

Case report

Aspartame-induced fibromyalgia, an unusual but curable cause of chronic pain

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ABSTRACT

We report for the first time an unusual musculoskeletal adverse effect of aspartame in two patients. A 50-year-old woman had been suffering from widespread pain and fatigue for more than 10 years leading to the diagnosis of fibromyalgia. During a vacation in a foreign country, she did not suffer from painful symptoms since she had forgotten to take her aspartame. All of the symptoms reappeared in the days following her return when she reintroduced aspartame into her daily diet. Thus, aspartame was definitively excluded from her diet, resulting in a complete regression of the fibromyalgia symptoms. A 43-year-old man consulted for a 3-year history of bilateral forearm, wrist, and hand and cervical pain with various unsuccessful treatments. A detailed questioning allowed to find out that he had been taking aspartame for three years. The removal of aspartame was followed by a complete regression of pain, without recurrence. We believe that these patients' chronic pain was due to the ingestion of aspartame, a potent flavouring agent, widely used in food as a calorie-saver. The benefit/risk ratio of considering the diagnosis of aspartame-induced chronic pain is obvious: the potential benefit is to cure a disabling chronic disease, to spare numerous laboratory and imaging investigations, and to avoid potentially harmful therapies; the potential risk is to temporarily change the patient's diet. Thus, practitioners should ask patients suffering from fibromyalgia about their intake of aspartame. In some cases, this simple question might lead to the resolution of a disabling chronic disease.

Introduction

Fibromyalgia syndrome is the third most commonly diagnosed rheumatologic disorder after osteoarthritis and

rheumatoid arthritis, with prevalence rates between 0.5% and 5% across different countries (1). This disabling disorder is characterised by widespread pain, tenderness, fatigue, sleep disturbance and is often accompanied by various psychological symptoms (1, 2). Unfortunately, the cause of fibromyalgia syndrome remains unclear. Among the several factors (neuroendocrine, genetic, etc.) involved in its pathophysiology (3, 4), environmental factors could have a critical role (1, 5). Therefore, clinicians should suspect fibromyalgia in patients who suffer from multifocal chronic pain which cannot be explained by physical examinations or by radiological and laboratory investigations. In most cases, pharmaceutical and non-pharmaceutical treatments are used to relieve pain and to improve patients' quality of life (1, 6). Before introducing such treatments, it is important to keep in mind certain adverse effects of drugs but also preservatives and food additives (7), responsible of painful manifestations which can mimic fibromyalgia.

Case report

We report for the first time two cases of patients who experienced a dramatic recovery from fibromyalgia syndrome by removing aspartame, a widely-used calorie-saver, from their diet. Thus, the intake of aspartame must be considered as an unusual cause of chronic pain, due to unsuspected components of the patients' lifestyle and particularly easy to treat compared to other idiopathic pain syndromes such as fibromyalgia. A 50-year-old French woman had been suffering from widespread pain, especially in the lower limbs, and fatigue for more than 10 years. The diagnosis of fibromyalgia, according to the ACR

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diagnosis criteria (8), had been proposed by her treating rheumatologist. Unfortunately, the symptoms were not improved by various drug therapies, including analgesics, non-steroidal anti-inflammatory drugs, carbamazepine, tricyclic antidepressants or by physical therapy. In 2006, the patient had a three-week vacation in a foreign country. During this period of time, she did not suffer from fatigue and pain. Unfortunately, all of the symptoms reappeared in the days following her return to France. She wondered if a difference in habits, behaviour or food between her three-week stay and her usual daily life could explain this spontaneous but transient improvement in health status. She remembered that she had not used food additives during the vacation as she had forgotten at home her aspartame that she had taken for ten years (intake of approximately 160mg a day). As soon as she had returned home, she reintroduced aspartame in her daily diet. Noticing that, she decided to withdraw aspartame from her diet and rapidly experienced total relief from fibromyalgia symptoms. A re-introduction test was made few months later which led to recurrence of pain and fatigue. Thus, aspartame was definitively excluded from her diet, resulting in a complete resolution of these disabling symptoms. At the last follow-up visit, three years after total abstention from aspartame, she was still free of any manifestations of fibromyalgia.

