

## Case Report

# SUCCESSFUL DESENSITISATION OF NON-IMMUNE TYPE SYMPTOMS SECONDARY TO SALICYLATE HYPERSENSITIVITY/INTOLERANCE

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### ABSTRACT

**Introduction:** Salicylate allergy/intolerance is a well-described entity that may present with typical hypersensitivity symptoms such as rhinitis, wheezing and urticaria or non-immune-type features such as headache, migraine, fatigue and abdominal cramps. Whereas aspirin desensitisation has been associated with success in patients presenting with Samter's triad of recurrent nasal polyps, asthma and aspirin sensitivity, the procedure has not been described in patients presenting with atypical or non-hypersensitivity-type symptoms.

**Case report:** A 48-year-old female presented with a two-year history of chronic headaches, migraines, fatigue and occasional upper-body myoclonic jerk-like movements upon exposure to a host of sodium salicylate-containing foods and beverages. The Flow-Cellular Antigen Stimulation Test (CAST) (Bühlmann Laboratories AG, Schönenbuch, Switzerland) for sodium salicylate was positive (stimulation index-3.9 [normal <2], percentage basophils-6.4% [normal <5%]). Aspirin desensitisation was successfully conducted in the ICU over a two-day period. At one month follow-up, she reported complete tolerance of salicylate-containing foods as well as a much better quality of life (QoL).

**Discussion:** Salicylate hypersensitivity/intolerance presenting with atypical or non-hypersensitivity-type symptoms may be successfully treated with aspirin desensitisation, resulting in a significant improvement in QoL.

**Key words:** salicylate intolerance; salicylate sensitivity; salicylate allergy; salicylate hypersensitivity; sodium salicylate

### CLINICAL IMPLICATIONS

Aspirin desensitisation has been well described in Aspirin Exacerbated Respiratory Disease (AERD). We present the first case report of resolution of atypical and non-hypersensitivity-type symptoms after aspirin desensitisation in a salicylate-intolerant patient.

### INTRODUCTION

Salicylates are natural or synthetic compounds that harbour anticancer, anti-aging and anti-oxidant properties as well as other beneficial health effects.<sup>1-3</sup> Natural salicylates are found mainly in plants and serve as a protection against environmental diseases and insects.<sup>4</sup> Varying concentrations of salicylates are present in various fruits, vegetables, teas, alcoholic beverages, herbs, spices, cosmetics, fragrances and medications.<sup>5</sup>

Symptoms of salicylate sensitivity/intolerance may include Gell and Coombs type-1 hypersensitivity related symptoms such as rhinitis, wheezing and urticaria as well as various non-specific and non-immune symptoms that include headaches, migraines, tinnitus, hyperacusis, hearing loss, palpitations, arrhythmias, irritable bowel symptoms (nausea, vomiting, reflux, bloating, flatulence, diarrhoea, constipation), joint pains, arthritis as well as possible behavioural and psychiatric disturbances (irritability, restlessness, inattention, Attention-Deficit Hyperactivity Disorder (ADHD), enuresis, depression, anxiety and panic attacks).<sup>4</sup> We present the first reported case of successful desensitisation in a patient that presented with non-specific and atypical symptoms of salicylate intolerance.

### CASE REPORT

A 48-year-old female presented with a two-year history of

chronic headaches, migraines and fatigue upon exposure to a host of sodium salicylate containing foods and beverages. She had also reported six previous hospital admissions with myoclonic jerk-like movements of her upper body after either using various non-steroidal anti-inflammatory class drugs or consuming a high salicylate content meal. Her symptoms were not associated with rhinitis, nasal polyps, wheezing, urticarial rash, dizziness, hypotension, deranged consciousness or any other symptoms in keeping with a Gell and Coombs type-1 hypersensitivity reaction. Of significance, the Flow-Cellular Antigen Stimulation Test (CAST) (Bühlmann Laboratories AG, Schönenbuch, Switzerland) for sodium salicylate was reported positive (stimulation index -3.9 [normal <2], percentage basophils-6.4% [normal <5%]). Her symptoms had improved upon initiation of a low salicylate diet. Owing to her concern about the restrictiveness and unsustainability of this diet, she asked to undergo a trial for an aspirin desensitisation procedure. Desensitisation was carried out over two days as per the protocol described by the Scripps clinic.<sup>6</sup> As per this protocol, three doses of aspirin were administered on Day 1 (20 mg at 8 am, 40 mg at 11 am and 90 mg at 2 pm), three doses on Day 2 (150 mg at 8 am, 250 mg at 11 am and 325 mg at 2 pm) and a final dose (600 mg at 8 am) on Day 3. During the procedure, after ingestion of the 2nd (40 mg), 4th (150 mg) and 5th (250 mg) doses of aspirin, she again developed severe myoclonic jerk-like movements that lasted approximately 20 minutes each. She tolerated the final aspirin dose of 600 mg on Day 3 without any adverse effects, however. Prior to discharge from hospital with high-dose maintenance aspirin therapy (600 mg twice daily), she had also tolerated 1 g of turmeric powder (high salicylate content) without developing any of her previous symptoms. At one month follow-up, she reported complete tolerance of salicylate-containing foods and a significant subjective improvement in QoL with no associated headaches or myoclonic jerky movements.

