

# Aniseed-Induced Nocturnal Tongue Angioedema

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## ■ Abstract

Aniseed is a spice native to the eastern Mediterranean region. Cases of simultaneous hypersensitivity to celery, mugwort pollen, and spices of the Umbelliferae family have been described as the celery–mugwort–spices syndrome. We report a case of aniseed-induced tongue angioedema. Skin prick tests to foods proved positive only to aniseed. Serum-specific immunoglobulin (Ig) E determination by enzyme allergosorbent test was 0.4 kU/L to aniseed extract and 0.6 kU/L to tare and cumin seeds. The molecular mass of the IgE-binding proteins studied by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) immunoblotting revealed a broad IgE-binding band of 12.9–13.7 kd in aniseed and tare extract assays and a broad band of 15–17.5 kd in cumin extract. This is the first case of type I hypersensitivity due to aniseed liqueur ingestion reported. SDS-PAGE immunoblotting study showed a broad specific IgE-binding band of 12.9–13.7 kd when aniseed extract was incubated with the patient's serum; this band might correspond to the protein responsible for the described symptoms.

**Key words:** Aniseed. Liqueur. Tongue angioedema.

## ■ Resumen

El anís es una especia originaria de la zona oriental del Mediterráneo. Se han descrito diferentes casos de hipersensibilidad a apio, polen de artemisa y especias de la familia Umbelliferae. Describimos un caso de angioedema lingual por anís. Las pruebas cutáneas en prick resultaron positivas para anís. La determinación de IgE específica por la técnica enzimo alergosorbente fue de 0.4 kU/L para anís y de 0.6 kU/L para alcaravea y comino. El estudio mediante inmunodetección tras electroforesis con dodecil sulfato de sodio (SDS-PAGE) reveló una banda fijadora de IgE específica de 12.9–13.7 kd para extracto de anís y alcaravea, así como una banda de 15–17.5 kd para extracto de comino. Se describe el primer caso de hipersensibilidad tipo I por la ingesta de licor de anís. El estudio mediante SDS-PAGE mostró una banda fijadora de IgE específica de 12.9–13.7 kd para el extracto de anís que podría corresponder a la proteína responsable de la sintomatología descrita.

**Palabras clave:** Anís. Licor. Angioedema lingual.

## Introduction

Aniseed (*Pimpinella anisum L*), an aromatic plant, belongs to the Umbelliferae family, which is native to the eastern Mediterranean region. Other spices in this family are cumin, tare, fennel, dill, coriander, and parsley; vegetables such as celery, carrot, and parsnip are also members. Aniseed is used to add aroma and flavor to pastry, preserves, sauces, fish, and meat as well as in the manufacture of certain liqueurs and pharmaceutical products. Cases of simultaneous hypersensitivity to celery, mugwort pollen, and spices of the Umbelliferae family have been described as the celery–

mugwort–spices syndrome. The prevalence of this syndrome is low in Spain, certainly due to the low consumption of spices.

A case of immediate hypersensitivity to an aniseed liqueur is reported. We found no report in the literature of hypersensitivity to aniseed as an alcoholic beverage.

## Case Description

A 58-year-old man, a bricklayer by trade and with no family or personal history of atopy, was referred from the

emergency department because of repeated episodes of tongue angioedema. He remembered having suffered 5 such episodes in the previous 2 years, all of them occurring at dawn, with no associated trigger factor and of increasing intensity. On the last 2 occasions, the symptoms were accompanied by difficulty in swallowing and breathing. He noticed that the last episode had followed the intake of aniseed liqueur preceded 24 to 48 hours earlier by intake of acetylsalicylic acid (AAS) to treat a migraine. He tolerated this drug by itself and did not remember having taken it before previous episodes. He also reported having consumed a large quantity of alcohol. Clinical symptoms remitted after intensive treatment in the emergency service (subcutaneous adrenalin and intravenous hydrocortisone and methylprednisolone) and later with treatment with oral ebastine and prednisone at home.

From the outset, AAS was considered to be an unlikely cause of the symptoms given the time elapsed (24-48 hours) since intake. An oral tolerance challenge test in hospital was scheduled and the patient was advised to avoid taking this drug until hypersensitivity to it was ruled out. However, the abovementioned tolerance challenge test was not carried out owing to his later inadvertent intake of AAS as part of a cold remedy on 2 occasions, with good tolerance.

