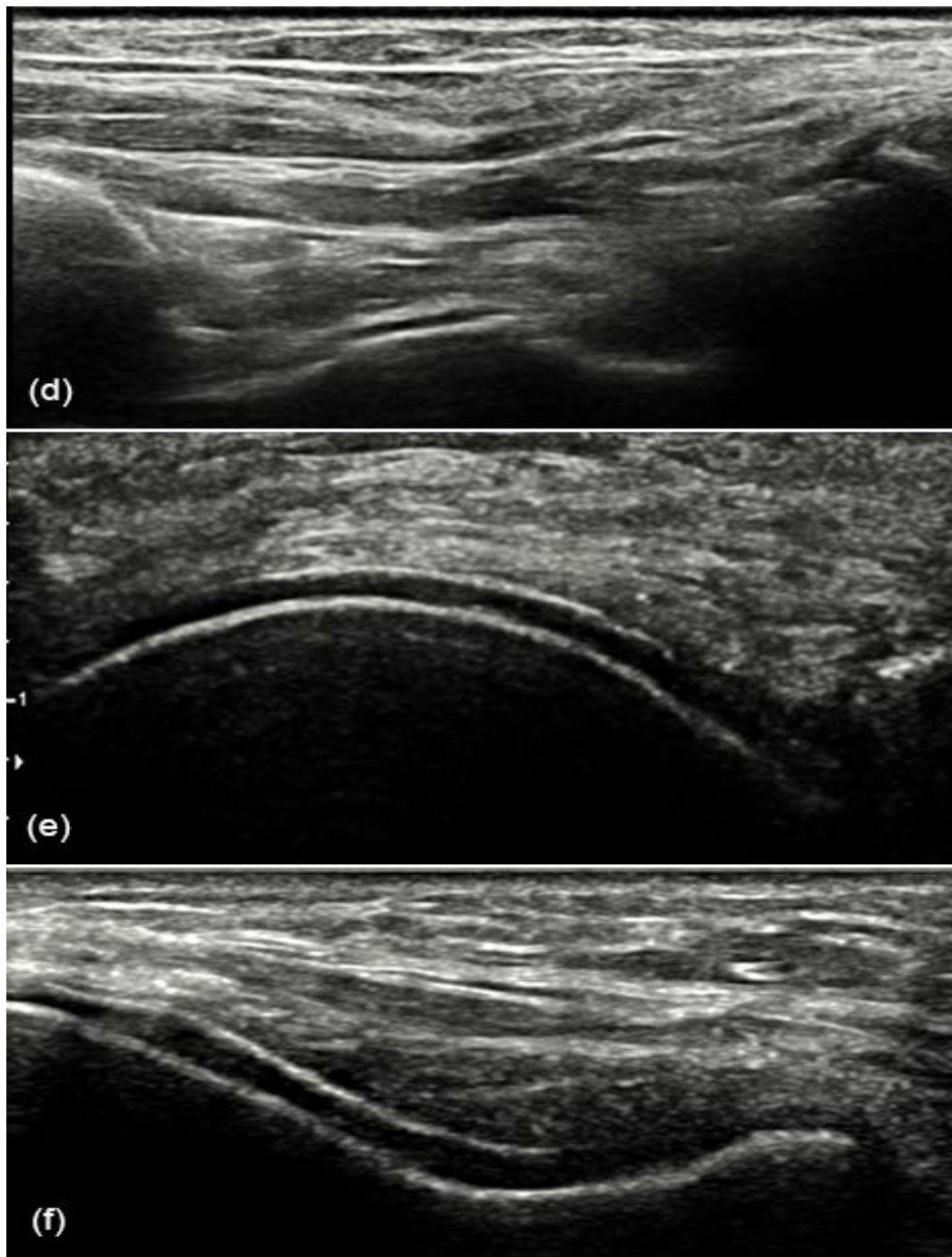


Fig.5. Longitudinal scan (d) of the ankle joint with the double contour sign as well as longitudinal and transversal scan (e, f) of the femoral trochlear cartilage with the same enhancement of the superficial margin of the cartilage independent of the ultrasound beam direction

Following the CRPS diagnosis, the patient received symptomatic pain therapy: antalgic with complex action on the central nervous system (Tramadol), anticonvulsant medication (Gabapentin 900mg/day) in painful paroxysmal crises, bisphosphonate therapy and. It has also been attempted to reduce the edema and fibrosis by nonsteroidal anti-inflammatory drugs and glucocorticoids, by centripetal massage and recovering the mobility of the affected extremity by complementary kinetotherapy. The patient

agreed and signed a written consent form regarding the publication of these data.

Discussion

CRPS types I and II are clinical syndromes with symptoms which include burning or aching pain, hyperalgesia or allodynia, edema, sudomotor and vasomotor changes predominantly in the distal extremity [11]. Most commonly, CRPS type I occurs after a soft

tissue trauma, while CRPS type II occurs after damage to a peripheral nervous trunk [12].

