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Review

Complex regional pain syndrome: A comprehensive and critical review

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ABSTRACT

Complex regional pain syndrome (CRPS) is a term used to describe a variety of disorders characterized by spontaneous or stimulus-induced pain that is disproportional to the inciting event and accompanied by a myriad of autonomic and motor disturbances in highly variable combinations. There are no standards which can be applied to the diagnosis and would fulfill definitions of evidence-based medicine. Indeed, there are almost as many diagnostic criteria as there are names to this disorder. The umbrella term CRPS has been subdivided into type I and type II. CRPS I is intended to encompass reflex sympathetic dystrophy and similar disorders without a nerve injury; while CRPS II occurs after damage to a peripheral nerve. There are numerous etiological pathophysiological events that have been incriminated in development of CRPS, including inflammation, autoimmune responses, abnormal cytokine production, sympathetic-sensory disorders, altered blood flow and central cortical reorganization. However, the number of studies that have included appropriate controls and have sufficient numbers of patients to allow statistical analysis with appropriate power calculations is vanishingly small. This has led to over-diagnosis and often excessive pharmacotherapy and even unnecessary surgical interventions. In this review we provide a detailed critical overview of not only the history of CRPS, but also the epidemiology, the clinical features, the pathophysiological studies, the proposed criteria, the therapy and, in particular, an emphasis that future research should apply more rigorous standards to allow a better understanding of CRPS, i.e. what it is, if it is, and when it is.

Contents

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1. Introduction

Complex regional pain syndrome (CRPS) is a term coined by the International Association for the Study of Pain (IASP) to describe disorders characterized by spontaneous or stimulus-induced pain that is disproportionate to the inciting event and accompanied by a wide variety of autonomic and motor disturbances in highly variable combinations. CRPS is a syndrome steeped in confusion and often inaccuracy.

Although there had been earlier reports of such disorders, Mitchell, Morehouse and Keen in 1864 [1] are generally credited for providing the first detailed account of the burning pain, swelling, skin color and temperature changes, the exquisite sensitivity to touch, and the tenderness and stiffness of the joints that sometimes result from peripheral nerve injury due to gunshot wounds. In a later publication, they coined the term causalgia, meaning burning pain, for this syndrome. A milestone came in 1900, when Sudeck [2,3] reported a painful, rapidly progressing, severe bone atrophy that developed after soft tissue injury and other forms of trauma and included many of the features of causalgia described by Mitchell et al. [1]. Importantly, Sudeck postulated an inflammatory origin for this condition. Some descriptions of the vasomotor and trophic changes that frequently accompany these syndromes already had been provided by Mitchell et al. and others in the late 19th century [1] as well as Sudeck [2,3]. In 1916, the French surgeon Leriche reported that causalgia could be successfully treated by surgical sympathectomy [4]. Subsequently, the possible role of the sympathetic nervous system became the focus of attention not only in causalgia but also in similar entities arising without obvious peripheral nerve injury. Approximately 80 different names for such disorders can be found in the English literature alone, more than 100 in other languages [5], reflecting the precipitating event, the predominant symptoms, the specialty and country of origin of the treating physician, or the presumed pathogenetic mechanism. The most common designations include Sudeck's atrophy (or dystrophy), algodystrophy, algoneurodystrophy, and reflex neurovascular dystrophy. However, the most widely accepted one was reflex sympathetic dystrophy (RSD) coined by Evans in 1946 in an attempt to unify causalgia and similar entities as both being due to a hyperactive sympathetic nervous system [6].

2. Diagnostic criteria

There are almost as many diagnostic criteria as there were names [7]. The resulting patient heterogeneity makes it impossible to compare the results of studies that attempted to elucidate pathophysiological mechanisms or to assess treatment outcomes. In addition, it was eventually recognized that there was little evidence of sympathetic hyperactivity and of the involvement of a reflex. In an attempt to address these problems, the IASP proposed a new taxonomy and consensus-based diagnostic criteria (see Table 1a) [8,9]. The new umbrella term CRPS is subdivided into types I and II. CRPS I is intended to encompass RSD and similar disorders arising without any nerve injury, while CRPS II is intended to be equivalent to causalgia, i.e. develops after damage to a peripheral nerve. There is no gold standard diagnostic test for CRPS, therefore, the diagnosis entirely rests on the assessment of clinical criteria and is a diagnosis of exclusion.

The IASP criteria have not been widely accepted [7] and were shown to lack specificity and internal validity [10–12]. Validation of diagnostic criteria in the absence of an objective diagnostic test involves circular reasoning, since criteria must be used both to define a patient sample and then to distinguish it from other diagnostic groups. According to factor analysis, patients originally diagnosed according to IASP criteria formed four clusters of covarying signs and symptoms, namely sensory, vasomotor, edema/sudomotor and motor/trophic clusters (see also Table 2) rather than the sensory and vasomotor/edema/sudomotor categories suggested by the IASP criteria. These four clusters then became the basis on which Bruehl and Harden proposed modified diagnostic criteria (see Table 1b) [11,12]. Whereas patient-reported symptoms alone are, at least theoretically, sufficient to fulfill the IASP

Table 1a
IASP Diagnostic Criteria for CRPS [19].

CRPS I
1. The presence of an initiating noxious event, or a cause of immobilization*2. Continuing pain, allodynia, or hyperalgesia in which the pain is disproportionate to any known inciting event3. Evidence at some time of edema, changes in skin blood flow, or abnormal sudomotor activity in the region of pain
4. This diagnosis is excluded by the existence of other conditions that would otherwise account for the degree of pain and dysfunction
*Not required for diagnosis

CRPS II
1. Type II is a syndrome that develops after nerve injury. Spontaneous pain or allodynia/hyperalgesia occurs and is not necessarily limited to the territory of the injured nerve.
2. There is or has been evidence of edema, skin blood flow abnormality, or abnormal sudomotor activity in the region of the pain since the inciting event.
3. This diagnosis is excluded by the existence of conditions that would otherwise account for the degree of pain and dysfunction.