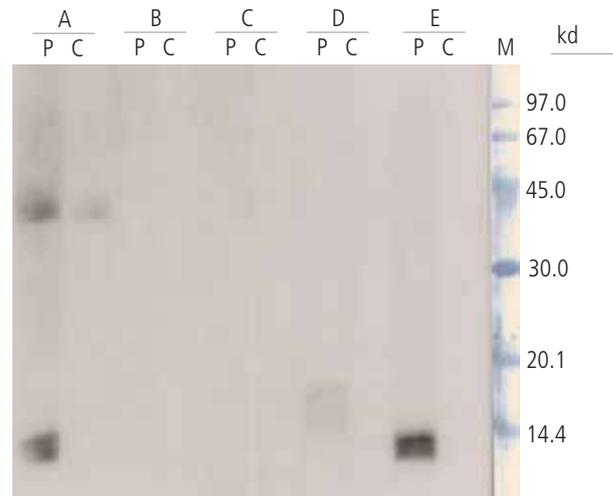
Blood tests performed included complete blood count, erythrocyte sedimentation rate, liver and kidney function tests, serum tests for hepatitis B and C viruses, thyroid function, C3, C4, immunoglobulin (Ig) A, IgG, IgM and IgE, antinuclear antibodies, antithyroglobulin and antiperoxidase antibodies. All test values obtained were within normal limits with the exception of total IgE at 283 IU/mL, a value slightly over the upper limit of normal (Pharmacia CAP System, Uppsala, Sweden). Stool analysis for parasite ova and chest X-rays were also normal.

Skin prick tests to a standard selection of common aeroallergens showed an immediate positive response to *Parietaria judaica* and mugwort pollens. Specific IgE levels (Pharmacia CAP System) to *P. judaica* and mugwort pollens were 3.19 kU/L and 2.47 kU/L, respectively. Skin prick tests to food (milk, egg, dried fruits, vegetables, flours, fruits, meats, fish, seafood, and spices) proved positive only to aniseed. Specific IgE level to aniseed extract (Pharmacia CAP System) was 0.91 kU/L.

Before the results were obtained, the patient was questioned again and he admitted to having been a heavy daily drinker of aniseed liqueur for up to 2 years before the first episode of tongue angioedema. At the time of the study, he continued drinking other liqueurs daily, but was only consuming aniseed liqueur sporadically. The episodes of tongue angioedema had coincided with drinking this liqueur. With the diagnosis of repeated tongue angioedema due to allergy to aniseed liqueur, blood was drawn for in vitro study, and extracts of different brands of aniseed liqueur and of other seeds of the Umbelliferae family were prepared. The patient was advised to avoid ingestion of aniseed in all its presentations.

Serum-specific IgE determination by enzyme allergosorbent test was 0.4 kU/L to aniseed extract, 0.6 kU/L to tare and cumin seeds, and < 0.35 kU/L to seeds from fennel, coriander and aniseed liqueur extract.

The molecular mass of the IgE-binding proteins was studied



Sodium dodecyl sulfate polyacrylamide gel electrophoresis immunoblotting. Immunoglobulin E bands: A) aniseed extract; B) aniseed liqueur extract, brand 1; C) aniseed liqueur extract, brand 2; D) cumin seed extract; E) tare seed extract. Lane P is the patient serum; C, control serum (pool of sera from nonatopic patients); M, molecular mass marker.

by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) immunoblotting: a broad IgE-binding band of 12.9-13.7 kd appeared in aniseed and tare extract assays and a broad band of 15-17.5 kd was revealed in cumin extract (figure). No specific IgE-binding band was detected in extracts from 2 different brands of aniseed liqueur. Since the patient has avoided aniseed ingestion, he has remained asymptomatic. A skin prick test to aniseed extract proved negative 20 months after aniseed liqueur abstention.

## Discussion

The clinical history and results of the in vitro study confirmed the diagnosis of tongue angioedema due to IgE-mediated hypersensitivity to aniseed. We found no case in the literature of hypersensitivity to aniseed in an alcoholic drink. Twenty months passed until skin prick tests were repeated and the fact that during this time the patient had not consumed aniseed liqueur, would explain negativization of the abovementioned skin prick tests.

Stäger and Wüthrich [1] studied the association between simultaneous celery allergy and allergy to different spices (including aniseed). Fraj and collaborators [2] described a case of occupational asthma due to aniseed powder in a butcher. Skin prick tests to mugwort pollen and other pollens and spices were negative. García-González and collaborators [3] reported a case, in a baker, of occupational rhinoconjunctivitis due to aniseed in which cross reactivity was detected between aniseed, tare, coriander, and fennel. In vitro study showed IgE-binding bands of 48, 42, 39, 37, 34, and 20 kd for the aniseed extract. Skin prick tests for celery, carrot, and mugwort pollen were negative.

This is the first report of type I hypersensitivity due to

aniseed liqueur intake. SDS-PAGE immunoblotting showed a broad specific IgE-binding band of 12.9-13.7 kd when aniseed extract was incubated with the patient's serum; this band might correspond to the protein responsible for the described symptoms.

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