A 43-year-old man with no relevant past medical history was seen at the Rheumatology Department of Dijon University Hospital for a 3-year history of bilateral forearm, wrist, hand and cervical pain present night and day, associated with fatigue and sleep disturbance. He had consulted numerous clinicians, including general practitioners, rheumatologists, neurologists and specialists of pain, but the diagnosis remained unclear. Physical examination was normal without synovitis, tenosynovitis, muscle weakness or neurological abnormalities. Routine laboratory examinations (erythrocyte sedimentation rate, C-reactive protein, blood count, serum standard biochemistry, liver function tests, blood cal-

cium and phosphorus levels, creatine phosphokinase) were within the normal limits. Anti-citrullinated peptide antibodies, rheumatoid factors and antinuclear antibody were negative as well as the hepatitis B and C virus serology. The hands, wrists, cervical column, and chest x-rays were without abnormalities. Magnetic resonance imaging of the hands and electromyography of the upper limbs were also considered as normal. Numerous pharmaceutical or non-pharmaceutical treatments had been tried without success since the beginning of the symptoms. A detailed questioning led to the discovery that he had been taking aspartame 3 times a day for three years (daily intake of 120mg). The removal of aspartame from his diet was followed by a complete regression of pain. Two years later, the patient had not experienced any recurrence of pain and fatigue. A reintroduction test was proposed to confirm this unusual cause of painful symptoms but the patient firmly refused.

We believe that the patient's chronic pain described in these two case reports was due to the ingestion of aspartame, at current use levels (9). In particular, the observation of the first patient, in which a re-introduction test was performed, is very suggestive.

Discovered in 1965 and marketed in France since 1979, aspartame is a dipeptide composed of aspartate and L-phenylalanine (10). It is a potent flavouring agent which is used in drugs, beverages, foods as a synthetic non-nutritive sweetener in over 90 countries worldwide in over 6000 products (9). In animals, aspartame has been linked with an increased incidence of brain tumours in one study, (11) but critical review of all carcinogenicity studies conducted on aspartame found no credible evidence that aspartame is carcinogenic in humans (9, 12). Adverse effects such as headaches, seizures, dizziness, skin diseases such as urticaria or angioedema have been reported with aspartame use (10, 12, 13). However, in placebo-controlled trials, only the potential for headache has been verified, even among self-identified susceptible patients (10). Moreover, aspartame is thought to have excitotoxic effects in the human cen-

tral nervous system. To our knowledge, the literature contains one comparable report of dietary excitotoxin-induced fibromyalgia (7). However, in the above-mentioned report, both monosodium glutamate and aspartame were involved, whereas aspartame is the only additive involved in the present observations. Such a difference is far from anecdotal: it is much easier to remove aspartame than monosodium glutamate from a diet, so an eviction test can easily be performed when aspartame-induced pains are suspected.

Although very suggestive, is not possible to establish from these case-reports a causal relationship between aspartame and certain chronic pain and/or fibromyalgia syndromes. Moreover, one could object that as aspartame is a widely used food additive (10), such hypothetical adverse effects should have been described for years, unless they are exceptional (12). However, given the huge number of subjects ingesting regularly aspartame as sugar substitute or in diet soft drinks, even an exceptional adverse effect might be of significant prevalence. In addition, the benefit/risk ratio of considering the diagnosis of aspartame-induced chronic pain is clear: the potential benefit is to improve or cure a disabling chronic disease, to spare numerous laboratory and imaging examinations, and to avoid potentially harmful therapies; the potential risk is to temporarily change the patient's diet. Thus, we believe that practitioners should ask patients suffering from fibromyalgia or chronic idiopathic pain about their intake of aspartame. In some cases, this simple question might lead to the resolution of a chronic disabling disease.

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