CRPS is more frequent in women and is very rare in children [13]. Its onset can be primary in 25% of the cases, but in most situations, it is secondary to a trauma (35% of the cases) [14], central neurologic (hemiplegia, Parkinson's disease) or cardiac (coronary heart disease) damage, pregnancy, or long-term treatment (antiepileptics, barbiturates or chemotherapy). It is considered that some patients might have a tendency for CRPS with an increased susceptibility to develop abnormal responses to painful stimuli and an extended sustenance of this reaction [15]. Anxiety, cholesterol, depression, diabetes, hyperuricemia can also be aggravating factors. Increased level of uric acid has been correlated with oxidative stress. Free radicals can intensify inflammation, enhance vascular permeability, release neuropeptides (substance P), and cause tissue damage. Hence, clinical studies have proved that the free radical scavengers like N-acetylcysteine, dimethylsulfoxide, mannitol and vitamin C can diminish CRPS signs and symptoms [16-18].

The patient presented in this study was a female with a history of metabolic syndrome, diagnosed with polyarticular chronic gout, which despite the specific drug treatment administered, had multiple predisposing factors for the development of CRPS type 2. The delay between the onset of symptoms and her presentation to the physician, conferred a poor prognosis for the developing pathology, with important functional and motor impairment. Thus, despite the treatment properly administered, the patient developed a chronic and extensive form of CRPS [19].

CRPS usually affects the limbs, but it can occur almost anywhere in the body [20]. The pleomorphic clinical appearance is more severe than it would normally be expected from the degree of the trigger event and might also extend beyond the area involved in the initial trauma. Thus, CRPS patients, even after minor trauma, are susceptible to exaggerated inflammatory response and multiple organ distress syndrome.

The activation of the sympathetic system following a trauma, induces the inflammatory stage of tissue healing, leading to peripheral vasoconstriction, increasing the edema and hyperalgesia in order to prevent worsening of the injuries [21]. This process could last from a few minutes up to a few hours, but in CRPS it persists, establishing a painful vicious circle. This sympathetic hyperactivity could be

associated to the development of new synapses between the large sensorial fibers A β and the afferent sympathetic fibers, creating a sensory-vegetative response that leads to the sympathetic hyperactivity and the constant activation of the sensorial neurons [22,23].

It has been taken in consideration that CRPS is more likely to affect people with psychological instability [24]. Patients with CRPS have been described as emotionally unstable, anxious, depressed, nervous, chronically complainers, sympathetic hyperreactors, in poor health, pathologic malingers, and susceptible to major life stresses.

The lack of a standard reference test for the diagnosis of CRPS may lead to over diagnosis of this condition [25]. Other neuropathic disorders, undifferentiated arthritis, inflammatory arthropathies, and unilateral vascular occlusive disorders should all be considered as possible differential diagnosis. Taken together, the clinical and imaging findings will help narrow the differential diagnoses.

The early diagnosis of CRPS contributes to an accurate therapeutic approach [26]. The main drugs selected in this pathology are glucocorticoids (with local administration), calcitonin (analgesic and vasoactive effect), analgesics and anticonvulsant medication (Gabapentin) in painful paroxysmal crises [27]. Bisphosphates are also used for preventing osseous demineralization, as well as sympatholytics for the inhibition of the α and β adrenergic receptors. Rehabilitation should start as early as possible in order to reduce the risk of functional sequelae. However, some principles must be followed, like working under the pain threshold and mobilizing to avoid possible adherences and retractions, reduce edema, and avoid the functional exclusion of the damaged limb. It is essential for the multidisciplinary team to establish a relationship of trust with the patient.

Conclusion

This case has revealed the predisposition of some patients to develop CRPS and their susceptibility to generate abnormal responses to painful stimuli. Early recognition of risk factors and diagnosis of CRPS, followed by occupational and physical therapies could result in reduced pain symptomatology and improve the outcome.

It is evident that the recovery period after injury is slightly different in each individual and depends on the severity of the injury and patient

factors such as age, general condition and the presence of other comorbidities. Thus, a multidisciplinary treatment approach should be pursued with such patients.

Conflict of interests

The authors declare no conflict of interests.

Authors' contribution

Cristina-Elena Gofiță and Paulina Lucia Ciurea equally contributed to the manuscript and thus share first authorship.

