The Evolution and Progression of Complex Regional Pain Syndrome (CRPS): Recent Insights into the Nociceptive Role of Cytokines and Management of CRPS with Anticytokine Therapy

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Dear Editor-in-Chief:

I read with great interest the recent article by Rand about complex regional pain syndrome (CRPS) in a recent issue of *Current Sports Medicine Reports* (6). Recent studies into the etiology and evolution of CRPS have reported a number of interesting results. One such aspect has been the evolving role of chemical mediators such as cytokines in the evolution and progression of CRPS.

For instance, recent studies suggest that a number of chemical modulators such as IL-1β and the calcitonin gene-related peptide (CGRP) play a major role in the progression of CRPS (1,2). Similarly, Sabsovich *et al.*, in a recent study involving tibia fracture models, have shown that TNF-α is another significant mediator of CRPS (7). TNF-α performs this role in part by upregulating the cellular expression of the transient potential receptor vanilloid type 1 (TRPV1) (5). The quantitative number of TNF-α positive mast cells in neural tissue is attenuated significantly following systemic administration of steroids such as triamcinolone (4). Similarly, the past year has seen a rapid increase in the clinical application of the TNF inhibitors such as etanercept for the successful treatment of CRPS (3). Pentoxifylline is another agent that recently has been shown to decrease the production of local nociceptive cytokines in patients with CRPS (9).

Another recent discovery has been the role of nerve growth factor in the modulation of nociceptive stimuli in CRPS (2). In fact, it is not surprising that a marked decline in CGRP as well as nociceptive stimulation is noted after administration of anti nerve growth factor antibodies (8).

These examples clearly illustrate the important role that TNF-α and nerve growth factor play in accentuation of nociception in CRPS. There is a clear need for further studies to find new agents to modulate the effects of these agents so that patients with CRPS can have a bright and pain-free existence.

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Response

Dear Editor-in-Chief:

I would like to thank Dr. Kapoor for extending the depth of this discussion.

Sincerely,
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