## DISCUSSION

Case presentations of salicylate intolerance-related non-immune-mediated symptoms are mostly self-described in web-based food and diet-intolerance forums.<sup>4,7</sup> Owing to the variation in presenting features and uncertain pathophysiology, the nomenclature is rather confusing. Terms such as 'salicylate allergy', 'salicylate sensitivity' and 'salicylate intolerance' have been used interchangeably in the literature. Although typical immediate hypersensitivity-type symptoms such as rhinitis, wheezing, urticaria and anaphylaxis have been well described on exposure to aspirin (acetyl salicylate acid) and related compounds, an IgE antigen-mediated mechanism has not been shown.<sup>8,9</sup> Non-hypersensitivity-type symptoms are believed to be non-immune-mediated.<sup>10</sup> Despite the positive CAST test result in our patient, which implies a non-IgE immune-mediated mechanism, her reported symptoms of headaches, migraine, fatigue and myoclonic jerky movements suggest a non-immune mechanism. It is possible that both immune

and non-immune mechanisms were present in our patient. Hence, in our description we have included the terms 'hypersensitivity' and 'intolerance'.

Salicylate hypersensitivity/intolerance is mostly diagnosed in patients with Aspirin Exacerbated Respiratory Disease (AERD) who present with the triad of symptoms described by Samter in 1968.<sup>8</sup> Salicylate sensitivity is reportedly present in approximately 20% of adults with asthma.<sup>11</sup> However, the true incidence of salicylate intolerance is not known as the diagnosis of salicylate hypersensitivity/intolerance is seldom considered in patients presenting with headache, migraine, gastrointestinal tract symptoms and fatigue.<sup>7</sup> Dose-related myoclonic jerky or pseudo-seizure-like symptoms that were reported in our patient were rather atypical and have not been previously reported.

With regard to the desensitisation procedure, we followed the two-day aspirin desensitisation protocol with lifelong high-dose maintenance therapy (600 mg twice daily for 1 month, then 600 mg in the morning and 300 mg in the evening for the second month, then 300 mg twice daily thereafter).<sup>6</sup> Although the literature is clear with regard to the benefits of aspirin desensitisation in the setting of AERD, we have not come across reports of successful desensitisation following non-immune-type symptoms that manifested in our patient. Of added significance in this case is the reported resolution of symptoms and marked improvement in QoL.

The successful resolution of non-immune-type symptoms in our patient paves the way and opens a new avenue for potential therapy of patients manifesting troublesome symptoms from salicylate intolerance. A possible mechanism for success in our case may be attributed to an increase in the tolerance threshold. This is supported by the fact that food and other intolerances have been shown to be dose-dependent, as some individuals may safely tolerate lower concentrations of salicylate without manifesting clinical symptoms.<sup>12</sup>

Current uncertainties and areas of potential research relate to the following questions:

- Will salicylate desensitisation for non-immune-type symptoms be associated with the same success as that in AERD?
- Does high-dose maintenance aspirin therapy with aspirin have to be continued lifelong?
- If so, what is the optimal daily maintenance dose?
- Do the risks associated with daily aspirin (renal, GIT) outweigh the benefits of desensitisation and the resolution of troublesome symptoms?

In designing a prospective study, first the diagnosis of salicylate intolerance must be confirmed by improvement of symptoms while following a low salicylate diet, prior to a desensitisation procedure.

## DECLARATION OF CONFLICT OF INTEREST

The authors hereby certify that this submission is not under consideration for publication elsewhere, and is free of conflict of interest.

## FUNDING

None

## ETHICS

Informed consent was obtained from the patient to make use of patient data and photographs/images for publication purposes.

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