

## Unexplained Nausea and Weight Loss in Two Cases of Longstanding CRPS

Dear Editor,

Complex regional pain syndrome (CRPS) is a highly painful, limb-confined condition that arises usually after trauma [1,2]. The objective of this letter is to highlight unusual presentations of nausea and rapid, dramatic, but then stabilizing weight loss associated with CRPS, which we observed in two of our patients. These are the only noted cases of this type among 190 cases of Budapest CRPS seen at our center since 2007 when a specialized service for this condition was set up.

Other investigators have reported that patients with CRPS report with some regularity gastrointestinal (GI) symptoms including weight changes [3]. In laboratory studies, we had previously demonstrated abnormal intestinal permeability in some patients [4], and other investigators have reported alterations in the GI microbial flora in patients with long-standing disease [5]. To our knowledge, to date, there have been no case reports describing any association between distressing weight loss and CRPS. We hope that our communication can perhaps give an opening for other clinicians who might have encountered similar cases.

The first case is of an 18-year-old female who suffered from relapsing/remitting CRPS involving the right shin and ankle, originally diagnosed by her orthopedic surgeon since she was 8 years old. Her CRPS episodes in the past had appeared to respond well to guanethidine blocks. She also suffered from abdominal pain, and constipation for a similar time, and from mild asthma and an overactive bladder. Following the last episode of CRPS, 9 months prior to presentation, she reported unusual nausea and weight loss with a reduction in her body mass index (BMI) from 22 (54 kg) to 13.7 (35 kg) over approximately 9 months, the rate of which was thought to have slowed by the time of presentation. She was thoroughly investigated by a Consultant Gastroenterologist. Investigations reported as normal included small bowel magnetic resonance imaging (MRI), MRI brain, psychiatric assessment for eating disorders, upper GI endoscopy, sigmoidoscopy with biopsies, gastric physiology, armband tests for metabolic requirements, liver functions, vitamin and mineral assays, and neurophysiological tests. Gastric emptying tests showed that she had delayed gastric emptying, but which by itself was not thought to explain the weight loss. Her medications included cetirizine and inhalers for asthma (salbutamol, fluticasone, and salmetrol). She consulted our unit with the perspective of identifying an

autoimmune cause for her condition [6,7], but following routine assessment when she was in a remission phase and fulfilled criteria for Budapest not otherwise specified [8], we were unable to recommend meaningful additions to her prior therapy, and she was discharged back to her regional tertiary care Pain Team. After she was seen at our unit, she was commenced by an outside gastroenterology team on high caloric dietary supplements, and Prucalopride, a prokinetic. This significantly improved her long-standing constipation, and over a period of approximately 6 months, she reported an increase in weight to 41.4 kg.

The second case is of a previously fit and well 42-year-old man who developed CRPS following a scaphoid fracture. Before being referred, he was trialed on first-line medications in accordance with CRPS treatment guidelines without any benefit [9]. The pain significantly interfered with his sleep, mood, and ability to work and interact socially. He had lost approximately 16 kg in weight over a period of 6 months following onset of CRPS (a reduction from BMI 24 to BMI 18) and had repeated emergency admissions for severe nausea and vomiting. During that time, his medications included amitriptyline 75 mg nocte, gabapentin 300 mg TDS, and morphine sulfate slow release 30 mg BD. On presentation, 14 months after disease onset, he met the research Budapest criteria for CRPS on examination [8]. Outpatient rehabilitation treatment did not seem to help him; however, we noted that he failed to attend most appointments because of his disability. He experienced some benefit from an increase of his slow-release morphine to 90 mg per day. He did not wish to attend a multidisciplinary pain management programme due to the distress of being in a group but was interested in undergoing a spinal cord stimulation trial. After referral, the consensus opinion of the multidisciplinary spinal cord stimulator assessment team after assessment was that he was not suitable for spinal cord stimulator treatment because he had independent psychological issues. He was very distressed, and his psychological problems seemed to severely hamper his ability to cope with his condition. He felt that it was his pain only precluding him from eating in a normal way. A consultant neurologist excluded underlying neurological causes. The following investigations initiated by an outside gastroenterology team after his first presentation at our unit were normal: short synacthen test, MRI abdomen, liver function tests, kidney function tests, iron studies, vitamin B12, and thyroid function tests. A cause to his weight loss problem was not identified. At the time

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of writing this letter, his weight is static; however, he continues to suffer from unchanged severe pain, and nausea and vomiting. It has remained unclear to the treatment team whether his weight loss problem was primarily due to a yet unidentified intestinal dysfunction or might have been largely caused a stress response in conjunction with the experience of having CRPS. His general practitioner wrote several letters highlighting a striking deterioration of this previously well young gentleman.

Although recent research has pointed toward an involvement of the GI system in some patients with CRPS [3], severe rapid weight loss has not specifically been reported. The weight loss in the two described cases was not explained by abnormal physiological tests and was unlikely solely caused by the medications, although a contribution from the combined intake of a strong opioid, tricyclic antidepressant, and gabapentinoid in patient 2 cannot be excluded. In our group of patients with CRPS seen since 2007, unexplained weight loss has been a very rare, time-limited yet very distressing complication. Unexplained weight loss is sometimes caused by psychologically defined eating behavior [10], but alternative explanations such as functional changes in the intestinal system should also be sought [4,5]. We would welcome a wider discussion on the prevalence of and potential causes for distressing, unexplained intestinal symptoms in CRPS.

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