References

1. Wasner G, Schattschneider J, Heckmann K, Maier C, Baron R. Vascular abnormalities in reflex sympathetic dystrophy (CRPS I): Mechanisms and diagnostic value. *Brain*, 2001, 124(3):587-599.
2. Libon DJ, Schwartzman RJ, Eppig J, Wambach D, Brahini E, Peterlin BL, Alexander G, Kalanuria A. Neuropsychological deficits associated with complex regional pain syndrome. *Journal of the International Neuropsychological Society*, 2010, 16(3):566-573.
3. Baron R, Levine JD, Fields HL. Causalgia and reflex sympathetic dystrophy: does the sympathetic nervous system contribute to the generation of pain? *Muscle Nerve*, 1999, 22(6):678-695.
4. Turner-Stokes L. Reflex sympathetic dystrophy-A complex regional pain syndrome. *Disability and Rehabilitation*, 2002, 24(18):939-947.
5. Schwartzman RJ, Kerrigan J. The movement disorder of reflex sympathetic dystrophy. *Neurology*, 1990, 40(1):57-61.
6. Zyluk A. The natural history of post-traumatic reflex sympathetic dystrophy. *Journal of Hand Surgery*, 1998, 23(1):20-23.
7. Dijkstra PU, Groothoff JW, ten Duis HJ, Geertzen JH. Incidence of complex regional pain syndrome type I after fractures of the distal radius. *European Journal of Pain*, 2003, 7(5):457-462.
8. Veldman PH, Goris RJ. Surgery on extremities with reflex sympathetic dystrophy. *Unfallchirurg*, 1995, 98(1):45-48.
9. Resmini G, Ratti C, Canton G, Murena L, Moretti A, Iolascon G. Treatment of complex regional pain syndrome. *Clinical Cases in Mineral and Bone Metabolism*, 2015, 12(Suppl 1):26-30.
10. Harden RN, Bruehl S, Perez RS, Birklein F, Marinus J, Maihofner C, Lubenow T, Buvanendran A, Mackey S, Graciosa J, Mogilevski M. Validation of proposed diagnostic criteria (the "Budapest Criteria") for Complex Regional Pain Syndrome. *Pain*, 2010, 150(2):268-274.
11. Oerlemans HM, Oostendorp RA, de Boo T, Goris RJ. Pain and reduced mobility in complex regional pain syndrome I: Outcome of a prospective randomised controlled clinical trial of adjuvant physical therapy versus occupational therapy. *Pain*, 1999, 83(1):77-83.
12. Woolf CJ, Shortland P, Coggeshall RE. Peripheral nerve injury triggers central sprouting of myelinated afferents. *Nature*, 1992, 355(6355):75-78.
13. De Mos M, De Bruijn AG, Huygen FJ, Dieleman JP, Stricker BC, Sturkenboom MC. The incidence of complex regional pain syndrome: A population-based study. *Pain*, 2007, 129(1-2):12-20.
14. Zyluk A. The natural history of post-traumatic reflex sympathetic dystrophy. *Journal of Hand Surgery*, 1998, 23(1):20-23.
15. Schwartzman RJ. Systemic complications of complex regional pain syndrome. *Neuroscience and Medicine*, 2012, 3(03):225.
16. Smith HS. The role of genomic oxidative-reductive balance as predictor of complex regional pain syndrome development: A novel theory. *Pain Physician*, 2010, 13(1):79-90.
17. Reuben SS. Preventing the development of complex regional pain syndrome after surgery. *Anesthesiology*, 2004, 101(5):1215-1224.
18. Van der Laan L, Kapitein PJ, Oyen WJ, Verhofstad AA, Hendriks T, Goris RJ. A novel animal model to evaluate oxygen derived free radical damage in soft tissue. *Free Radical Research*, 1997, 26(4):363-372.
19. Bruehl S, Harden RN, Galer BS, Saltz S, Backonja M, Stanton-Hicks M. Complex regional pain syndrome: Are there distinct subtypes and sequential stages of the syndrome? *Pain*, 2002, 95(1-2):119-124.
20. Van Rijn MA, Marinus J, Putter H, Bosselaar SR, Moseley GL, van Hilten JJ. Spreading of complex regional pain syndrome: Not a random process. *Journal of Neural Transmission*, 2011, 118(9):1301-1309.
21. Gracely RH, Lynch SA, Bennett GJ. Painful neuropathy: altered central processing maintained dynamically by peripheral input. *Pain*, 1992, 51(2):175-194.
22. Birklein F, Riedl B, Claus D, Neundörfer B. Pattern of autonomic dysfunction in time course of complex regional pain syndrome. *Clinical Autonomic Research*, 1998, 8(2):79-85.
23. Wasner G, Schattschneider J, Binder A, Baron R. Complex regional pain syndrome-diagnostic, mechanisms, CNS involvement and therapy. *Spinal Cord*, 2003, 41(2):61-75.
24. Galer BS, Henderson J, Perander J, Jensen MP. Course of symptoms and quality of life measurement in complex regional pain syndrome: A pilot survey. *Journal of Pain and Symptom Management*, 2000, 20(4):286-292.
25. Stutts JT, Kasdan ML, Hickey SE, Bruner A. Reflex sympathetic dystrophy: misdiagnosis in patients with dysfunctional postures of the upper extremity. *The Journal of Hand Surgery*, 2000, 25(6):1152-1156.
26. Rockett M. Diagnosis, mechanisms and treatment of complex regional pain syndrome. *Current Opinion in Anesthesiology*, 2014, 27:494-500.
27. Mellick GA, Mellick LB. Reflex sympathetic dystrophy treated with gabapentin. *Archives of Physical Medicine and Rehabilitation*, 1997, 78(1):98-105.

Corresponding Author: Anca Emanuela Muștescu, Department of Rheumatology, University of Medicine and Pharmacy of Craiova, Romania, e-mail: anca_muștescu@yahoo.com